A National Prospective Cohort Study in Lebanon to Evaluate the Impact of the Lebanese Mediterranean Diet on Maternal and Infant Outcomes

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Table of Contents

Abstract

Background: Lebanon, a low and middle-income country, is experiencing a dietary shift from the traditional Mediterranean diet (MeD) to a more Westernized one that is accompanied by increased obesity rates and sedentary lifestyle among women of childbearing age. However, adherence to the MeD has been associated with lowered risk of gestational diabetes mellitus (GDM), hypertensive disorders of pregnancy (HDPs), and adverse infant birth outcomes.

Objectives: Three studies were designed: 1) Study 1 investigated the association of adherence to the Lebanese Mediterranean diet (LMeD) and other maternal factors including psychosocial factors (stress, sleep quality, and depression) and gestational weight gain with blood pressure indices including systolic blood pressure (SBP), diastolic blood pressure (DBP) and mean arterial pressure (MAP). Study 2 explored the association between LMeD and maternal factors on GDM and on impaired glucose tolerance (IGT). Study 3 evaluated the adherence to the LMeD and maternal factors, and their association with birth of AGA, SGA and LGA infants.

Methods: For this longitudinal study, a total of 618 pregnant women were recruited prior to 12 weeks of pregnancy. Socio-demographic (age, place of residence, level of income, marital status, education and employment), medical history (family history of diabetes, previous macrosomia, previous GDM and HDPs), physical activity (PA), dietary adherence to the LMeD and psychosocial factors (e.g. stress, sleep quality, and depression) were assessed using validated questionnaires. Gestational weight gain (GWG) (total and per trimester) was classified as low, adequate or excessive according to the pre-pregnancy BMI using the recommendations of the Institute of Medicine (IOM).

Results: In paper 1, a low percentage (<5%) of the population had elevated SBP and/or DBP, however more than 30% had elevated MAP (eMAP) in each trimester. We observed that SBP, DBP and MAP significantly differed by level of adherence to the LMeD in trimester 2 and 3. Moreover, in trimester 1, 1 tsp. of olive oil per day was associated with a reduced the risk of eMAP. In trimester 2, a high adherence to the LMeD and a daily consumption of dried fruits (≥0.3 servings/day) was associated with decreased risk of eMAP. A higher pre-pregnancy BMI increased eMAP risk in trimester 2 and 3.

In paper 2, adherence to the LMeD was neither associated with IGT nor with GDM but individual food groups were. For instance, higher intakes of burghol and legumes were associated with increased risk of high FBG≥100 mg/dl in trimester 1, whereas higher vegetable intake decreased its risk in trimester 3. Moreover, higher perceived stress in trimester 1 and excessive GWG in trimester 3 increased the risk of having impaired FBG ≥100 mg/dl, respectively. On the other hand, excessive GWG and higher eMAP in trimester 2 were associated with increased GDM risk.

In paper 3, adherence to the LMeD was significantly higher among women who delivered AGA infants compared to SGA and LGA, and was significantly associated with lower birth weight among AGA infants. Moreover, higher maternal burghol intake increased SGA risk while higher olive oil intake increased LGA risk. Other factors including poor sleep quality in trimester 2 and higher total GWG were associated with increased infant birth weight for gestational age.

Conclusion: Collectively, these three studies demonstrate the importance of the inter-relationship between socio-demographic, medical history, psychosocial factors, obesity and weight gain as well as maternal adherence to the LMeD on improving maternal and infant outcomes during pregnancy. Adherence to LMeD is recommended to achieve normal MAP and birth of AGA infants, and intakes of its specific food groups protect against adverse maternal-fetal outcomes. However, adhering to LMeD might not be sufficient alone to lower risk of pregnancy complications. Weight gain should be appropriate especially in the 2^{nd} and 3^{rd} trimester. Finally, early screening and counselling is recommended for women with high risk factors such as family history of diabetes, previous macrosomia, high blood pressure, pre-pregnancy overweight and/obesity, high stress and poor sleep.

Resume

Introduction: Le Liban, pays à revenu faible et intermédiaire, est témoin d'une occidentalisation du système alimentaire. Ce changement du régime alimentaire traditionnellement méditerranéen et l'adoption d'une diète occidentale, coincide avec une augmentation des taux d'obésité et de sédentarité chez les femmes en âge de procréer. Cependant, l'adhérence à une diète méditerranéenne est associée à une réduction du risque de diabète gestationnel (GDM), des troubles hypertensifs de la grossesse et des complications liées à l'accouchement.

Objectifs: Cette étude repose sur 3 axes. Le premier investigue la relation entre l'adhérence à la diète méditerranéenne libanaise (LMeD) et les facteurs maternels tels que les paramètres psychologiques et le gain de poids durant la période de grossesse d'une part, et les indices de l'hypertension artérielle systolique (SBP), l'hypertension artérielle diastolique (DBP) et la pression artérielle moyenne (MAP) d'autre part. Le deuxième axe explore l'impact de la LMeD et les facteurs maternels sur le développement du GDM et l'intolérance au glucose (IGT). L'axe 3 évalue l'adhérence à la LMeD et les facteurs maternels, en association avec le poids à la naissance pour l'âge gestationnel du nouveau-né (approprié pour l'âge gestationnel AGA, gros pour l'âge gestationnel LGA, petit pour l'âge gestationnel SGA).

Méthodes: Cette étude longitudinale a recruté un total de 618 femmes enceintes avant 12 semaines de grossesse. Plusieurs questionnaires validés ont été utilisés pour collecter les données socio- démographiques (l'âge, le lieu residence, le salaire, le statut marital, l'éducation et l'emploi), l'histoire médicale (histoire familiale de diabète, une histoire de macrosomie pendant une grossesse antérieure, une histoire de GDM et des troubles hypertensifs de la grossesse), l'activité physique (PA), l'adhérence à la LMeD et les facteurs psychologiqyes (e.g. stress,

qualité de sommeil et dépression). De plus, le gain de poids gestationnel (GWG) (total et per trimestre) a été stratifié en faible, adéquat ou excessif en comparaison avec l'indice de masse corporelle BMI avant la grossesse suivant les recommendations de l'Institute of Medicine (IOM).

Résultats: Selon le premier manuscrit, un petit pourcentage de la population avait une hypertension systolique et/ou diastolique (<5%). Cependant, plus de 30% de l'échantillon présentait une pression arterielle moyenne élevée (eMAP) pendant chaque trimestre. Nos observations notent que les pressions artérielles SBP, DBP et MAP diffèrent significativement selon le niveau d'adhérence à la LMeD aux trimestres 2 et 3. De plus, durant le 1er trimestre, la consummation d'1 cuillère à thé d'huile d'olive par jour, est associée à une diminution du risqué de développer une eMAP. Nous avons également noté que lors du 2ème trimestre, une forte adhérence à la LMeD ainsi qu'une consummation journalière de fruits secs (≥0.3 portions/jour) s'est avérée associée à une diminution du risque de eMAP. Plus loin, un IMC élevé est positivement associé au risque de eMAP durant le 2ème et le 3ème trimestres.

Selon le deuxième manuscrit, l'adhérence à la LMeD ne semblait pas influencer le risque de l'IGT ni le risque de developer le GDM. Néanmoins, certains groupes alimentaires affectent ces risques. Par exemple, une consommation élevée de burghol et de légumineuses a été positivement associée à une augmentation du risque d'hyperglycémie à jeun ≥100 mg/dl pendant le 1er trismestre, au moment où une consommation élevée de legumes a diminuée ce risque durant le 3ème trimestre. De plus, un haut niveau de stress pendant le 1er trimestre et un gain de poids excessif durant le 3ème trimestre augmentent le risque d'une glycémie à jeun ≥100 mg/dl. Parallèlement, un gain de poids excessif et une eMAP élevée pendant le 2ème trimestre sont associés à un risque élevé de GDM.

Selon le 3ème manuscrit, l'adhérence à la LMeD est significativement plus élevée chez les femmes avec des nouveaux-nés AGA en comparaison avec SGA et LGA, et est significativement associée à un poids de naissance plus bas pour les nouveaux-nés AGA. De plus, une consummation maternelle élevée de burghol augmente le risque d'avoir un nouveaux-né SGA alors qu'une consommation élevée d'huile d'olive augmente le risque de nouveau-né LGA. Plus loin, d'autres facteurs tels qu'une mauvaise qualité de sommeil durant le 2ème trimestre, et un gain de poids gestationnel excessif, sont associés à une augmentation du poids à la naissance pour l'âge gestationnel chez le nouveau-né.

Conclusion: Collectivement, ces 3 études mettent en relief l'importance de la relation entre les facteurs socio-démographiques, l'histoire médicale, les facteurs psychologiques, l'obesité et surpoids ainsi que l'adhérence de la femme enceinte à la LMeD afin d'améliorer les conditions foetales et maternelles durant les periode pré- et post-natales. Cependant, l'adoption de la LMeD seule n'est pas suffisante pour réduire le risque des complications. Un gain de poids adéquat surtout durant le 2ème et le 3ème trimestres est crucial. Finalement, une prise en charge et un dépistage précoce sont recommandés pour les femmes à haut risque telles que celles ayant une histoire dediabète familial, une histoire de macrosomie ou d'hypertension arterielle, un surpoids/obesitéavant la grossesse, un niveau eleve de stress et une mauvaise qualité de sommeil.

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Lastly, this journey would not have been possible without the support of my husband, Dany and our daughters, Christa and Alexia. Thank you for your understanding, encouragement, support, love, patience and listening over the years that it has taken to complete this degree. This accomplishment would not have been possible without them.

Contribution of Authors

The thesis is written in paper format according to the 'Guidelines Concerning Thesis Preparation' by McGill University. Paula Hage Boutros wrote this thesis. This study was a collaboration between McGill University and the two universities in Lebanon: Notre Dame University-Louaize and the Lebanese American University. Dr. Kristine Koski and I developed the overall conceptual framework and specific study design for each paper, and Dr. Daiva Nielsen provided input on them. Dr. Maya Bassil from the Lebanese American University and Dr. Jessy El Hayek from Notre Dame University-Louaize played a critical role in the implementation of the national data collection as they added recognition that the study was being supervised by two credible institutions, and they also oversaw the implementation of the study. Moreover, they were involved in participant recruitment, management of the data collected and provided an appropriate environment for training of research assistants. Moreover, Dr. Maya, Dr. Jessy and I were involved in the training and supervision of all research assistants and students on effectively approaching participants, administering questionnaires and extracting information from medical charts with minimal bias. Dr. Khalil Asmar, the epidemiologist from AUB, assisted in the development of an analytical strategy and supervised the data analysis for study I and II, and given that Dr. Asmar was not available at the time of conducting the analysis for paper 3, Dr. Bachir Atallah from MUBS stepped in and provided statistical support and introduced new approaches for the hierarchical logistic regression model in Study III.

The thesis contains three studies, all of which were developed in collaboration with my academic advisors, Dr. Kristine G. Koski, Dr. Daiva Nielsen, Dr. Jessy El Hayek and Dr. Maya Bassil. I, Paula Hage Boutros, also collaborated in the final inclusion of study questions, completed the statistical analysis of the data, and interpreted the data within the context of the current body of literature. Each study, was developed by myself and Dr. Kristine Koski, and was reviewed by Dr. Daiva Nielsen, Dr. Jessy El Hayek and Dr. Maya Bassil, and will be submitted for publication in the near future.

Dr. Kristine Koski, Dr. Daiva Nielsen, Dr. Jessy El Hayek and Dr. Maya Bassil served as thesis committee members and read this dissertation and individual papers. Dr. Khalil Asmar reviewed studies I and II, and Dr. Bachir Atallah reviewed study III as co-authors.

Statement of Originality

This thesis, composed of three original papers, contributed several novel findings.

For the first time in Lebanon, Study I assessed the prevalence of high systolic blood pressure (SBP), diastolic blood pressure (DBP) and mean arterial pressure (MAP) during pregnancy on a national level in Lebanon with the latter being an early indicator of hypertensive disorders of pregnancy (HDPs).

- Study I highlighted that elevated SBP and DBP was low in the population (<5%) whereas elevated MAP (eMAP) was high in all trimesters (>30%)

- Study I showed that adherence to the Lebanese Mediterranean diet (LMeD) and specific food groups decreased eMAP risk.

- Moreover, urban regions including Beirut and Mount Lebanon had lower adherence to the LMeD and increased risk of eMAP compared to other regions.

Study II was the first study to determine the prevalence of gestational diabetes mellitus (GDM) and impaired glucose tolerance (IGT) on a national level in Lebanon.

- Study II highlighted that GDM diagnosis was low (5.6%) whereas IGT prevalence was high (12.4% in trimester 1 and 26.5% in trimester 3).

- Study II also showed that sleep quality, stress and physical activity levels worsened by trimester whereas adherence to the LMeD improved from trimester 1 to trimester 3.

- Family history of diabetes, high gestational weight gain (GWG) and high MAP were significant predictors of GDM. On the other hand, high stress, burghol and legumes intake increased IGT risk in trimester 1 while high GWG increased IGT risk in trimester 3. Vegetable consumption was protective of IGT risk in trimester 3.

Study III was the first national study in Lebanon to assess prevalence of infant birth weight for gestational age and predictors of small for gestational age (SGA) and large for gestational age (LGA) risk.

- SGA prevalence was 12% whereas LGA prevalence was 16%. Interestingly, women who delivered appropriate for gestational age (AGA) infants had better sleep scores in trimester 2 and higher adherence to the LMeD in trimester 2 and 3 compared to women who delivered SGA and LGA infants.

- Predictors for infant birth weight varied for SGA and LGA. For instance, higher MAP in trimester 3 and higher consumption of burghol in trimester 1 increased SGA risk, whereas previous macrosomia, greater parity and higher consumption of olive oil in trimester 2 increased LGA risk

List of Tables

Chapter V- Predictors of Infant Birth Weight for Gestational Age (SGA and LGA) in a Lebanese Pregnant Population

List of Figures

Chapter I: Introduction

Chapter III: Association of the Lebanese Mediterranean Diet with Blood Pressure Measurements among a National Sample of Pregnant Women in Lebanon

Chapter IV- Predictors of Impaired Glucose Tolerance and Gestational Diabetes Mellitus in a Lebanese Pregnant Population

Chapter V: Predictors of Infant Birth Weight for Gestational Age (SGA and LGA) in a Lebanese Pregnant Population

List of Abbreviations

ACOG: American College of Obstetrics and Gynecology

AGA: Appropriate for Gestational Age

BMI: Body Mass Index

eMAP: Elevated Mean Arterial Pressure

EMC: Eastern Mediterranean Countries

EPDS: Edinburgh Perinatal-Postnatal Depression Scale

FBG: Fasting Blood Glucose

GDM: Gestational Diabetes Mellitus

GWG: Gestational Weight Gain

HDPs: Hypertensive Disorders of Pregnancy

IGT: Impaired Glucose Tolerance

LGA: Large for Gestational Age

LIMC: Low and Middle Income Countries

LMeD: Lebanese Mediterranean Diet

MAP: Mean Arterial Pressure

MeD: Mediterranean Diet

PA: Physical Activity

PARMED-X: Physical Activity Readiness Medical Examination for Pregnancy

PE: Pre-eclampsia

PP: Pulse Pressure

PSQI: Pittsburgh Sleep Quality Index

PSS: Perceived Stress Scale

SES: Socio-Economic Status

SGA: Small for Gestational Age

CHAPTER I

Introduction

1.1. Overview

Obesity is a global challenge with an alarmingly high burden among Lebanese women (Papazian et al., 2016). Moreover, these women are entering pregnancy with a high body mass index (BMI) which has negative consequences for mothers and their offspring (Papazian et al., 2016). Both high pre-pregnancy BMI and gestational weight gain (GWG) in excess of recommendations have been associated with adverse maternal outcomes including gestational diabetes mellitus (GDM) and hypertensive disorders of pregnancy (HDPs), as well as poor infant outcomes that include birth of either a premature, large for gestational age (LGA) or small for gestational age (SGA) infant (M. K. Kjøllesdal & G. Holmboe-Ottesen, 2014; Mamun et al., 2011; Marchi et al., 2015; Vasudevan et al., 2011). Furthermore, pregnancy is a period that causes increased insulin resistance in normal weight women particularly in the third trimester due to a rise in lipoprotein concentrations, which is further exacerbated in those who are overweight and obese and leading to a higher prevalence of GDM, HDPs, pre-eclampsia (PE), and SGA (Bautista-Castaño et al., 2013; Haugen et al., 2008). To prevent these sequelae, the Institute of Medicine (IOM), recommends that women have a BMI at the beginning of pregnancy, gain weight within the proposed guidelines for their BMI (Bautista-Castaño et al., 2013; Hanson et al., 2015; Haugen et al., 2008; Marchi et al., 2015) (Table 1-1) and follow a healthy diet to enhance maternal and infant health (Hanson et al., 2015). The Mediterranean diet (MeD) has been highlighted in various studies as optimizing gestational weight gain (GWG) (Spadafranca et al., 2016) and reducing risk of GDM (Karamanos et al., 2014), HDP, SGA (Parlapani et al., 2019), LGA (Fernández-Barrés et al., 2019) and prematurity (Parlapani et al., 2019), possibly due to its anti-inflammatory properties and cholesterol lowering effects (Khoury et al., 2005).

Presently, Eastern Mediterranean countries (EMC) are experiencing a nutrition transition. Both economic and population growth are contributing to the adoption of a Westernized diet and a more sedentary lifestyle (Zhu & Zhang, 2016) that is now linked to a rise in abdominal and visceral obesity, impaired glucose tolerance (IGT) and type 2 diabetes in the general population. These same behavioral components have also been associated with excessive GWG (Mourady et al., 2017), GDM (Sanabria-Martínez et al., 2015), and HDPs (Magro-Malosso et al., 2017) during pregnancy. The American College of Obstetrics and Gynecology advises pregnant women to engage in moderate intensity physical activity (PA) for 30 minutes on most days of the week (Vargas-Terrones et al., 2019), however women in Lebanon now report lower PA levels than the recommended 150 minutes per week (Mourady et al., 2017) which in turn is leading to compromised maternal-infant health (Sanabria-Martínez et al., 2015). There is also growing evidence that psychosocial factors including stress, depression and sleep disorders adversely affect gestational outcomes (Karam et al., 2006; Mourady et al., 2017; Omidvar et al., 2018). One study among a convenience sample of pregnant females in Lebanon’s capital showed that worry, depression and insomnia are highly prevalent (Mourady et al., 2017). These factors are often disregarded by healthcare professionals (Chaaya et al., 2002; Mourady et al., 2017). Although demonstrating a positive relationship, to date, few studies have investigated either diet and PA interventions or education and counselling on maternal-infant wellbeing (Bo et al., 2014; Hoppichler & Lechleitner, 2001; Pérez-Ferre et al., 2015; Tamborrino et al., 2016; Tawfik, 2017).

Table 1-1. Recommended Weight Gain in Singleton Pregnancies

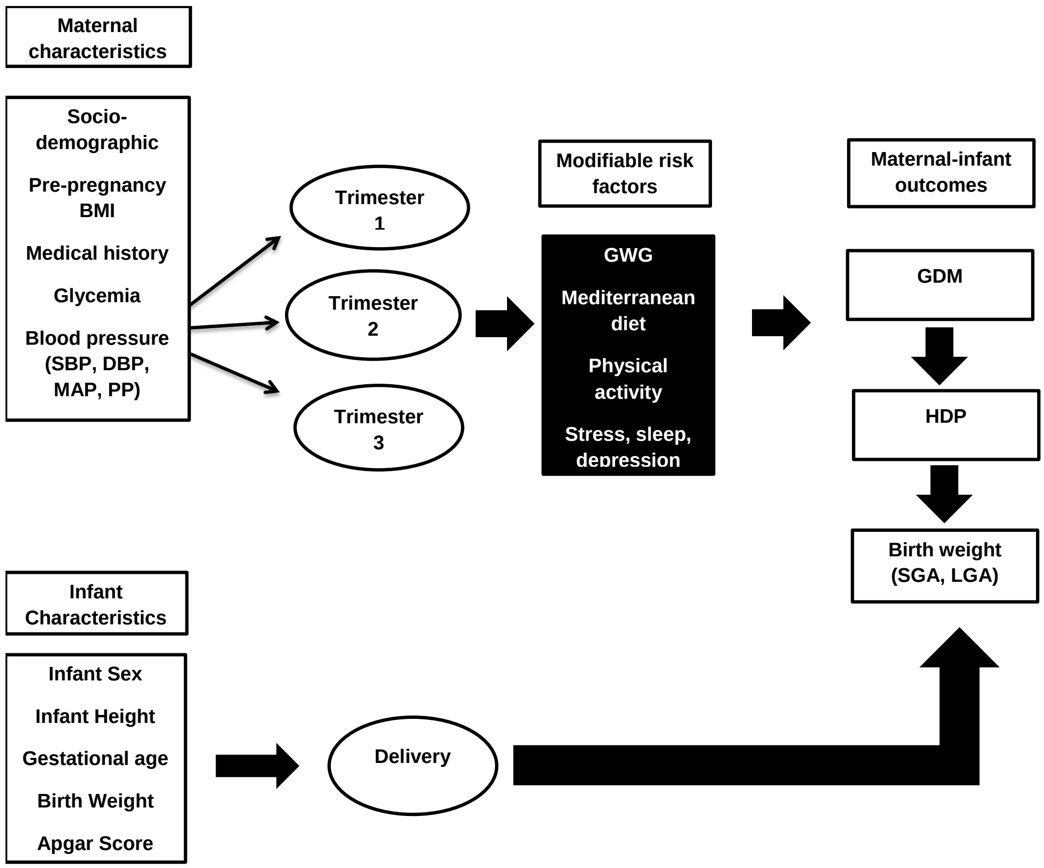
Pre-pregnancy BMI	**Range of Recommended Weight Gain (Kg)**
Underweight (<18.5 Kg/m^2)	12.5-18.0
Normal Weight (18.5-24.9 Kg/m^2)	11.5-16.0
Overweight (25.0-29.9 Kg/m^2)	7.0-11.5
Obese (≥30 Kg/m^2)	5.0-9.0

Source: (IOM, 2009)

1.2. Conceptual Framework

Based on existing literature, a conceptual framework was designed to assess the impact of socio-demographic, medical, behavioral, dietary and psychosocial factors on the development of maternal and infant outcomes: GDM, HDPs, and infant outcomes (SGA and LGA) (Figure 1-1). Unmodifiable factors (socio-demographic, pre-pregnancy BMI, health status and medical history) play an important role in pregnancy outcomes, yet they are not suitable intervention targets. However, modifiable factors which include adherence to the LMeD, psychosocial factors (stress, sleep and depression), PA and gestational weight gain may play a role but have not been studied yet in Lebanon. Their simultaneous assessment will assist in understanding their contribution to lowering the risk of having GDM, HDPs, and/or a SGA or LGA infant.

Figure 1-1. A Conceptual Framework for the Relationship between Maternal Characteristics on Pregnancy Outcomes



1.3. Rationale, Research Context and Objectives

With the rising prevalence of maternal obesity, GDM, HDPs and unfavorable infant outcomes in low and middle income countries (LMIC) (Abalos et al., 2014; Savona-Ventura et al., 2013; Wahabi et al., 2016), including Lebanon (Blondel et al., 2006; El-Khoury et al., 2012; Papazian et al., 2017), there is an immediate need to identify modifiable risk factors and determine the prevalence of each of these outcomes on a national level. Currently, excessive GWG (Roberts et al., 2011), stress (Soto-Balbuena et al., 2018), depression (Shakeel et al., 2015), poor sleep (Dorheim et al., 2012), and sedentary lifestyle (Sanabria-Martínez et al., 2015) are being targeted in addition to a low adherence to the MeD (Karamanos et al., 2014) given that there is a shift from the MeD in pregnant women (Papazian et al., 2016) and non-pregnant populations to a Westernized diet in Lebanon and other Mediterranean countries (Farhat et al., 2016; Issa et al., 2014; Jomaa et al., 2016; Naja et al., 2011; Sibai et al., 2010). Furthermore, there is a growing concern, but limited information, on the factors influencing the adoption of the MeD and/or its specific dietary components that are associated with increased risk of adverse maternal (GDM, HDPs) or infant (SGA, LGA) outcomes. A recent review in the EMC countries characterized the main gaps as related to a focus on laboratory-based studies with minimal cohort or intervention studies. Moreover, few investigated the impact of dietary patterns on health outcomes using validated assessment tools. According to AbdulMalik et al 2019, pregnancy data was not addressed in EMC and little is known about prevalence and determinants of risk factors and outcomes during pregnancy.

We believe that this emerging nutrition transition provides an important opportunity to investigate the elements of this dietary shift in real time and to identify LMeD patterns that optimize maternal-infant health in Lebanon. Anchoring distinct health benefits of the LMeD to specific pregnancy outcomes is needed by healthcare providers in Lebanon. Additionally, pre-pregnancy BMI, GWG, PA levels, psychosocial factors and medical history should also be assessed among pregnant females in the different regions of Lebanon. We expect that our findings will inform health professionals on the importance of recommending the LMeD to all pregnant women, and in particular to those who are at risk of developing adverse complications. Other implications include early screening for risk factors such as weight, psychosocial factors and sedentary lifestyle. These will become an important target for future interventions and randomized controlled trials.

Therefore, the goals of this dissertation were as follows:

In Study I, we aimed to 1) determine the prevalence of HDPs (including high SBP, DBP, MAP and HDPs), 2) study the association between adherence to the LMeD and maternal factors on elevated SBP, DBP and MAP, and 3) explore the impact of individual components of the LMeD on each of the blood pressure measurements. In Study II, we aimed to 1) determine the prevalence of GDM in trimester 2 and IGT in trimester 1 and 3, 2) assess the impact of adherence to the LMeD and maternal factors on each of GDM and IGT, and 3) study the individual impact of LMeD food groups on GDM and IGT. In Study III, we aimed to 1) determine the prevalence of SGA and LGA infants, 2) explore the factors that are associated with higher or lower birth weight for gestational age in the total study population and in the AGA population specifically, and 3) study the association between adherence to the LMeD and maternal factors on infant birth weight for gestational age and on SGA and LGA risk.

The findings from Studies I, II and III will improve our understanding on the role of the LMeD in improving maternal and infant outcomes, in addition to the role of other potential modifiable

[(GWG, psychosocial (stress, sleep, depression) and PA, and unmodifiable risk factors (socio-demographic, pre-pregnancy BMI, and medical history) on each of the main outcomes. A comprehensive assessment of these factors will allow us to fill important gaps in the literature, particularly for Lebanon that lacks national studies among pregnant women and will set benchmarks for future interventions and counselling by healthcare professionals. The findings of this study may assist in the development of health promotion strategies that aim to increase awareness on dietary, behavioral and psychosocial factors.

1.4. Measures

To assess the dietary, PA and psychosocial factors that may influence maternal and infant outcomes, the following measures were used:

i. Dietary Factors: Adherence to the Lebanese Mediterranean Diet: Data on food intake was collected using a previously validated 61-item food frequency questionnaire (FFQ) specifically for the Lebanese diet by Naja et al. (2015) (Naja et al., 2015) that is representative of the LMeD and incorporates traditional Lebanese dishes. The FFQ consisted of 9 food categories and under each category there were specific food items listed: 1) breads and cereals (white bread, brown bread, breakfast cereals, rice, pasta, burghol), 2) dairy products (low fat milk, full fat milk, fat free/low fat yogurt, whole fat yogurt, cheese regular, cheese low fat, labneh), 3) fruits and juices (citrus fruits/grapefruit, deep yellow or orange fruits, grapes, strawberries, other: bananas, apples, dried fruits, fresh fruit juice, canned or bottled fruit drinks), 4) vegetable (salad-green: lettuce, celery, cucumber, green pepper), dark green or deep yellow vegetable, tomatoes, corn/green peas, potatoes, squash/eggplant, cauliflower/cabbage/broccoli), 5) meat and alternates (legumes, nuts and seeds, red meat, poultry, fish including tuna, eggs, organ meats, luncheon meats, sausages/makanek/hotdogs), 6) fats and oils (oil: corn/olive/soy/sunflower, olives, butter, mayonnaise), 7) sweets and desserts (cakes/cookies/donuts/muffins, ice cream, chocolate bar, sugar/honey/molasses, Arabic sweets), 8) beverages (soft drinks regular, soft drinks diet, Turkish coffee, coffee/nescafe or tea, hot chocolate or cocoa, beer, wine, liquor) and 9) miscellaneous (manakish zaatar or cheese, pizza, French fries, chips, falafel sandwich, chawarma sandwich, burger). Serving sizes for each food item and the frequency of consumption of each food item was recorded as the number of servings consumed on a daily, weekly, monthly, or never basis. To minimize recall bias and measurement errors, we used food models, cups and spoons to illustrate portion sizes of all the food items.

Lebanese Mediterranean Diet Index (LMeD): This index was developed to assess the adherence to a Lebanese version of the MeD and was derived from the aforementioned-61 item- FFQ by Naja et al. (2015) (Naja et al., 2015). This tool was initially developed to identify different dietary patterns in the population using factor analysis. Authors were able to identify a Lebanese MeD pattern from the FFQ with the following 9 food groups because of their consistently high loading on this pattern which included: fruits, vegetable, legumes, olive oil, burghol (crushed whole wheat), milk and dairy products, starchy vegetable (potato, corn and beans), dried fruits and eggs. The LMeD index used in this study shares common food groups with other indices developed in Italy: Italian Mediterranean Index (Agnoli et al., 2011), Spain: rMED (Buckland et al., 2009), Greece: nMED (Panagiotakos et al., 2007), France: Mediterranean Diet Quality Index (Gerber, 2003), and 9 Mediterranean European countries: Mediterranean Diet Scale (Trichopoulou et al., 2003) such as fruits, vegetable, olive oil, legumes, dairy products and starchy vegetable, however, in the Lebanese MeD other main components were missing such as fish, red meat, poultry, and wine consumption (Naja et al., 2015).

Adherence to the LMeD was measured based on consumption of each of these food groups with 1, 2 and 3 points assigned to consumption within the first, second and third tertile of intake respectively. Subsequently, a score was derived after adding the points for every participant with a minimum score of 9 reflecting the least adherence and a maximum score of 27 reflecting the highest adherence to the Lebanese MeD. This tool had a good correlation (r=0.56) with the Italian MeD tool (Agnoli et al., 2011). Similar to other studies done in pregnant women (E. Gesteiro et al., 2012; Tatiana Papazian et al., 2019), alcohol intake was excluded as consumption is virtually absent in this study population. We presented our results as the number of servings that were consumed on a daily basis for each of the food groups that comprise the MeD index.

ii. Physical Activity: Canadian Physical Activity Readiness Examination (PARmed-X): A section of the lifestyle questionnaire addressed the frequency, intensity and duration of participation in recreational exercise over the past month to assess for PA using the Physical Activity Readiness Examination (PARmed-X). The PARmed-X was initially used as a screening tool for pregnant women prior to participation in any exercise and is comprised of 4 parts: 1) General health status, 2) Status of current pregnancy, 3) Activity habits during the past month and 4) Physical activity intentions. For the purpose of this study we only used the third part of the questionnaire "Activity habits during the past month" which categorizes participants into three categories according to the frequency, intensity and duration of PA: unfit (frequency <1-2 times/ week and <20 min duration; PA index=0), active (1-2 times/ week for 20 min or more than twice/week for < 20 min; PA index=1) and fit (>2 times/week for more than 20 min; PA index=2). This tool has been validated against peak oxygen consumption (Hui et al., 2012), and was translated to Arabic and back-translated since it was not validated in an Arabic population before. Since the vast majority of the women in this study were sedentary, we combined fit and active together due to the small percentages found in the two groups.

iii: *Depression: Edinburgh Perinatal/Postnatal Depression Scale (EPDS)* is a commonly used 10-item scale in research and clinical practice to identify women at risk of perinatal depression. The questions included reflect the ability of the person to integrate normally in social life. A score of 0-3 is given for each question and a global sum of 0-30 is obtained. A score of 10 or greater indicates possible depression (Cox et al., 1987). This tool has been validated in pregnant women with a cut-off point of 10 (Murray & Carothers, 1990), and in an Arab population with a Cronbach's alpha=0.84 and a Correlation r=0.57 compared with the Present State Examination which is a semi-structured interview intended to provide an objective evaluation of symptoms associated with mental disorders (Ghubash et al., 1997).

iv. Stress: *Perceived Stress Scale (PSS10)* is a 14-item questionnaire that assesses perception of stress in the past month (Almadi et al., 2012) and was shortened to 10 items. The questions referred to feelings and thoughts that were experienced in the past month by participants and that could affect their social integration. Each of the 10 questions had a score between 0-4 with a global sum score of 0-40 with higher scores indicating higher perceived stress. The categories are the following: Low stress (score 0-13), moderate stress (score 14-26), and high stress (score 27-40). It has been previously validated in a Lebanese pregnant population with a test-retest reliability and Cronbach's alpha=0.74 and a Correlation r=0.48 and r=0.58 with the General health questionnaire and the EPDS, respectively (Almadi et al., 2012).

v. Sleep: Pittsburgh Sleep Quality Index (PSQI) assesses sleep quality over a 1-month period and classifies sleep as good versus bad sleep using 9 questions that are based on seven domains: subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleep medications, and daytime dysfunction with the latter component having an impact on social aspects of life. Each of the 7 components is scored between 0 and 3 indicating no difficulty and extreme difficulty respectively. A global score is obtained after adding up the 7 components with a sum ranging between 0-21. A score equal to or greater than 5 indicates poor sleep, while a score of less than 5 indicates good sleep. It has been previously validated in an Arabic population with an internal consistency and a reliability coefficient (Cronbach's alpha) of 0.74 for its seven components (Suleiman et al., 2012).

CHAPTER II

Review of the Literature

2.1. Hypertensive Disorders of Pregnancy (HDPs) as an Outcome - Overview

Hypertension, once a distinctive attribute of the Western societies, has become more common in the Eastern Mediterranean countries (EMC) and Middle Eastern region (Abdul-Rahim et al., 2001; Hasab et al., 1999; Sarraf-Zadegan & Sajady, 2003). Several studies have shown that countries in the Middle East including Iran, Oman, Egypt and Turkey had the highest prevalence of hypertension ranging between 19-30% (Bramham et al., 2014; Payne et al., 2016; Sarrafzadegan et al., 2017; Wahabi et al., 2016), (Al-Riyami & Nadar, 2022) with Lebanon having the greatest prevalence of 37% (Najem et al., 2021). This is attributed to the sedentary lifestyle and change in dietary habits which are leading to high rates of overweight and obesity in this region. At the same time, one third of the Lebanese population has been shown to have diabetes which shares common metabolic risk factors with hypertension (Al-Riyami & Nadar, 2022).

Hypertensive disorders of pregnancy (HDPs) are common medical conditions that affect 5-10% of pregnancies worldwide, however their prevalence have not been assessed in Lebanon. This increase in HDPs can be linked to the rise in cardio-metabolic risk factors that are present among women of child-bearing age (Nagraj et al., 2020). Pregnancy is a period with significant alterations in metabolic processes and results in blood volume expansion as well as increase in vascular resistance, therefore maladaptation to these biological processes may result in adverse maternal and infant outcomes including the development of HDPs (Khedagi & Bello, 2021). The American College of Obstetricians and Gynecologists (ACOG) defines hypertension during pregnancy as systolic blood pressure (SBP) greater than or equal to 140 mm Hg and/or diastolic blood pressure (DBP) greater than or equal to 90 mm Hg on 2 or more occasions at least 4 hours apart (American College of Obstetricians and Gynecologists, 2019). Severe hypertension is diagnosed if there is consistent elevated SBP greater than or equal to 160 mm Hg and/or DBP greater than or equal to 110 mm Hg. Early intervention and treatment for women diagnosed with HDPs is recommended to prevent adverse pregnancy outcomes and future cardiovascular risk (Khedagi & Bello, 2021).

2.2 Risk Factors and Modifiers of HDPs

Several risk factors have been associated with increased HDP risk which include high pre-pregnancy body mass index (BMI) and excessive gestational weight gain (GWG), low physical activity (PA) levels among pregnant women (Magro-Malosso et al., 2017; Mourady et al., 2017), as well as increased prevalence of psychosocial factors including stress, depression and poor sleep (Karam et al., 2006; Mourady et al., 2017; Omidvar et al., 2018). The Institute of Medicine (IOM) recommends that women have a normal BMI at the beginning of pregnancy, gain weight within the proposed guidelines for their BMI (Hanson et al., 2015; Marchi et al., 2015) and follow a healthy diet to enhance maternal and infant health (Hanson et al., 2015). Being overweight or obese and having gestational diabetes mellitus (GDM) can increase the risk of HDPs more than either factor alone (El Sagheer & Hamdi, 2018; Erem et al., 2015; Goueslard et al., 2016; Marchi et al., 2015; Metzger, 2007; Sesmilo et al., 2017; Tomic et al., 2016; Zhang et al., 2014). The Mediterranean diet (MeD) has been highlighted in various studies as optimizing

GWG (Spadafranca et al., 2016) and reducing risk of HDPs (Parlapani et al., 2019) possibly due to its anti-inflammatory properties and cholesterol lowering effects (Khoury et al., 2005). Moreover, a recent study reported that not only systolic and diastolic can identify women at risk of HDPs (Martínez-González et al., 2019), but elevated mean arterial pressure (MAP) has clinical value and can be more important to screen for women at early risk of HDPs (Conde-Agudelo et al., 1993; Martínez-González et al., 2019). SBP, DBP, MAP, and pulse pressure (PP) are known to be elevated in early pregnancy before the development of HDPs whereas low DBP and MAP have been associated with poor fetal outcomes (Martínez-González et al., 2019). Both Wright et al. (2015) and Mayrink et al. (2019) also highlighted that certain maternal risk factors including age, weight, height and medical history should be considered when using MAP as a screening and risk assessment tool.

Socio-demographic factors: The role of socio-demographic characteristics in the etiology of HDP remains controversial (Abalos et al., 2014). There is evidence to show that both older (>40 years) and younger (<20 years) mothers have a higher risk of experiencing HDPs (Abalos et al., 2014; Khader et al., 2018). The rapid urbanization in EMC has caused a shift in dietary habits and activity levels (Payne et al., 2016; Wahabi et al., 2016) leading to a rise in obesity and cardio-vascular problems (McDonald et al., 2008; Payne et al., 2016).

Medical History: History of GDM (Koual et al., 2013), pre-eclampsia (PE) (Lecarpentier et al., 2013), nulliparity (Di Lorenzo et al., 2012; Erez et al., 2006), and multiple gestation (Erez et al., 2006; Funai et al., 2005) have been shown to increase the risk of developing HDPs.

Pre-pregnancy BMI: Obesity can significantly increase the risk of developing HDPs (Khader et al., 2018; Parazzini et al., 1996; Samuels-Kalow et al., 2007). A prospective cohort study identified that every 1 kg/m^2 increase in pre-pregnancy BMI was associated with 6% and 9% higher risk for gestational hypertension and PE respectively independent of GWG. SBP and DBP were also positively associated with higher pre-pregnancy BMI (Savitri et al., 2016). Lewandowska et al., 2020 found that pre-pregnancy BMI was the most significant factor that increased the probability of having HDPs Additionally, a meta-analysis showed that being overweight or obese is associated with higher risk of developing PE (Motedayen et al., 2019; Nekkanti et al., 2023), while Hutcheon et al. (2018) identified an association between higher pre-pregnancy BMI and PE among nulliparous women.

Gestational weight gain (GWG): Various studies have investigated the impact of GWG on blood pressure measurements during pregnancy and development of HDPs. In particular, the timing of the weight gain influenced the risk of hypertension during pregnancy. One study showed that early GWG was associated with increased blood pressure throughout pregnancy (Macdonald-Wallis et al., 2013), while another study showed an association between either early or late GWG and HDPs (Song et al., 2023). A more recent study by Yuan et al. (2022) identified that early GWG predicted HDPs and was partially mediated by elevated MAP. On the other hand, (Dude et al., 2020) showed that mid and late trimester GWG increased the risk of HDPs. Moreover, Ito et al., 2023 identified an increased risk of HDPs among overweight women with high total GWG, and increased risk of PE among obese women with high total GWG. A meta-analysis showed that excessive GWG increased the odds of HDPs by 45% (Ren et al., 2018). However, the distinct impact of GWG on HDPs remains inconclusive since weight gain is confounded by the fluid retention associated with HDPs (Heude et al., 2012; Jeyabalan, 2013).

Psychosocial factors: Stress, poor sleep, and depression can increase cortisol levels and make women more vulnerable to obesity and hypertension which are predictors for HDPs (Karam et al., 2006; Omidvar et al., 2018). This was emphasized in a meta-analysis by Liu et al. (2017) that showed an association between stress and hypertension in the general population, as well as another meta-analysis by (Zhang et al., 2013) that identified mental stress as a risk factor for gestational hypertension (GH), and work stress, anxiety and depression as risk factors for PE (Zhang et al., 2013). Another study showed a combined effect of stress and chronic hypertension on the development of PE during pregnancy (Yu et al., 2013). A more recent study showed a 50% increased risk of HDPs among women with high stress independent of other risk factors (Caplan et al., 2021). Moreover, two reviews showed an association between poor sleep quality, duration and sleep disordered breathing on increasing blood pressure during pregnancy and HDPs (Haney et al., 2013; Querejeta Roca et al., 2020). Depression was also associated with HDPs as seen in a recent review and women with more severe depression had a greater risk of PE (Chapuis-de-Andrade, 2019). A meta-analysis confirmed these findings where depressed women were reported to have an increased prevalence of HDPs compared to non-depressed women (Shay et al., 2020).

Physical activity: PA can prevent the development of HDPs and PE through several mechanisms including improving uterine-placental blood flow, adaptation to cardiovascular changes, and decreasing insulin resistance (Gao et al., 2020). This was also confirmed by a meta-analysis that showed an association between cardiorespiratory fitness and HDP risk (Al-Huda et al., 2022), and another that reported a significant reduction in hypertension in women receiving early pregnancy (first 20 weeks) exercise interventions (Magro-Malosso et al., 2017), Zhu et al. (2022) also identified an association between PA and HDPs, while another study showed a benefit for pre-pregnancy PA on blood pressure, due to improved cardiovascular fitness (Arvizu et al., 2022). However, to our knowledge only one study explored the effect of PA on HDPs in Mediterranean countries, and identified that pregnant women who did not engage in PA were 3 times more likely to develop HDPs (Barakat et al., 2016). Still, in Lebanon studies are lacking on the relationship between PA and HDPs, and culturally appropriate guidelines for PA are missing.

Adherence to the Mediterranean diet: Women in the Mediterranean countries are more likely to develop HDPs. Adherence to the MeD can decrease predisposing factors for hypertension including dyslipidemia, high blood pressure, inflammation, diabetes, GDM, obesity and stress (Bonaccio et al., 2013; Domenech et al., 2015; Fischer et al., 2017; Koual et al., 2013; Schoenaker et al., 2015), and can lower the risk of HDPs possibly due to the MeD's anti-inflammatory components; however, more research is needed to further assess this relationship (Flor-Alemany et al., 2023; Parlapani et al., 2019). A recent meta-analysis showed an association between adherence to the MeD and high SBP (Bakaloudi et al., 2021), while a large cohort in the USA by Makarem et al. (2022) reported a 21% reduction in HDP risk among women with high adherence to the MeD. Moreover, a study done in Germany identified that a low compliance to the MeD was associated with higher SBP in early and mid-gestation, with no impact on HDPs (Timmermans et al., 2011) similarly to Al Wattar et al. (2019) who reported no significant relationship between adherence to the MeD and PE. Moreover, an Australian longitudinal study revealed that a high pre-pregnancy adherence to the MeD was associated with 42% lower chance of developing HDPs compared to those with low adherence (Schoenaker et al., 2015). Among the three studies conducted in Mediterranean countries, adoption of a MeD during pregnancy was shown to significantly lower the risk of HDPs (Assaf-Balut et al., 2019; Benhammou et al., 2016; Parlapani et al., 2019). Other studies also showed a decreased risk of PE with higher adherence to the MeD (Minhas et al., 2022). MAP is a significant predictor for HDPs and was found to be improved with higher adherence to the MeD in the general population (Tyrovolas et al., 2014). Furthermore, a large cohort study identified a linear relationship between adherence to the MeD and decreasing SBP, DBP and MAP (Ahmed et al., 2020).

2.3. Gestational Diabetes Mellitus (GDM) as an Outcome - Overview

GDM is a common metabolic complication that is first diagnosed in pregnancy between 24-28 weeks (Orós et al., 2023). All Mediterranean countries report a high GDM prevalence between 8-32% (Guariguata et al., 2014; Law & Zhang, 2017; Savona-Ventura et al., 2012; Zhu & Zhang, 2016), and the Middle East in particular has the highest prevalence of diabetes (Oros et al., 2023). In fact, Lebanon is among the top 10 countries with a diabetes prevalence of 20.2% (International Diabetes Federation (IDF), 2011) and the highest rate of impaired glucose tolerance (IGT) (26.6%) in the general population (Savona-Ventura et al., 2012). National data on prevalence of GDM in the country is lacking, however two recent studies showed a prevalence between 6-15% in Beirut and South Lebanon (Al-Rifai et al., 2021).

The etiology of GDM is multi-factorial (Orós et al., 2023) and coincides with the increase of maternal age and obesity as well as the high rates of diabetes among women of child-bearing age in the Middle East (Al-Rifai et al., 2021). Furthermore, pregnancy is a period with increased insulin resistance, which is further exacerbated in women with metabolic dysfunction or predisposition to diabetes (Orós et al., 2023). A recent meta-analysis by Ye et al. (2022) reported that women with GDM had higher odds of caesarean delivery, preterm delivery, poor Apgar scores, macrosomia, and large for gestational age (LGA) infants. Moreover, the Hyperglycemia and Adverse Pregnancy Outcomes (HAPO) study identified that even a small elevation in fasting blood glucose (FBG) is a predominant determinant of unfavorable gestational complications including fetal overgrowth and adiposity (Leary et al., 2010).

The prevalence and determinants of GDM have not been previously assessed on a national level in Lebanon. Recent evidence suggests that early lifestyle intervention for risk factors can modify the risk of GDM (Simmons et al., 2018). Indeed, it was previously established that metabolic perturbations are associated with higher amniotic fluid glucose in mothers with GDM before 15 weeks gestation (Tisi et al., 2011), suggesting a metabolic need for earlier dietary guidelines.

2.4. Risk Factors and Modifiers of GDM

Socio-demographic and behavioral factors: Interestingly, the rise in obesity and type 2 diabetes (International Diabetes Federation (IDF), 2011) in EMC has occurred in parallel with urbanization (El Sagheer & Hamdi, 2018; Khader et al., 2018; Musaiger, 2004) and higher socio-economic status (SES) (Khader et al., 2018; Musaiger, 2004) and has been attributed to shifts in both dietary habits and PA levels (El Sagheer & Hamdi, 2018). On the other hand, some studies identified that maternal obesity was more prevalent among Eastern Mediterranean women with lower SES and that these were more prone to glucose intolerance and GDM (Alkasseh & Aljeesh, 2014; El Sagheer & Hamdi, 2018) as a result of poor nutrition and inactive lifestyle (Alsairafi et al., 2016; International Diabetes Federation (IDF), 2011). Higher maternal age was also significantly correlated to GDM risk (Amiri et al., 2021; Kouhkan et al., 2021).

Medical conditions and previous history: Maternal characteristics including previous diabetes (Erem et al., 2015; Goueslard et al., 2016), previous GDM (Kouhkan et al., 2021), hypertensive disorders (El Sagheer & Hamdi, 2018; Goueslard et al., 2016; Savona-Ventura et al., 2012), previous macrosomia (Kouhkan et al., 2021; Savona-Ventura et al., 2012), first degree family history of diabetes (Amiri et al., 2021; IDF Clinical Guidelines Task Force, 2009; Kouhkan et al., 2021), miscarriage (AlKasseh et al., 2013; Savona-Ventura et al., 2012), stillbirth (AlKasseh et al., 2013), and caesarian delivery (AlKasseh et al., 2013) have been also associated with GDM in Mediterranean women.

Pre-pregnancy BMI: Maternal adiposity is the most significant risk factor for GDM (Hashim et al., 2019; Law & Zhang, 2017; World Health Organization (WHO), 2016) with central obesity being the most prominent as seen in a recent meta-analysis (Yao et al., 2020). Several studies showed an association between higher pre-pregnancy BMI and risk of IGT (Mi et al., 2021) and GDM (Amiri et al., 2021; Lotfi et al., 2018; Quotah et al., 2022; Sun et al., 2023) with the latter study showing a mediating effect of advanced age on the relationship between pre-pregnancy BMI and GDM (Sun et al., 2023). Furthermore, recent findings suggest the role of adipose tissue dsyfunction in the pathophysiology of GDM (Šimják et al., 2018). Mediterranean women on average report a pre-pregnancy BMI$\geq$25 kg/m^2 (Abu-Heija et al., 2017; El Sagheer & Hamdi, 2018; Imen et al., 2018) and excessive GWG with a third trimester BMI ≥30 kg/m^2 (Savona-Ventura et al., 2012).

Gestational Weight Gain: Of interest are reports that show high first trimester weight gain being associated with abnormal glucose tolerance (Eades et al., 2017) and GDM (Rasmussen et al., 2009). In fact, a randomized controlled trial by Simmons et al. (2018) reported a significant benefit of having normal GWG as early as the first trimester on fasting blood glucose, whereas second to third trimester GWG did not have any impact. To our knowledge, in Lebanon, some pregnant women are unaware of the recommended weight gain which may increase their risk of developing GDM (El Rafei et al., 2016; Zgheib et al., 2017).

Psychosocial factors: Studies have demonstrated that stress, depression (Silveira et al., 2014) and poor sleep (Sirimon Reutrakul et al., 2011) can increase the risk for GDM. Various mechanisms have linked psychological disorders among women with oxidative stress, elevated cortisol level, sympathetic activity and inflammation (Gooley et al., 2018). There is also evidence that pregnant women who suffered from depression and stress were more likely to have inappropriate dietary patterns, reduced PA levels and to gain weight below or above the IOM recommendations (Molyneaux et al., 2016; Omidvar et al., 2018). Depression is prevalent among Middle Eastern pregnant females compared to Western European countries (Shakeel et al., 2015). Anxiety and depression are also common in Lebanese females (Karam et al., 2006), yet no studies have assessed their impact on maternal and infant health. Feng et al. (2020) identified a possible relationship between elevated stress hormones and/or stress maladaptation with GDM, while Mishra et al. (2020) reported a 13-fold increase in GDM among women who had high stress. Additionally, various studies showed that poor sleep was a predictor for GDM (Eleftheriou et al., 2023; Peivandi et al., 2021; B. Zhu et al., 2020) and Zhong et al. (2018) reported an association between early gestational sleep disturbances and GDM. Sleep duration was found to be important with short sleep durations increasing GDM risk (S. Reutrakul et al., 2011) and fasting blood glucose among pregnant women (Myoga et al., 2019), while higher sleep durations (>10 hours) also increased GDM risk (Myoga et al., 2019). This was further exacerbated in overweight women (Qiu et al., 2010). With respect to depression, a recent systematic review by Fischer & Morales-Suárez-Varela (2023) showed a two-way link between depression and GDM, and Hinkle et al. (2016) identified that first and second trimester depression increased GDM risk.

Dietary intake and adherence to the Mediterranean diet: Several studies have highlighted the role of the MeD in improving risk factors for GDM by optimizing GWG (H. Al Wattar et al., 2019; Koutelidakis et al., 2018; Parlapani et al., 2019; Silva-del Valle et al., 2013; Spadafranca et al., 2016), lowering pre-pregnancy BMI, and decreasing blood pressure (Hoppichler & Lechleitner, 2001; Issa et al., 2014; Naja et al., 2011; Papazian et al., 2016; Sibai et al., 2010) which was also seen among a Lebanese pregnant population (Papazian et al., 2019).

A large body of evidence identified that the MeD significantly decreased GDM risk (Assaf-Balut et al., 2017; Assaf-Balut et al., 2019; Donazar-Ezcurra et al., 2017; H. Al Wattar et al., 2019; Izadi et al., 2016; Karamanos et al., 2014; Makarem et al., 2022; Schoenaker et al., 2015; Zaragoza-Martí et al., 2022), and glucose levels in women without GDM (Karamanos et al., 2014). Specifically, Mohtashaminia et al. (2023) showed a 41% reduction in GDM risk among women in the highest tertile of adherence to the MeD early during pregnancy. Three large clinical trials reported a significant reduction in GDM risk by using a MeD intervention in early pregnancy (Hoppichler & Lechleitner, 2001), a MeD diet supplemented with extra virgin olive oil (EVOO) and pistachios (Soto-Balbuena et al., 2018), and MeD adherence to the following 6 food items: >12 servings/week of vegetable, >12 servings/week of fruits, 3 servings/week of nuts, >6 days/week consumption of extra virgin olive oil (EVOO), and ≥40 mL/day of EVOO (Shakeel et al., 2015). Additionally, two case control studies reported a significant reduction in FBG among GDM women who adhered to a MeD (Dorheim et al., 2012), and 80% decrease in GDM risk in women who adhered to the highest tertile of the MeD (Tamborrino et al., 2016). In a large prospective cohort study covering 10 Mediterranean countries, a decrease in GDM risk was identified among women who had a high adherence to the MeD prior to the OGTT test at 24-32 weeks, as well as an improved glucose tolerance during the oral glucose tolerance test (OGTT) test in women without GDM, who had a better adherence to the MeD (Pérez-Ferre et al., 2015). However, the evidence on diet and GDM is inconclusive due to the heterogeneity of the studied diets (Assaf-Balut et al., 2019; Bo et al., 2014; Hoppichler & Lechleitner, 2001; Pérez-Ferre et al., 2015; Tamborrino et al., 2016; Tawfik, 2017).

Table 2-1. Differences between Mediterranean Diet Indices across Mediterranean Countries

Med Index	Food Groups Included	Adherence Scoring
MeD Diet Scale (Trichopoulou, 2003) 9 Med Countries	5 MeD food: vegetables, legumes, fruits, cereals and fish 3 non MeD items: meat, dairy products, alcohol, and ratio of MUFA+PUFA to SFA	Classified by sex specific median intake Higher scores for MeD food
Greek nMeD (Panagiotas, 2007)	11 food items of Greek MeD pyramid: 7 MeD items: Non-refined cereals, fruits, veg, legumes, potatoes, fish, olive oil 4 Non-MeD items: Meat, poultry, full fat dairy, alcohol	Classified by weekly intake of foods on MeD pyramid Higher scores for foods at bottom of pyramid
French MeD Index (Gerber, 2003)	5 MeD food:cereals, veg, fruits, fish, olive oil 3 non MeD items: saturated fats, cholesterol and meat	Classified with higher scores for MeD food Lower scores for non-MeD food
Spanish rMeD (Buckland, 2009)	6 MeD food: fruits excluding juices, vegetables, legumes, fish, olive oil 2 non-MeD food: meat and dairy products, and alcohol	Classified with higher scores for MeD food Lower scores for non-MeD food
Italian MeD Index (Agnoli, 2011)	6 MeD food: pasta, veg, fruits, legumes, olive oil, fish 4 non-MeD food: soft drinks, butter, red meat, potatoes, and alcohol	Classified with higher scores for MeD food Lower scores for non-MeD food

Physical activity: A meta-analysis of randomized controlled trials (RCTs) in Mediterranean countries demonstrated that PA during pregnancy significantly decreased the likelihood of developing GDM (Sanabria-Martínez et al., 2015) while another meta-analysis of RCTs and cohort studies identified leisure time activity as having the greatest effect (Aune et al., 2016). Moreover exercise was proven to reduce the risk of excessive GWG which is a well-known predictor for GDM (Ming et al., 2018), however no significant association was reported in a cohort study conducted in Lebanon and Qatar (Abdulmalik et al., 2019).

2.5. SGA and LGA as an Outcome – Overview:

Small for gestational age (SGA) infants have a birth weight for gestational age less than the 10^{th} percentile. The prevalence of SGA is around 10% in high income countries, whereas in LIMC approximately 32.5 million infants (27%) are born SGA (Osuchukwu & Reed, 2023; Younes et al., 2021). SGA indicates fetal growth restriction during pregnancy, and these infants are at greater risk of having future complications including prematurity, hypoglycemia, sepsis and death. Placental factors can contribute to the birth of SGA infants including placental abruption and placental previa, whereas maternal factors include cardiovascular problems, hypertension, substance use, poor maternal nutrition, being underweight and/or low weight gain during pregnancy (Osuchukwu & Reed, 2023; Younes et al., 2021).

LGA infants on the other hand have a birth weight for gestational age greater than the 90^{th} percentile. The prevalence of LGA in LIMC is greatly variable and ranges between 5-20% and this is primarily due to socio-economic differences and heterogeneity in the types of assessment used (Falcão et al., 2021). LGA indicates rapid fetal development during pregnancy and can lead to complications in infants upon delivery including postpartum hemorrhage and birth injuries. Common maternal risk factors associated with LGA include overweight and obesity, diabetes and multi-parity (Younes et al., 2021).

2.6. Risk Factors and Modifiers of SGA and LGA

Socio-demographic Characteristics: Advanced maternal age, family history of diabetes and multi-parity are known to increase the risk of LGA (Ennazhiyil et al., 2019; Khan et al., 2013). Moreover, place of residence is considered a risk factor with urban areas having a greater prevalence of LGA compared to rural regions (Khan et al., 2013).

Medical Conditions: Several maternal medical conditions have been linked to higher risk of SGA and/or LGA. For instance, previous and current GDM were shown to be a significant risk factor of LGA (Erem et al., 2015; Erjavec et al., 2016; Savona-Ventura et al., 2013; Sesmilo et al., 2017; Wahabi et al., 2016; Younes et al., 2021). This is because insulin resistance is an underlying mechanism in GDM and it can lead to greater glucose availability for the fetus, hence increasing fetal growth (Nahavandi et al., 2019). GDM has been proven to strengthen the relationship between high maternal pre-pregnancy BMI and GWG with LGA (Saito et al., 2022). HDPs on the other hand have been associated with low birth weights, neonatal complications (Abalos et al., 2014; Khader et al., 2018) and prematurity (Khader et al., 2018). A recent large cohort by (Li et al., 2023) found that women with HDPs compared to those without, had increased risk of low birth weight and SGA infants but reduced risk of LGA, after controlling for possible confounders including maternal age, race/ethnicity, education level, cigarette use during last 3 months of pregnancy, total household income in the 12 months before delivery, pre-pregnancy BMI, weight gain, history of preterm birth, infant sex, health insurance, prenatal care adequacy, and visit for depression or anxiety in the 12 months before pregnancy.

Pre-pregnancy BMI and GWG: Maternal obesity (Shi et al., 2021; Alberico et al., 2014; Teshome et al., 2021) and excessive GWG (Alberico et al., 2014; El Rafei et al., 2016; Goldstein et al., 2017; Papazian et al., 2017; Shi et al., 2021; Teshome et al., 2021) are both significant predictors for delivery of LGA infants (Bautista-Castaño et al., 2013), whereas inadequate GWG, even in the obese, has been linked with birth of SGA infants (El Rafei et al., 2016; Papazian et al., 2017; Shi et al., 2021). There is also evidence that 1^{st} to 2^{nd} trimester GWG can predict fetal growth before birth (Neufeld et al., 2004; Young et al., 2017).

Psychosocial Factors: Other factors including maternal stress can elevate the risk of lower fetal weight gain from the second trimester until birth (Pinto et al., 2017), and both stress and depression before 20 weeks of pregnancy increased the likelihood of SGA infants (Khashan et al., 2014). Moreover, Liu et al. (2021) reported a significant reduction in birth weight among female newborns of mothers who had poor sleep quality in the 1^{st} and 3^{rd} trimester, whereas Howe et al. (2015) did not find any association between sleep disorders and SGA or LGA.

Dietary Intake and Adherence to the Mediterranean Diet: Maternal diet during pregnancy is among the most significant factors that can affect fetal growth. The importance of the MeD in optimizing infant outcomes has been previously highlighted in the literature (Chia et al., 2019; Kheirouri & Alizadeh, 2021). Poor adherence to the MeD, particularly in early gestation (before

24 weeks), has been shown to decrease placental growth and cause reduced infant birth weight (Timmermans et al., 2012). In contrast a protective effect of high fruit, vegetable and dairy product intake has been reported (Colón-Ramos et al., 2015; M. K. Kjøllesdal & G. Holmboe-Ottesen, 2014) as well as that of a MeD supplemented with extra virgin olive oil (Assaf-Balut et al., 2017). Accordingly, research in several Mediterranean countries has shown that adopting a MeD was associated with lower odds of poor intrauterine growth (Chatzi et al., 2012; Parlapani et al., 2019), as well as lower odds of high infant birth weight (Fernández-Barrés et al., 2019), SGA (Assaf-Balut et al., 2017; Assaf-Balut et al., 2019; Martínez-Galiano et al., 2018), LGA, insulin resistance in offspring (Assaf-Balut et al., 2017; Assaf-Balut et al., 2019), and prematurity (Assaf-Balut et al., 2017; Assaf-Balut et al., 2019; Parlapani et al., 2019; Saunders et al., 2014; Smith et al., 2015). On the other hand, some studies demonstrated no significant association of the MeD on SGA when controlling for all potential confounders (Peraita-Costa et al., 2018). To date, few cohort studies have been conducted in LMIC (Abdollahi et al., 2021; Papazian et al., 2022) and the majority assessed dietary patterns either in early or late pregnancy, and only one intervention cohort (Goueslard et al., 2016) investigated the MeD at several points during gestation, which reinforces the pressing need for prospective research that follows women from the first trimester until delivery.

Physical Activity: Conflicting results on the impact of exercise on birth weight and gestational age have been found in previous studies (Bisson et al., 2017; Pathirathna et al., 2019; Pinzón et al., 2012). One review reported that moderate intensity PA was associated with promoting adequate GWG in mothers and consequently protecting against LGA without increasing the risk for SGA (Vargas-Terrones et al., 2019), whereas another cohort study conducted in Lebanon and

Qatar did not show any significant relationship between PA and GWG (Abdulmalik et al., 2019). Another study reported that a higher PA levels decreased SGA risk but had no impact on LGA (Watkins et al., 2022) whereas (Ehrlich et al., 2020) reported increased SGA risk and decreased LGA risk with higher PA levels. Moreover, (Hoffmann et al., 2019) reported an increase in low-birth-weight infants among sedentary pregnant women.

Given the gaps in the literature, inconsistent findings from prior research and lack of studies in Lebanon, this dissertation aimed to 1) assess whether adherence to the LMeD and psychosocial factors can protect against the risk of HDPs, 2) determine predictors of IGT and GDM, and 3) evaluate the risk factors associated with infant birth outcomes including birth of SGA and LGA infants.

CHAPTER III

Association of the Lebanese Mediterranean Diet with Blood Pressure Measurements among a National Sample of Pregnant Women in Lebanon

3.1 Abstract

Lebanon, a low- and middle-income country, is experiencing a dietary shift from the traditional Mediterranean diet (MeD) to a Westernized one that is accompanied by increased obesity rates and sedentary lifestyle among women of childbearing age. Adherence to the MeD has been associated with protecting against adverse pregnancy outcomes including hypertensive disorders of pregnancy (HDPs). However, this has not been studied yet in Lebanon. This study aimed to explore the association between the Lebanese Mediterranean diet (LMeD) and blood pressure indices including systolic blood pressure (SBP), diastolic blood pressure (DBP) and mean arterial pressure (MAP); the latter being an early predictor of HDPs during pregnancy. A total of 618 pregnant women were recruited (mean age=29.1±5.0 years) before 12 weeks of gestation. A baseline questionnaire assessed socio-demographic characteristics, psychosocial factors including stress, sleep and depression, as well as a food frequency questionnaire (FFQ) and adherence to the LMeD. Questionnaires were re-administered at 24-28 weeks and at 34-37 weeks of gestation. Medical chart information was also retrieved upon enrollment and in the 2nd and 3rd trimester which included pre-pregnancy body mass index (BMI), weight gain per trimester and total gestational weight gain (GWG), medical history, anemia, vitamin/supplement use, maternal health status and blood pressure measurements (SBP, DBP and MAP). Univariate testing was done to summarize the sample profile as well as the frequency of consumption of every food group. Pearson correlation coefficients were used to assess the association between MAP and the risk factors. We used one way ANOVA to compare the average MAP across the 3 adherence categories of the LMeD, and chi-square tests to study associations between blood pressure measurements and level of adherence to the LMeD. Hierarchical logistic regression

models were used to test the association between MAP and adherence to the LMeD controlling for potential confounders. An alpha level of 0.05 was used to indicate statistical significance. All the analyses were conducted using SAS V9.4. The majority of the population were primiparous and college educated, while half lived in Beirut and Mount Lebanon. Approximately 33% of the women were overweight and/or obese, and most of them exceeded weight gain recommendations in all trimesters. The prevalence of HDPs was low with 1.6% having gestational hypertension, and 1.9% having pre-eclampsia. The majority of the population (95%) had normal SBP and/or DBP while elevated MAP emerged as more prevalent in all trimesters. In trimester 1, poor sleep quality and living in Beirut and Mount Lebanon increased the risk of eMAP, while consumption of 1 tsp/day olive oil lowered the risk. In trimester 2, high pre-pregnancy BMI was associated with increased odds of having eMAP. On the other hand, living in Bekaa, North and Akkar decreased the risk. Moreover, a high adherence to the LMeD and dried fruits consumption ≥0.3 servings/day reduced the risk of eMAP. In trimester 3, neither LMeD nor any food group were associated with eMAP. Early counselling by healthcare professionals, particularly for weight and sleep quality should be targeted in addition to recommending the LMeD and specific food groups such as olive oil and dried fruits in early pregnancy to lower the risk of having eMAP which is an early indicator for HDPs.

3.2. Introduction

Hypertension, once a distinctive attribute of the Western societies, has become more common in the Eastern Mediterranean countries (EMC) (Abdul-Rahim et al., 2001; Hasab et al., 1999; Sarraf-Zadegan & Sajady, 2003). As of 2020, the EMC countries are having the highest rates of hypertension worldwide (Bramham et al., 2014; Payne et al., 2016; Sarrafzadegan et al., 2017; Wahabi et al., 2016) and recent studies have shown that countries in the Middle East including Iran, Oman, Egypt and Turkey had the highest prevalence of hypertension ranging between 19-30% (Bramham et al., 2014; Payne et al., 2016; Sarrafzadegan et al., 2017; Wahabi et al., 2016), Al Riyami and Nadar, 2022., with Lebanon having the greatest prevalence of 37% (Najem et al, 2021). This is attributed to the sedentary lifestyle and change in dietary habits which are leading to high rates of overweight and obesity in this region. At the same time, one third of the Lebanese population has been shown to have diabetes which shares common metabolic risk factors with hypertension, or hypertension alone, or both. (Al-Riyami and Nadar, 2022). Often, these health factors are associated with the lack of knowledge and proper treatment (Al-Riyami and Nadar, 2022).

Hypertensive disorders of pregnancy (HDPs) are common medical conditions that affect 5-10% of pregnancies worldwide, however its prevalence has not been established in Lebanon. The increase in HDPs can be linked to the rise in cardio-metabolic risk factors that are present among women of child-bearing age (Nagraj et al., 2020). Pregnancy is a period that increases metabolic processes and results in blood volume expansion as well as increase in vascular resistance, therefore maladaptation to these biological processes may result in adverse maternal and infant outcomes including the development of HDPs (Khedagi and Bello, 2021). The American College of Obstetricians and Gynecologists (ACOG) defines hypertension during pregnancy as systolic blood pressure (SBP) greater than or equal to 140 mm Hg and/or diastolic blood pressure (DBP) greater than or equal to 90 mm Hg on 2 or more occasions at least 4 hours apart (ACOG, 2019). Severe hypertension is diagnosed if there is consistent high SBP greater than or equal to 160 mm Hg and/or DBP greater than or equal to 110 mm Hg. Pre-eclampsia (PE) is diagnosed when having high blood pressure (BP) and proteinuria. Early intervention and treatment for women diagnosed with HDPs is recommended to prevent adverse pregnancy outcomes and future cardiovascular risk (Khedagi & Bello, 2021). Several studies reported that mean arterial pressure (MAP) which is calculated as [MAP = DP + 1/3 (SBP – DBP)] and elevated MAP (eMAP) can identify women at early risk of HDPs (Conde-Agudelo et al., 1993; Martínez-González et al., 2019; Page & Christianson, 1976; Wright et al., 2015). MAP has been shown to be elevated in early pregnancy before the development of HDPs (Gonzalez et al., 2020). Both Mayrink et al. (2019) and Wright et al. (2015) also highlighted that certain maternal risk factors including age, weight, height and medical history should be considered when using MAP as a screening and risk assessment tool.

Several factors are affecting the development of HDPs which include high pre-pregnancy body mass index (BMI) and excessive gestational weight gain (GWG), low PA among pregnant women (Magro-Malosso et al., 2017; Mourady et al., 2017), and increased prevalence of psychosocial factors including stress, depression and poor sleep (Karam et al., 2006; Mourady et al., 2017; Omidvar et al., 2018). The Institute of Medicine (IOM) recommends that women have a normal BMI at the beginning of pregnancy, gain weight within the proposed guidelines for their BMI (Hanson et al., 2015; Marchi et al., 2015) and follow a healthy diet to enhance maternal and infant health (Hanson et al., 2015). The Mediterranean diet (MeD) has been highlighted in various studies as optimizing GWG (Spadafranca et al., 2016) and reducing risk of

HDPs (Parlapani et al., 2019) possibly due to its anti-inflammatory properties and cholesterol lowering effects (Khoury et al., 2005).

Presently, EMC are experiencing a nutrition transition. Both economic and population growth are contributing to the adoption of a Westernized diet and a more sedentary lifestyle (Zhu & Zhang, 2016) that is now linked to a rise in abdominal and visceral obesity, impaired glucose tolerance (IGT) and type 2 diabetes in the general population which are all risk factors for HDPs during pregnancy (Magro-Malosso et al., 2017). In Mediterranean countries (including Lebanon) that are moving away from the traditional MeD and adopting a more Westernized diet (Farhat et al., 2016; Jomaa et al., 2016), there is evidence to show that a poor adherence to the MeD in pregnancy is associated with increased BMI, excessive GWG (Spadafranca et al., 2016), and HDPs (Assaf-Balut et al., 2019; Bonaccio et al., 2013; Domenech et al., 2015; Fischer et al., 2017; Koual et al., 2013; Parlapani et al., 2019; Schoenaker et al., 2015).

With the rising prevalence of maternal obesity and risk factors for HDPs in low and middle income countries (LMIC) (Abalos et al., 2014; Savona-Ventura et al., 2013; Wahabi et al., 2016), including Lebanon (Blondel et al., 2006; El-Khoury et al., 2012; Papazian et al., 2017), there is an immediate need to identify the determinants of HDPs and determine the burden of HDPs at a national level. Furthermore, there is a growing concern, but limited information, on the factors influencing the adoption of the MeD and/or its specific dietary components that are associated with risk of HDPs. A recent review in the EMC characterized the main gaps as related to a focus on laboratory based studies with minimal cohort or intervention studies, and remarkably few investigated relevance of dietary patterns to health outcomes using validated assessment tools (Abdulmalik et al., 2019). Moreover, only few studies in the Mediterranean countries explored the impact of the MeD, psychosocial factors and physical activity (PA) on HDPs, whereas in the Arab countries including Lebanon these studies are lacking.

We believe that this emerging nutrition transition provides an important opportunity to investigate the elements of this dietary change in real time and to identify Lebanese MeD (LMeD) patterns that reduce the incidence HDPs in Lebanon. We expect that our findings will inform health professionals on the importance of recommending the LMeD to all pregnant women, and in particular to those who are at risk of developing adverse complications, as well as emphasize the critical role of pre-pregnancy BMI, weight gain, mental health and PA for women of child-bearing age.

We are hypothesizing that a low adherence to the LMeD, along with excessive GWG and psychosocial factors including stress, poor sleep quality, and depression, will be associated with higher risk of HDPs. Our secondary hypothesis is that specific dietary components of the LMeD are more likely to protect against HDPs. The primary objective for this study is to evaluate the differences between modifiable risk factors among women with or without HDPs. Secondary objectives are to examine potential interaction between each predictor and HDPs, and identify the association between distinct LMeD dietary components and HDPs. Moreover, we want to explore the association between MAP and the development of HDPs.

3.3. Material and Methods

3.3.1. Study population

This study is a national prospective cohort study on pregnant women of various ethnic and religious backgrounds living in the 6 different governorates of Lebanon including Mount Lebanon, Beirut (capital of Lebanon), Bekaa, South (and Nabatieh), North, and Akkar. Beirut and Mount Lebanon are the main urban regions and account for the majority of the country's socio-economic, trade, political and cultural activities; however, poverty exists in the suburbs of these regions. The other governorates consist of both urban cities and rural villages where the latter have poor socio-economic and educational levels (Chamieh et al., 2015).

For this study, a simple random sampling among all obstetric clinics in Lebanon was done using the statistical software SPSS (Statistical Package for Social Sciences), version 22.0. Out of 732 obstetric clinics, a total of 20 private and hospital based private clinics were selected: Mount Lebanon (n=3), Beirut (n=5), Bekaa (n=4), South (n=3), North (n=4), and Akkar (n=1), and a minimum of 30 women were recruited from each clinic.

Recruitment was initiated by the two universities in Lebanon: Notre Dame University-Louaize and Lebanese American University who provided training to their senior students as part of their research program. Data collection was initiated in August 2019 and was completed by June 2021. Written consent and approval was obtained from each physician at the respective clinic to survey the clientele and access medical records. Individual hospitals also provided written consent after reviewing the questionnaires and medical chart data prior to data collection. Healthy pregnant women (< 15 weeks) were invited to participate and were approached by the research team during their routine obstetric visit after being informed about the purpose of this study. We recruited the first 30 women who consented to participate and were eligible to participate. They were informed of their anonymity and that they could withdraw at any time. Inclusion criteria for the study were Lebanese women: 1) > 18 years. Exclusion criteria included women 1) with multiple gestations, 2) pre-pregnancy diabetes, 3) women who were carrying a fetus with structural malformation, chromosomal anomalies or TORCH (toxoplasmosis, rubella, cytomegalovirus, herpes and other agents) infection.

3.3.2. Study design

This prospective cohort study followed consenting pregnant women from the 1st trimester (<15 weeks of gestation) until delivery with follow up interviews in the 2nd (24-28 weeks), and 3rd trimester (34-37 weeks). The initial interview was conducted in person, and the survey included socio-demographic data such as age, place of residence, level of income, education, occupation and marital status, and 5 validated questionnaires 1) Perceived Stress Scale (PSS10) (Cohen et al., 1983), 2) Pittsburgh Sleep Quality Index (PSQI) (Suleiman et al., 2012), 3) Edinburgh Perinatal/Postnatal Depression Scale (EPDS) (Ghubash et al., 1997), 4) FFQ and LMeD (Naja et al. (2015), and 5) Canadian Physical Activity Readiness Medical Examination (PARmed-X for pregnancy), wherewe categorized women as sedentary or active. Questionnaires were re-administered in the 2nd and 3rd trimester of pregnancy via phone interviews. A section of the survey included advice on diet and PA (Forbes et al., 2018) and food security (Gary et al., 2000) which were collected upon the first trimester visit.

Medical records were reviewed by our research team in each trimester during routine follow-up visits and this data was used to evaluate changes in clinical measures across gestation. Clinical data was obtained from medical chart review including self-reported pre-pregnancy weight, vitamin/mineral intake, anemia and medical history. At follow up visits at each trimester, additional clinical indicators were collected from medical charts including weight gain per trimester, blood pressure measurements SBP and DBP, and general maternal health status.

Our main exposure variable was the adherence to LMeD which was assessed in each trimester, and we evaluated its associations with the outcome variable HDPs including elevated SBP, DBP, eMAP and presence of PE.

3.3.3. Sample Size Calculation

The main outcome of this study was HDPs. We used Epiinfo Software to calculate the sample size needed using formula by Fleiss with correction. The confidence interval was set at 95%, power at 80% and ratio (unexposed/exposed to the MeD=1). A sample of 618 participants was needed after adjusting for a 20% loss to follow up (Assaf-Balut et al., 2019). A simple random sampling was conducted among all obstetric clinics in Lebanon using the statistical software SPSS (Statistical Package for Social Sciences), version 22.0. Out of 732 obstetric clinics, a total of 20 clinics were selected from the 6 governorates of Lebanon with a minimum of 30 women recruited from each clinic [Mount Lebanon (n=190), Beirut (n=100) (capital of Lebanon), Bekaa (n=100), South including Nabatieh (n=182), North (n=46), and Akkar (n=23)]. After completing the study, we had a total of 660 participants of which 42 dropped out due to miscarriages and/or other reasons. Data for dietary intake was collected from 618 participants using questionnaires, whereas blood pressure (BP) measurements including SBP, DBP and MAP were collected from n=574 in trimester 1, n=574 in trimester 2, and n=583 in trimester 3 from medical charts by research trainees.

3.3.4 Questionnaires

Edinburgh Perinatal/Postnatal Depression Scale (EPDS)

Edinburgh Perinatal/Postnatal Depression Scale (EPDS) is a commonly used 10-item scale in research and clinical practice to identify women at risk of perinatal depression. A score of 0-3 is given for each question and a global sum of 0-30 is obtained. A score of 10 or greater indicates possible depression (Cox and Sagovsky, 1998). This tool has been validated in pregnant women with a cut-off point of 10 (Murray & Carothers, 1990), and in an Arabic population with a Cronbach's alpha=0.84; Correlation r=0.57 with the Present State Examination (Ghubash et al., 1997).

Perceived Stress Scale (PSS10)

Perceived stress was evaluated using the Perceived Stress Scale (PSS10) which was originally developed as a 14-item scale in 1983 to assess perception of stress in the past month in people (Cohen et al., 1983) and was shortened to 10 items. The questions referred to feelings and thoughts that were experienced in the past month by participants. Each of the 10 questions had a score between 0-4 with a global sum score of 0-40 with higher scores indicating higher perceived stress. The categories are the following: Low stress (score 0-13), moderate stress (score 14-26), and high stress (score 27-40). It has been previously validated in a Lebanese pregnant population with a test-retest reliability and Cronbach's alpha=0.74; Correlation r=0.48 and r=0.58 with General health questionnaire and the EPDS (Almadi et al., 2012).

Pittsburgh Sleep Quality Index (PSQI)

Sleep quality and patterns were assessed using Pittsburgh sleep quality index (PSQI) which is a self-reported tool that assesses sleep quality over a 1 month period and classifies sleep as good versus bad sleep using 9 questions that are based on seven domains: subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleep medications, and daytime dysfunction. Each of the 7 components is scored between 0-3 indicating no difficulty and extreme difficulty, respectively. A global score is obtained after adding up the 7 component sum, ranging between 0-21. A score of equal or greater to 5 indicates poor sleep, while a score of less than 5 indicates good sleep. It has been previously validated in an Arabic population with an internal consistency and a reliability coefficient (Cronbach's alpha) of 0.74 for its seven components (Suleiman et al., 2012).

Canadian Physical Activity Readiness Examination (PARmed-X):

A section of the lifestyle questionnaire addressed the frequency, intensity and duration of participation in recreational PA over the past month to assess for physical activity using the Physical Activity Readiness Examination (PARmed-X). The PARmed-X was initially used as a screening tool for pregnant women prior to participation in any exercise and is comprised of 4 parts: 1) General health status, 2) Status of current pregnancy, 3) Activity habits during the past month and 4) Physical activity intentions (Shephard et al., 2000). For the purpose of this study we only used the third part of the questionnaire "Activity habits during the past month" which categorizes participants into three categories according to the frequency, intensity and duration of PA: unfit (frequency <1-2 times/ week and <20 min duration; PA index=0), active (1-2 times/ week for 20 min or more than twice/week for < 20 min; PA index=1) and fit (>2 times/week for more than 20 min; PA index=2) and we translated and back translated into Arabic. This tool has been validated against peak oxygen consumption to predict target heart rate zones based on age and fitness levels (Hui et al., 2012). Since the vast majority of the women in this study were sedentary, we combined fit and active together due to the small percentages found in the two groups and re-categorized the groups into sedentary and active.

Dietary assessment and adherence to the Mediterranean diet

Data on food intake was collected using a previously validated 61-item FFQ specifically for the Lebanese diet by Naja et al. (2015) (Naja et al., 2015) that is representative of the LMeD and incorporates traditional Lebanese dishes. The FFQ consisted of 9 food categories and under each category there were specific food items listed: 1) breads and cereals (white bread, brown bread, breakfast cereals, rice, pasta, burghol), 2) dairy products (low fat milk, full fat milk, fat free/low fat yogurt, whole fat yogurt, cheese regular, cheese low fat, labneh), 3) fruits and juices (citrus fruits/grapefruit, deep yellow or orange fruits, grapes, strawberries, other: bananas, apples, dried fruits, fresh fruit juice, canned or bottled fruit drinks), 4) vegetable (salad-green: lettuce, celery, cucumber, green pepper), dark green or deep yellow vegetable, tomatoes, corn/green peas, potatoes, squash/eggplant, cauliflower/cabbage/broccoli), 5) meat and alternates (legumes, nuts and seeds, red meat, poultry, fish including tuna, eggs, organ meats, luncheon meats, sausages/makanek/hotdogs), 6) fats and oils (oil: corn/olive/soy/sunflower, olives, butter, mayonnaise), 7) sweets and desserts (cakes/cookies/donuts/muffins, ice cream, chocolate bar, sugar/honey/molasses, Arabic sweets), 8) beverages (soft drinks regular, soft drinks diet, Turkish coffee, coffee/nescafe or tea, hot chocolate or cocoa, beer, wine, liquor) and 9) miscellaneous (manakish zaatar or cheese, pizza, French fries, chips, falafel sandwich, chawarma sandwich, burger). Serving sizes for each food item were set at the beginning, and the frequency of consumption of each food item was recorded as the number of servings consumed on a daily, weekly, monthly, or never basis. To minimize recall bias and measurement errors, we took food models, cups and spoons to illustrate portion sizes of all the food items.

LMeD: This index was developed to assess the adherence to a Lebanese version of the MeD and was derived from the aforementioned-61 item- FFQ by Naja et al. (2015) (Naja et al., 2015).

This tool was initially developed to identify different dietary patterns in the population using factor analysis. Authors were able to identify a LMeD pattern from the FFQ with the following 9 food groups because of their consistently high loading on this pattern which included: fruits, vegetable, legumes, olive oil, burghol (crushed whole wheat), milk and dairy products, starchy vegetable (potato, corn and beans), dried fruits and eggs. The LMeD index used in this study shares common food groups with other indices developed in Italy: Italian Mediterranean Index (Agnoli et al., 2011), Spain: rMED (Buckland et al., 2009), Greece: nMED (Panagiotakos et al., 2006), France: Mediterranean Diet Quality Index (Gerber, 2006), and 9 Mediterranean European countries: Mediterranean Diet Scale (Trichopoulou et al., 2005) such as fruits, vegetable, olive oil, legumes, dairy products and starchy vegetable, however in the LMeD other main components were missing such as fish, red meat, poultry, and wine consumption (Naja et al., 2015).

Adherence to the LMeD was measured based on consumption of each of these food groups with 1, 2 and 3 points assigned to low, average and high intake respectively. Then, a score was derived after adding the points for every participant with a minimum score of 9 reflecting the least adherence and a maximum score of 27 reflecting the highest adherence to the LMeD. This tool had a good correlation (r=0.56) with the Italian MeD tool (Agnoli et al., 2011). Similarly to other studies done in pregnant women (E Gesteiro et al., 2012; Tatiana Papazian et al., 2019), alcohol intake was excluded as consumption is virtually absent in this study population. We presented in our results the number of servings that were consumed on a daily basis for each of the food groups that comprise the LMeD index.

3.3.5. Clinical Measurements

Pre-pregnancy BMI and GWG

Pre-pregnancy BMI was collected at baseline from obstetrical charts at clinics and was used to classify women as being underweight (<18.5 kg/m^2), normal (18.5-24.9 kg/m^2), overweight (25-29.9 kg/m^2) or obese (≥30 kg/m^2). Weight was re-assessed at 15 weeks, 28 weeks, and 37 weeks during routine clinic visit. Total GWG in Kg was calculated by subtracting total weight gain from pre-pregnancy weight, and GWG was classified as low, adequate or excessive according to the pre-pregnancy BMI using the recommendations of the Institute of Medicine (IOM) (underweight 12.5-18 kg, normal weight 11.5-16 kg, overweight 7-11.5 kg, and obese 5-9 kg) (Rasmussen et al., 2009). Weight gain per trimester was calculated by subtracting weight at each trimester from the preceding trimester (American College of Obstetricians Gynecologists, 2013). GWG per trimester was classified as adequate, excessive or low according to the following recommendations: For 1st trimester: above 2 kgs or below 1 kg was considered excessive or low, respectively for all categories of BMI. For 2nd and 3rd trimester, the recommended weight gain per week for each BMI category is the following: 0.45-0.6 kg/wk for underweight women, 0.35-0.45 kg/wk for normal weight women, 0.2-0.3 kg/wk for both overweight, and obese women. Weight gain below or above these values was classified as low or excessive, respectively (American College of Obstetricians Gynecologists, 2013).

HDPs

In Lebanon, HDP diagnosis is made after 20 weeks of pregnancy according to the American College of Obstetricians and Gynecologists guidelines with two readings of SBP ≥ 140 mmHg and/or DBP ≥ 90 mmHg at least 4 hours apart or one reading of SBP ≥ 160 mmHg and/or DBP ≥

110 mmHg. HDPs are classified into 4 categories: 1) gestational hypertension (diagnosed after 20 weeks of gestation), 2) chronic hypertension (high BP before gestation or in the first half of pregnancy), 3) pre-eclampsia (PE) (high BP accompanied by proteinuria or pre-eclampsia (PE) symptoms including thrombocytopenia, renal insufficiency, impaired liver function, pulmonary edema high BP, headache, nausea and blurry vision after 20 weeks of gestation and 4) chronic hypertension accompanied by PE (development of PE after 20 weeks of gestation) (Brown et al., 2001).

PE is diagnosed as having high BP stated previously coupled with either proteinuria ≥300 mg in a 24 hour urine collection or one reading of dipstick-proteinuria ≥ 2+ if a quantitative measurement is not available, or presence of PE symptoms after the 20th week of pregnancy including thrombocytopenia, renal insufficiency, impaired liver function and pulmonary edema (American College of Obstetricians and Gynecologists, 2019b).

Mean Arterial Pressure (MAP)

Other BP measurements have been used to determine risk of developing HDPs. These include MAP (MAP = DBP + 0.33 [SBP-DBP]) (Kane, 2016) and PP (PP = SBP - DBP) (Klabunde, 2012). Previous studies have shown that MAP (Lai et al., 2013) and PP (Adsumelli et al., 2006; Hale et al., 2010) are elevated in early pregnancy before the development of HDPs, while low MAP and PP have been associated with poor fetal outcomes (Warland et al., 2008; Zhang & Klebanoff, 2001). The highest sensitivity (69-81%) for diagnosing HDPs was identified using a combination of these maternal factors and history of PE and high MAP (Kane, 2016; Scazzocchio et al., 2013). Both SBP and DBP were retrieved from obstetric charts at each assessment point. Trimester-specific cutoffs for eMAP in pregnancy were defined as >87 mmHg

(10-18 wks), >84 mmHg (18-34 weeks), and >86 mmHg (after 34 weeks) (Women's Health and Education Center (WHEC), 2009), and low MAP as <70 mmHg (Henry et al., 2002). A prior large population study of normal pregnant women was used to define high PP (>68 mmHg) and low PP (<42 mmHg) (Ayala & Hermida, 2013).

3.3.6. Statistical analyses

Univariate analyses (measures of central tendency, percentage and frequencies) were used to summarize the maternal characteristics as well as the frequency of consumption of every food group of the LMeD. The distribution of SBP, DBP and MAP per trimester was shown using scatter plots as well as the distribution of total and per trimester GWG across pre-pregnancy BMI. Pearson correlation coefficients were used to study the association between MAP and each of the risk factors. We used one way ANOVA to compare the average MAP across the 3 adherence categories of the LMeD, and chi-square tests to study associations between BP measurements (SBP, DBP and MAP) and level of adherence to the LMeD. We also explored associations between maternal characteristics and MAP per trimester by the three adherence categories. Chi square tests were conducted for categorical variables and one way ANOVA was conducted for continuous variables. A mixed model with a random intercept was conducted to test the time-adherence interaction. Hierarchical logistic regression models were used to test for predictors of eMAP. In the 1st layer, we entered maternal characteristics including place of residence, employment, occupation, pre-pregnancy BMI, GWG and psychosocial factors (stress, sleep, and depression). In the 2nd layer, we entered the main exposure variable adherence to the LMeD along with the significant variables from the 1st layer. In the 3rd layer, we entered each individual food group in 9 separate models along with significant variables from the 2nd layer. Only significant food models were presented. An alpha level of 0.05 was used to indicate statistical significance. All the analyses were conducted using SAS V9.4.

3.4 Results

3.4.1. Population Characteristics

Table 3-1 represents the population characteristics of the sample population. A total of 618 pregnant women were recruited from the 6 governorates of Lebanon. The mean age of participants was 29 years ±5.0. Almost half of the women (43.0%) lived in Mount Lebanon and Beirut, whereas the least percentage lived in North Lebanon (7.4%) and Akkar (3.7%). A very high percentage of women (76.0%) were educated and had either a Bachelor's degree or a Master's degree and beyond, while 13.0 % did not reach high school. Almost an equal number of women were homemakers (49.0%) and employed (51.0%) either self-employed (8.7%) full time (31.2%) or part time (9.9%). The average monthly income was between 700-2000. 14% of women were smokers in the first trimester, and this proportion declined in trimester 2 (9.0%) and trimester 3 (6.0%). A high % of women were sedentary in trimester 1 and 2 (84.0% and 89.0%, respectively), and this percentage increased to 95.0% in trimester 3. Pregnant women in this population engaged in daily activities such as occasional or frequent walking, stair climbing, and household chores. Assessment of pre-pregnancy BMI showed that more than half of the population (63.8%) had a normal pre-pregnancy BMI, whereas a small percentage (3.9%) were underweight, and 32.4% were overweight and obese. Furthermore, most of them (68.3%) gained excessive weight with respect to the recommendations. The majority of women (64.2%) had a parity of 1 or 2, while 23.0% of the women had a parity of 0, and a small percentage (13.0%) had a parity of 3 or more. With regards to maternal medical history, the results showed that most women did not have previous GDM (98.1%) or previous HDPs (96.3%), while 20.0% of participants had previous miscarriages. Only 8.5% of women were infected with COVID-19 during their pregnancy, and 25% had anemia. As for the primary outcome (HDPs), less than 2.0 % of the population had either gestational hypertension or pre-eclampsia, and only 1.45% had chronic hypertension. Only 20% of the women answered on food security hence the data was not used for the bivariate analyses.

3.4.2. Distribution of Blood Pressure Measurements (SBP, DBP and MAP) for the Population across Trimesters

Figure 3-1 illustrates the outcome variables SBP, DBP and MAP in the sample population. Fig 1a shows the distribution of the SBP versus DBP in the population in the 1st trimester. The majority of women had SBP between 100-140 mmHg (98%) and DBP between 60-90 mmHg (94%)). Only a small percentage had high SBP≥140 (<2%) and DBP≥90 (<4%) as well as low DBP<60 (n=7), while a higher number reported to have low SBP <100 mmHg (n=26) which indicates the occurrence of low BP in our population. Likewise in trimester 2 and 3 (fig 1b and 1 c respectively) most of the population had SBP 100-139 mmHg (n=548 and n=546, respectively) and DBP 60-89 mmHg (n= 547 and n=545, respectively), however the number of women with low SBP <100 mmHg slightly decreased in trimester 2 (n=21) and continued to decrease in trimester 3 (n=15). Fig 1d represents MAP across the trimesters and it is clear how the number of women with eMAP in trimester 1, 2 and 3 has increased dramatically compared to SBP and/or

DBP alone where only few were reported to have elevated BP using the traditional systolic or diastolic BP criteria. The number of women with eMAP increased gradually across trimesters from 24% in trimester 1 to 41% in trimester 2 and 49% in trimester 3.

3.4.3. Distribution of GWG across Trimesters for the Sample Population

Figure 3-2 represents the scattered plots for the distribution of GWG among the sample per trimester according to their pre-pregnancy BMI. Cut-offs for GWG were defined as above or below the IOM recommendations for different pre-pregnancy BMI categories which are the following: For 1st trimester: above 2 kgs or below 1 kg for all categories of BMI. For 2nd and 3rd trimester, the cut-offs used for GWG below the IOM guidelines were as follows (pink dashed lines): <0.44 kg/week for underweight women (BMI < 18.5 kg/m2), <0.35 kg/week for normal-weight women (BMI 18.5 to 24.99 kg/m2), <0.23 kg/week for overweight women (BMI 25 to 29.99 kg/m2), and <0.17 kg/week for obese women (BMI > 30 kg/m2). GWG above the IOM guidelines (purple dashed lines) was defined as follows: >0.58 kg/week for underweight, >0.50 kg/week for normal weight, >0.33 kg/week for overweight, and >0.27 kg/week for obese women. The plots show that the majority of women who had a pre-pregnancy BMI that is normal or overweight exceeded the cut-offs for normal GWG in all trimesters, while among those who were underweight less than 20% exceeded these cut-offs for GWG during pregnancy.

3.4.4. Trimestral Differences in Blood Pressure Measurements across Level of Adherence to the Mediterranean Diet

In trimester 1, no significant differences were reported for SBP, DBP and MAP among low, medium and high adherence to the LMeD, whereas in trimester 2 and 3 significant differences were observed. In trimester 2, women with SBP≥140 mmHg were more likely to have a low adherence (66.7%), and women with SBP<140 mmHg were more likely to have a medium adherence (52.9%) to the LMeD ($p<0.001$). Likewise, women with DBP<90 mmHg reported to have medium adherence (52.5%) and high adherence (26.4%) ($p<0.001$). Similarly for women with MAP≤84 mmHg, women were more likely to have medium adherence (53.1%) and high adherence (30%) ($p<0.001$). In trimester 3, 30.1% of women who had SBP≥140 mmHg had a low adherence to the LMeD, while the majority of women with SBP<140 mmHg had medium adherence (45.1%) and high adherence (32.3%) ($p<0.001$). Similarly, women with DBP≥90 mmHg were more likely to have low adherence to the LMeD (33.3%) ($p<0.001$). Moreover, 80 % of women with medium adherence and high adherence to the diet had a MAP≤86 mmHg ($p<0.001$). This indicates that either a medium or high adherence to the LMeD was associated with improved BP measurements (SBP, DBP and MAP) in trimester 2 and 3 (Table 3-2).

3.4.5. Dietary Characteristics and Adherence to the Mediterranean Diet across the Population

Table 3-3 represents the mean serving consumption of each food group of the LMeD across trimester 1, 2 and 3. Fruit consumption decreased gradually from trimester 1 to trimester 3, whereas dried fruit consumption slightly increased across the trimesters. Olive oil and eggs consumption increases from trimester 1 to trimester 2. On the contrary, starchy vegetable and dairy consumption decreased across the trimesters.

Adherence to the LMeD was significantly different across the governorates, where Beirut had the highest percentage of low adherence in trimester 1 (26.32%), 2 (38.95%) and 3 (46.32%) compared to the others, and South Lebanon had the second highest percentage of low adherence in trimester 1 (21.74%), 2 (30.43%) and 3 (39.13%) ($p<0.0039$, $p<0.0001$, and $p<0.0001$, respectively). With regards to the governorates that had the highest adherence, Akkar and Bekaa were identified in the 1st trimester ($p<0.0039$), Bekaa and Mount Lebanon in the 2nd trimester ($p<0.0001$) and Mount Lebanon and North Lebanon were identified in the 3rd trimester ($p<0.0001$). (Supplemental table 3-1)

3.4.6. Other Factors That May Influence Adherence to the Mediterranean Diet during Pregnancy

A mixed model with a random intercept was conducted to test the time-adherence interaction for the maternal outcomes HDPs, sleep quality, stress and depression. Stress and chronic hypertension were significantly associated with LMeD adherence. The prevalence of chronic hypertension decreased with time for pregnant women who had a high adherence to the LMeD. As for stress, the prevalence of women with high stress decreased with time for those having a low adherence whereas the prevalence of women with high stress increased for those having a high adherence suggesting that diet did not improve or decrease high stress among these women.

3.4.7. Hierarchical Logistic Regression Models

We initially investigated the effect of adherence to the LMeD on high vs. non high MAP using hierarchical logistic regression models for each trimester. In layer 1 we entered age, education, place of residence, occupation, GWG, pre-pregnancy BMI and smoking. In layer 2 we entered adherence to the LMeD with each individual food group in 9 separate models. Only significant food group models are shown (Tables 3-4A, 3-4B, 3-4C).

Trimester 1

Table 3-4A identified factors associated with eMAP (>87 mmHg) in the first trimester emerging in a multiple logistic regression while controlling for age, education, place of residence, occupation, GWG, pre-pregnancy BMI and smoking. Adherence to the LMeD was not significant in the model but 1 tsp olive oil consumption per day was associated with a lower risk (OR 0.559, $p<0.02$) where higher intakes did not confer added benefit. Poor sleep quality, but not hours of sleep alone, was associated with higher odds of eMAP (OR 1.019, $p<0.035$) when compared to those having a good sleep score. Among other covariates, place of residence contributed to eMAP with women living in Beirut (OR 5.2, $p<0.0001$) and Mount Lebanon (OR 5.0, $p<0.0001$) being at greatest risk while those living in Bekaa having a lower risk of eMAP (OR 0.186, $p<0.01$). Stress and depression were not significant ($p>0.05$).

Trimester 2

Table 3-4B reports factors associated with eMAP (>84 mmHg) in the second trimester emerging in a multiple logistic regression model while controlling for the same covariates like trimester 1. One model was identified – a dried fruit food model. Daily consumption of dried fruits (≥0.3 servings/day) was associated with a lower risk of eMAP (OR 0.544 $p< 0.0106$). Pregnant women who were self-employed had a higher risk of elevated MAP compared to those who were full-time employed (p<0.13). Pre-pregnancy BMI was positively associated with eMAP (OR 1.125, p <0.0356). Regarding the place of residence, women living in North (OR 0.237 p<0.0018), Bekaa (OR 0.192 p<0.001) and Akkar (OR 0.22, p<0.0112) had a lower risk of high MAP while living in Beirut did not impact eMAP. The remaining covariates (age, education, smoking, GWG, stress, sleep and depression) did not have an effect. A high adherence to the LMeD significantly lowered the risk of eMAP [OR 0.258, p<0.0002] compared to a low adherence to the MeD.

Trimester 3

Table 3-4C reports factors associated with eMAP (>86 mmHg) in the third trimester emerging in a multiple logistic regression model while controlling for the same covariates like trimester 1 and 2. No specific food group entered the model in the 3rd trimester, but pre-pregnancy BMI played an important role. Although a higher pre-pregnancy BMI (OR 1.123, p<0.029) was linked to a greater risk of eMAP (p<0.029), GWG in the 3rd trimester was not significant. Furthermore, the LMeD in the 3rd trimester did not have any effect on MAP. Among the covariates, only place of residence was significantly associated with MAP, where women living in Beirut had greater risk of eMAP (OR 3.054, p<0.003) and women living in North (OR 0.309, p<0.01) and Bekaa (OR 0.26, p<0.0006) had a lower risk of eMAP. The other covariates (education, age, GWG, smoking) and psychosocial factors (stress, sleep, depression) were not significant.

3.5. Discussion

Our study is the first in the region to look at the impact of adherence to the LMeD on eMAP during pregnancy. The majority of previous studies looked only at associations with SBP and

DBP measurements, while neglecting MAP which has been shown to be an early indicator of HDP risk and has a great impact on maternal and infant outcomes. Studies are lacking in the Middle Eastern area and specifically in Lebanon, and our study highlighted significant findings which can be beneficial for this population. Four major findings emerged in this study. First, a low percentage of the population had elevated SBP and/or DBP in all trimesters, however when it came to eMAP a greater percentage was identified in each trimester. Second, adherence to the LMeD differed by governorates with Beirut and South Lebanon having the least adherence among the regions. Third, BP measurements were different across the levels of adherence to the MeD in trimester 2 and 3 only, while in trimester 1 they did not differ. More women were reported to have elevated SBP, DBP and or/MAP in the low adherence group compared to the medium and high adherence group. Finally, with respect to predictors of eMAP per trimester, poor sleep quality and place of residence specifically those living in Beirut and Mount Lebanon significantly increased eMAP risk in trimester 1, whereas adherence to the LMeD did not. Olive oil, on the other hand, reduced the risk of eMAP when consuming 1 teaspoon per day. In trimester 2, a high adherence to the LMeD and a daily consumption of dried fruits (≥0.3 servings/day) in addition to those living in Bekaa, North and Akkar decreased risk of eMAP, whereas a high pre-pregnancy BMI and being self-employed increased its risk. In trimester 3, adherence to the LMeD was not associated with MAP while a high pre-pregnancy BMI and living in Beirut elevated the odds of eMAP.

Our results showed that BP differed by governorates. MAP significantly varied across the different regions of residence of Lebanon. Living in Beirut was associated with eMAP across all trimesters ($p<0.001$, $p=0.019$, $p=0.004$ respectively per trimester) compared to South Lebanon, whereas living in Mount Lebanon showed a greater risk of eMAP only in the 1st trimester (p<0.001) compared to South Lebanon. This is because each governorate has unique and specific traits, socio-demographic characteristics and culture. For instance, Beirut is a governorate and the capital of Lebanon and is considered the most important region in Lebanon because of its political, economic, cultural and social activity. Mount Lebanon has the greatest population density among the governorates and has mostly urban regions. It includes the highest percentage of industrial establishments in Lebanon and most of these establishments work in the food industries sector. People residing in Beirut and Mount Lebanon usually follow a more Western diet than those living in other governorates which can explain the higher risk of MAP found in these regions (Nasreddine et al., 2006). This was supported by the analyses where a significant difference was found for the adherence to the LMeD among the different regions in Lebanon where Beirut had the least adherence in all trimesters (p<0.05). Similarly, a recent study showed that an annual increase in HDPs was greater in urban compared to rural areas from 2007 to 2019 (Cameron et al., 2022).

Bekaa on the other hand consists of three districts Zahle (urban), Rachaya and West Bekaa, the latter being mostly rural areas. Akkar is Lebanon's poorest region and has the country's highest illiteracy rate and suffers from lack of basic infrastructure and services (Hoteit et al., 2021). The lower MAP reported in Bekaa and Akkar could be due to the consumption of organic and locally grown foods rather than a Western diet which is not readily available in this area. South Lebanon on the other hand has few mixed rural areas concentrated around 3 main cities with a majority of natural areas and agricultural lands. A low adherence to the LMeD was also identified in South Lebanon compared to the other governorates in the three trimesters (p<0.05). Contrary to our findings, another study showed that women living in rural areas had a higher risk of developing HDPs (Hinkosa et al., 2020).

Contrary to other studies that reported older age to be a risk factors for HDPs (Hinkosa et al., 2020; Zhao et al., 2021), this study did not show any association. Moreover, education, GWG and smoking did not differ across the trimesters and did not affect eMAP, whereas occupation did. Pregnant women who were self-employed experienced an increased risk of eMAP in the 2nd trimester than those working full-time (p=0.014). This can be explained because women who are self-employed experience higher stress levels due to the overwhelming demands of a running a certain business compared to those who are full-time employed, part-time employed or those who stay at home. One study found that women who worked in specific areas such as business, management, legal and social services, and healthcare professions were at greater risk of developing HDPs compared to housekeepers or non-employed women (Bilhartz & Bilhartz, 2013). The impact of pre-pregnancy BMI and sleep quality on eMAP also differed by trimesters. Pre-pregnancy BMI increased the risk of eMAP in the 2nd and 3rd trimester (p=0.041 and p=0.028, respectively), and was most important in the latter suggesting that having excessive weight was problematic and cannot be prevented by a Mediterranean diet alone. Similarly, women who were overweight before conception had a higher risk of developing HDPs (Hinkosa et al., 2020; Ren et al., 2018; Shubham Prasad, 2022; Zhao et al., 2021). Although a high percentage of women were exceeding GWG (68.29%), but it did not significantly affect MAP in any trimester indicating that pre-pregnancy BMI is more important than GWG, and this can be shown by the different distribution of GWG across the 4 categories of BMI. Contrary to our finding, a recent meta-analysis by (Ren et al., 2018) reported a significant association between high GWG and the emergence of HDPs.

Poor sleep was linked to a higher risk of eMAP in the 1st trimester only. Since the PSQI that was used to assess sleep quality is composed of 7 components, we investigated the impact of the component “sleep hour duration” in the model. However, it was not associated with MAP which suggests that subjective sleep quality is more important. Sleep alterations can occur during pregnancy and poor sleep has also been linked to stress and depression later in pregnancy with increased cortisol levels and poorer health-related quality of life that can lead to pregnancy complications including elevated blood pressure (Dorheim et al., 2012). Poor sleep is also a precursor to poor mental health. In our population, 47.5% of pregnant women experienced poor sleep quality which is similar to a study done in Lebanon among pregnant women where 74.5% experienced clinically significant insomnia (Mourady et al., 2017). Similar to our results, two recent reviews identified that sleep problems including insomnia, obstructive sleep apnea, restless leg syndrome and sleep disordered breathing were associated with increased risk of HDPs (Querejeta Roca et al., 2020; Silvestri & Aricò, 2019). We also explored the impact of stress and depression on MAP, however they were not associated with MAP despite the fact that a high percentage of women 85.7% of the pregnant females in this study experienced moderate or high stress. On the contrary, Njukang et al. (2020) and Morgan et al. (2022) reported a significant association between stress and gestational hypertension. A recent review also identified that severe depression increased the risk of HDPs (Chapuis-de-Andrade, 2019), and another meta-analysis reported the same association with depression and stress (Shay et al., 2020). Another study highlighted the potential role of pre-pregnancy stress and depression on increasing the risk of HDPs (Thombre et al., 2015). These results draw a special attention on the poor mental health status of the Lebanese pregnant population and the importance of screening for the presence of psychological conditions during their routine visits to the obstetricians. Our study was the first to look at the relationship between psychosocial factors and MAP, which may explain the reason why our study findings differed from others.

Our main independent variable adherence to the LMeD differed by trimesters and dominated in the 2nd trimester only, where a high adherence lowered the risk of eMAP. Although studies on BP and specifically MAP during pregnancy are few, but previous research in Australia and 2 Mediterranean countries (Spain and Greece) have showed a similar association between adherence to the MeD and BP (Parlapani et al., 2019; Assaf-Ballut et al., 2019; Schoenaker et al., 2015). One study reported a significant reduction in MAP in the general population with a high adherence to the MeD (Ahmed et al., 2020). The MeD is rich in vegetables, fruits, whole grains and low in fat, and has high anti-inflammatory components which can contribute to lowering the risk factors of high BP such as overweight, dyslipidemia, inflammation, high blood glucose levels, and diabetes (Bonaccio et al., 2013; Benhammou et al., 2016). In this study, the LMeD did not relate to any benefit in the 1st and 3rd trimester of pregnancy. In the 1st trimester, pregnant women usually experience nausea, decreased appetite and lower food intake, whereas in the 2nd trimester, they regain their appetite and hence it becomes a turning point for both the mother and her fetus. Maternal nutrition in the 2nd trimester can affect overall fetal growth and brain development (Pathirathna et al., 2017). Moreover, the placenta starts forming at the end of the 1st trimester and a low adherence to the MeD during this period is linked to lower placental weight (Timmermans et al., 2012). Similarly, elevated BP can exacerbate placental problems and cause a decline in placental function (Krielessi et al., 2012). In the third trimester, adherence to the LMeD was not associated with MAP which suggests that adherence to this diet cannot prevent the oxidative stress which may have resulted from a high pre-pregnancy BMI reported in the 3rd trimester.

We also explored the relationship between specific food groups of the LMeD and eMAP, and among the 9 food groups, olive oil and dried fruits were protective of eMAP. Olive oil in particular has been shown to lower the risk of cardiovascular diseases including high BP in pregnant women in a prior study (Assaf-Ballut et al., 2017). The high content of mono-unsaturated fatty acids (anti-inflammatory) can protect against oxidative stress and the oxidation of the placenta (Schwingshackl et al., 2015). Furthermore, the usage of olive oil favors the consumption of vegetables (Assaf-Ballut et al., 2017). In this study, a moderate consumption of olive oil (1 tsp) in the 2nd tertile lowered the risk of eMAP in the 1st trimester which suggest an optimal daily consumption of 1 tsp/day to protect against high MAP. Furthermore, a high consumption of dried fruits(≥0.3 serving/day) in the 3rd tertile in the 2nd trimester was associated with lower eMAP, since dried fruits are rich in anti-oxidants and can limit the oxidative stress for the placenta which could be related to a low BP (Assaf-Ballut et al., 2019).

3.6. Strengths and Limitations

The major strength of this study is its national prospective cohort design that is the first in the EMC conducted among a representative sample of pregnant women in the different regions of Lebanon. This study is the first to assess predictors of the outcome MAP in the region. Moreover, all questionnaires that were used were validated and administered by trained professionals. Another major strength of this study is the novelty of the findings with regards to the association of LMeD and its specific components, particularly olive oil and dried fruits on eMAP. Moreover, other predictors such as living in urban regions, being self-employed, having poor sleep quality, and a high pre-pregnancy BMI also emerged as predictors of eMAP.

At the same time, we acknowledge that prospective cohort study designs have limitations as they are prone to measurement and recall bias such as for self-reported data on diet, psychosocial factors, physical activity, and smoking. We also acknowledge that the nature of the study design can lead to loss of follow up, however only 6.4% dropped out either due to miscarriage (n=21) or loss to follow up (n=21) which was less than the 20% we had added to our original sample size. Moreover, the economic crisis and the emergence of COVID-19 during the period of this study might have affected our results by increasing psychosocial factors such as stress, depression and/or poor sleep among participants and affecting their dietary intake. Another limitation is that we were not able to enter the following variables: food security, PA and advice on diet in our models due to the very low response rate.

Our focus on LMeD adherence did not consider other dietary factors (e.g. processed food intake, total caloric intake, and specific nutrient intakes).

3.7. Conclusion

In conclusion, the results of this study conferred the importance of the LMeD on lowering eMAP in pregnant women particularly in the 2nd trimester, in addition to the effect of socio-demographic variables such as employment and place of residence, biological variables such as pre-pregnancy BMI and lifestyle variables such as sleep quality on pregnancy outcomes specifically BP. Moreover, specific food groups such as olive oil and dried fruits had the most significant contribution on lowering eMAP risk. This study is the first national study to assess the association between the LMeD and MAP (early indicator of HDPs during pregnancy) in Lebanon and across the different governorates, and provided novel findings on this issue. This reinforces the importance of promoting nutrition, mental health and lifestyle counseling for pregnant women.

Table 3-1. Maternal Characteristics of the sample population (N=618)

MATERNAL SOCIO-DEMOGRAPHICS	N (%) or Mean ± SD
Mean age in years	29.2 ± 5.0
Place of Residence	
Akkar	23 (3.72)
Beirut	77 (12.46)
Bekaa	100 (16.18)
Mount Lebanon	190 (30.74)
North Lebanon	46 (7.44)
South Lebanon	182 (29.45)
Education	
Brevet or less	81 (13.11)
High school	67 (10.84)
BSc. Degree	251 (40.61)
Master's degree and beyond	219 (35.44)
Occupation	7 (1.13)
Student	303 (49.03)
Homemaker	54 (8.74)
Self-employed	61 (9.87)
Employee part-time	193 (31.23)
Employee full-time	
Food Security*	
High food security	81 (65.85)
Low food security	22 (17.89)
Very low food security	20 (16.27)
MATERNAL HEALTH STATUS	
Pre-pregnancy BMI**	
Underweight (BMI <18.5)	24 (3.88)
Normal (BMI 18.5-24.9)	394 (63.76)
Overweight (BMI 25-29.9)	137 (22.17)
Obese (BMI≥30)	63 (10.19)
Total GWG***	
Low	62 (11.170)
Adequate	114 (20.54)
Excessive	379 (68.29)
Previous HDPs	
Yes	21 (3.65)
No	554 (96.35)
Gestational Hypertension	10 (1.61)

Pre-Eclampsia	
Yes	11 (1.95)
Chronic Hypertension	
Yes	9 (1.45)
Perceived Stress Score (Trimester 1)	
Low stress ((Score ≤13)	88 (14.24)
Moderate stress (Score 14-26)	462 (74.60)
High stress (Score ≥27)	68 (11.0)
Perceived Stress Score (Trimester 2)	
Low stress (Score ≤13)	79 (13.57)
Moderate stress (Score 14-26)	400 (68.73)
High stress (Score ≥27)	103 (17.70)
Perceived Stress Score (Trimester 3)	
Low stress ((Score ≤13)	78 (13.45)
Moderate stress (Score 14-26)	367 (63.28)
High Stress (Score ≥27)	135 (23.28)
Edinburgh Depression Score (Trimester 1)	
Depressed (Score≥10)	277 (45.19)
Non-depressed (Score<10)	336 (54.81)
Edinburgh Depression Score (Trimester 2)	
Depressed (Score≥10)	257 (45.49)
Non-depressed (Score<10)	308 (54.51)
Edinburgh Depression Score (Trimester 3)	
Depressed (Score≥10)	250 (43.78)
Non-depressed (Score<10)	321 (56.22)
Pittsburgh Sleep Quality Index (Trimester 1)	
Good sleep (score <5)	279 (46.27)
Bad sleep (score ≥5)	324 (53.73)
Pittsburgh Sleep Quality Index (Trimester 2)	
Good sleep (score <5)	141 (24.31)
Bad sleep (score ≥5)	439 (75.69)
Pittsburgh Sleep Quality Index (Trimester 3)	
Good sleep (score <5)	94 (16.26)
Bad sleep (score ≥5)	484 (83.74)

*Food security was assessed using a six-item scale derived from the United States Department of Agriculture guide to measuring food insecurity. A score 0-1 indicates high food security, 2-4 indicates low food security, and 5-6 indicates very low food security **BMI was classified into underweight, normal, overweight and obese according to IOM **(Total gestational weight gain was calculated by subtracting total weight gained from pre-pregnancy BMI. GWG was classified as inadequate, appropriate or excessive applying the following recommendations: To be

considered adequate GWG, women who are underweight should gain a total of 12.5-18 kg, normal weight between 11.5-16 kg, overweight between 7-11.5 kg, and obese between 5-9 kg. Those with low GWG have a weight gained below these recommendations whereas those with excessive weight gain have above these recommendations.
Abbreviations: BMI, body mass index, GWG, gestational weight gain, HDPs, hypertensive disorders of pregnancy

Figures 3-1. Population Characteristics describing Blood Pressure Measurements including SBP, DBP, and MAP

Fig 3-1a. SBP vs. DBP in the 1st trimester

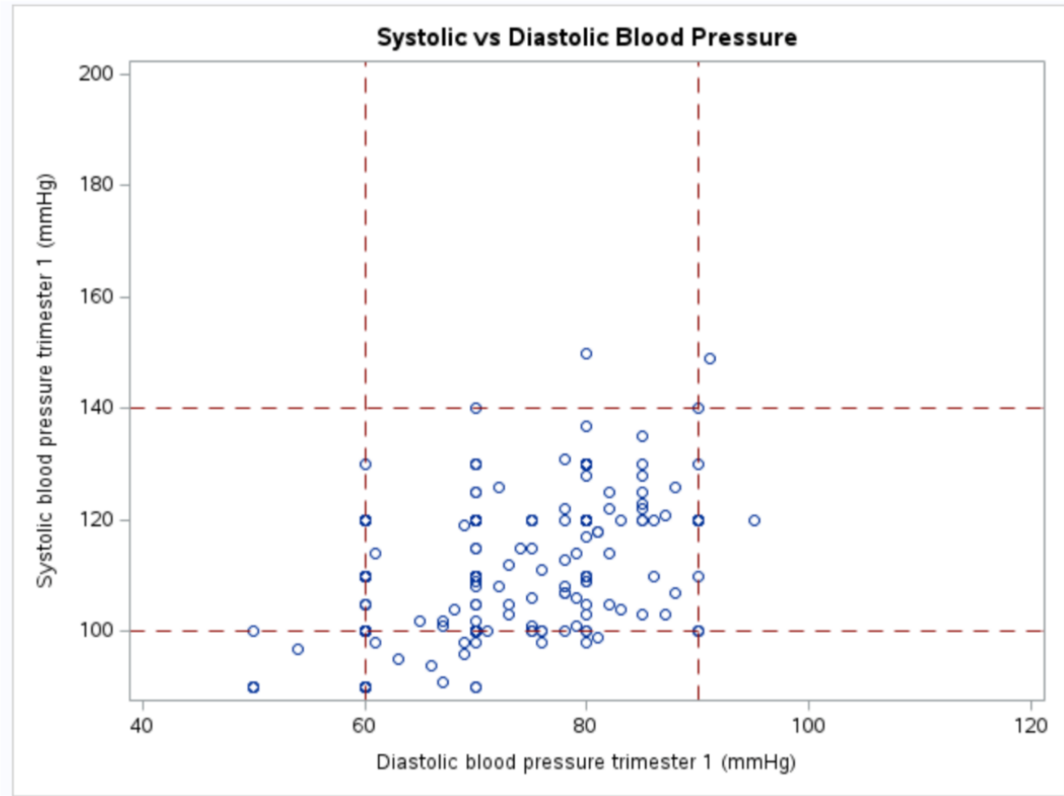


Figure 3-1a: Scatter plot of systolic vs. diastolic blood pressure in 574 pregnant Lebanese women in their first trimester. Dashed lines represent blood pressure limits for hypertension during pregnancy (≥140 mmHg for SBP and ≥ 90 mmHg for DBP, lower limits were defined following the most conservative cut-offs (<100 mmHg for SBP and <60 mm Hg for DBP) for pregnant women.

Fig 3-1b. SBP vs DBP in the 2nd trimester

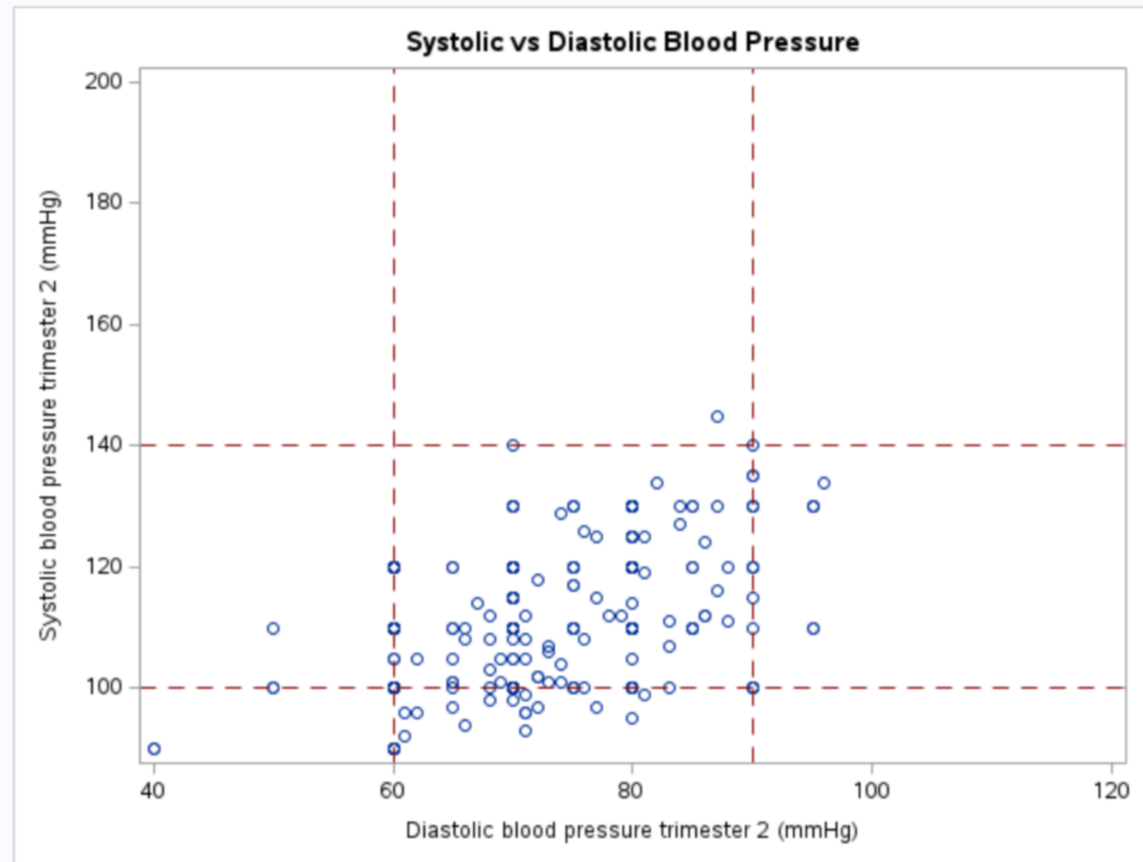


Figure 3-1b: Scatter plot of systolic vs. diastolic blood pressure in 572 pregnant Lebanese women in their second trimester. Dashed lines represent blood pressure limits for hypertension during pregnancy (≥ 140 mmHg for SBP and ≥ 90 mmHg for DBP, lower limits were defined following the most conservative cut-offs (<100 mmHg for SBP and <60 mm Hg) for pregnant women.

Fig 3-1c. SBP vs. DBP in the 3rd trimester

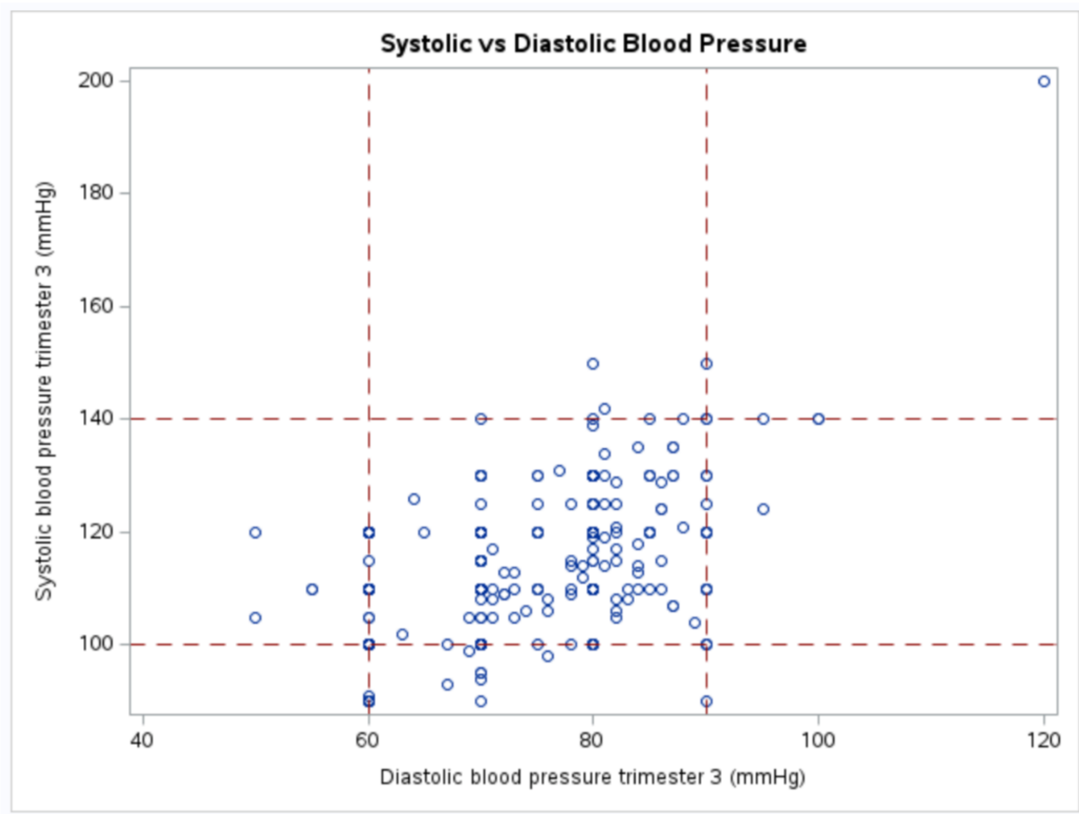


Figure 3-1c: Scatter plot of systolic vs. diastolic blood pressure in 580 pregnant Lebanese women in their third trimester. Dashed lines represent blood pressure limits for hypertension during pregnancy (≥ 140 mm Hg for SBP and ≥ 90 mm Hg for DBP, lower limits were defined following the most conservative cut-offs (<100 mm Hg for SBP and <60 mm Hg) for pregnant women.

Fig 3-1d. MAP by Gestational Age across the Trimesters

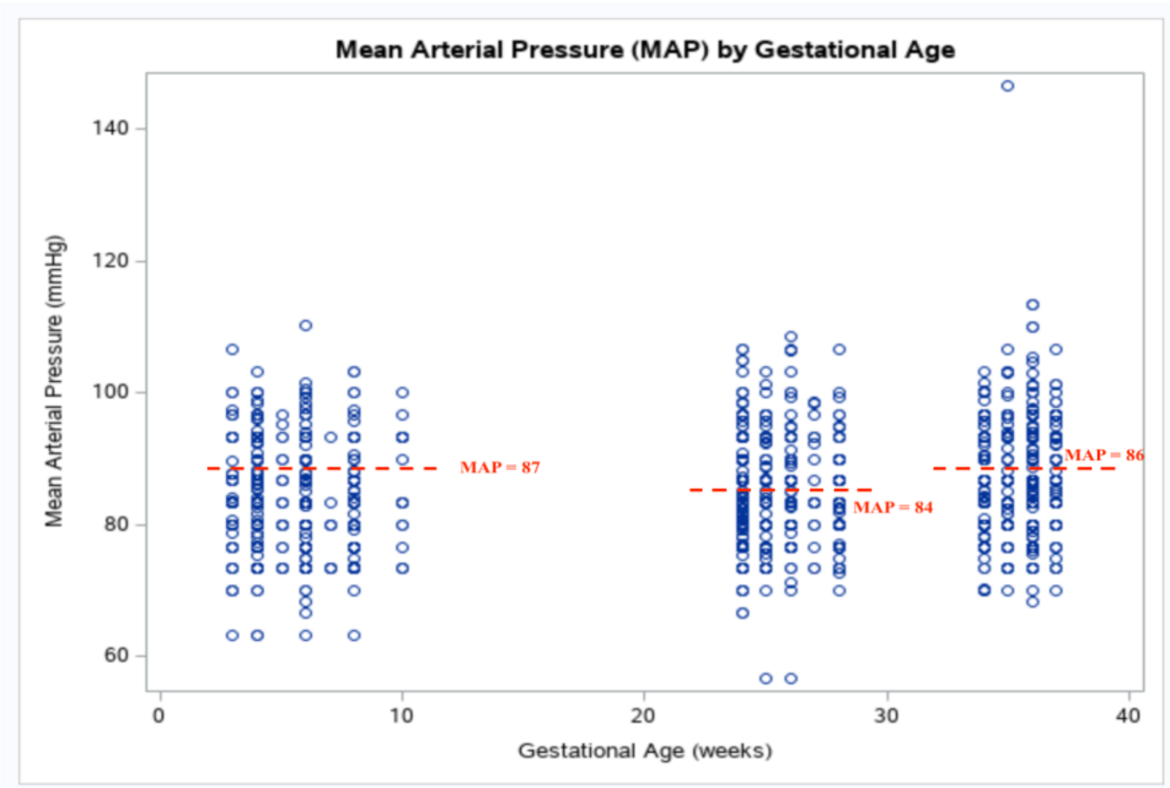


Figure 3-1d: Scatter plot of mean arterial pressure (MAP) according to gestational age. Dashed lines represent cutoffs for elevated MAP >87 mm Hg between weeks 10 – 18, > 84 mm Hg in weeks 18 – 34, and > 86 mm Hg after week 34.

Figures 3-2. Gestational Weight Gain across the Trimesters for the Different Pre-pregnancy BMI Categories

Fig 3-2a. Total GWG for women with pre-pregnancy BMI≤18.5 kg/m2

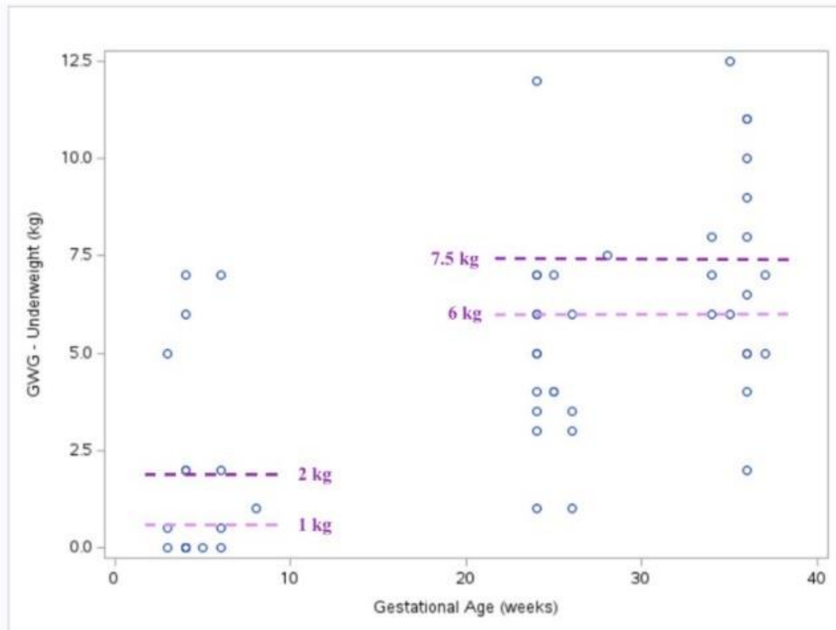


Fig 3-2b. Total GWG for women with pre-pregnancy BMI 18.5-24.99 kg/m2

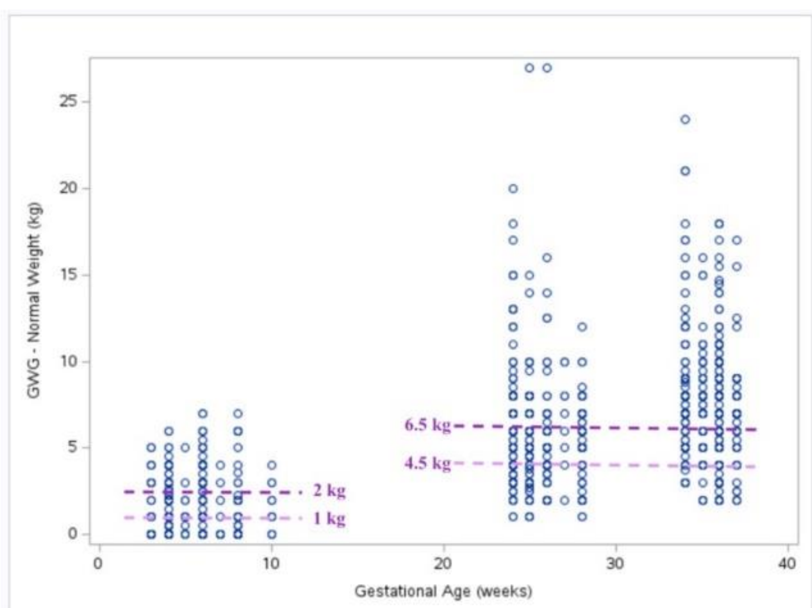


Fig 3-2c. Total GWG for women with pre-pregnancy BMI 25-29.99 kg/m2

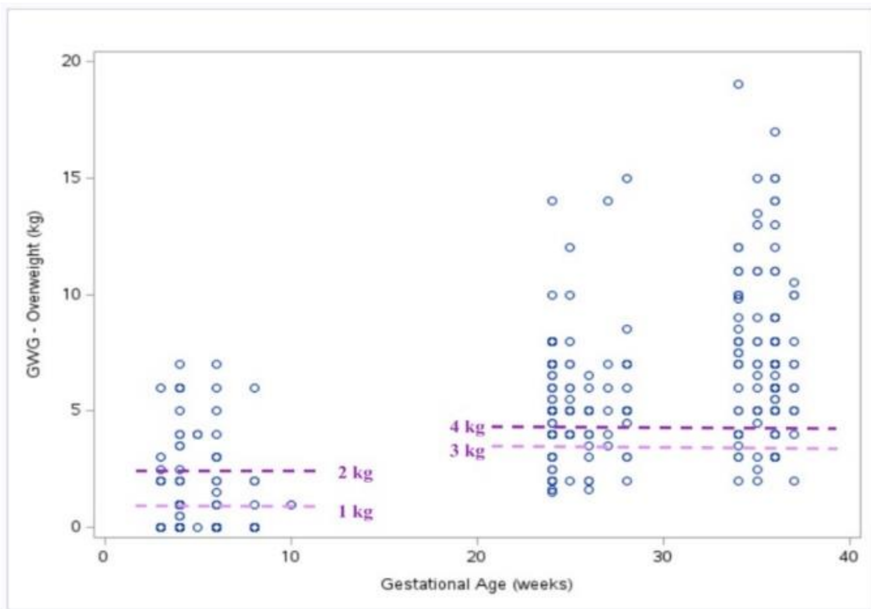
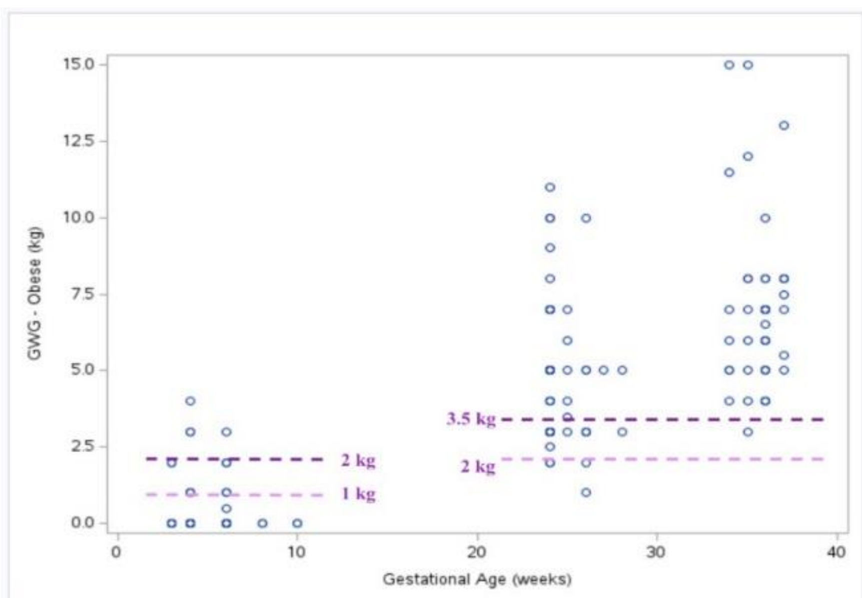


Fig 3-2d. Total GWG for women with pre-pregnancy BMI≥30 kg/m2



Cut-offs for GWG were defined as above or below the IOM recommendations for different pre-pregnancy BMI categories which are the following: For 1st trimester: above 2 kgs (purple dashed lines) or below 1 kg (pink dashed lines) for all categories of BMI. For 2nd and 3rd trimester, the cut-offs used for GWG below the IOM guidelines were as follows (pink dashed lines): <0.44 kg/week for underweight women (BMI < 18.5 kg/m^2), <0.35 kg/week for normal-weight women (BMI 18.5 to 24.99 kg/m^2), <0.23 kg/week for overweight women (BMI 25 to 29.99 kg/m^2), and <0.17 kg/week for obese women (BMI > 30 kg/m^2). GWG above the IOM guidelines (purple dashed lines) was defined as follows: >0.58 kg/week for underweight, >0.50 kg/week for normal weight, >0.33 kg/week for overweight, and >0.27 kg/week for obese women

Table 3-2. Trimester Blood Pressure Measurements by Level of Adherence to the Lebanese Mediterranean Diet*

Blood Pressure Measurements	**Low Adherence (Score 9-15)**	**Medium Adherence (Score 16-20)**	**High Adherence (Score 21-27)**	**p**
Trimester 1				
SBP<140	109 (19.12%)	337 (59.12%)	124 (21.75%)	0.35
SBP≥140	0 (0%)	4 (100%)	0 (0%)	
DBP<90	107 (19.21%)	331 (59.43%)	119 (21.36%)	0.62
DBP≥90	2 (11.76%)	10 (58.82%)	5 (29.41%)	
MAP≤87	80 (18.39%)	257 (59.08%)	98 (22.53%)	0.60
MAP>87	29 (20.86%)	84 (60.43%)	26 (18.71%)	
Trimester 2				
SBP<140	120 (21.02%)	302 (52.89%)	149 (26.09%)	**<0.001****
SBP≥140	2 (66.67%)	1 (33.33%)	0 (0.00%)	
DBP<90	116 (21.01%)	290 (52.54%)	146 (26.45%)	**<0.001****
DBP≥90	6 (28.57%)	13 (61.90%)	2 (9.52%)	
MAP≤84	57 (16.91%)	179 (53.12%)	101 (29.97%)	**<0.001****
MAP>84	65 (27.54%)	124 (52.54%)	47 (19.92%)	
Trimester 3				
SBP<140	127 (22.64%)	253 (45.10%)	181 (32.26%)	**<0.001****
SBP≥140	4 (30.77%)	6 (46.15%)	3 (23.08%)	
DBP<90	123 (22.40%)	247 (44.99%)	179 (32.60%)	**<0.001****
DBP≥90	8 (33.33%)	12 (50.00%)	4 (16.67%)	
MAP≤86	58 (20%)	140 (48.28%)	92 (31.72%)	**<0.001****
MAP>86	73 (25.80%)	119 (42.05%)	91 (32.16%)	

*Chi square test was conducted. **Indicates significant associations. Abbreviations: SBP, systolic blood pressure, DBP, diastolic blood pressure, MAP, mean arterial pressure

Table 3-3. Daily Mean Food Group Consumption of the Lebanese Mediterranean Diet among Pregnant Women per Trimester (N=618)*

Food Group (Serving Size)	Trimester 1	Trimester 2	Trimester 3
Burghol (1cup)	0.12±0.2	0.13±0.2	0.12±0.2
Fruits (1 cup/1 item)	2.44±1.8	2.35±1.7	2.12±1.5
Dried fruits (2tbsp raisins or cranberries, 2 pieces dates, 4 pieces apricots)	0.17±0.4	0.17±0.4	0.19±0.4
Olive oil (1 tsp)	1.05±0.8	1.07±0.8	1.32±1.0
Eggs (one large egg)	0.32±0.4	0.35±0.4	0.36±0.4
Starchy vegetables (1 cup)	0.40±0.4	0.35±0.3	0.31±0.3
Dairy (1cup milk/yogurt, 1 slice cheese/2 tbsp labneh)	2.35±1.5	1.56±1.2	1.51±1.3
Vegetables (1 cup)	1.79±1.1	1.90±1.4	1.64±1.2
Legumes (1 cup)	0.24±0.3	0.27±0.3	0.25±0.2

*Numbers represent mean serving consumption per day of each food group of the Lebanese Mediterranean diet per trimester

Supplemental Table 3-1: Comparison of Adherence to the Lebanese Mediterranean Diet across Place of Residence in Trimester 1, 2 and 3

	LOW ADHERENCE		MEDIUM ADHERENCE		HIGH ADHERENCE		Total		
	N	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**p**
PLACE OF RESIDENCE - Trimester 1									**0.0039**
Akkar	13	16.88	43	55.84	21	27.27	77		
Beirut	50	26.32	107	56.32	33	17.37	190		
Bekaa	7	15.22	22	47.83	17	36.96	46		
Mount Lebanon	33	18.13	122	67.03	27	14.84	182		
North Lebanon	11	11.00	63	63.00	26	26.00	100		
South Lebanon	5	21.74	12	52.17	6	26.09	23		
PLACE OF RESIDENCE - Trimester 2									**<0.0001**
Akkar	21	27.27	43	55.84	13	16.88	77		
Beirut	74	38.95	99	52.11	17	8.95	190		
Bekaa	11	23.91	21	45.65	14	30.43	46		
Mount Lebanon	24	13.19	66	36.26	92	50.55	182		
North Lebanon	13	13.00	73	73.00	14	14.00	100		
South Lebanon	7	30.43	14	60.87	2	8.70	23		
PLACE OF RESIDENCE - Trimester 3									**<0.0001**
Akkar	24	31.17	36	46.75	17	22.08	77		
Beirut	88	46.32	85	44.74	17	8.95	190		
Bekaa	14	30.43	25	54.35	7	15.22	46		
Mount Lebanon	21	11.54	50	27.47	111	60.99	182		
North Lebanon	6	6.00	59	59.00	35	35.00	100		
South Lebanon	9	39.13	13	56.52	1	4.35	23		

Table 3-4A, 3-4B, 3-4C- Logistic Regression Models (LRM) on the Association between Adherence to the Mediterranean Diet and high vs non-high MAP in Trimesters 1, 2 and 3

Table 3-4A. LRM between Adherence to the LMeD and high MAP (>87) vs non-high MAP (≤87) in Trimester 1

Olive Oil Model

Variables	OR **	CI **	p-value
Adherence to the LMeD			
High (Score 21-27)	1.043	0.495-2.196	0.9116
Medium (Score 16-20)	1.288	0.717-2.314	0.3968
Low (Score 9-15)			
Olive oil consumption			
High (≥1.4 tsp/day)	0.681	0.32-1.447	0.3176
Medium (1 tsp/day)	0.559	0.331-0.945	**0.0240***
Low (≤0.8 tsp/day)			
Pittsburgh Sleep Quality Index			
Poor Sleep (Score≥5)	1.019	0.534-1.943	**0.0351***
Good Sleep (Score<5)			
Place of Residence			
Beirut	5.228	2.417-11.31	**<0.0001***
Mount Lebanon	5.056	2.536-10.08	**<0.0001***
North Lebanon	0.893	0.302-2.643	0.8381
Bekaa	0.186	0.051-0.675	**0.0105***
Akkar	2.663	0.791-8.968	0.1138
South Lebanon			

Olive oil model represents the logistic model of adherence to the LMeD (main independent variable) and olive oil consumption, and outcome categorical MAP using trimester cut-off for high vs not high MAP in trimester 1, controlling for age, GWG in the 1st trimester, pre-pregnancy BMI, education, place of residence, occupation, smoking, sleep, stress, and depression scores from questionnaires. * Indicates significant associations with high MAP. ** OR indicates the odds ratio for the logistic model and CI indicates 95% Wald Confidence Limits

Table 3-4B. LRM between Adherence to the LMeD and high MAP (>84) vs non-high MAP (≤84) in trimester 2

Dried Fruits Model

Variables	**OR**	**CI**	**p-value**
Adherence to the LMeD			
High (Score 21-27)	0.258	0.126-0.53	**0.0002***
Medium (Score 16-20)	0.647	0.38-1.101	0.1083
Low (Score 9-15)			
Dried fruits consumption			
High (≥0.3 serving/day)	0.544	0.341-0.868	**0.0106***
Medium (0.2 serving/day)	1.083	0.505-2.323	0.8378
Low (≤0.1 serving/day)			
Pre-pregnancy BMI	1.125	1.008-1.255	**0.0356***
Occupation			
Student	2.684	0.396-18.172	0.3116
Homemaker	1.43	0.872-2.345	0.1565
Self-employed	2.443	1.202-4.968	**0.0136***
Employee part time	1.14	0.565-2.301	0.7141
Employee full time			
Place of Residence			
Beirut	1.964	0.971-3.971	0.0602
Mount Lebanon	0.68	0.377-1.226	0.1997
North Lebanon	0.237	0.096-0.584	**0.0018***
Bekaa	0.192	0.095-0.39	**<0.0001***
Akkar	0.22	0.068-0.709	**0.0112***
South Lebanon			

Dried fruits model represents the logistic model of adherence to the LMeD (main independent variable) and dried fruits consumption, and outcome categorical MAP using trimester cut-off for high vs not high MAP in trimester 2, controlling for age, GWG, pre-pregnancy BMI, education, place of residence, occupation, smoking, sleep, stress, and depression. * Indicates significant associations with MAP

Table 3-4C. LRM between Adherence to the LMeD and high MAP (>86) vs non-high MAP (≤86) in trimester 3

Variables	**OR**	**CI**	**p-value**
Adherence to the LMeD			
High (Score 21-27)	1.123	0.593-2.126	0.7212
Medium (Score 16-20)	0.981	0.584-1.649	0.9421
Low (Score 9-15)			
Pre-Pregnancy BMI	1.123	1.012-1.245	**0.0282***
Place of Residence			
Beirut	2.945	1.403-6.181	**0.0043***
Mount Lebanon	1.109	0.591-2.08	0.7476
North Lebanon	0.287	0.118-0.7	**0.0061***
Bekaa	0.264	0.139-0.503	**<0.0001***
Akkar	0.375	0.123-1.148	0.0857
South Lebanon			

This model represents the logistic model of adherence to the LMeD (main independent variable, and outcome categorical MAP using trimester cut-off for high vs not high MAP in trimester 3, controlling for age, total GWG, pre-pregnancy BMI, education, place of residence, occupation, smoking, sleep, stress, and depression. No food group emerged in this model. * Indicates significant associations with MAP

Connecting Statement I

In Chapter III, we assessed the prevalence of high SBP, DBP and MAP during pregnancy on a national level in Lebanon, and found that elevated SBP and MAP were low in the population (<5%) whereas eMAP was high in all trimesters (>30%). MAP was shown in previous studies to be an early indicator of HDPs. The predictors of eMAP in every trimester were also studied, and we hypothesized that a high adherence to the LMeD and good psychosocial factors including low stress, good sleep quality and no depression were associated with decreasing eMAP risk. We found that adherence to the LMeD and specific food groups of the LMeD including olive oil and dried fruits decreased eMAP risk. Moreover, urban regions including Beirut and Mount Lebanon had a lower adherence to the LMeD and an increased risk of eMAP compared to other regions. Moreover, poor sleep quality and high pre-pregnancy BMI were found to be associated with eMAP as well.

In Chapter IV, the specific objectives of the study were to determine the prevalence of GDM and impaired glucose tolerance (IGT) on a national level among pregnant women in Lebanon and to assess the predictors of GDM and IGT per trimester among these women. We hypothesized that a high adherence to the LMeD and good psychosocial factors including low stress, good sleep quality and no depression were associated with a decreased GDM and IGT risk among pregnant women in Lebanon. Therefore our aim was to study the association between adherence to the LMeD and its specific food groups with GDM and IGT, and explore the role of other maternal factors including eMAP, psychosocial factors, family history of diabetes, GWG and pre-pregnancy BMI on GDM and IGT.

CHAPTER IV

Predictors of Impaired Glucose Tolerance and GDM in a Lebanese Pregnant Population

4.1. Abstract

Obesity is on the rise in Lebanon and women are exceeding weight gain recommendations during pregnancy. Lebanon is among the top 10 countries with highest diabetes prevalence (20.2%) and impaired glucose tolerance (IGT) (26.6%). Gestational diabetes mellitus (GDM), which is first diagnosed in pregnancy is also increasing and the highest prevalence was found in the Eastern Mediterranean countries (EMC) (23%). Despite the high incidence in EMC, predictors of GDM and IGT have not been studied yet in Lebanon. This study aimed to assess risk factors that are associated with the diagnosis of GDM in trimester 2, as well as predictors of IGT in trimester 1 and trimester 3. A total of 618 pregnant women were recruited (mean age=29.1±5.0 years) before 12 weeks of gestation. A baseline questionnaire assessed socio-demographic characteristics, psychosocial factors including stress, sleep and depression, as well as a food frequency questionnaire (FFQ) and adherence to the Lebanese Mediterranean diet (LMeD). Questionnaires were re-administered at 24-28 weeks and at 34-37 weeks of gestation. Medical chart information was also retrieved upon enrollment and in the 2nd and 3rd trimester which included pre-pregnancy body mass index (BMI), weight gain per trimester and total gestational weight gain (GWG), medical history, anemia, vitamin/supplement use, maternal health status, blood pressure measurements [(systolic blood pressure (SBP), diastolic blood pressure (DBP) and mean arterial pressure (MAP)], diagnosis of GDM, and fasting blood glucose values (FBG) in trimester 1 and 3. Univariate analyses were used to summarize the population characteristics as well as the mean serving size consumption of each LMeD food group. Lifestyle characteristics, psychosocial factors including stress, sleep and depression, and dietary characteristics were compared across the trimesters using the McNemar test. Maternal

factors and dietary characteristics were also compared among women in the normal FBG group <100 mg/dl vs IGT group>=100 mg/dl in trimester 1 and 3.A hierarchical multiple logistic regression modeling approach was used to test the association between each potential predictor including lifestyle and psychosocial variables in trimester 1 and 3, respectively and elevated FBG within the same trimester, and in trimester 2, models were used to test the association between GDM and each predictor variable within the same trimester. Models were first adjusted for GWG, pre-pregnancy BMI, family history of diabetes, stress, sleep, depression and MAP (Model 1-Maternal Characteristics), then the significant variables from model 1 were entered and adjusted for adherence to the LMeD (Model 2-Adherence to the LMeD), and finally model 3 was adjusted for individual food groups (Model 3-Individual Food Groups). All the analyses were conducted using SAS V9.4. The majority of the population were primiparous (38%) and college educated (75%), while half lived in Beirut and Mount Lebanon. Approximately 33% of the women were overweight and/or obese, and most of them exceeded weight gain recommendations in all trimesters. The prevalence of GDM was low (5.6%) whereas the prevalence of IGT was greater in trimester 1 (13%) and trimester 3 (26%). Family history of diabetes, high GWG in trimester 2 and high MAP increased the risk of GDM. Moreover, high perceived stress and high burghol and legumes intake increased the odds of having IGT in trimester 1, whereas higher T3 GWG increased the risk of IGT in trimester 3 and higher intake of vegetables lowered the risk. LMeD was neither associated with GDM nor with IGT, however specific food groups such as burghol and legumes increased the risk of IGT while vegetables decreased the odds of IGT. Furthermore, counseling on GWG should be initiated early during pregnancy as well as screening for family history of diabetes and elevated BP measurements.

4.2. Introduction

Gestational diabetes mellitus (GDM) is the most common pregnancy complication diagnosed between 24 and 32 weeks of pregnancy and is on the rise worldwide due to increasing age and obesity (Benhalima, 2018). GDM can cause adverse maternal and infant outcomes including large for gestational age (LGA) offspring, macrosomia, caesarean section, hypertensive disorders of pregnancy (HDPs), and pre-eclampsia (PE). Also, on the long term GDM can increase the risk of impaired glucose tolerance (IGT), diabetes, and abnormal blood lipids in women (Benhalima, 2018). Pre-existing conditions such as previous diabetes (Erem et al., 2015; Goueslard et al., 2016), hypertensive disorders (El Sagheer & Hamdi, 2018; Goueslard et al., 2016; Savona-Ventura et al., 2012) previous macrosomia (Savona-Ventura et al., 2012), first degree family history of diabetes (IDF Clinical Guidelines Task Force, 2009), miscarriage (AlKasseh et al., 2013; Savona-Ventura et al., 2012), stillbirth (AlKasseh et al., 2013), and caesarian delivery (AlKasseh et al., 2013) have been strongly linked with GDM in Mediterranean women. Additional risk factors were also identified including socio-demographic and behavioral factors. Furthermore, the Hyperglycemia and Adverse Pregnancy Outcomes (HAPO) study identified hyperglycemia and IGT as a major burden even in women without GDM due to their predominant role in increasing gestational complications (Leary et al., 2010).The highest prevalence of hyperglycemia in pregnancy was reported among Middle Eastern and North African countries (22.3%) compared to other regions (Guariguata et al., 2014).

Adiposity has been identified as the most significant risk factor for GDM (Hashim et al., 2019; Haugen et al., 2008; World Health Organization (WHO), 2016). Both high pre-pregnancy body mass index (BMI) and gestational weight gain (GWG) in excess of recommendations have been associated with GDM (M. K. Kjøllesdal & G. Holmboe-Ottesen, 2014; Mamun et al., 2011;

Marchi et al., 2015; Vasudevan et al., 2011). Being overweight prior to pregnancy showed to increase the risk of elevated fasting blood glucose (FBG) levels among women with GDM (Mi, 2021). Moreover, high first trimester weight gain was associated with GDM (Hedderson, 2010; Lan, 2019) and abnormal glucose tolerance (Macdonald, 2017) regardless of pre-pregnancy BMI. Mediterranean women have previously been reported to have an average pre-pregnancy BMI $\geq$25 kg/m^2 (Abu-Heija et al., 2017; El Sagheer & Hamdi, 2018; Imen et al., 2018) and excessive GWG with a third trimester BMI $\geq$30 kg/m^2 (Savona-Ventura et al., 2012).

Diet also has emerged as a predictor of GDM (Altemani, 2022). In particular, the Mediterranean diet (MeD) adopted by most Mediterranean countries has emerged as beneficial for decreasing GDM risk (Assaf-Balut et al., 2017; Assaf-Balut et al., 2019; H. Al Wattar et al., 2019; Izadi et al., 2016; Karamanos et al., 2014) and improving glucose levels in women without GDM (Karamanos et al., 2014). More than 22 indexes have been developed specific for Mediterranean countries including Lebanon to assess adherence to the MeD in the general population and among these, several ones were modified for use with pregnant women by removing alcohol and/or including micronutrients needed for pregnancy such as calcium, folic acid, and iron (Eckl, 2021; Naja et al., 2015). Two recent meta-analyses showed that adherence to the MeD during pregnancy can decrease the risk of GDM. Further, recent evidence highlighted that a low glycemic index diet accompanied with a high intake of vegetables, fruits, and fibers decreases inflammation in the body (Schiattarella, 2021). Other studies showed a benefit of a pre-pregnancy adherence to the MeD (Donazar-Ezcurra et al., 2017; Schoenaker et al., 2015; Trenidou, 2023) or an early MeD intervention during pregnancy (De la Torre, 2019). Three large clinical trials reported a significant reduction in GDM risk by using a MeD intervention in early pregnancy (H. Al Wattar et al., 2019), a MeD diet supplemented with extra virgin olive oil (EVOO) and pistachios (Zhao, 2022), and MeD adherence to the following 6 food items: >12 servings/week of vegetable, >12 servings/week of fruits, 3 servings/week of nuts, >6 days/week consumption of extra virgin olive oil (EVOO), and ≥40 mL/day of EVOO (Assaf-Balut, 2018). Additionally, two case control studies reported the following: a significant reduction in FBG among GDM women who adhered to a MeD (Mahjoub, 2021), and 80% decrease in GDM risk in women who adhered to the highest tertile of the MeD (Izadi et al., 2016). In a large prospective cohort study covering 10 Mediterranean countries, a decrease in GDM risk was identified among women who had a high adherence to the MeD prior to the oral glucose tolerance test (OGTT) test at 24-32 weeks, as well as an improved glucose tolerance during the OGTT test in women without GDM, who had a better adherence to the MeD (Karamanos et al., 2014). However, the evidence on diet and GDM is inconclusive due to the heterogeneity of studied diets (Altemani, 2022; Assaf-Balut et al., 2017; Assaf-Balut et al., 2019; H. Al Wattar et al., 2019; Izadi et al., 2016; Karamanos et al., 2014). Risk factors for IGT such as elevated blood pressure and excessive GWG were also found to be improved with the MeD (H. Al Wattar et al., 2019; Koutelidakis et al., 2018; Parlapani et al., 2019; Silva-del Valle et al., 2013; Spadafranca et al., 2016).

In addition to diet, psychosocial factors including high stress, depression (Silveira et al., 2014) and poor sleep (Sirimon Reutrakul et al., 2011) are emerging as important determinants that can increase the risk for GDM which was highlighted in a recent large meta-analysis (Mena, 2022). Depression is highly prevalent among Middle Eastern pregnant females compared to Western European countries (Shakeel et al., 2015). Stress has been shown to increase the levels of stress hormones contributing to insulin resistance and GDM pathogenesis (Feng, 2020). A recent meta-analysis also confirmed that depression can increase cortisol levels and inflammatory markers in pregnant women leading to abnormal glucose levels and GDM (Riggin., 2020), while on the other hand, having GDM can further exacerbate poor mental health (Delanerolle, 2021). Sleep quality and short sleep duration were also independently associated with GDM (Cai, 2017; Chen, 2022; Myoga, 2019; Zhang et al., 2020; Bingqian Zhu et al., 2020) and abnormal glucose tolerance (Cai, 2017; Chen, 2022; Myoga, 2019), and one study highlighted the role of first trimester sleep quality in GDM development (Zhou, 2022). Evidence from studies reported that pregnant women who suffered from depression and stress were more likely to have inappropriate dietary patterns, reduced physical activity (PA) levels and to gain weight below or above the IOM recommendations (Molyneaux et al., 2016; Omidvar et al., 2018; Riggin., 2020).

It is important to understand the roles of various predictors such as pre-pregnancy weight and GWG, diet and psychosocial factors in maintaining normal glucose values during pregnancy in modulating the risk of GDM. All Mediterranean countries have reported public health concerns related to elevated rates of impaired carbohydrate metabolism in the general population, specifically type 2 diabetes and IGT with prevalence ranging between 16.3%-17%, while the highest prevalence was found in the EMC including Lebanon (Savona-Ventura et al., 2012; Zhu & Zhang, 2016). Lebanon is among the top 10 countries in diabetes prevalence that reached 20.2% in the general population (International Diabetes Federation (IDF), 2011) and has the highest rate of IGT (26.6%) which is expected to rise sharply by 2030 (Savona-Ventura et al., 2012). However, the prevalence and determinants of IGT and GDM have not been previously assessed on a national level in Lebanon. Therefore, our objectives were 1) to identify predictors of IGT in trimester 1 and 3 and GDM at 24-28 weeks of pregnancy, and 2) to assess the association between the LMeD on IGT and GDM and 3) to determine the role of specific dietary components of the LMeD on GDM diagnosis and FBG in trimester 1 and 3. We hypothesized that a poor adherence to the LMeD, excessive GWG along with psychosocial factors (stress, poor sleep, and depression), will be associated with increased IGT and GDM risk.

4.3. Materials and Methods

4.3.1. Study population

This study is a national prospective cohort study on pregnant women of various ethnic and religious backgrounds living in the 6 different governorates of Lebanon including Mount Lebanon, Beirut (capital of Lebanon), Bekaa, South (and Nabatieh), North, and Akkar. Beirut and Mount Lebanon are the main urban regions and account for the majority of the country's socio-economic, trade, political and cultural activities; however, poverty exists in the suburbs of these regions. The other governorates consist of both urban cities and rural villages where the latter have poor socio-economic and educational levels (Chamieh et al., 2015).

For this study, a simple random sampling among all obstetric clinics in Lebanon was done using the statistical software SPSS (Statistical Package for Social Sciences), version 22.0. Out of 732 obstetric clinics, a total of 20 private and hospital based private clinics were selected: Mount Lebanon (n=3), Beirut (n=5), Bekaa (n=4), South (n=3), North (n=4), and Akkar (n=1), and a minimum of 30 women were recruited from every clinic.

Recruitment was initiated by the two universities in Lebanon: Notre Dame University-Louaize and Lebanese American University who provided training to their senior students as part of their research program. Data collection was initiated in September 2019 and was completed in June 2021. Written consent and approval was obtained from each physician at the respective clinic to survey the clientele and access medical records. Individual hospitals also provided written consent after reviewing the questionnaires and medical chart data prior to data collection. Healthy pregnant women (< 15 weeks) were invited to participate and were approached by the research team during their routine obstetric visit after being informed about the purpose of this study. We recruited the first 30 women who consented to participate and were eligible to participate. They were informed of their anonymity and that they could withdraw at any time. Inclusion criteria for the study were Lebanese women: 1) > 18 years. Exclusion criteria included women 1) with multiple gestations, 2) pre-pregnancy diabetes, 3) women who were carrying a fetus with structural malformation, chromosomal anomalies or TORCH (toxoplasmosis, rubella, cytomegalovirus, herpes and other agents) infection.

4.3.2. Study design

This prospective cohort study followed consenting pregnant women from the 1st trimester (<15 weeks of gestation) until delivery with follow up interviews in the 2nd (24-28 weeks), and 3rd trimester (34-37 weeks). The initial interview was conducted in person, and the survey included socio-demographic data such as age, place of residence, level of income, education, occupation and marital status, and 5 validated questionnaires 1) Perceived Stress Scale (PSS10) (Cohen et al., 1983), 2) Pittsburgh Sleep Quality Index (PSQI) (Suleiman et al., 2012), 3) Edinburgh

Perinatal/Postnatal Depression Scale (EPDS) (Ghubash et al., 1997), 4) FFQ and Lebanese Mediterranean Diet Index (LMeD) (Naja et al., 2015), and 5) Canadian Physical Activity Readiness Medical Examination (PARmed-X for pregnancy) where we categorized women as sedentary or active (Shepard et al. 2000) . Questionnaires were re-administered in the 2nd and 3rd trimester of pregnancy via phone interviews. A section of the survey included advice on diet and PA (Forbes et al., 2018) and food security (Gary et al., 2000) which were collected in the first interview upon recruitment only.

Medical records were reviewed by our research team in each trimester during routine follow-up visits and this data was used to evaluate changes in clinical measures across gestation. Clinical data was obtained from medical chart review including self-reported pre-pregnancy weight, vitamin/mineral intake, anemia and medical history (previous GDM and family history of diabetes). At follow up visits at each trimester, additional clinical indicators were collected from medical charts including weight gain per trimester, MAP, glycemia, and general maternal health status.

Our main exposure variable was the adherence to LMeD which was assessed in each trimester, and we evaluated its associations with the outcome variables including diagnosis of GDM between 24-28 weeks and impaired FBG in trimester 1 and 3. GDM diagnosis was retrieved between 24-28 weeks of pregnancy based on the two step 50 g glucose tolerance test. IGT was diagnosed with FBG between 100-125 mg/dl (5.5-6.9 mmol/L).

4.3.3 Sample Size

The main outcomes of our study were IGT and GDM. We used Epiinfo Software to calculate the sample size needed for our study using formula by Fleiss with correction. The confidence interval was set at 95%, power at 80% and ratio (unexposed/exposed to the MeD=1). A sample of 618 participants was needed after adjusting for a 20% loss to follow up (Assaf-Balut et al., 2019). A simple random sampling was conducted among all obstetric clinics in Lebanon using the statistical software SPSS (Statistical Package for Social Sciences), version 22.0. Out of 732 obstetric clinics, a total of 20 clinics were selected from the 6 governorates of Lebanon with a minimum of 30 women recruited from each clinic [Mount Lebanon (n=190), Beirut (n=100) (capital of Lebanon), Bekaa (n=100), South including Nabatieh (n=182), North (n=46), and Akkar (n=23)]. After completing the study, we had a total of 660 participants of which 42 dropped out due to miscarriages and/or other reasons. Data for dietary intake was collected from 618 participants using questionnaires, whereas GDM was collected from n=569 women, FBG in trimester 1 was retrieved from n=543 women, and in trimester 3 from n=528 women from the medical charts by research trainees.

4.3.4 Questionnaires:

Edinburgh Perinatal/Postnatal Depression Scale (EPDS)

Edinburgh Perinatal/Postnatal Depression Scale (EPDS) is a commonly used 10-item scale in research and clinical practice to identify women at risk of perinatal depression. The questions included reflect the ability of the person to integrate normally in social life. A score of 0-3 is given for each question and a global sum of 0-30 is obtained. A score of 10 or greater indicates possible depression (Cox et al., 1987). This tool has been validated in pregnant women with a cut-off point of 10 (Murray & Carothers, 1990), and in an Arab population with a Cronbach's alpha=0.84; Correlation r=0.57 with the Present State Examination (Ghubash et al., 1997).

Perceived Stress Scale (PSS10)

Perceived stress was evaluated using the Perceived Stress Scale (PSS10) which was originally developed as a 14-item scale in 1983 to assess perception of stress in the past month (Almadi et al., 2012) and was shortened to 10 items. The questions referred to feelings and thoughts that were experienced in the past month by participants and that could affect their social integration. Each of the 10 questions had a score between 0-4 with a global sum score of 0-40 with higher scores indicating higher perceived stress. The categories are the following: Low stress (score 0-13), moderate stress (score 14-26), and high stress (score 27-40). It has been previously validated in a Lebanese pregnant population with a test-retest reliability and Cronbach's alpha=0.74; Correlation r=0.48 and r=0.58 with General health questionnaire and the EPDS (Almadi et al., 2012).

Pittsburgh Sleep Quality Index (PSQI)

Sleep quality and patterns were assessed using Pittsburgh sleep quality index (PSQI) which is a self-reported tool that assesses sleep quality over a 1 month period and classifies sleep as good versus bad sleep using 9 questions that are based on seven domains: subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleep medications, and daytime dysfunction with the latter component having an impact on social aspects of life. Each of the 7 components is scored between 0 and 3 indicating no difficulty and extreme difficulty respectively. A global score is obtained after adding up the 7 component sum, ranging between 0-21. A score of equal or greater to 5 indicates poor sleep, while a score of less than 5 indicates good sleep. It has been previously validated in an Arabic population with an internal consistency and a reliability coefficient (Cronbach's alpha) of 0.74 for its seven components (Suleiman et al., 2012).

Canadian Physical Activity Readiness Examination (PARmed-X)

A section of the lifestyle questionnaire addressed the frequency, intensity and duration of participation in recreational PA over the past month to assess for physical activity using the Physical Activity Readiness Examination (PARmed-X) (Shephard et al., 2000). The PARmed-X was initially used as a screening tool for pregnant women prior to participation in any exercise and is comprised of 4 parts: 1) General health status, 2) Status of current pregnancy, 3) Activity habits during the past month and 4) Physical activity intentions. For the purpose of this study we only used the third part of the questionnaire "Activity habits during the past month" which categorizes participants into three categories according to the frequency, intensity and duration of PA: unfit (frequency <1-2 times/ week and <20 min duration; PA index=0), active (1-2 times/ week for 20 min or more than twice/week for < 20 min; PA index=1) and fit (>2 times/week for more than 20 min; PA index=2). This tool has been validated against peak oxygen consumption to predict target heart rates for exercise for pregnant women based on age and fitness level (Hui et al., 2012), and was translated to Arabic and back-translated since it was not validated in an Arabic population before. Since the vast majority of the women in this study were sedentary, we combined fit and active together due to the small percentages found in the two groups.

Dietary assessment and adherence to the Mediterranean diet

Data on food intake was collected using a previously validated 61-item FFQ specifically for the Lebanese diet by Naja et al. (2015) (Naja et al., 2015) that is representative of the LMeD and incorporates traditional Lebanese dishes. The FFQ consisted of 9 food categories and under each category there were specific food items listed: 1) breads and cereals (white bread, brown bread, breakfast cereals, rice, pasta, burghol), 2) dairy products (low fat milk, full fat milk, fat free/low fat yogurt, whole fat yogurt, cheese regular, cheese low fat, labneh), 3) fruits and juices (citrus fruits/grapefruit, deep yellow or orange fruits, grapes, strawberries, other: bananas, apples, dried fruits, fresh fruit juice, canned or bottled fruit drinks), 4) vegetables (salad-green: lettuce, celery, cucumber, green pepper), dark green or deep yellow vegetable, tomatoes, corn/green peas, potatoes, squash/eggplant, cauliflower/cabbage/broccoli), 5) meat and alternates (legumes, nuts and seeds, red meat, poultry, fish including tuna, eggs, organ meats, luncheon meats, sausages/makanek/hotdogs), 6) fats and oils (oil: corn/olive/soy/sunflower, olives, butter, mayonnaise), 7) sweets and desserts (cakes/cookies/donuts/muffins, ice cream, chocolate bar, sugar/honey/molasses, Arabic sweets), 8) beverages (soft drinks regular, soft drinks diet, Turkish coffee, coffee/nescafe or tea, hot chocolate or cocoa, beer, wine, liquor) and 9) miscellaneous (manakish zaatar or cheese, pizza, French fries, chips, falafel sandwich, chawarma sandwich, burger). Serving sizes for each food item and the frequency of consumption of each food item was recorded as the number of servings consumed on a daily, weekly, monthly, or never basis. To minimize recall bias and measurement errors, we used food models, cups and spoons to illustrate portion sizes of all the food items.

LMeD: This index was developed to assess the adherence to a Lebanese version of the MeD and was derived from the aforementioned-61 item- FFQ by Naja et al. (2015) (Naja et al., 2015). This tool was initially developed to identify different dietary patterns in the population using factor analysis. Authors were able to identify a Lebanese MeD pattern from the FFQ with the following 9 food groups because of their consistently high loading on this pattern which included: fruits, vegetable, legumes, olive oil, burghol (crushed whole wheat), milk and dairy products, starchy vegetable (potato, corn and beans), dried fruits and eggs. The Lebanese MeD index used in this study shares common food groups with other indices developed in Italy: Italian Mediterranean Index (Agnoli et al., 2011), Spain: rMED (Buckland, 2009), Greece: nMED (Panagiotakos et al., 2007), France: Mediterranean Diet Quality Index (Gerber, 2003), and 9 Mediterranean European countries: Mediterranean Diet Scale (Trichopoulou, 2003) such as fruits, vegetable, olive oil, legumes, dairy products and starchy vegetable, however in the Lebanese MeD other main components were missing such as fish, red meat, poultry, and wine consumption (Naja et al., 2015).

Adherence to the LMeD was measured based on consumption of each of these food groups with 1, 2 and 3 points assigned to low, average and high intake, respectively. Then, a score was derived after adding the points for every participant with a minimum score of 9 reflecting the least adherence and a maximum score of 27 reflecting the highest adherence to the Lebanese MeD. This tool had a good correlation (r=0.56) with the Italian MeD tool (Agnoli et al., 2011). Similarly to other studies done in pregnant women (Gesteiro et al., 2012; Papazian et al., 2019), alcohol intake was excluded as consumption is virtually absent in this study population. We presented in our results the number of servings that were consumed on a daily basis for each of the food groups that comprise the MeD index.

4.3.5. Clinical Measurements

Pre-pregnancy BMI and GWG

Pre-pregnancy BMI was collected at baseline from the obstetrical charts at the clinics and was used to classify women as being underweight (<18.5 kg/m^2), normal (18.5-24.9 kg/m^2), overweight (25-29.9 kg/m^2) or obese (≥30 kg/m^2) (Moore Simas et al., 2013). Weight was re-assessed at 15 weeks, 28 weeks, and at 37 weeks during routine clinic visit. Total GWG in Kg was calculated by subtracting total weight gain from pre-pregnancy weight, and GWG was classified as inadequate, appropriate or excessive according to the pre-pregnancy BMI using the recommendations of the Institute of Medicine (IOM) (underweight 12.5-18 kg, normal weight 11.5-16 kg, overweight 7-11.5 kg, and obese 5-9 kg) (Rasmussen et al., 2009). Weight gain per trimester was calculated by subtracting weight at each trimester from the preceding trimester (American College of Obstetricians Gynecologists, 2013). GWG per trimester was classified as adequate, excessive or low according to the following recommendations: For 1st trimester: above 2 kgs or below 1 kg was considered excessive or low respectively for all categories of BMI. For 2nd and 3rd trimester, the recommended weight gain per week for each BMI category is the following: 0.45-0.6 kg/wk for underweight women, 0.35-0.45 kg/wk for normal weight women, 0.2-0.3 kg/wk for overweight and obese women. Weight gain below or above these values are classified as low or excessive, respectively (American College of Obstetricians Gynecologists, 2013).

Vitamin/mineral intake

Vitamin and mineral supplement usage was self-reported at the end of the first trimester, and medical charts were used to confirm supplementation recommended by their physician. Supplement usage was categorized into iron, vitamin D and multi-vitamin supplement.

Anemia

Anemia diagnosis was made by laboratory testing and a complete blood count early at the beginning of pregnancy. A serum ferritin concentration <30 μg/L together with an Hb concentration <11 g/dL was used to determine the presence of anemia during the 1st trimester of pregnancy (Api, 2015).

Fasting Blood Glucose (FBG), Impaired glucose tolerance, and Diagnosis of GDM

FBG values were collected from obstetric charts in trimester 1 and 3 only and were categorized into normal FBG: < 100mg/dl and impaired FBG ≥100 mg/dl; and during the second trimester visit, GDM diagnosis (yes/no) was confirmed. Obstetricians in Lebanon followed the two-step 50 g oral glucose tolerance test between 24-28 weeks in line with the American College of Obstetricians and Gynecologists for diagnosis of GDM. If the 50 g glucose tolerance test was ≥140 mg/dL after one hour, a 100 g 3-hour oral glucose tolerance test was done. Blood glucose was tested at t=0 (fasting), t=1 hour, t=2 hours and t=3 hours with cut-off values of 95, 180, 155, and 140 mg/dL, respectively. GDM diagnosis was made when two or more these cut-off values met or exceeded the Carpenter and Coustan criteria (American College of Obstetricians and Gynecologists, 2018).

Mean Arterial Pressure (MAP)

Mean arterial pressure is a blood pressure measurement used to predict HDP risk and is calculated as MAP = DBP + 0.33 [SBP-DBP] (Kane, 2016) Trimester-specific cutoffs for elevated MAP (eMAP) in pregnancy were defined as >87 mmHg (10-<18 weeks), >84 mmHg (18-34 weeks), and >86 mmHg (after 34 weeks) (Women's Health and Education Center (WHEC), 2009); low MAP is defined as <70 mmHg (Henry et al., 2002).

4.3.6. Statistical analyses

Univariate analyses (measures of central tendency, percentage and frequencies) were used to summarize the population characteristics of pregnant women as well as the mean serving size consumption of each food group of the LMeD. Lifestyle characteristics including GWG, smoking and PA, and psychosocial factors including stress, sleep and depression were compared across the trimesters using the McNemar test. Dietary characteristics including adherence to the LMeD and individual food group consumption were compared across the trimesters using the McNemar test. Frequencies and percentages were used to determine categorical dietary variables: adherence to the LMeD, while means were used to determine mean adherence of the population as well as mean intake of each of the 9 food groups of the MeD. Scatter plots were used to describe the FBG measurements in trimester 1 and 3 of the sample population and dashed lines represented the cut-offs for normal, impaired FBG and diabetes. The following maternal characteristics: pre-pregnancy BMI, GWG, MAP, stress, sleep, depression, adherence to the LMeD and individual food group consumption were also compared among women in the normal FBG group <100 mg/dl vs IGT group>=100 mg/dl in trimester 1 and 3..

A hierarchical multiple logistic regression modeling approach was used to test the association between each potential predictor including adherence to the LMeD, maternal factors (pre-pregnancy BMI, GWG, family history of diabetes, eMAP) and psychosocial variables in trimester 1 and 3, respectively and elevated FBG within the same trimester, and in trimester 2, models were used to test the association between GDM and the same predictor variables within the same trimester. Variables such as adherence to the LMeD and GWG from the 1st trimester were also tested for association with GDM in the 2nd trimester and FBG in the 3rd trimester, respectively. Significant association was defined as p-value < 0.05. Models were first adjusted for GWG, pre-pregnancy BMI, family history of diabetes, stress, sleep, depression and MAP (Model 1-Maternal Characteristics), then the significant variables from model 1 were entered and adjusted for adherence to the LMeD (Model 2-Adherence to the LMeD), and finally we entered each of the 9 food groups in individual models along with the significant variables from model 2 (Model 3-Individual Food Groups). All the analyses were conducted using SAS V9.4.

4.4. Results

4.4.1 General Population Characteristic

Table 4-1 describes the population characteristics of our sample. A total of 618 pregnant women were recruited from the 6 governorates of Lebanon. The mean age of participants at enrollment was 29.2 ±5.0 years, and mean parity was 1.3 child. Less than half of the women lived in Mount Lebanon and Beirut (main urban regions), and a higher percentage lived in rural areas (South Lebanon, Bekaa, Akkar and North Lebanon). More than 75% of women had a university degree. Out of the total sample, an equal number of homemakers and self-employed was reported. The average monthly income was between 700$-2000 US dollars ($) and did not significantly differ by regions. Assessment of pre-pregnancy BMI showed that 83.8% of the women had a normal pre-pregnancy BMI, while 22.2% were overweight and 10.2% were obese. Only 3.8% of the women were underweight prior to pregnancy. Most gained excessive weight with respect to their BMI recommendations. With regards to maternal medical history, the results showed that most women did not have previous GDM (98%) or previous HDPs (96.4%) while 25% had anemia at the time of the study. Approximately 70% took their multivitamin supplements, while 30.8%

took iron and 34.4% took Calcium/Vitamin D. Only 20% of the women answered on food security hence the data was not used for the bivariate analyses.

4.4.2 Maternal Characteristics Per Trimester

Table 4-2 represents the differences in lifestyle and psychosocial factors in each trimester of pregnancy. Smoking incidence was less than 9% and did not differ across trimesters. With regards to PA, despite that the majority of women were sedentary across trimesters, there was a significant decline in PA between the first and third trimester ($p<0.001$). Among the psychosocial variables, depression did not differ by trimester, but stress and sleep quality did. The greatest percentage of women with high stress was reported in trimester 3 (20.52%) ($p<0.001$). The PSQI also showed the greatest percentage of poor sleep in trimester 3 compared to trimester 1 and 2 ($p<0.001$).

Table 4-3 represents maternal dietary intake and the consumption of the individual food groups of the LMeD in each trimester. Adherence to the LMeD was significantly different between trimester 1, 2 and 3. In trimester 3, a higher percentage of women (26.0%) had low adherence scores compared to trimester 1 and 2 (19.0% and 24.0% respectively) ($p<0.001$), and in trimester 2 more women were identified in the high adherence group (30.0%) compared to trimester 1 (21.0%) and trimester 3 (25.0%). The mean daily consumption of the 9 food groups of the LMeD were also reported per trimester. However, the daily mean serving consumption of the food groups did not significantly vary across the trimesters except for dairy products where the highest consumption was reported in trimester 1 ($p<0.0350$) followed by vegetables where the highest consumption was reported in trimester 2 ($p<0.0440$).

4.4.3. Diagnosis of GDM

Out of 569 pregnant women, 5.6% were diagnosed with GDM between 24-28 weeks, and among those diagnosed with GDM, 50% already had IGT in the 1st trimester and continued having abnormal glucose through trimester 3.

Maternal characteristics were compared between women with GDM and without GDM. Place of residence was significantly different between the two groups ($p<0.02$), where the majority of women with GDM lived in Beirut and Mount Lebanon. Furthermore, a higher % of women with a family history of diabetes developed GDM compared to those who did not have a family history in the non-GDM group. Excessive total GWG was higher in women with GDM (28%) compared to those who did not develop GDM (17%) (Supplemental table 4-1).

Table 4-4 represents the multiple logistic regression models describing the predictors associated with the diagnosis of GDM at 24-28 weeks of gestation in trimester 2. In Model 1-Maternal characteristics, the following variables entered as significant predictors and were associated with increasing the odds of having GDM: trimester 2 GWG [OR=1.057, $p<0.0246$], family history of diabetes [OR=3.79, $p<0.0012$] and MAP [OR=1.057, $p<0.0311$]. In Model 2-Adherence to the LMeD, we entered the significant variables in model 1 (trimester 2 GWG, family history of diabetes and MAP) and included the adherence to the LMeD. Only family history of diabetes [OR=3.672, $p<0.0010$] and MAP [OR=1.066, $p<0.0093$]), were positively associated with GDM. Adherence to the LMeD in trimester 2 did not have an impact on the diagnosis of GDM. In Model 3-Identification of Food Groups, we entered the significant variables from model 2 (family history of diabetes and MAP), adherence to the LMeD and each food group in an individual model. No food groups were identified to have an association with GDM ($p>0.05$).

4.4.4. Comparison of Women Having Normal FBG <100 mg/dl vs Impaired FBG ≥ 100 mg/dl in Trimester 1 and 3

Figure 4-1 describes the fasting blood glucose in the 1st and 3rd trimester of pregnancy, (Figures 4-1a and 4-1b respectively). In trimester 1, out of 543 pregnant women, 87.6% had a normal FBG <100 mmHg, while 10.4 % had IGT (100-125 mg/dl) and less than 2% had elevated FBG (≥ 126 mg/dl). The percentage of women who had IGT increased from 10% to 23% out of 549 participants from trimester 1 through trimester 3 and those with elevated FBG also increased from 1.8% to 3.5% from trimester 1 through trimester 3.

Maternal Characteristics

Maternal characteristics of pregnant women having normal FBG <100 mg/dl (control group) vs. women having impaired FBG ≥ 100 mg/dl were compared in trimester 1 and 3 (Table 4.5). No statistical differences between the two groups were identified for the following variables: place of residence, pre-pregnancy BMI, GWG, MAP, stress, sleep, depression, and adherence to the LMeD in trimester 1 and trimester 3 (p>0.05). However, with regards to individual food group consumption between the two groups, daily consumption of vegetables was significantly higher in the normal (FBG<100 mg/dl) vs IGT group (FBG ≥126 mg/dl) (p<0.0019), while dried fruits consumption was higher in the IGT vs normal FBG group (p<0.0413) in trimester 1 only.

4.4.5 Multiple Logistic Regression Models for Impaired Glucose Tolerance for Trimester 1 and 3

Table 4-6 represents the multiple logistic regression models describing the predictors of impaired FBG≥100 mg/dl in trimester 1 and trimester 3. In trimester 1, Model 1- Maternal Characteristics, we investigated the effect of the following factors which included trimester 1 GWG, pre-pregnancy BMI, family history of diabetes, stress, sleep, depression scores and MAP on the main outcome FBG≥100 mg/dl. None of the variables were significant. In Model 2-Adherence to the LMeD, we entered both the stress variable which was borderline significant in Model 1 and included adherence to the LMeD as a predictor. A high perceived stress score compared to a low stress score increased the risk of having impaired FBG [OR=2.885, p<0.0392]. However, adherence to the LMeD was not associated with FBG. In Model 3-Identification of Food Groups, two food group models emerged, including Burghol [OR=3.023, p<0.0361] such that a higher daily burghol intake was associated with an increased risk of elevated FBG. Legumes also emerged as significant where a higher daily intake of legumes increased the risk of impaired FBG [OR=2.100, p<0.0361], while stress remained significant [OR=3.054, p<0.0296].

In trimester 3, in Model 1-Maternal Characteristics 1st model: Trimester 3 GWG [OR=1.036, p<0.0444] was associated with increased risk of GDM. In Model 2-Adherence to the MeD, we entered only the significant variable which is trimester 3 GWG and added the third trimester adherence to the LMeD. GWG remained significant [OR=1.036, p<0.0334], however adherence to the LMeD was not associated with the outcome. In Model 3-Individual Food Groups, we entered trimester 3 GWG, adherence to the LMeD and each food group in a separate model and we obtained only one significant food group model, which was Vegetables. A higher intake of vegetables decreased the odds of having impaired FBG [OR=0.742, p<0.0120], while GWG remained positively associated with impaired FBG [OR=1.036, p<0.0321].

4.5. Discussion

This study is the first national study to assess the impact of the LMeD and its 9 associated food groups, as well as that of the psychosocial and maternal risk factors per trimester of pregnancy on GDM and FBG per trimester. Interestingly, despite the high prevalence of diabetes and IGT that was reported in Lebanon to be 20.2% (Musaiger, 2004) and 27% (Marchi et al., 2015) in the general population respectively, only 5.6% of the population developed GDM. However, the percentage of women with IGT in this study ranged between 12.5% in the 1st trimester and 27% in the 3rd trimester which is similar to the national prevalence.

Five novel findings emerged. First, adherence to the LMeD differed by trimesters and was the highest in trimester 3, however, adherence was neither associated with IGT nor with GDM but individual food groups were. Our second finding was that specific food items of the LMeD differed across women with normal FBG vs. IGT. In trimester 1, dried fruit consumption was significantly higher in mothers with FBG≥100 mg/dl while vegetable consumption was lower in those women. Moreover, burghol and legumes were associated with increased risk of high FBG>=100 mg/dl in trimester 1, whereas vegetable intake decreased the risk in trimester 3. Third, among the psychosocial factors, high perceived stress in trimester 1 increased the risk of having impaired FBG ≥100 mg/dl but did in trimester 2 and 3. Fourth, excessive GWG in trimester 3 and not in trimester 1 and 2 increased the risk of high FBG≥100 mg/dl. Fifth, with regards to the diagnosis of GDM at 24-28 weeks of pregnancy, excessive GWG and eMAP in trimester 2 as well as family history of diabetes were associated with the increased likelihood of the diagnosis of GDM, however neither adherence to the LMeD nor individual food groups were associated with GDM diagnosis in trimester 2.

Association of Maternal Factors with Diagnosis of GDM (Family History of Diabetes, GWG, and MAP)

Family history of diabetes was an important variable that contributed to the emergence of GDM in trimester 2, and excessive GWG increased both GDM risk in trimester 2 and high FBG in trimester 3. GDM shares common etiology with type 2 diabetes which suggests that there is a genetic predisposition to develop GDM (Zhan, 2013). Similar to a recent meta-analysis (Lee, 2018), women who had a family history of diabetes were twice as likely to develop GDM, while in this study women with a family history were 3.7 times more likely to develop GDM. A previous study showed an 8.4 fold increased risk of GDM in women having a sibling with diabetes (Williams, 2003).

Excessive GWG also was significantly associated with GDM and glucose levels where higher GWG in trimester 2 and 3 increased both GDM and impaired FBG risk, which highlights the importance of maintaining appropriate weight gain based on pre-pregnancy BMI that is recommended by the IOM in each trimester. Pregnancy is a period that causes insulin resistance in normal weight women. This is due to the rise in lipoprotein concentrations specifically in the second and third trimester that is further exacerbated in overweight and obese women (Catalano, 2019). Moreover, both economic and population growth in the EMC are contributing to a rise in abdominal and visceral obesity, IGT and type 2 diabetes in the general population (El Sagheer &

Hamdi, 2018; Khader et al., 2018; Musaiger, 2004; Zhu & Zhang, 2016). The association between excessive weight gain and hyperglycemia is in line with two recent reviews (Luo, 2022; Sun, 2020), however the majority of these studies examined total GWG towards the end of pregnancy only whereas our study was the first to assess GWG per trimester. Moreover, two other studies showed a significant association between first trimester weight gain and GDM regardless of pre-pregnancy BMI (Lan, 2019; Zheng, 2014). Contrary to other studies which showed a direct relationship between high pre-pregnancy BMI and GDM (De la Torre, 2019; Heude et al., 2012; Li, 2021; Sun, 2020; Wu, 2022; Zhang, 2006), and IGT (Mi, 2021), or optimal BMI early in pregnancy (Zhang, 2022), our study did not find an association. Our observation is in line with a recent meta-analysis which concluded that there is no clear association between pre-pregnancy BMI and GDM (Fuller, 2022). This could be explained that around 63% of the women had a normal pre-pregnancy BMI in this study and therefore no association was identified. Moreover, weight gain during pregnancy was highlighted as being more important.

Although previous studies have consistently highlighted the role of SBP and DBP on GDM risk (Vanlalhruaii, 2013) and on elevated FBG (Vanlalhruaii, 2013), our study was among the first few studies to show a significant association between eMAP and GDM risk. Given that a small percentage of women had elevated SBP and DBP, we were not able to look at the association between them and GDM. Similarily, Zhang et al. 2022 identified an association between eMAP and GDM. Moreover, hypertensive disorders were reported to be more common among women with GDM and can occur in subsequent pregnancies prior to GDM diagnosis in a study done by (Li, 2018). This can be explained that conditions that cause insulin resistance in mothers can also increase their susceptibility to HDPs Li (2018). A recent review also identified common risk factors between GDM and HDPs, such as older age, overweight and obesity, and adoption of a Western dietary pattern (Jiang, 2022).

Association of Psychosocial factors with IGT in Trimester 1

Our study was the first that assessed the relationship between psychosocial factors including stress, sleep and depression on a trimester basis and both FBG and GDM risk. We reported that high stress and poor sleep quality differed by trimester and worsened in the 3rd trimester. High stress was linked to a greater risk of impaired FBG in the 1st trimester only as shown in the logistic regression model. Similarly, a study showed a 2.5 increase in GDM risk among women who experienced stressful events in the past 12 months before delivery (Hosler et al., 2011) while another study (Mishra et al., 2020) showed a 13-fold increase in GDM risk among those with high perceived stress before 24-28 weeks. This can be explained by the fact that stress acts on the hypothalamic-pituitary-adrenal cortex and releases hormones that prevent insulin secretion and raise blood glucose (Feng, 2020; Silveira et al., 2014). Moreover, a recent review proved that anxiety significantly increased the risk of GDM, while data on depression and GDM was controversial. Women with GDM and abnormal glucose levels had higher levels of anxiety, stress and/or depression (OuYang, 2021). On the contrary, Silveira et al. did not report any significant association between stress in early or mid-pregnancy and glucose tolerance (Silveira et al., 2014).

Other psychosocial factors were also assessed in this study. Sleep quality and depression did not affect either glucose tolerance or GDM. This can be explained that a higher proportion of women in this study were not depressed throughout the trimesters. It is also possible that effect of poor sleep is mediated through increased stress levels in the 1st trimester as shown in a study by Dorheim et al. that reported increased cortisol levels with poor sleep, and that a poorer health-related quality of life that can lead to pregnancy complications (Dorheim et al., 2012). This was shown in our study with stress being associated with a greater FBG in trimester 1. Data on sleep quality and GDM is contradictory. While Ahmed *et al.*, 2018 and Hashemipour *et al.* 2022 (Ahmed et al., 2019; Hashemipour et al., 2022) did not report any significant association between poor sleep quality and blood glucose levels which is similar to our findings, Zhou *et. al* 2022 did find an association (Zhou, 2022).

Association between Food Groups of the Lebanese Mediterranean diet and FBG in Trimester 1 and 3

Our main independent variable adherence to the LMeD was not associated with the diagnosis of GDM at 24-28 weeks or FBG. In a recent meta-analysis, MeD was shown to decrease the incidence of GDM possibly due to lowering inflammatory markers and oxidative stress, and the reduction which ranged from 15 to 38% was dependent on compliance, genetics and the method used to diagnose GDM. However, in a meta-analysis on the effect of different diets on GDM including MeD and the Dietary Approaches to Stop Hypertension (DASH), the latter showed superiority to the MeD (Altemani, 2022) and aligns with our observation of eMAP emerging as a determinant of GDM. Although the majority of studies showed a significant association between MeD and GDM (Assaf-Balut et al., 2017; Assaf-Balut et al., 2019; H. Al Wattar et al., 2019; Izadi et al., 2016; Karamanos et al., 2014), our findings did not confer any benefit. This could be explained that the majority of the women had a good compliance to the LMeD and only 20% or less had a low adherence while in another recent study almost 50% had a low compliance (Mahjoub, 2021). Another explanation is that previous literature reported associations between MeD and GDM in low risk populations (Assaf-Balut et al., 2017; Pistollato, 2015), and given that our sample population had excessive weight gain and other factors contributing to the development of GDM such as high stress, elevated MAP and family history of diabetes, there is a possibility that diet alone was not able to counteract their combined effect on impaired FBG. Moreover, even though pregnant women were following the LMeD, yet it seems that they were exceeding their calorie intake as evidenced by an excessive GWG.

The majority of previous studies have routinely studied associations between dietary patterns and GDM while neglecting the individual food groups which comprise the MeD (Altemani, 2022). In this study, individual food groups emerged as predictors for FBG in trimester 1 and 3. The MeD is rich in vegetables, fruits, whole grains and low in fat, and has high anti-inflammatory components which can contribute to lowering the risk factors of high FBG including overweight, dyslipidemia, inflammation, high blood glucose levels, and diabetes (Benhammou et al., 2016; Bonaccio et al., 2013). In this study we used a culturally adapted and validated tool for our population that is representative of their dietary intake to assess for adherence to a Middle Eastern version of the MeD (Naja et al., 2015), and it was different from other tools that were used in studies conducted in Mediterranean countries (Altemani, 2022). Burghol, eggs and dried fruits were identified as main components of the LMeD only and were not common in other indices (Naja et al., 2015) which could be another factor explaining why other observational studies that assessed the impact of healthy diets including the MeD showed a protective effect on GDM (Fuller, 2022) whereas our findings did not.

Among the 9 food groups of the LMeD, legumes and burghol elevated FBG in trimester 1. These two food groups are high sources of carbohydrates that may lead to impaired glycemia especially during pregnancy (Mahjoub, 2021). Although it is recommended that women diagnosed with GDM or elevated BG consume complex carbohydrates including legumes and whole grains, however the total amount of carbohydrate should not exceed 40-45% of their total caloric intake (Hernandez, 2014) and foods with high glycemic load including burghol can negatively affect glycemia (Allehdan et al., 2022; Mahjoub, 2021).

Moreover, even though women had a high GWG in the third trimester, vegetable intake lowered the risk of impaired FBG in trimester 3. Vegetables are low in carbohydrate and rich in antioxidants, fibers and low in saturated fats which can reduce inflammation and improve glycemia (Schiattarella, 2021). A daily vegetable consumption of $\geq$ 2 cups is beneficial which was seen in women with healthy glucose tolerance test, while those in the IGT group were consuming around 1.7 cups per day. This result is similar to a study done on pregnant women in Iran however in that study a greater daily intake of $\geq$ 4.9 servings of vegetable was inversely associated with GDM (Mirmiran et al., 2019). Two recent meta-analyses on pregnant women identified that a MeD diet rich in vegetables, fruits, low fat dairy products and a plant-based diet are beneficial for improving glycemia and GDM during pregnancy (Hernandez, 2014; Moslehi, 2022; Schiattarella, 2021). Hence, more light is being shed on dietary patterns that focus on plant foods such as MeD or low glycemic diet which is in line with our findings. Other food groups in the MeD such as fish, olive oil and mixed nuts were also beneficial in decreasing GDM risk in two previous clinical trials (Assaf-Balut et al., 2019; H. Al Wattar et al., 2019), but this was not observed in this study.

IGT was identified in the first trimester and around 40% of these women developed GDM. Because we observed the emergence of GDM related to family history, GWG and MAP in the 2nd trimester, it is recommended to screen early for abnormal glucose during pregnancy in order to implement lifestyle and dietary interventions at an early stage during pregnancy. We found that a decrease in burghol and legumes intake and a lower weight gain and lower stress protected against the risk of IGT in the 1st trimester, and an increase in vegetable intake and abiding by weight gain recommendations in the 3rd trimester were associated with a decreased risk of IGT among those women.

4.6. Strengths and Limitations

The major strength of this study is its national prospective cohort design that is the first in the EMC conducted among a representative sample of pregnant women in the different regions of Lebanon. Additionally, most questionnaires that were used were validated and administered by trained professionals. Another major strength of this study is the novelty of the findings with regards to the impact of specific components of the LMeD where burghol and legumes increased the risk of elevated FBG in trimester 1, and vegetable in trimester 3 decreased the risk. Moreover, excessive GWG increased the risk of elevated FBG in trimester 3 while stress had an impact in trimester 1. With regards to GDM diagnosis, eMAP, family history of diabetes and excessive GWG were also significant determinants.

At the same time, we acknowledge that prospective cohort study designs have limitations as they are prone to measurement and recall bias such as for self-reported data on diet, psychosocial factors, PA, and smoking. We also acknowledge that the nature of the study design can lead to loss of follow up, however only 6.4% dropped out either due to miscarriage (n=21) or loss to follow up (n=21) which was less than the 20% we anticipated. Moreover, the economic crisis and the emergence of COVID-19 during the period of this study might have affected our results by increasing psychological disorders such as stress, depression and/or poor sleep among participants and affecting their dietary intake. Another limitation is that we were not able to enter the following variables: food security and advice on diet and physical activity in our models due to the very low response rate. Additionally, caloric intake for the pregnant women was not assessed in this study to explore its relationship with the main outcomes of this study.

4.7. Conclusion

Adherence to the LMeD was not associated with our main outcomes high FBG and GDM at any point during pregnancy. However, this study identified the importance of certain elements of the LMeD on decreasing the risk of IGT in pregnant women particularly in early and late pregnancy in addition to the importance of stress reduction, emphasizing appropriate weight gain, and lowering MAP. Our findings reinforce the importance of early screening for family history of diabetes and management of risk factors for hyperglycemia as well as GDM including elevated blood pressure in particular MAP, excessive GWG, stress and dietary factors. The role of pre-pregnancy BMI was not identified as being significant in this study, however other factors such as dietary patterns prior to pregnancy would be important to assess in relation to elevated FBG and/or GDM during pregnancy.

Table 4-1. Population Characteristics of a National Sample of Pregnant Women in Lebanon

Variable	Mean ± SD or %
Maternal characteristics	
[1] Age, years	29.2 ± 5.0
Parity	1.3 ±1.1
[1] Place of Residence	
Akkar,	3.7
Beirut, %	12.4
Bekaa, %	16.1
Mount Lebanon, %	30.7
North Lebanon, %	7.4
[a] South Lebanon, %	29.4
[1] Occupation	
Student, %	1.1
Homemaker, %	49.0
Self-employed, %	8.7
Employee part-time, %	9.8
Employee full-time, %	31.2
[1] Education	
High school or less, %	23.9
Bachelor degree, %	40.6
Masters degree or higher, %	35.4
Maternal Health Status	
[1] Pre-pregnancy BMI, kg/m^2	
[b]Underweight (<18.5, %)	3.8
Normal (18.5-24.9, %)	63.8
Overweight (25.0-29.9, %)	22.2
Obese (≥30.0, %)	10.2
[2] Total GWG [c], kg	
Low, %	11.1
Adequate, %	20.5
Excessive, %	68.3
[6] Previous Hypertensive Disorders of Pregnancy, % Yes	3.6
[3] Family History of Diabetes, % Yes	20.8
[6] Previous GDM, % Yes	1.9
[3] Current GDM [d], % Yes	5.6
[7] IGT 1st trimester [e], % Yes	12.4
[8] IGT 3rd trimester [e], % Yes	26.5
[5] Vitamin Supplement Intake, % Yes	98.8
OTC Multivitamins/minerals	68.9
Iron	30.8
Calcium/Vitamin D	34.4
[3] Current Anemia [f], % Yes	25.0
[4] COVID Infection during Pregnancy, % Yes	7.7

Sample size= 618 ([1]n=618, [2]n= 555, [3]n= 573, [4]n=117, [5]n=499, [6]n=575, [7]n=543, [8]n=549). Values are means ± standard deviation (SD) if normally distributed, median (min-max) if not normally distributed, or percentages (%) if binary, unless otherwise specified. [a]South Lebanon includes the sample of Nabatieh. [b] Pre-pregnancy BMI was calculated as weight in Kg over height in meters squared, and was classified as underweight, normal, overweight and obese. [c] Total gestational weight gain was calculated by subtracting total weight gained from pre-pregnancy BMI. GWG was classified as low, adequate or excessive applying the following recommendations: To be considered adequate GWG, women who are underweight should gain a total of 12.5-18 kg, normal weight between 11.5-16 kg, overweight between 7-11.5 kg, and obese between 5-9 kg. Those with low GWG have a weight gained below these recommendations whereas those with excessive weight gain have above these recommendations. [d] GDM diagnosis was made using the two-step 50 g oral glucose tolerance test between 24-28 weeks in line with the American College of Obstetricians and Gynecologists for diagnosis of GDM. If the 50 g glucose tolerance test was ≥140 mg/dL after one hour, a 100 g 3-hour oral glucose tolerance test was done. Blood glucose was tested at t=0 (fasting), t=1 hour, t=2 hours and t=3 hours with cut-off values of 95, 180, 155, and 140 mg/dL, respectively. GDM diagnosis was made when two or more these cut-off values met or exceeded the Carpenter and Coustan criteria. [e] Impaired glucose tolerance (IGT) was diagnosed with FBG ≥100 mg/dl in trimester 1 and 3. [f] Serum ferritin concentration <30 μg/L together with an Hb concentration <11 g/dL was used to determine the presence of anemia during the 1st trimester of pregnancy. Abbreviations: BMI, body mass index, GWG, gestational weight gain, GDM, gestational diabetes mellitus, IGT, impaired glucose tolerance, OTC, over the counter medication

Table 4-2. Differences in Lifestyle and Psychosocial Factors in Trimester 1, 2 and 3 in a National Sample of Pregnant Women in Lebanon

Variables	**Trimester 1**	**Trimester 2**	**Trimester 3**	
Lifestyle Characteristics	**Mean ± SD; %**	**Mean ± SD; %**	**Mean ± SD; %**	**p**
[1] **GWG**				
Low	48.95	29.48	35.70	0.256
Adequate	23.24	25.0	22.0	
Excessive	27.70	45.52	42.30	
[2] **Smoking**				
Yes	8.99	7.29	5.85	0.212
No				
[3] **Physical Activity** [a]				
Sedentary	84.53	89.48	94.81	**<0.001***
Active	15.47	10.52	5.19	**<0.001***
Psychological Factors				
[4] **Perceived Stress Score**				
Low stress (Score ≤13)	5.0 ± 2.8	6.5 ± 2.7	7.3 ± 2.8	**<0.001***
	14.24	13.57	13.45	
Moderate Stress (Score 13-26)	16.2 ± 3.4	16.38 ± 2.5	16.2 ± 1.6	
	74.76	68.73	63.28	
High stress (Score ≥27)	29.0 ± 0.0	29.5± 1.1	30.5 ± 2.5	
	11.00	17.7	23.28	
[5] **Edinburgh Depression Score**				
Depressed (Score≥10)	14.0 ± 2.5	13.5 ± 3.5	14.1 ± 3.3	0.897
	42.10	39.06	37.99	
Non-depressed (Score<10)	6.0 ± 2.5	6.5 ± 2.8	6.0 ± 2.6	
	57.90	60.94	62.01	
[6] **Pittsburgh Sleep Quality Index**				
Bad sleep (score ≥5)	7.7 ± 3.2	8.2 ± 3.1	8.64 ± 3.0	**<0.001***
	49.24	66.72	73.56	
Good sleep (Score<5)	2.8 ±1.1	3.2 ±0.8	3.4 ± 0.8	
	50.76	33.28	26.44	

Sample size=618 ([1]n=574 T1, n=563 T2, n=555 T3; [2] n= 612 T1, 577 T2, 575 T2; [3] n= 614 T1, 580 T2, 578 T3; [4] n= 578 T1, 542 T2, 540 T3; [5] n= 575 T1, 533 T2, 531 T3, [6] n= 578 T1, 540 T2, 538 T3) Values are means ± standard deviation (SD) if normally distributed, median (min-max) if not normally distributed, or percentages (%) if binary, unless otherwise specified. McNemar test for proportions. [a] Sedentary was defined as engaging in physical activity for less than 1-2 times/week for <20 min duration, active was defined as having greater than 1-2 times/week for >20 min duration. *Indicates significant associations between percentages across trimesters

Table 4-3. Dietary Characteristics of the Population and the Consumption of the Individual Food Groups of the Lebanese Mediterranean Diet (N=618)

	Trimester 1	Trimester 2	Trimester 3	
Maternal Dietary Intake	**Mean ± SD; %**	**Mean ± SD; %**	**Mean ± SD; %**	**p**
Mean Adherence Score	17.47 ± 3.4	17.43 ± 4.04	17.5 ± 4.46	
Categories of Adherence				
Low (Score 9-15)	12.7 ±1.3 19.0	11.8 ± 1.9 24.0	11.5 ± 2.0 26.0	**<0.001***
Medium (Score 16-20)	17.3 ± 1.7 60.0	17.7 ± 1.7 51.0	17.7 ± 1.6 43.0	
High (Score 21-27)	22.4 ± 1.4 21.0	22.4 ± 1.3 25.0	22.6 ± 1.5 30.0	
[1] Food Group Intake per Day, Serving Size				
Burghol, 1cup	0.12 ± 0.23	0.13 ± 0.22	0.13 ± 0.22	0.430
Starchy Vegetables, 1 cup	0.40 ± 0.48	0.36 ± 0.37	0.32 ± 0.36	0.256
Vegetables, 1 cup	1.79 ± 1.17	1.90 ± 1.43	1.64 ± 1.22	**0.044***
Fruits, 1 piece	2.44 ± 1.83	2.36 ± 1.76	2.13 ± 1.52	0.560
[2] Dried Fruits, 1 serv	0.18 ± 0.45	0.18 ± 0.45	0.19 ± 0.45	0.875
[2] Dairy products, 1 serv	2.36 ± 1.58	1.56 ± 1.28	1.51 ± 1.33	**0.035***
Olive oil, 1 tsp	1.05 ±.84	1.08 ± 0.87	1.32 ± 1.03	0.567
Eggs, 1 large	0.33 ± 0.44	0.36 ± 0.49	0.36 ± 0.48	0.789
Legumes, 1 cup	0.25 ± 0.32	0.28 ± 0.35	0.26 ± 0.30	0.567

Sample size= 618. Values are means ± standard deviation (SD) if normally distributed, median (min, max, interquartile range) if not normally distributed, or percentages (%) if binary. [1]Food group intake was reported as the daily average number of servings consumed for each food group of the MeD.in each trimester: [2] 1 ex for dried fruits (2tbsp raisins or cranberries, 2 pieces dates, 4 pieces apricots), and dairy products (1 cup milk or yogurt, 1 slice cheese or 2 tbsp labneh). *Indicates significant associations using McNemar test for proportions. Abbreviations: IGT, impaired glucose tolerance, LMeD, Lebanese Mediterranean diet, tsp, teaspoon

Supplemental Table 4-1: Maternal Characteristics of Women having GDM vs those without GDM*

	GDM (N=32)	**No GDM (N=541)**	**p**
Maternal Characteristics	**N (%) or Mean ± SD**	**N (%) or Mean ± SD**	
Mean age in years (N=618)	N= 32 29.5 ± 5.8	N=541 29.3 ± 4.9	
Place of Residence			
Beirut + Mount Lebanon	21 (66)	230 (43)	**0.028***
North Lebanon + Akkar	1 (3)	66 (12)	
South Lebanon + Bekaa	10 (31)	245 (45)	
Education			
<High school (High school or brevet)	8 (25)	116 (21)	0.634
University degree or higher	24 (75)	425 (79)	
Occupation			
Non-employed	16 (50)	263 (49)	0.878
Employed	16 (50)	278 (51	
Family History of Diabetes			
Yes	14 (44)	105 (20)	**0.001***
No	18 (56)	433 (80)	
Pre-pregnancy BMI [1]			
Normal (BMI 18.5-24.9)	8 (25)	121 (29)	0.414
Overweight (BMI 25-29.9) + Obese	24 (75)	400 (71)	
Total GWG [2]			
Low	5 (17)	200 (38)	**0.048***
Adequate	16 (55)	234 (44)	
Excessive	8 (28)	92 (17)	

* Indicates significant associations using Chi Square test. [1] Pre-pregnancy BMI was calculated as weight in Kg over height in meters squared, and was categorized into underweight, normal, overweight and obese according to IOM. Among women with GDM, no one was underweight. [2] Total gestational weight gain was calculated by subtracting total weight gained from pre-pregnancy BMI. GWG was classified as inadequate, appropriate or excessive applying the following recommendations: To be considered adequate GWG, women who are underweight should gain a total of 12.5-18 kg, normal weight between 11.5-16 kg, overweight between 7-11.5 kg, and obese between 5-9 kg. Those with low GWG have a weight gained below these recommendations whereas those with excessive weight gain have above these recommendations

Table 4-4 Multiple Logistic Regression Models (MLR) Describing Predictors of GDM in a National Sample of Pregnant Women in Lebanon in Trimester 2 (N=569)

[1] Model 1-Maternal Characteristics			
GDM	**OR**	**95% CI**	**p**
Trimester 2 GWG, Kg	1.057	1.014-1.226	**0.024***
Pre-pregnancy BMI, Kg/m^2	1.078	0.996-1.167	0.062
Family History of Diabetes			
Yes	3.79	1.69-8.48	**0.001***
No			
Pittsburgh Sleep Quality Index, Trimester 2			
Poor Sleep (Score<5)	0.592	0.258-1.360	0.216
Good Sleep (Score>=5)			
Edinburgh Depression Scale, Trimester 2			
Depressed (Score≥10)	1.215	0.552-2.677	0.628
Non-Depressed (Score<10)			
Perceived Stress Score, Trimester 2			
High (Score ≥27)	0.634	0.160-2.516	0.516
Medium (Score 13-26)	0.601	0.201-1.792	0.361
Low (Score ≤13)			
MAP Trimester 2, mmHg	1.057	1.005-1.112	**0.031***
[2] Model 2-Adherence to the LMeD			
Adherence to the LMeD, Trimester 2			
High (Score 21-26)	0.676	0.213-2.438	0.507
Medium (Score 16-20)	0.894	0.343-2.331	0.818
Low (Score 9-15)			
Family History of Diabetes			
Yes	3.673	1.694-7.964	**0.001***
No			
MAP Trimester 2, mmHg	1.066	1.016-1.119	**0.009***
[3] Model 3-Identification of Food Groups			
Adherence to the LMeD, Trimester 2			
High (Score 21-26)	0.676	0.213-2.438	0.507
Medium (Score 16-20)	0.894	0.343-2.331	0.818
Low (Score 9-15)			
Family History of Diabetes			
Yes	3.673	1.694-7.964	**0.001***
MAP Trimester 2, mmHg	1.066	1.016-1.119	**0.009***

Sample size: n=560 in model 1, and n=569 in model 2 and model 3. [1] Model 1 represents the logistic model of the variables: family history of diabetes, pre-pregnancy BMI, GWG, stress, sleep, depression and MAP with the outcome GDM in trimester 2. [2] Model 2 represents the significant variables in model 1 (GWG, family history of diabetes, MAP) and adherence to the LMeD. [3] Model 3 represents the food groups that were significant. *Indicates significant associations

Figures 4-1. Fasting Blood Glucose Measurements in the 1st and 3rd Trimester of Pregnancy among a National Sample of Pregnant Women in Lebanon

Fig 4-1a. FBG in Trimester 1

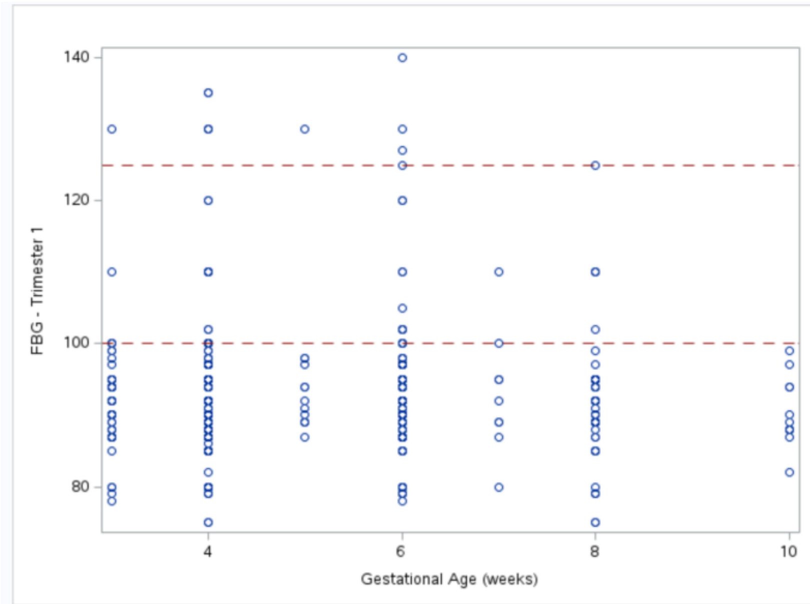


Fig 4-1a. Scatter-Plot of Fasting Blood Glucose in Pregnant Women (n=543) in trimester 1. Dashed lines represent the cut-offs for FBG. Normal<100 mg/dL, Impaired Glucose Tolerance 100-125 dL, and Diabetes ≥ 126 mg/dL

Fig 4-1b- FBG in Trimester 3

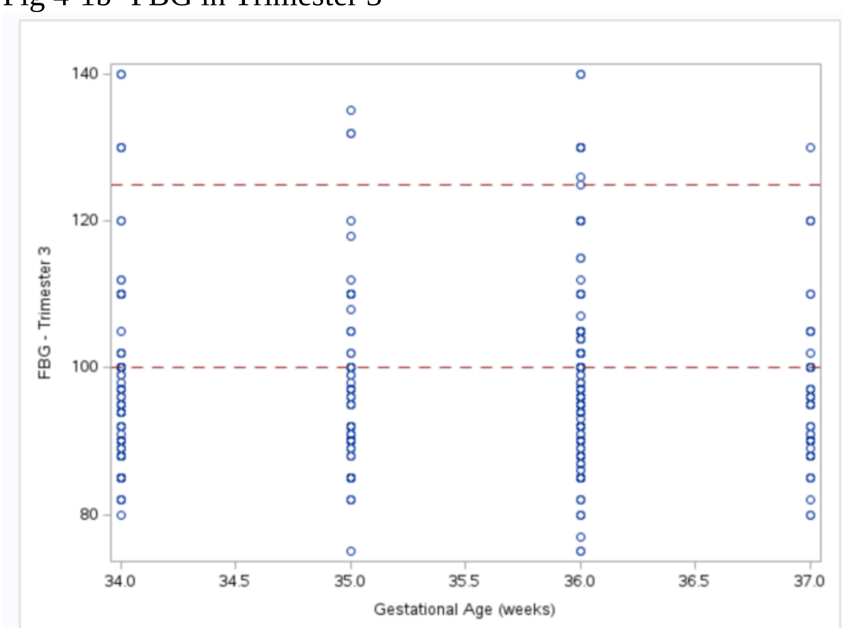


Fig 4-1b. Scatter-Plot of Fasting Blood Glucose in Pregnant Women (n=559) in trimester 1. Dashed lines represent the cut-offs for FBG. Normal<100 mg/dL, Impaired Glucose Tolerance 100-125 dL, and Diabetes ≥ 126 mg/dL

Table 4-5. Comparison of Maternal Characteristics among Women in the Control (FBG<100 mg/dl) vs. Impaired Glucose Tolerance (IGT) (FBG≥100 mg/dl) in Trimesters 1 and 3 in a National Sample of Pregnant Women in Lebanon

	Trimester 1			Trimester 3		
	Control	**IGT**		**Control**	**IGT**	
	Mean (SD); %	**Mean (SD); %**	**p**	**Mean (SD); %**	**Mean (SD); %**	**p**
Health Status						
[1] Mean FBG Values (mg/dl)	90.3±4.9 88.0	109.6 ±11.6 12.0	0.214	90.4 ±4.2 73.0	109.5±11.2 27.0	0.345
[1] Pre-pregnancy BMI, kg/m^2						
<18.5	17.1±1.1 4.0	18.0±0.4 2.0	0.562	17.1±14.7 4.0	18.0±0.4 0.0	0.759
18.5-24.9	21.9±1.8 62.0	22.0±1.6 65.0		21.9±1.8 62.0	21.9±1.6 57.0	
≥30	29.2±3.7 34.0	30.3±4.1 33.0		29.3±3.7 34.0	29.2±3.9 43.0	
[2] Mean GWG, Kg	1.9±4.4 88.0	1.5±4.3 12.0		14.0±5.8 73.0	15.2±6.2 27.0	
GWG Categories [a]						
Low	1.4±3.2 97.0	0.86±3.0 96.0	0.288	8.6±3.3 37.0	9.1±3.7 33.0	0.234
Adequate	15.2±1.4 2.0	16.0±1.7 4.0		15.3±1.7 46.0	15.5±1.7 44.0	
Excessive	25.1±2.6 1.0	27.1 ± 3.4 0.0		22.9±4.7 16.0	23.6±4.7 23.0	
[3] Mean MAP, mmHg	82.9±7.7 88.0	84.0±8.0 12.0		86.0±8.1 74.0	86.8±7.8 26.0	
MAP [b]						
Not High	79.6±5.0 78.0	80.2±5.3 73.0	0.345	80.2±3.6 64.0	80.2±3.7 46.0	0.103
High	94.2±4.0 22.0	94.2±4.0 27.0		92.8±6.6 46.0	92.5±5.6 54.0	
Psychological Factors						
[4] Perceived Stress Score						
Low (Score≤13)	9.6±2.8 15.0	9.9±3.8 10.0	0.061	10.2±2.5 14.0	9.7±2.6 13.0	0.191
Moderate (Score 14-26)	20.3±3.5 75.0	20.6±3.5 70.0		20.3±3.4 61.0	20.7±3.5 65.0	
High (Score≥27)	29.4±2.3 10.0	29.6±2.2 19.0		30.9±2.9 24.0	30.0±2.3 22.0	
[5] Pittsburgh Sleep Quality						
Good Sleep (Score<5)	2.8±1.2 48.0	7.0±3.1 43.0	0.440	3.3±0.8 17.0	3.5±0.8 16.0	0.615
Poor Sleep (Score≥5)	7.7±3.1	7.0±3.1		8.5±3.0	8.8±3.2	

	52.0	57.0		83.0	84.0	
[6] Edinburgh Depression Score						
Depressed (Score≥10)	14.0±3.5	14.8±4.8	0.229	14.2±3.4	14.6±3.8	0.575
	47.0	39.0		43.0	46.0	
Non-depressed (Score<10)	5.9±2.6	6.2±2.1		6.0±2.7	5.4±2.7	
	53.0	61.0		57.0	54.0	

Sample size=618 ([1]n= 476 control, 67 IGT Tr 1, 410 control, 149 IGT Tr 3; [2]n= 475 Control, 67 IGT Tr 1, 388 Control, 140 IGT Tr3; [3]n= 475 Control, 67 IGT Tr 1, 401 Control, 144 IGT Tr 3; [4]n= 476 Control, 67 IGT Tr 1, 358 Control, 147 IGT Tr 3; [5]n= 476 Control, 67 IGT Tr 1, 395 Control, 147 IGT Tr 3; [6]n= 474 Control, 67 IGT Tr 1, 389 Control, 146 IGT Tr 3). Values are means ± standard deviation (SD) if normally distributed, median (min-max) if not normally distributed, or percentages (%) if binary, unless otherwise specified. [a] Total gestational weight gain was calculated by subtracting total weight gained from pre-pregnancy BMI. GWG was classified as low, adequate or excessive applying the following recommendations: To be considered adequate GWG, women who are underweight should gain a total of 12.5-18 kg, normal weight between 11.5-16 kg, overweight between 7-11.5 kg, and obese between 5-9 kg. Those with low GWG have a weight gained below these recommendations whereas those with excessive weight gain have above these recommendations. [b] Not high MAP in trimester 1 is ≤ 87 mm Hg, and high MAP > 87 mm Hg, and in trimester 3 not high MAP is ≤ 86 mm Hg,and high MAP is >86 mm Hg.*Indicates significant associations using McNemar test for proportions. Abbreviations: IGT, impaired glucose tolerance, MeD, IGT, impaired glucose tolerance, FBG, fasting blood glucose, GWG, gestational weight gain, MAP mean arterial pressure

Table 4-6. Comparison of Dietary Intake among Women in the Control (FBG<100 mg/dl) vs. IGT Group (FBG≥100 mg/dl) in Trimesters 1 and 3 in a National Sample of Pregnant Women in Lebanon

Dietary Variable	Trimester 1			Trimester 3		
	Control	IGT		Control	IGT	
	Mean (SD); %	Mean (SD); %	p	Mean (SD); %	Mean (SD); %	p
[1]Adherence to the MeD						
Low (Score 9-15)	12.8±1.2 17.6	13.3±1.0 20.9	0.806	12.4±1.8 22.4	12.0±1.4 23.8	0.406
Medium (Score 16-20)	17.2±1.7 60.6	17.7±1.7 55.8		17.7±1.6 45.0	17.7±1.6 57.1	
High (Score 21-27)	22.3±1.3 21.8	22.7±2.2 23.2		22.6±1.5 32.5	22.4±1.4 19.0	
[2] Food Group Intake per Day, Serving Size						
Burghol, 1 cup	0.11+-0.19	0.22+-0.48	0.212	0.12+-0.17	0.16+-0.32	0.135
Starchy Vegetable, 1 cup	0.54+-0.97	0.39+-0.40	0.433	1.59+-1.02	1.81+-1.23	0.278
Vegetable, 1 cup	1.95+-1.29	1.79+-1.16	**0.032***	1.58+-1.02	1.81+-1.23	0.795
Fruit, 1 item	2.75+-2.35	2.47+-1.80	0.672	2.28+-1.57	2.26+-1.46	0.875
[3] Dried Fruits, 1 serv	0.06+-0.17	0.19+-0.48	**0.001***	0.21+-0.49	0.20+-0.46	0.721
[4]Dairy products, 1 serv	2.53+-1.59	2.38+-1.62	0.118	1.62+-1.33	1.62+-1.32	0.965
Olive oil, 1 tsp	0.95+-0.75	1.07+0.83	0.205	1.36+-0.89	1.43+-1.08	0.458
Eggs, 1 large	0.33+-0.44	0.32+-0.42	0.632	0.39+-0.53	0.39+-0.47	0.747
Legumes, 1 cup	0.37+-0.63	0.24+-0.29	0.111	0.28+-0.28	0.26+-0.29	0.622

[1] Sample size= 618 ([1] n= 476 in Control group, n= 67 IGT group; [2] n= 410 Control group, n= 149 IGT group). [2] Food group intake was reported as the daily average number of servings for each food group of the MeD. [3] 1 serving for dried fruits (2tbsp raisins or cranberries, 2 pieces dates, 4 pieces apricots), and [4] 1 ex for dairy products (1 cup milk or yogurt, 1 slice cheese or 2 tbsp labneh). *Indicates significant associations using McNemar test for proportions. Abbreviations: IGT, impaired glucose tolerance, MeD, Mediterranean diet, tsp, teaspoon.

Table 4-7 Multiple Logistic Regression (MLR) Describing Predictors of Impaired FBG≥100 mg/dl in a National Sample of Pregnant Women in Lebanon in Trimester 1 (N=543) and Trimester 3 (N=525)

	[a] Trimester 1			[b] Trimester 3		
	[1] Model 1-Maternal Characteristics					
FBG ≥ 100 mg/dl	**[1a] OR**	**95% CI**	**p**	**[1b]OR**	**95% CI**	**p**
GWG, kg	0.972	0.909-1.039	0.401	1.036	1.001-1.072	**0.044***
Pre-pregnancy BMI, kg/m^2	0.977	0.919-1.039	0.459	0.990	0.944-1.037	0.667
Family History of Diabetes, Yes	1.376	0.741-2.551	0.312	2.842	0.875-2.232	0.161
Pittsburgh Sleep Quality Index						
Poor Sleep (Score<5)	1.118	0.645-1.937	0.692	1.136	0.668-1.931	0.638
Good Sleep (Score>=5)						
Edinburgh Depression Scale						
Depressed (Score≥10)	0.656	0.382-1.126	0.126	1.176	0.783-1.766	0.434
Non-Depressed (Score<10)						
Perceived Stress Score						
High (Score ≥27)	2.842	0.987-8.193	**0.053***	1.152	0.565-2.349	0.697
Medium (Score 13-26)	1.385	0.590-3.252	0.454	1.404	0.752-2.622	0.286
Low (Score ≤13)						
MAP, mmHg	1.019	0.986-1.054	0.259	1.014	0.990-1.039	0.246
	[2] Model 2-Adherence to the LMeD					
Adherence to the LMeD						
High (Score 21-26)	0.978	0.407-2.349	0.959	0.905	0.510-1.605	0.733
Medium (Score 16-20)	1.339	0.656-2.735	0.422	1.249	0.735-2.122	0.410
Low (Score 9-15)						
GWG, Kg	--	--	--	1.036	1.003-1.070	**0.033***
Perceived Stress Score						
High (Score 21-26)	2.885	1.053-7.743	**0.039***	--	--	--
Medium (Score 16-20)	1.355	0.588-3.125	0.476	--	--	--
Low (Score ≤13)						
	[3] Model 3-Identification of Specific Food Groups					
Adherence to the MeD	--	--	--	--	--	--
Perceived Stress Score						
High (Score≥27)	2.605	0.948-7.155	0.063	--	--	--
Medium (Score 13-26)	1.369	0.592-3.162	0.462	--	--	--
Low (9-13)						
Legumes, serving/day	2.100	1.049-4.205	**0.036***	--	--	--

GWG, Kg	--	--	--	1.036	1.003-1.071	**0.032***
Perceived Stress Score						
High (Score ≥27)	3.054	1.117-8.354	**0.029***	--	--	--
Medium (Score 13-26)	1.390	0.600-3.221	0.443	--	--	--
Low (Score≤13)						
Burghol, serving/d	3.023	1.190-7.679	**0.020***	--	--	--
Adherence to the MeD	-	-	NS	-	-	NS
Perceived Stress Score	--	--	--	-	-	NS
Vegetables, serving/d	--	--	--	0.742	0.587-0.936	**0.012***

[a] Trimester 1 Sample size= 543 (Number of observations used were 539 in model 1 and 543 in model 2 and 3).
[1a] Model 1 represents the logistic model of the variables: family history of diabetes, pre-pregnancy BMI, GWG trimester 1, stress trimester 1, sleep trimester 1, depression trimester 1 and MAP trimester 1 with the outcome impaired FBG (≥100 mm Hg).
[2a] Model 2 represents the significant variables in model 1 (stress) and adherence to the LMeD in trimester 1.
[3a] Model 3 represents the significant variables in model 2 (stress trimester 1), adherence to the LMeD trimester 1 and significant food groups (burghol and legumes) trimester 1.
[b] Trimester 3 Sample size: n=525 in model 1, and n=528 in model 2 and 3.
[1b] Model 1 represents the logistic model of the variables: family history of diabetes, pre-pregnancy BMI, GWG trimester 3, stress trimester 3, sleep trimester 3, depression trimester 3 and MAP trimester 3 with the outcome impaired FBG in trimester 3.
[2b] Model 2 represents the significant variable GWG in model 1 and adherence to the LMeD.
[3b] Model 3 represents the significant variables in model 2: GWG, adherence to the LMeD and significant food group (vegetable) in trimester 3. The results shown represent the values for the significant variables only.
* Indicates significant associations with FBG≥100.
- Indicates non-significant associations with FBG≥100
--Variable not included in the model
Abbreviation: OR, odds ratio for the logistic model, 95% CI, 95% Wald Confidence Limits

Connecting Statement II

In Chapter IV, our aim was to determine the prevalence of GDM and IGT on a national level among pregnant women in Lebanon and to assess the predictors of GDM and IGT per trimester among these women. We hypothesized that a high adherence to the LMeD and good psychosocial factors including low stress, good sleep quality and no depression were associated with a decreased GDM and IGT risk among pregnant women in Lebanon. The results showed that GDM prevalence was low (<5.6%), whereas IGT prevalence was high (12.4% in trimester 1 and 26.5% in trimester 3). Moreover, sleep quality, stress, and PA levels worsened by trimester whereas adherence to the LMeD improved from trimester 1 to trimester 3. Family history of diabetes, high GWG and eMAP were significant predictors of GDM. On the other hand, high stress, burghol and legumes intake increased IGT risk in trimester 1, whereas high GWG increased IGT risk in trimester 3. Vegetable consumption was protective of IGT in trimester 3.

In Chapter V, our specific objectives were to assess the prevalence of small for gestational age (SGA), appropriate for gestational age (AGA) and large for gestational age (LGA) and the predictors of SGA and LGA risk. We hypothesized that a high adherence to the LMeD and good psychosocial factors including low stress, good sleep quality and no depression were associated with a decreased risk of SGA and LGA. Our aim was to study the association between adherence to the LMeD and each of SGA, LGA risk, and to explore the role of other maternal factors including pre-pregnancy BMI, GWG, GDM, IGT, MAP, and previous macrosomia on SGA, LGA risk.

Chapter V

Predictors of Infant Birth Weight for Gestational Age (SGA and LGA) in a Lebanese Pregnant Population

5.1. Abstract

Obesity is a global challenge that impacts pregnant females with an alarming high burden among Lebanese women. Both high pre-pregnancy body mass index (BMI) and gestational weight gain (GWG) in excess of recommendations have been associated with adverse infant outcomes that include birth of large for gestational age (LGA) or small for gestational age (SGA) infant. Moreover, high prevalence of gestational diabetes mellitus (GDM) and impaired glucose tolerance (IGT) and elevated blood pressure further exacerbate the risk. The specific objective of this study is to explore the association between LMeD adherence and infant birth weight for gestational age including birth of SGA and LGA infants as well as other risk factors which include pre-pregnancy BMI and GWG, psychosocial, socio-demographic and medical history covariates. Statistical analyses were conducted using the statistical software SPSS (Statistical Package for the Social Sciences) version 25. A descriptive analysis was conducted to report qualitative and quantitative variables. The dependent variable in our study was the "FWGA" (Fetal Birth Weight Gestational Age) and was categorized into three categories SGA, AGA and LGA. All the study variables were presented in function of the three groups using one-way ANOVA test followed by post-hoc Tukey test. A linear regression model approach was used to test the factors associated with FWGA of the total population and for AGA alone. The multiple linear regression model was performed via multiple layers where model 1 was adjusted for smoking at trimester 1 (T1), trimester 2 (T2), and trimester 3 (T3), total GWG, pre-pregnancy BMI, parity, infant sex, maternal height in meters and family history of diabetes, then model 2 was adjusted for GDM, FBG≥100 mg/dl at T1 and T3, pulse pressure at T1, T2 and T3, sleep quality I at T1, T2 and T3, and adherence to the LMeD at T1, T2, and T3, and model 3 was adjusted for individual food groups. A logistic regression model approach was used to test the

association between each potential predictor per trimester and SGA to AGA infants, and LGA to AGA infant risk. All maternal characteristics were entered in model 1, and model 2 included 9 food groups in 9 individual models. The majority of the population were primiparous (38.3%) and college educated (75%), while half lived in Beirut and Mount Lebanon. Approximately 33% of the women were overweight and/or obese, and most of them exceeded weight gain recommendations in all trimesters. Among the infants, 13% were classified as SGA, 73% as AGA and 16% as LGA. Moreover, the predictors of AGA infants included good maternal sleep and higher maternal adherence to the LMeD in T2 and T3. FWGA was positively associated with greater parity and previous macrosomia, higher total GWG, poor sleep in T2, higher olive oil and eggs consumption in T3, higher dairy products intake in T2, whereas higher dairy products consumption in T1 was associated with lower FWGA. AGA was positively associated with greater parity and higher dried fruits intake in T3. Adherence to LMeD and high consumption of dairy products in T1 was associated with lower FWGA. Moreover, higher MAP in T3 and higher burghol intake in T1 was associated with higher SGA risk, whereas a higher total GWG and higher MAP in T2 decreased SGA risk. On the other hand, greater parity, previous macrosomia and higher olive oil intake in T2 were associated with LGA risk, while a higher pulse pressure in T1 decreased its risk. Adherence to the LMeD was not associated with SGA or LGA, however different food groups were. Screening for risk factors such as previous macrosomia, greater parity and abnormal MAP and pulse pressure measurements should be assessed early during gestation.

5.2. Introduction

Obesity is a global challenge that impacts pregnant females with an alarming high burden among Lebanese women, and it carries adverse consequences for their offspring. Both high pre-pregnancy body mass index (BMI) and gestational weight gain (GWG) in excess of recommendations have been associated with adverse maternal outcomes and infant outcomes that include birth of either a large for gestational age (LGA) or small for gestational age (SGA) infant (M. K. Kjøllesdal & G. Holmboe-Ottesen, 2014; Mamun et al., 2011; Marchi et al., 2015; Vasudevan et al., 2011). Furthermore, pregnancy is a period that causes increased insulin resistance in normal weight women particularly in the third trimester due to a rise in lipoprotein concentrations and is further exacerbated in those who are overweight and obese. This is leading to a higher risk of delivering SGA infants (Bautista-Castaño et al., 2013; Haugen et al., 2008). To prevent these sequelae, the Institute of Medicine (IOM), recommends that women have a normal BMI at the beginning of pregnancy, gain weight within the proposed guidelines for their BMI (Bautista-Castaño et al., 2013; Hanson et al., 2015; Haugen et al., 2008; Marchi et al., 2015) and follow a healthy diet to enhance maternal and infant health (Hanson et al., 2015). MeD has been highlighted in various studies as optimizing birth weight and preventing SGA (Parlapani et al., 2019) and LGA (Fernández-Barrés et al., 2019) possibly due to its anti-inflammatory properties (Khoury et al., 2005).

Several maternal factors can contribute to poor infant outcomes. Maternal obesity and excessive gestational weight gain (GWG) (El Rafei et al., 2016; Papazian et al., 2017) are both significant predictors for delivery of LGA infants (Bautista-Castaño et al., 2013), whereas inadequate GWG, even in the obese, has been linked with birth of SGA infants (El Rafei et al., 2016; Papazian et al., 2017). Prior research identified that women with either low or high GWG as well as those who were underweight or obese were more likely to deliver premature babies (El Rafei et al., 2016). There is also evidence that 1st to 2nd trimester GWG can predict fetal growth before birth (Neufeld et al., 2004; Young et al., 2017). Moreover, gestational diabetes mellitus (GDM) has been shown to adversely affect infant outcomes, leading to higher chance of LGA or low birth weight babies (Erem et al., 2015; Erjavec et al., 2016; Savona-Ventura et al., 2013; Sesmilo et al., 2017; Wahabi et al., 2016). In EMC, HDPs were often associated with low birth weights, neonatal complications (Abalos et al., 2014; Khader et al., 2018) and prematurity (Khader et al., 2018). Other factors including maternal stress increased the risk of lower fetal weight gain from the second trimester until birth (Pinto et al., 2017), and both stress and depression before 20 weeks of pregnancy increased the likelihood of SGA infants (Khashan et al., 2014). Conflicting results on the impact of exercise on birth weight and gestational age have been found in previous studies (Bisson et al., 2017; Pathirathna et al., 2019; Pinzón et al., 2012). One review reported that moderate intensity physical activity (PA) was associated with promoting adequate GWG in mothers and consequently protecting against LGA without increasing the risk for SGA (Vargas-Terrones et al., 2019), whereas another cohort study conducted in Lebanon and Qatar did not show any significant relationship between PA and GWG (Abdulmalik et al., 2019).

Maternal diet during pregnancy is among the most significant factors that can affect fetal growth. The importance of the Mediterranean diet (MeD) in optimizing infant outcomes has been previously highlighted in the literature. Poor adherence to the MeD, particularly in early gestation (before 24 weeks), has been shown to decrease placental growth and reduce infant birth weight (Timmermans et al., 2012). In contrast a protective effect of high fruit, vegetable and dairy product intake has been reported (Colón-Ramos et al., 2015; Kjøllesdal & G. Holmboe-Ottesen, 2014) as well as that of a MeD supplemented with extra virgin olive oil (Assaf-Balut et al., 2017). Accordingly, research in several Mediterranean countries has shown that adopting a MeD was associated with lower odds of poor intrauterine growth (Chatzi et al., 2012; Parlapani et al., 2019), elevated infant birth weight (Fernández-Barrés et al., 2019), SGA (Assaf-Balut et al., 2017; Assaf-Balut et al., 2019; Martínez-Galiano et al., 2018), LGA, insulin resistance in offspring (Assaf-Balut et al., 2017; Assaf-Balut et al., 2019), and prematurity (Assaf-Balut et al., 2017; Assaf-Balut et al., 2019; Parlapani et al., 2019; Saunders et al., 2014; Smith et al., 2015). On the other hand, some studies demonstrated no significant impact of the MeD on SGA when controlling for all potential confounders (Peraita-Costa et al., 2018) or on prematurity (Haugen et al., 2008). To date, few cohort studies have been conducted in LMIC and the majority assessed dietary patterns either in early or late pregnancy, while only one intervention cohort (Goueslard et al., 2016) investigated the MeD at several points during gestation.

Presently, Eastern Mediterranean countries (EMC) are experiencing a nutrition transition. Both economic and population growth are contributing to the adoption of a Westernized diet and a more sedentary lifestyle (Zhu & Zhang, 2016) that is now linked to a rise in abdominal and visceral obesity, impaired glucose tolerance (IGT), type 2 diabetes and elevated blood pressure in the general population. These same behavioral components have also been associated with excessive GWG (Mourady et al., 2017), GDM (Sanabria-Martínez et al., 2015), and hypertensive disorders of pregnancy (HDPs) (Magro-Malosso et al., 2017) during pregnancy. The American College of Obstetrics and Gynecology advises pregnant women to engage in moderate intensity PA for 30 minutes on most days of the week (Vargas-Terrones et al., 2019), however women now report lower levels than the recommended 150 minutes per week (Mourady et al., 2017) which in turn is leading to compromised maternal-infant health (Sanabria-Martínez et al., 2015). There is also growing evidence that psychological factors including stress, depression and sleep disorders adversely affect gestational outcomes (Karam et al., 2006; Mourady et al., 2017; Omidvar et al., 2018). In Mediterranean countries (including Lebanon) that are transitioning away from the traditional MeD and adopting a more Westernized diet (Farhat et al., 2016; Jomaa et al., 2016), poor adherence to the MeD in pregnancy is associated with increased BMI, excessive GWG (Spadafranca et al., 2016), GDM (Karamanos et al., 2014), HDPs and birth of SGA and LGA infants (Assaf-Balut et al., 2019; Parlapani et al., 2019).

It is important to understand the roles of the various predictors in modulating infant birth weight. Our specific objectives were 1) to identify predictors of infant birth weight for gestational age, 2) study the association between Lebanese MeD (LMeD) adherence on infant birth weight for gestational age including SGA, LGA, and 3) to determine the role of specific components of the LMeD on infant birth weight for gestational age including SGA, LGA risk.. We hypothesized that a high adherence to the LMeD will protect against SGA and LGA risk, while excessive GWG will increase LGA risk, and psychosocial factors including stress, poor sleep and depression will increase SGA risk.

5.3. Materials and Methods

5.3.1. Study population

This study is a national prospective cohort study on pregnant women of various ethnic and religious backgrounds living in the 6 different governorates of Lebanon including Mount Lebanon, Beirut (capital of Lebanon), Bekaa, South (and Nabatieh), North, and Akkar. Beirut and Mount Lebanon are the main urban regions and account for the majority of the country's socio-economic, trade, political and cultural activities; however, poverty exists in the suburbs of these regions. The other governorates consist of both urban cities and rural villages where the latter have poor socio-economic and educational levels (Chamieh et al., 2015).

For this study, a simple random sampling among all obstetric clinics in Lebanon was done using the statistical software SPSS (Statistical Package for Social Sciences), version 22.0. Out of 732 obstetric clinics, a total of 20 private and hospital based private clinics were selected: Mount Lebanon (n=3), Beirut (n=5), Bekaa (n=4), South (n=3), North (n=4), and Akkar (n=1).

Recruitment was initiated by two universities in Lebanon: Notre Dame University-Louaize and Lebanese American University who provided training to their senior students as part of their research program. Written consent and approval were obtained from each physician at the respective clinic to survey the clientele and access medical records. Individual hospitals also provided written consent after reviewing the questionnaires and medical chart data prior to data collection. Healthy pregnant women (< 15 weeks) were invited to participate and were approached by the research team during their routine obstetric visit after being informed about the purpose of this study. We recruited the first 30 women who consented to participate and were eligible to participate. They were informed of the study anonymity and that they could withdraw at any time. Inclusion criteria for the study were Lebanese women: 1) > 18 years. Exclusion criteria included women 1) with multiple gestations, 2) pre-pregnancy diabetes, 3) women who were carrying a fetus with structural malformation, chromosomal anomalies or TORCH (toxoplasmosis, rubella, cytomegalovirus, herpes and other agents) infection.

5.3.2. Study design

This prospective cohort study followed consenting pregnant women from the 1st trimester (<15 weeks of gestation) until delivery with follow up interviews in the 2nd (24-28 weeks), and 3rd trimester (34-37 weeks). The initial interview was conducted in person, and the survey included socio-demographic data such as age, place of residence, level of income, education, occupation and marital status, and 5 validated questionnaires 1) Perceived Stress Scale (PSS10) (Cohen et al., 1983), 2) Pittsburgh Sleep Quality Index (PSQI) (Suleiman et al., 2012), 3) Edinburgh Perinatal/Postnatal Depression Scale (EPDS) (Ghubash et al., 1997), 4) food frequency questionnaire (FFQ) and LMeD (Naja et al., 2015) and 5) Canadian Physical Activity Readiness Medical Examination (PARmed-X for pregnancy) (Hui et al., 2012), where we categorized women as sedentary or active. Questionnaires were re-administered in the 2nd and 3rd trimester of pregnancy via phone interviews. A section of the survey included advice on diet and PA (Forbes et al., 2018) and food security (Gary et al., 2000) which were collected in the first trimester visit only.

Medical records were reviewed by our research team in each trimester during routine follow-up visits and this data was used to evaluate changes in clinical measures across gestation. Clinical data was obtained from medical charts including self-reported pre-pregnancy weight, vitamin/mineral intake, anemia and medical history (previous GDM and family history of diabetes). At follow up visits at each trimester, additional clinical indicators were collected from medical charts including weight gain per trimester, mean arterial pressure (MAP), glycemia, and general maternal health status. Upon delivery, maternal and infant data were retrieved from hospital charts which include maternal delivery type (vaginal/caesarian) and location, maternal delivery complications, and infant sex, birth weight and height, abdominal and head circumference, Apgar scores at 1 and 5 minutes, and gestational age at delivery.

Our main exposure variable was the adherence to LMeD which was assessed in each trimester, and we evaluated its associations with the outcome variable birth weight for gestational age including birth of SGA and LGA infants. We controlled for the following risk factors: pre-pregnancy BMI, total and per trimester GWG, stress, sleep, depression, elevated MAP (eMAP), pulse pressure, GDM, IGT as well as previous macrosomia, family history of diabetes, smoking, infant sex, parity, and maternal height.

5.3.3 Sample Size

The main outcome of our study was infant birth weight. We used Epiinfo Software to calculate the sample size needed for our study using formula by Fleiss with correction. The confidence interval was set at 95%, power at 80% and ratio (unexposed/exposed to the MeD=1). A sample of 618 participants was needed after adjusting for a 20% loss to follow up (Assaf-Balut et al., 2019). A simple random sampling was conducted among all obstetric clinics in Lebanon using the statistical software SPSS (Statistical Package for Social Sciences), version 22.0.

After completing the study, we had a total of 660 participants of which 42 dropped out due to miscarriages and/or other reasons. Data for maternal dietary intake and infant birth weight were collected from 618 participants using questionnaires.

5.3.4 Questionnaires:

Perceived Stress Scale (PSS10)

Perceived stress was evaluated using the Perceived Stress Scale (PSS10) which was originally developed as a 14-item scale in 1983 to assess perception of stress in the past month (Almadi et al., 2012) and was shortened to 10 items. The questions referred to feelings and thoughts that were experienced in the past month by participants and that could affect their social integration. Each of the 10 questions had a score between 0-4 with a global sum score of 0-40 with higher scores indicating higher perceived stress. The categories are the following: Low stress (score 0-13), moderate stress (score 14-26), and high stress (score 27-40). It has been previously validated in a Lebanese pregnant population with a test-retest reliability and Cronbach's alpha=0.74; Correlation r=0.48 and r=0.58 with General health questionnaire and the EPDS (Almadi et al., 2012).

Pittsburgh Sleep Quality Index (PSQI)

Sleep quality and patterns were assessed using Pittsburgh sleep quality index (PSQI) which is a self-reported tool that assesses sleep quality over a 1 month period and classifies sleep as good versus bad sleep using 9 questions that are based on seven domains: subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleep medications, and daytime dysfunction with the latter component having an impact on social aspects of life. Each of the 7 components is scored between 0 and 3 indicating no difficulty and extreme difficulty, respectively. A global score is obtained after adding up the 7 component sum, ranging between 0-21. A score equal or greater to 5 indicates poor sleep, while a score of less than 5 indicates good sleep. It has been previously validated in an Arabic population with an internal consistency and a reliability coefficient (Cronbach's alpha) of 0.74 for its seven components (Suleiman et al., 2012).

Edinburgh Perinatal/Postnatal Depression Scale (EPDS)

Edinburgh Perinatal/Postnatal Depression Scale (EPDS) is a commonly used 10-item scale in research and clinical practice to identify women at risk of perinatal depression. The questions included reflect the ability of the person to integrate normally in social life. A score of 0-3 is given for each question and a global sum of 0-30 is obtained. A score of 10 or greater indicates possible depression (Cox et al., 1987). This tool has been validated in pregnant women with a cut-off point of 10 (Murray & Carothers, 1990), and in an Arab population with a Cronbach's alpha=0.84; Correlation r=0.57 with the Present State Examination (Ghubash et al., 1997).

Canadian Physical Activity Readiness Examination (PARmed-X):

A section of the lifestyle questionnaire addressed the frequency, intensity and duration of participation in recreational PA over the past month to assess for physical activity using the Physical Activity Readiness Examination (PARmed-X). The PARmed-X was initially used as a screening tool for pregnant women prior to participation in any exercise and is comprised of 4 parts: 1) General health status, 2) Status of current pregnancy, 3) Activity habits during the past month and 4) Physical activity intentions (Shephard et al., 2000). For the purpose of this study we only used the third part of the questionnaire "Activity habits during the past month" which categorizes participants into three categories according to the frequency, intensity and duration of PA: unfit (frequency <1-2 times/ week and <20 min duration; PA index=0), active (1-2 times/ week for 20 min or more than twice/week for < 20 min; PA index=1) and fit (>2 times/week for more than 20 min; PA index=2). This tool has been validated against peak oxygen consumption to predict target heart rates for exercise for pregnant women based on age and fitness levels (Hui et al., 2012), and was translated to Arabic and back-translated since it was not validated in an Arabic population before. Since the vast majority of the women in this study were sedentary, we combined fit and active together due to the small percentages found in the two groups and obtained two categories: sedentary and active.

Dietary assessment and adherence to the Lebanese Mediterranean diet

Data on food intake was collected using a previously validated 61-item FFQ specifically for the Lebanese diet by Naja et al. (2015) (Naja et al., 2015) that is representative of the LMeD and incorporates traditional Lebanese dishes. The FFQ consisted of 9 food categories and under each category there were specific food items listed: 1) breads and cereals (white bread, brown bread, breakfast cereals, rice, pasta, burghol), 2) dairy products (low fat milk, full fat milk, fat free/low fat yogurt, whole fat yogurt, cheese regular, cheese low fat, labneh), 3) fruits and juices (citrus fruits/grapefruit, deep yellow or orange fruits, grapes, strawberries, other: bananas, apples, dried fruits, fresh fruit juice, canned or bottled fruit drinks), 4) vegetables (salad-green: lettuce, celery, cucumber, green pepper), dark green or deep yellow vegetables, tomatoes, corn/green peas, potatoes, squash/eggplant, cauliflower/cabbage/broccoli), 5) meat and alternates (legumes, nuts and seeds, red meat, poultry, fish including tuna, eggs, organ meats, luncheon meats, sausages/makanek/hotdogs), 6) fats and oils (oil: corn/olive/soy/sunflower, olives, butter, mayonnaise), 7) sweets and desserts (cakes/cookies/donuts/muffins, ice cream, chocolate bar, sugar/honey/molasses, Arabic sweets), 8) beverages (soft drinks regular, soft drinks diet, Turkish coffee, coffee/nescafe or tea, hot chocolate or cocoa, beer, wine, liquor) and 9) miscellaneous (manakish zaatar or cheese, pizza, French fries, chips, falafel sandwich, chawarma sandwich, burger). Serving sizes for each food item and the frequency of consumption of each food item was recorded as the number of servings consumed on a daily, weekly, monthly, or never basis. To minimize recall bias and measurement errors, we used food models, cups and spoons to illustrate portion sizes of all the food items.

Lebanese Mediterranean Diet Index (LMeD): This index was developed to assess the adherence to a Lebanese version of the MeD and was derived from the aforementioned-61 item- FFQ by Naja et al. (2015) (Naja et al., 2015). This tool was initially developed to identify different dietary patterns in the population using factor analysis. Authors were able to identify a Lebanese MeD pattern from the FFQ with the following 9 food groups because of their consistently high loading on this pattern which included: fruits, vegetables, legumes, olive oil, burghol (crushed whole wheat), milk and dairy products, starchy vegetables (potato, corn and beans), dried fruits and eggs. The Lebanese MeD index used in this study shares common food groups with other indices developed in Italy: Italian Mediterranean Index (Agnoli et al., 2011), Spain: rMED (Buckland, 2009), Greece: nMED (Panagiotakos et al., 2007), France: Mediterranean Diet Quality Index (Gerber, 2003), and 9 Mediterranean European countries: Mediterranean Diet Scale (Trichopoulou, 2003) such as fruits, vegetables, olive oil, legumes, dairy products and starchy vegetable, however in the LMeD other main components were missing such as fish, red meat, poultry, and wine consumption (Naja et al., 2015).

Adherence to the LMeD was measured based on consumption of each of these food groups with 1, 2 and 3 points assigned to low, average and high intake respectively. Then, a score was derived after adding the points for every participant with a minimum score of 9 reflecting the least adherence and a maximum score of 27 reflecting the highest adherence to LMeD. This tool had a good correlation (r=0.56) with the Italian MeD tool (Agnoli et al., 2011). Similarly to other studies done in pregnant women (E Gesteiro et al., 2012; Tatiana Papazian et al., 2019), alcohol intake was excluded as consumption is virtually absent in this study population. We presented in our results the number of servings that were consumed on a daily basis for each of the food groups that comprise the LMeD index.

5.3.5. Clinical Measurements

Pre-pregnancy BMI and GWG

Pre-pregnancy BMI was collected at baseline from the obstetrical charts at the clinics and was used to classify women as being underweight (<18.5 kg/m^2), normal (18.5-24.9 kg/m^2), overweight (25-29.9 kg/m^2) or obese (≥30 kg/m^2). Weight was re-assessed at 28 weeks, and at 37 weeks during routine clinic visit. Total GWG in Kg was calculated by subtracting total weight gain from pre-pregnancy weight, and GWG was classified as inadequate, appropriate or excessive according to the pre-pregnancy BMI using the recommendations of the Institute of Medicine (IOM) (underweight 12.5-18 kg, normal weight 11.5-16 kg, overweight 7-11.5 kg, and obese 5-9 kg) (Rasmussen et al., 2009). Weight gain per trimester was calculated by subtracting weight at each trimester from the preceding trimester (American College of Obstetricians Gynecologists, 2013). GWG per trimester was classified as adequate, excessive or low according to the following recommendations: For 1st trimester: above 2 kgs or below 1 kg was considered excessive or low respectively for all categories of BMI. For 2nd and 3rd trimester, the recommended weight gain per week for each BMI category is the following: 0.45-0.6 kg/wk for underweight women, 0.35-0.45 kg/wk for normal weight women, 0.2-0.3 kg/wk for overweight,and for obese women. Weight gain below or above these values are classified as low or excessive respectively (American College of Obstetricians Gynecologists, 2013).

Vitamin/mineral intake

Vitamin and mineral supplement usage was self-reported at the end of the first trimester, and medical charts were used to confirm supplementation recommended by their physician. Supplement usage was categorized into iron, vitamin D and multi-vitamin supplement.

Anemia

Anemia diagnosis was made by laboratory testing and a complete blood count early at the beginning of pregnancy. A serum ferritin concentration <30 μg/L together with an Hb concentration <11 g/dL was used to determine the presence of anemia during the 1st trimester of pregnancy (Api, 2015).

Fasting Blood Glucose (FBG), Impaired glucose tolerance, and Diagnosis of GDM

FBG values were collected from obstetric charts in trimester 1 and 3 only, and were categorized into normal FBG: < 100mg/dl and impaired glucose ≥100 mg/dl;. during the second trimester visit, GDM diagnosis (yes/no) was confirmed. Obstetricians in Lebanon followed the two-step 50 g oral glucose tolerance test between 28-32 weeks in line with the American College of Obstetricians and Gynecologists for diagnosis of GDM. If the 50 g glucose tolerance test is ≥140 mg/dL after one hour, a 100 g 3-hour oral glucose tolerance test is done. Blood glucose is tested at t=0 (fasting), t=1 hour, t=2 hours and t=3 hours with cut-off values of 95, 180, 155, and 140 mg/dL respectively. GDM diagnosis was made when two or more these cut-off values met or exceeded the Carpenter and Coustan criteria (American College of Obstetricians and Gynecologists, 2018).

Mean Arterial Pressure (MAP) and Pulse Pressure (PP)

MAP is a blood pressure measurement used to predict HDP risk and is calculated as MAP = DBP + 0.33 [SBP-DBP] (Kane, 2016) Trimester-specific cutoffs for elevated MAP (eMAP) in pregnancy were defined as >87 mmHg (10- <18 weeks), >84 mmHg (18-34 weeks), and >86 mmHg (after 34 weeks) (Women's Health and Education Center (WHEC), 2009); low MAP is defined as <70 mmHg (Henry et al., 2002). Pulse pressure (PP) is calculated as follows: PP = SBP - DBP (Klabunde, 2012). A prior large population study on normal pregnant women was used to define high PP (>68 mmHg) and low PP (<42 mmHg) (Ayala & Hermida, 2013). Previous studies have shown that high MAP and both low or high PP have been associated with poor fetal outcomes (Warland et al., 2008; Zhang & Klebanoff, 2001).

Infant Birth Outcomes

Infants with birth weight <10th percentile and >90th percentile according to their gestational age were classified as SGA and LGA respectively using data from the National Center for Health Statistics from 2011 (Duryea et al., 2014). Infants born <37 weeks were considered premature and <33 weeks very premature and an Apgar score of <7 is an indicator of poor infant health status (American College of Obstetricians and Gynecologists, 2019a). Head circumference (HC) and abdominal circumference (AC) were also retrieved from medical charts, where a normal HC is between 33 to 35 cm, and a normal AC is between 31 to 33 cm.

5.3.6 Statistical Analyses

Statistical analyses were performed using the statistical software SPSS (Statistical Package for the Social Sciences) version 25.

A descriptive analysis was conducted where qualitative data (nominal) was represented through tables by frequencies and percentages or through pie or bar charts, and quantitative data (scale) was represented by mean, standard deviation, median, minimum, and maximum. Graphically, quantitative data were represented by histograms.

The dependent variable in our study was the "FWGA" (Fetal Weight Gestational Age), which was calculated via the electronic calculator (INTERGROWTH_EFW calculator) and was categorized into three categories SGA, AGA, and LGA (Papageorghiou et al., 2018).

All the study variables were presented in function of the three groups SGA, AGA and LGA including GDM, blood pressure measurements (SBP, DBP and MAP at T1, T2 and T3), PP (at T1, T2 and T3), HDPs including preeclampsia, gestational age, pre-pregnancy BMI, maternal height (meters), maternal age, education, monthly income, place of residence, occupation, smoking status (at T1, T2 and T3), PA (at T1, T2 and T3), parity, previous miscarriage, previous HDPs, family history of diabetes, FBG at T1 and T3, previous GDM, anemia, infant sex, infant weight, infant height, infant head circumference, infant abdominal circumference, Apgar at 1 and 5 min, delivery complications, maternal delivery type, previous caesarian, previous macrosomia, sleep score (at T1, T2 and T3), depression score (at T1, T2 and T3), stress score (at T1, T2 and T3), FBG (at T1 and T3), GWG (at T1, T2 and T3), and adherence to LMeD (at T1, T2 and T3). Additionally, adherence to the LMeD and food categories at T1, T2 and T3 were also compared across the three categories. The tests used in the bivariate analysis were the chi-square test and the ANOVA test. A statistically significant association was set at 5% (p-value less than 0.05). One way ANOVA was followed by post-hoc Tukey test to identify where the difference is observed.

A linear regression model approach was used to test the test the factors associated with FWGA of the total population and for AGA alone. The multiple linear regression was conducted via multiple layers where the models included all the factors which were statistically associated to the dependent (SGA, AGA, or LGA) in the bivariate settings. Significant association was defined as p-value<0.05. Model 1 was controlled for smoking T1, T2, T3, total GWG, pre-pregnancy BMI, parity, infant sex, maternal height in meters and family history of diabetes, then the significant variables from model 1 were entered in Model 2 and adjusted for GDM, FBG≥100 mg/dl T1 and T3, pulse pressure at T1, T2 and T3, PSQI at T1, T2 and T3, and adherence to the MeD at T1, T2, and T3, and finally in Model 3, we entered each of the 9 food groups in individual models along with the significant variables from model 2. The final adjusted models were done via stepwise model.

A logistic regression model approach was used to test the association between each potential predictor per trimester and SGA to AGA infants, and LGA to AGA infant risk. Significant association was defined as p-value<0.05. In Model 1, we controlled for family history of diabetes, smoking at T1, T2 and T3, total GWG, pre-pregnancy BMI, infant sex, maternal height in meters, FBG≥100 mg/dl, GDM, MAP at T1, T2 and T3, pulse pressure at T1, T2 and T3, PSQI at T1, T2 and T3, and adherence to the LMeD at T1, T2 and T3. In the second model, we entered the significant variables from model 1 and entered each of the 9 food groups in individual models. The final adjusted models were done via Forward Wald model.

5.4. Results

5.4.1 General Population Characteristics

Table 5-1 describes the population characteristics of our sample. A total of 618 pregnant women were recruited from the 6 governorates of Lebanon. The mean age of participants at enrollment was 29.2 ±5.0 years, and mean parity was 1.3 child. Less than half of the women lived in Mount Lebanon and Beirut (main urban regions), and a higher percentage lived in rural areas (South Lebanon, Bekaa, Akkar and North Lebanon). More than 75% of women had a university degree. Out of the total sample, 49% were homemakers and another 49% were either self-employed, full time or part time, and 1.1% were students. The average monthly income was between 700$-2000 US dollars ($) and did not significantly differ by regions. Assessment of pre-pregnancy BMI showed that 83.8% of the women had a normal pre-pregnancy BMI, while 22.2% were overweight and 10.2% were obese. Only 3.8% of the women were underweight prior to pregnancy. More than 62% of women gained excessive weight with respect to their BMI recommendations in trimester 1, 2 and 3. With regards to maternal medical history, the results showed that most women did not have previous GDM (98%) or previous HDPs (96.4%), while 29.6% had previous caesarian section and 4.3% had previous macrosomia. Moreover, 25% of the women had anemia at the time of the study. Approximately 70% took their multivitamin supplements, while 30.8% took iron and 34.4% took Calcium/Vitamin D. Only 20% of the women answered on food security hence the data was not used for the bivariate analyses. With respect to maternal delivery data during the study, 54.9% had a Caesarian section and 14.4% had delivery complications.

5.4.2 Newborn Characteristics

Newborn characteristics of the sample population were described in table 5-2. The mean gestational age at delivery was 37.62±1.98 weeks. A greater percentage of newborns (58%) were boys. With respect to birth weight percentiles, 11.8% were SGA infants, 72.3% were AGA infants, and 15.9% were LGA infants. The majority of women (85.6%) delivered an infant with a birth weight between 2500-4500 grams. Mean birth weight was 3118 ± 598, Mean birth height was 49.40 ±2.91 cm, while mean head circumference was 33.20 ±3.17 cm and mean abdominal circumference was 27.44 ±3.35 cm. The mean Apgar scores at 1 and 5 minutes were 8.31±1.06 and 9.55±1.07.

5.4.3. Comparison of Maternal and Infant Characteristics across SGA, AGA and LGA Infants

Among the maternal factors, gestational age significantly differed across the three groups with the highest mean reported among AGA infants ($p<0.000$). Maternal weight at Trimester 3 significantly differed across the three groups with the highest mean weight 82.57±13.86 Kg identified in the LGA infants ($p<0.003$). The greatest percentage (28.6%) of maternal delivery complications was reported among the SGA infants ($p<0.011$). Moreover, the greatest percentage of previous macrosomia (13.0%) was reported among women who delivered LGA infants ($p<0.000$). With respect to total GWG, more women with low GWG were identified in the SGA group (34.5%), while the greatest percentage of women who had excessive GWG were found in the LGA group (54.9%) ($p<0.003$). With respect to infant characteristics, more boys were found in the SGA and LGA group compared to girls ($p<0.013$). Infant birth weight, birth height and head circumference significantly differed across the three groups ($p<0.000$). Agar Scores at 1 and 5 min were significantly higher among AGA infants compared to SGA and LGA infants

($p<0.000$) (Table 5.3). Moreover, women who delivered LGA infants had the highest total GWG (16 Kg) and a total weight gain of 14 Kg was associated with AGA infants ($p<0.001$). In trimester 1, weight gain of 3 Kg was associated with LGA infants, whereas a weight gain of 1.5 Kg was associated with AGA infants ($p<0.011$) (Figure 5-1).

5.4.4. Differences between Maternal Factors per Trimester across SGA, AGA and LGA Infants

PA in trimester 1 significantly differed across the three groups with the greatest percentage (19.7%) of active women reported among women who delivered SGA infants ($p<0.027$) compared to AGA and LGA infants. Moreover, poor sleep in trimester 2 was significantly higher among women with LGA infants (86.5%) compared to SGA and AGA infants ($p<0.038$). PP was lowest among women who delivered LGA infants in trimester 1, 2 and 3 compared to SGA and AGA infants ($p<0.002$, $p<0.016$, $p<0.001$ respectively), while MAP in trimester 1 and 3 was highest among women who delivered SGA infants ($p<0.016$ and $p<0.002$ respectively) (Table 5-4)

Table 5-5 represents the dietary characteristics of the pregnant women delivering SGA, AGA and LGA infants. In trimester 1, only mean eggs consumption significantly differed with the highest intake in the LGA group ($p<0.05$). In T2 and T3, adherence to the LMeD was significantly different across the three groups, where the highest mean adherence was identified among AGA infants compared to SGA and LGA ($p<0.05$). With respect to individual food groups of the LMeD, eggs, mean olive oil consumption in T2 and T3 was highest among women delivering LGA infants ($p<0.05$). Mean dairy products and vegetable consumption in T2 and T3 were lowest among women delivering SGA infants ($p<0.05$), and dairy products was highest among women delivering AGA infants ($p<0.05$).

5.4.5. Linear Regression Models for Fetal Birth Weight for Gestational Age

Table 5-6 represents the linear regression that describes predictors of FWGA in infants in N=618 pregnant women in Lebanon. In Model 1- Maternal Characteristics, we entered smoking at T1, T2 and T3, pre-pregnancy BMI and total GWG, parity, infant sex, maternal height and family history of diabetes. In the unadjusted model, parity, history of macrosomia, total GWG and pre-pregnancy BMI increased infant birth weight for gestational age [B=3.683, $p<0.001$; B=19.054, $p<0.007$; B=0.937, $p<0.000$; B=0.799 $p<0.007$]. Infant sex was also associated with FWGA where being a girl increased it [B= -9.299, $p<0.000$]. After adjustment using the Stepwise model, the same variables remained significant: parity, history of macrosomia, infant sex, total GWG and pre-pregnancy BMI [B=3.935, $p<0.015$; B=19.686, $p<0.001$; B=-9.208, $p<0.042$; B=0.951, $p<0.000$; B=0.750, $p<0.001$]. In Model 2-Maternal Markers, we entered the significant variables total GWG, parity and infant sex in addition to GDM, IGT (FBG≥100 mg/dl) at T1 and T3, MAP at T1, T2 and T3, pulse pressure at T1, T2 and T3, Pittsburgh Sleep Quality Index at T1, T2 and T3, and adherence to the LMeD at T1, T2 and T3. In the unadjusted model, parity, infant sex, history of macrosomia, total GWG and pre-pregnancy BMI remained significant [B=3.495, $p<0.003$; B=-10.706, $p<0.000$; B=21.067, $p<0.003$; B=0.983, $p<0.000$; B=0.825, $p<0.008$], in addition to PP at T2 [B=-0.413, $p<0.029$] and T3 [B=-0.369, $p<0.026$], and sleep quality at T2 [B=1.819, $p<0.004$]. After adjustment, parity [B=3.701, $p<0.001$], infant sex [B=-9.841, $p<0.000$], history of macrosomia [B=19.736, $p<0.005$], total GWG [B=0.960, $p<0.000$] and pre-pregnancy BMI [B=0.713, $p<0.015$], PP at T2 [B=0.397, $p<0.009$] and T3 [B=-0.491, $p<0.001$], and sleep quality at T2 [B=1.169, $p<0.002$] remained significantly associated with FWGA. In

Model 3-Food Groups, we entered each food group of the LMeD along with the significant variables from Model 2. Three food group models emerged: 1-Olive oil model: Parity, history of macrosomia, total GWG, poorer sleep quality and greater olive oil consumption in T3 were associated with higher FWGA [B=4.017, p<0.000; B=15.466, p<0.019; B=0.765, p<0.000; B=1.088, p<0.004; B=2.656, p<0.027]. Infant sex (females) was negatively associated with FWGA [B=-8.990, p<0.000]. 2-Dairy products model: parity, history of macrosomia, total GWG, poorer sleep scores, and higher dairy products consumption increased FWGA [B=3.934, p<0.000; B=16.186, p<0.013; B=3.934, p<0.000; B=1.171, p<0.002; B=2.656, p<0.027]. Infant sex (females) and dairy products consumption in T1 were inversely associated with FWGA [B=-9.169, p<0.000; B=-3.132, p<0.001]. 3-Eggs Model: Parity, history of macrosomia, total GWG, poorer sleep scores and higher eggs consumption in T3 were associated with higher FWGA [B=3.738, p<0.001; B=13.814, p<0.037; B=0.733, p<0.001; B=1.131, p<0.003; B=7.279, p<0.005]. Infant sex (females) was negatively associated with FWGA [B=-9.119, p<0.000].

Table 5-7 represents the linear regression that describes the determinants of AGA infants in pregnant women (N=447). In Model 1-Maternal Characteristics, the following variables were entered: smoking at T1, T2 and T3, total GWG, pre-pregnancy BMI, parity, infant sex, maternal height and family history of diabetes. Only parity emerged as significant even after adjustment where greater parity increased FWGA [B=3.220, p<0.006]. In Model 2-Maternal Health Markers, parity was entered along with IGT (FBG≥100 mg/dl) at T1 and T3, MAP at T1, T2 and T3, PP at T1, T2 and T3, PSQI at T1, T2 and T3, and adherence to the LMeD at T1, T2 and T3. Greater parity and poorer sleep scores were associated with AGA infants (B=3.338, p<0.009; B=1.462, p<0.013). After adjustment, they remained significant [B=3.291, p<0.005; B=0.674, p<0.045]. Adherence to the LMeD was not associated with AGA. In Model 3-Food Groups, parity was entered along with every individual food group in separate models. Two food group models emerged: 1) Dried fruits emerged as significant at T3 after adjustment [B=6.324, p<0.014] where a higher daily intake of dried fruits increased birth weight for gestational age. Adherence to the LMeD was associated with decreased birth weight within the AGA group [B=-3.807, p<0.040]. Parity remained significant [B=3.726, p<0.002]. 2) Dairy products model emerged where a higher dairy products intake significantly decreased birth weight for AGA at T1 [B=-1.892, p<0.006] even after adjustment while parity increased birth weight for AGA [B=3.293, p<0.004].

5.4.6. Multiple Logistic Models for SGA to AGA Infants

Table 5-8 represents the multiple logistic regression predicting the likelihood of SGA to AGA infants in N=520 pregnant women. In Model 1-Maternal Characteristics, the following variables were entered: parity, smoking at T1, T2 and T3, total GWG, pre-pregnancy BMI, infant sex, maternal height, family history of diabetes, IGT (FBG≥100 mg/dl), GDM, MAP at T1, T2 and T3, PP at T1, T2 and T3, PSQI at T1, T2 and T3, and adherence to the LMeD at T1, T2 and T3. A higher total GWG decreased SGA risk [OR=0.894, p<0.001], whereas higher MAP at T3 increased the odds of SGA [OR=1.047, p<0.004]. After adjustment, total GWG, MAP at T2 and T3 were significant [OR=0.511, p<0.002, OR=0.958, p<0.009; OR=1.045, p<0.001]. In Model 2-Food Groups, individual food groups were entered with the significant variables from model 1 in 9 separate models. One food model emerged: Burghol. In this model, burghol at T1 significantly increased the risk of SGA infants [OR=16.329, p<0.024] Total GWG and higher MAP at T2 were also associated with elevated SGA risk [OR=0.430, p<0.001; OR=0.948, p<0.012], whereas higher MAP at T3 increased SGA risk [OR=1.047, p<0.009]. Burghol, total GWG, MAP at T2 and T3 remained significantly associated with SGA risk even after adjustment [OR=3.130, p<0.026; OR=0.483, p<0.001; OR=0.956, p<0.007, OR=1.049, p<0.001].

5.4.7. Multiple Logistic Models for LGA to AGA Infants

Table 5-9 represents the multiple logistic regression predicting the likelihood of LGA to AGA infants in N=545 pregnant women. In Model 1-Maternal Characteristics, the following variables were entered: smoking at T1, T2 and T3, total GWG, pre-pregnancy BMI, infant sex, maternal height, family history of diabetes, IGT (FBG≥100 mg/dl), GDM, MAP at T1, T2 and T3, PP at T1, T2 and T3, sleep quality at T1, T2 and T3, and adherence to the LMeD at T1, T2 and T3. Before adjustment, parity and previous macrosomia significantly increased the odds of having LGA infants [OR=1.369, p<0.010; OR=8.482, p<0.001], girls had a lower odds to be LGA [OR=0.340, p<0.002]. Higher MAP at T3 was significantly associated with increased risk of LGA infants [OR=1.039, p<0.016]. After adjustment, parity, infant sex, and previous macrosomia remained significant [OR=1.452, p<0.001; OR=0.314, p<0.000; OR=6.447, p<0.001]. Family history of diabetes and higher PP decreased the risk [OR=0.456, p<0.041; OR=0.977, p<0.007]. In Model 2-Food Groups, the significant variables from model 1 were entered with each food group in separate models. Only one food group emerged: Olive Oil. In this model, parity, infant sex, and history of macrosomia, remained significant even after adjustment [OR=1.498, p<0.000; OR=0.352, p<0.001; OR=6.145, p<0.000]. Higher olive oil intake was associated with a greater LGA risk [OR=1.447, p<0.010].

5.5. Discussion

This study was the first national study that explored the association between LMeD and its 9 associated food groups in addition to psychosocial and maternal variables per trimester of pregnancy on FWGA in Lebanon. Five novel findings emerged. First, adherence to the LMeD was significantly higher among women who delivered AGA infants compared to SGA and LGA and was significantly associated with lower birth weight among AGA infants. Second, specific food groups of the LMeD were associated with infant birth weight, where a higher burghol consumption increased SGA risk and higher olive oil intake increased LGA risk. Third, a higher total GWG was associated with greater FWGA and decreased SGA risk. Fourth, among the psychosocial factors, poor sleep quality in trimester 2 was associated with increased FWGA. Fifth, greater parity and previous macrosomia increased both FWGA and LGA risk.

Association of the Mediterranean Diet with Infant Birth Weight for Gestational Age in Trimester 2

The highest adherence to the LMeD (47%) in this population was reported in trimester 2 among women who delivered AGA infants compared to SGA and LGA ($p<0.003$). Moreover, adherence to the LMeD in trimester 2 was associated with lower birth weights within the AGA infants but was neither associated with SGA or LGA risk. The MeD is characterized by high consumption of vegetables, fruits, legumes, nuts, seeds, whole grains, and olive oil; moderate intakes of fish and alcohol; low to moderate intakes of dairy; and low intakes of meat and poultry. Therefore, the MeD is a plant-based diet that is rich in fiber and antioxidants as well as monounsaturated and polyunsaturated fatty acids. The second and third trimester of pregnancy are critical periods for fetal growth and therefore good maternal nutrition by adhering to the MeD can prevent fat deposition in the baby throughout this period and lower birth weight within the acceptable range (Ashwin et al., 2022). This is in line with a cohort study conducted in Spain that reported an association between a high adherence to the MeD in late pregnancy and a lower risk of having infants with large birth weight (Fernández-Barrés et al., 2019). Furthermore, evidence showed that a Western diet contributed to a greater risk of having low birth weight infants (Hajianfar et al., 2018).

On the contrary, two recent studies showed that a greater adherence to the MeD was associated with increased birth weight (Parlapani et al., 2019; Timmermans et al., 2012) and larger infants along with a lower risk of SGA infants (Yisahak et al., 2021). Similarly, adherence to the MeD was shown to decrease the risk of SGA infants in a longitudinal population based study (Díaz-López et al., 2022), cohort study using MeD and olive oil (Martínez-Galiano et al., 2018) and in an intervention study using MeD supplemented with extra virgin olive oil and nuts (Assaf-Balut et al., 2019). This can be explained that the MeD supplies all essential nutrients which are important to the fetus and hence can improve their growth (Yisahak et al., 2021). Our results did not report similar findings which may be attributed to the difference in the LMeD index that was being used in this study versus other studies.

Association between Food Groups of the Lebanese Mediterranean Diet and Infant Birth Weight for Gestational Age

In this study we looked at the individual effect of each of the 9 food groups of the LMeD on FWGA. Several food groups did not emerge as significant. However, the following food groups were identified: Eggs, Dairy Products, Dried Fruits, Burghol and Olive Oil.

Higher eggs consumption was associated with higher FWGA. On average, women who delivered LGA infants were consuming on average half an egg per day. Higher dried fruits consumption in trimester 3 was associated with greater birth weight of AGA infants, whereas dairy products consumption in trimester 1 was associated with lower birth weights of AGA infants. This in line with a previous study that showed that a diet rich in dairy products, meat, snacks and potatoes decreased fetal growth and contributed to low birth weight infants (Timmermans et al., 2012). A study done by Eckl et al. 2021 reported that dairy products may increase CVD risk factors such as blood pressure which may in turn lead to lower birth weights due to blood volume expansion and placental problems. Additionally, one study showed that eggs (Kjøllesdal & Holmboe-Ottesen, 2014) and another showed that dried fruits increased birth weight (Murphy et al., 2014).

Higher burghol consumption in trimester 1 increased the risk of SGA infants, while higher olive oil consumption increased LGA risk. In general, most studies showed that healthy diets that are rich in fruits, vegetables, whole grains, nuts, olive oil, fish, poultry and low fat dairy products were positively associated with birth weight (Assaf-Balut et al., 2018). However, a review showed that Western diets and a diet rich in unspecified or refined wheat products increase the risk of SGA while protein rich diets and MeD showed a positive association with birth weight (Kjøllesdal & Holmboe-Ottesen, 2014). Moreover, Yisahak et al. 2021 reported that a vegetarian pattern including pulses decreased infant birth weight. This can explain the inverse relationship between burghol and birth weight in this study, and the positive impact of eggs and MeD on birth weight. Similarly, a recent meta-analysis also identified a trend for healthy dietary patterns rich in vegetables, fruits, whole grains, low fat dairy and lean protein foods and a decrease in SGA risk and higher birth weight for data-driven dietary patterns obtained from population-based data, but no association was reported for LGA risk due to high heterogeneity (Chia et al., 2019).

With respect to olive oil, an intervention study done by Assaf-Ballut et al. (Assaf-Balut et al., 2018) showed that adherence to 6 food groups of the MeD including the consumption of olive oil for at least 6 days/week reduced the risk of SGA.

Association of Maternal Factors with Infant Birth Weight for Gestational Age (Total GWG and Parity)

Of the maternal characteristics, higher total GWG was associated with higher FWGA and lower SGA risk. This was highlighted in figure 5-1, where women who delivered LGA infants had the highest total GWG (16 Kg) and a total weight gain of 14 Kg was associated with AGA infants ($p<0.001$). In trimester 1, weight gain of 3 Kg was associated with LGA infants, whereas a weight gain of 1.5 Kg was associated with AGA infants ($p<0.011$). These findings imply that gaining weight during pregnancy according to the IOM recommendations may be important to lower risk of LGA infants. The association between high weight gain during pregnancy and larger neonates has been largely demonstrated in prior studies (El Rafei et al., 2016; Mogensen et al., 2023; Sato & Miyasaka, 2019; Uchinuma et al., 2021; Young et al., 2017), however one study showed that increasing GWG in low birth weight infants does not contribute to higher birth weights (Uchinuma et al., 2021). Although various studies have shown a linear relationship between pre-pregnancy BMI and birth weight (Yan, 2015), our study did not. Bautista-Castaño et al. (2013) and Papazian et al. (2017) reported a significant association between pre-pregnancy overweight and obesity and delivering large and/or macrosomic babies, while a low pre-pregnancy BMI was associated with low birth weight infants (Papazian et al., 2017). This was not observed in our population maybe because the majority of the women (69%) had a normal BMI or were underweight prior to pregnancy. On the other hand, overweight and obese women exceeded the cut-offs for normal GWG in all trimesters while only a very small percentage of those who were underweight did (paper 1) which might infer the importance of GWG during pregnancy especially for those who are overweight or obese.

Parity also emerged as a significant predictor of infant birth where it increased FWGA and was associated with higher birth weight of AGA infants. This might be explained that those with a higher parity are having a higher total GWG which is positively related to infant birth weight as seen in figure 5-1.

Association of MAP with Infant Birth Weight for Gestational Age

Hypertension during pregnancy is a strong determinant of impaired uterine growth rate during pregnancy especially high SBP and high DBP (Bakker et al., 2011; González-Fernández et al., 2020; Lim et al., 2021). In this study, the low number of women with high SBP and DBP did not allow to study their association with of HDPs. However, eMAP was more prevalent in this population as seen in Study I and can contribute to HDPs and utero-placental fetal growth impairments. In the current study, high MAP in trimester 3 was associated with increased SGA risk whereas high MAP in trimester 2 decreased the risk of SGA infants. A study by Iwama et al. (2016) identified that a high MAP before 20 weeks of gestation can increase the risk of SGA.

Association of Poor Sleep Quality with Higher Infant Birth Weight for Gestational Age

Of the maternal psychosocial factors, only poor sleep emerged as significant in trimester 3, where poor sleep was associated with higher infant birth weight for gestational age. Only one study was in line with our findings where sleep distress in particular sleep apnea increased the risk of LGA (Howe et al., 2015). A possible explanation for the relationship between poor sleep and LGA is that disturbed sleep can increase the risk of GDM and subsequently increase the risk of macrosomia (Cai et al., 2017). On the contrary, two recent studies showed that poor sleep increased the risk of SGA infants (Liu et al., 2021; Murata et al., 2021). This can be explained that a poor sleep quality is associated with inflammatory responses in the placenta that cause fetal growth restriction and lead to low infant birth weight (Murata et al., 2021). Although stress and depression did not impact birth weight in this study, but previous findings showed a significant association between maternal anxiety (Khashan et al., 2014; Pinto et al., 2017), stress and depression (Khashan et al., 2014) and SGA infants. A recent meta-analysis by Eichler et al. (2021) reported a significant impact of stress only on low birth weight for infants while another meta-analysis highlighted the effect of depression on low birth weight (Grote et al., 2010). The mechanism behind has not been yet well established, however researchers predict that the increased glucocorticoids that are delivered to the fetus due to high stress or anxiety levels can lead to low birth weight (Khashan et al., 2014).

The Relationship between FBG, GDM and Infant Birth Weight

In this study population, FBG and GDM did not affect infant birth weight. This is in contrast to a previous study by Savona-Ventura et al. (2013) that reported a significant association between GDM and delivering either SGA or LGA infants in Mediterranean women. Wahabi et al. (2016)

also reported an increased risk of LGA infants in women with GDM or pre-GDM in Saudi Arabia, and (Sesmilo et al., 2017) showed a direct association between elevated FBG and macrosomia. Interestingly, despite the high prevalence of diabetes (20.2%) (Musaiger, 2004) and IGT (27%) (Marchi et al., 2015) reported in Lebanon , only 5.6% of the women developed GDM which is lower than the percentage reported in other Mediterranean countries. Moreover, the average FBG in trimester 1 and 3 for SGA, AGA and LGA infants was below 100 mg/dl. This highlights that the majority of our population has normal FBG and is considered healthy. Even though 20.8% of the women had a family history of diabetes, however this did not contribute to larger birth weight infants.

5.6. Strengths and Limitations

The major strength of this study is its national prospective cohort design that was the first in the EMC to be conducted among a representative sample of pregnant women in the different regions of Lebanon. The fact that we took gestational age and infant sex into consideration while calculating birth weight is another strength of this study in addition to measuring maternal characteristics at three points during pregnancy. Additionally, most questionnaires that were used were previously validated in Lebanon and administered by trained professionals. Another major strength of this study is the novelty of its findings with regards to the association of specific components of the LMeD with infant birth weight, where eggs increased FWGA and LGA risk and burghol consumption increased SGA risk. Dried fruits on the other hand increased the odds of having AGA infants while dairy products decreased the odds of having AGA infants. Furthermore, excessive total GWG and poor sleep in trimester 3 contributed to higher FWGA and increased LGA risk. Blood pressure indices were also important in this study. High PP in trimester 1 decreased LGA risk, while high MAP varied by trimester where in trimester 2 it decreased SGA risk and in trimester 3 it increased SGA risk.

At the same time, we acknowledge that prospective cohort study designs have limitations as they are prone to measurement and recall bias such as for self-reported data on diet, psychosocial factors, PA and smoking. Moreover, food security could not be controlled for since data was missing. We also acknowledge the nature of the study design can lead to loss of follow-up, however only 6.4% dropped out either due to miscarriage (n=21) or loss to follow up (n=21) which was less than the 20% anticipated. Moreover, the economic crisis and the emergence of the COVID-19 during the period of this study might have affected our results by increasing psychological disorders such as poor sleep among participants and also affecting their dietary intake.

5.7. Conclusion

Adherence to the LMeD in trimester 2 was associated with lowering infant birth weight among AGA infants but was not associated with decreasing SGA or LGA risk. This study, however, identified the importance of specific food groups of the LMeD such as eggs and dairy products which are protein rich foods in increasing infant birth weight. The findings also emphasized that higher intake of burghol which is a type of cracked wheat elevated SGA risk and higher intake of olive oil increased LGA risk. In addition, good sleep quality, maintaining adequate weight gain according to the IOM guidelines, as well as having lower MAP values were also important elements to reduce the risk of delivering SGA and/or LGA infants. Although our findings did not show an association between GDM and IGT on birth outcomes, however it is important to emphasize the role of early screening for other related risk factors such as elevated blood pressure, pre-pregnancy overweight and obesity, excessive GWG, poor sleep, and previous macrosomia.

Table 5-1. Population Characteristics of Pregnant Women in Lebanon

Maternal Characteristics	Mean ± SD or %
[1] Age, years	29.2 ± 5.0
Parity, number of gestation	1.3 ± 1.1
[1] Place of Residence	
Akkar, %	3.7
Beirut, %	12.4
Bekaa, %	16.1
Mount Lebanon, %	30.7
North Lebanon, %	7.4
[a] South Lebanon, %	29.4
[1] Occupation	
Student,	1.1
Homemaker, %	49.0
Self-employed, %	8.7
Employee part-time , %	9.8
Employee full-time, %	31.2
[1] Education	
High school or less, %	23.9
Bachelor degree, %	40.6
Masters degree or higher, %	35.4
Maternal Health Characteristics	
[1] Pre-pregnancy BMI, kg/m^2 [b]	
Underweight (<18.5, %)	3.9
Normal (18.5-24.9, %)	63.4
Overweight (25.0-29.9, %)	22.5
Obese (≥30.0, %)	10.2
[2] Total GWG [c], kg	
Low, %	11.1
Adequate, %	20.5
Excessive, %	68.3
GWG at T1	1.17 ± 4.33
Low, %	3.6
Adequate, %	9.6
Excessive, %	86.9
GWG at T2	5.34 ± 3.46
Low, %	34.5
Adequate, %	4.1
Excessive, %	61.5

GWG at T3	7.09 ± 3.80
Low, %	4.5
Adequate, %	2.3
Excessive, %	93.2
HDPs	
[3] Previous Hypertensive Disorders of Pregnancy, % Yes	3.6
[3] Gestational Hypertension, % Yes	1.6
[6] Pre-eclampsia, % Yes	1.9
Diabetes	
[3] Family History of Diabetes, % Yes	20.8
[6] Previous GDM, % Yes	1.9
[3] GDM [d], % Yes	5.6
[3] Anemia [e], % Yes	25.0
[4] COVID Infection during Pregnancy, % Yes	7.7
[3] Previous caesarian, %	29.6
[3] Previous macrosomia, %	4.3
[1] Delivery type	
Vaginal, %	45.1
Caesarian section, %	54.9
Maternal delivery complications [f], %	14.4
[5] Vitamin Supplement Intake, % Yes	98.8
OTC Multivitamins/minerals	68.9
Iron	30.8
Calcium/Vitamin D	34.4

Sample size= 618 ([1]n=618, [2]n= 555, [3]n= 573, [4]n=117, [5]n=499, [6]n=563). Values are means ± standard deviation (SD) if normally distributed, median (min-max) if not normally distributed, or percentages (%) if binary, unless otherwise specified. [a] South Lebanon includes the sample of Nabatieh. [b] Pre-pregnancy BMI was calculated as weight in Kg over height in meters squared, and was classified as underweight, normal, overweight and obese. [c] Total gestational weight gain was calculated by subtracting total weight gained from pre-pregnancy BMI. GWG was classified as low, adequate or excessive applying the following recommendations: To be considered adequate GWG, women who are underweight should gain a total of 12.5-18 kg, normal weight between 11.5-16 kg, overweight between 7-11.5 kg, and obese between 5-9 kg. Those with low GWG have a weight gained below these recommendations whereas those with excessive weight gain have above these recommendations. [d] GDM diagnosis was made using the two-step 50 g oral glucose tolerance test between 24-28 weeks in line with the American College of Obstetricians and Gynecologists for diagnosis of GDM. If the 50 g glucose tolerance test was ≥140 mg/dL after one hour, a 100 g 3-hour oral glucose tolerance test was done. Blood glucose was tested at t=0 (fasting), t=1 hour, t=2 hours and t=3 hours with cut-off values of 95, 180, 155, and 140 mg/dL, respectively. GDM diagnosis was made when two or more these cut-off values met or exceeded the Carpenter and Coustan criteria. [e] Serum ferritin concentration <30 μg/L together with an Hb concentration <11 g/dL was used to determine the presence of anemia during the 1st trimester of pregnancy. [f] Maternal complications included those upon delivery. Abbreviations: BMI, body mass index, GWG, gestational weight gain, HDPs, hypertensive disorders of pregnancy, GDM, gestational diabetes mellitus, OTC, over the counter

Figure 5-1. Gestational Weight Gain at T1, T2 and T3 and total GWG in function of Fetal Birth Weight for Gestational Age

Fig 5-1a. GWG at T1 in Function of Fetal Birth Weight for Gestational Age

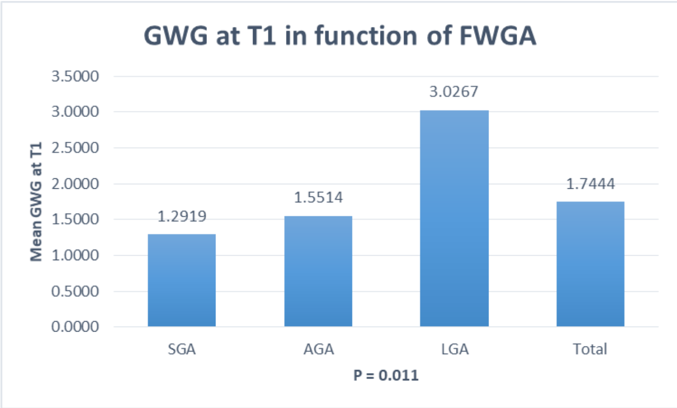


Fig 5-1b. GWG at T2 in Function of Fetal Birth Weight for Gestational Age

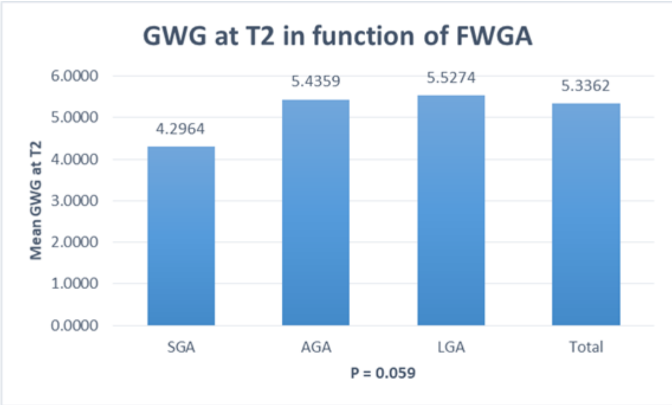


Fig 5-1c. GWG at T3 in Function of Fetal Birth Weight for Gestational Age

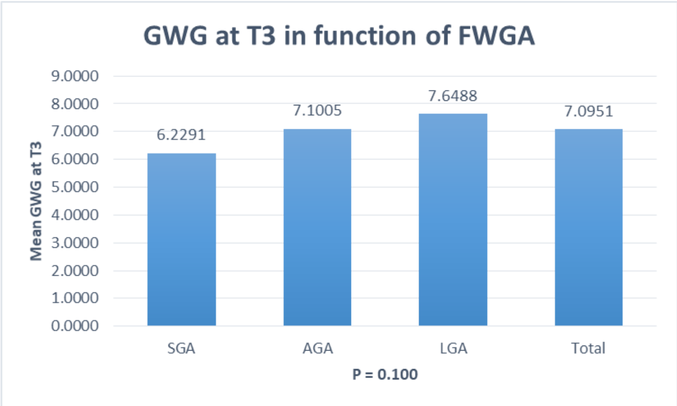
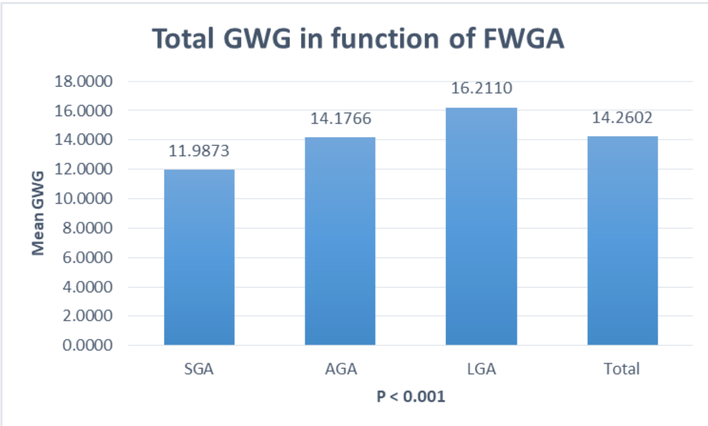


Fig 5-1d. Total GWG in Function of Fetal Birth Weight for Gestational Age



One way Anova was done to test for significant associations. Abbreviations: SGA, small for gestational age, AGA, appropriate for gestational age, LGA, large for gestational age, FWGA, fetal birth weight for gestational age

Table 5-2. Newborn Characteristics of the Sample Population

Newborn Characteristics	**Mean ± SD or %**
Gestational age at delivery, weeks*	37.62 ± 1.98
Infant sex	
Boy, %	58
Girl, %	42
Mean Birth Weight, grams	3118.68 ± 598.62
Birth Weight (percentiles) z scores**	
SGA <10th percentile, %	11.8
AGA between 10 and 90 percentiles, %	72.3
LGA>90th percentile, %	15.9
Birth Weight, grams	
<2500 g, %	11.0
2500–4500 g, %	85.6
≥4500 g, %	3.4
Infant birth length, cm	49.40 ± 2.91
Head circumference, cm	33.20 ± 3.17
Abdominal circumference, cm	27.44 ± 3.35
Apgar score	
At 1 min	8.31 ± 1.06
5 min	9.55 ± 1.07

*Gestational age at delivery was calculated from the first day of the last menstrual period **Birth weight percentiles were categorized according to the fetal growth calculator percentile range

Table 5-3. Differences in Maternal and Infant Risk Factors across SGA, AGA and LGA Infants

	SGA (N=73)	AGA (N=447)	LGA (N=98)	
Maternal Factors	**Mean±SD or %**	**Mean±SD or %**	**Mean±SD or %**	**p**
Maternal Age, years	29.48± 5.94	29.23±4.93	28.97±4.92	0.804
Gestational age, weeks	37.7±2.5 [A]	37.8±1.6 [A]	36.3±2.7 [B]	**0.000***
Maternal Height, meters	1.63±0.06	1.63±0.06	1.64±0.07	0.305
Weight T3, Kg	75.65±11.62 [A]	78.52±11.76 [A]	82.57±13.86 [B]	**0.003***
Parity, number of gestations				
0-1	57.5	57.7	49.0	**0.000***
2-4	19.2	36.2	33.7	
>4	23.3	6.0	17.3	
Pre-pregnancy BMI, Kg/m^2				
Underweight (<18.5, %)	5.5	4.0	2.0	0.095
Normal (18.5-24.9, %)	60.3	62.2	71.4	
Overweight (25-29.9, %)	27.4	23.9	12.2	
Obese (≥30, %)	6.8	9.8	14.3	
Delivery Complications				
No, %	71.4	87.4	84.9	**0.011***
Yes, %	28.6	12.6	15.1	
Maternal Delivery Type				
Vaginal, %	43.8	44.3	50.0	0.573
Caesarian, %	56.2	55.7	50.0	
Previous Caesarian				
No, %	81.0	69.3	68.0	0.167
Yes, %	19.0	30.7	32.0	
Previous Macrosomia				
No, %	95.1 [A]	97.4 [AB]	87.0 [B]	**0.000***
Yes, %	4.9	2.6	13.0	
GDM				
No, %	90.3	95.8	90.7	0.058
Yes, %	9.7	4.2	9.3	
Mean Total GWG	11.98±4.97	14.17±5.71	16.21±7.13	
Total GWG				
Low, %	34.5 [A]	18.9 [B]	14.6 [B]	**0.001**
Adequate, %	41.8	38.0	30.0	
Excessive, %	23.6	43.1	54.9	
Infant sex				0.013
Boy, %	54.8 [A]	55.5 [B]	71.4 [C]	
Girl , %	45.2	44.5	28.6	
Infant Weight, grams	2332.5±451.6 [A]	3111.0±391.5 [B]	3735.9±756.8 [C]	**0.000***

Values are means ± standard deviation (SD) if normally distributed, median (min-max) if not normally distributed, or percentages (%) if binary, unless otherwise specified. One way ANOVA was conducted followed by post-hoc Tukey test. *Indicates significant associations. Abbreviations: SGA, small for gestational age, AGA, appropriate for gestational age, LGA, large for gestational age, T3, trimester 3, BMI, body mass index, GDM, gestational diabetes mellitus, GWG, gestational weight gain.

Table 5-4. Comparison of Maternal Health Factors across SGA, AGA, LGA: the following variables were taken at Trimester 1, Trimester 2 and Trimester 3

Maternal Health Factors	SGA (N=73) Mean±SD or %	AGA (N=447) Mean±SD or %	LGA (N=98) Mean±SD or %	p
FBG T1, mg/dl	94.19 ±11.04	92.39±8.54	92.95±8.57	0.335
FBG T3, mg/dl	95.59±11.15	95.29±10.67	96.44±11.75	0.686
IGT T1 (FBG≥100 mg/dl)				
Yes	12.3	10.3	12.2	0.776
No	87.7	89.7	87.8	
IGT T3 (FBG≥100 mg/dl)				
Yes	21.9	24.6	23.5	0.872
No	78.1	75.4	76.5	
[a] Physical Activity T1				
Sedentary	80.6	84.0	87.6	0.453
Active	19.4	16.0	12.4	
Physical Activity T2				
Sedentary	80.3 [A]	88.8 [AB]	94.4 [B]	**0.027***
Active	19.7	11.2	5.6	
Physical Activity T3				
Sedentary	90.2	94.6	97.7	0.131
Active	9.8	5.4	2.3	
Smoking T1				
Yes, %	4.4	9.8	8.3	0.336
No, %	95.6	90.2	91.7	
Smoking T2				
Yes, %	3.6	9.3	8.0	0.351
No, %	96.4	91.7	92.0	
Smoking T3				
Yes, %	1.8	6.7	6.9	0.351
No, %	98.2	93.3	93.1	
Mean Perceived Stress Score T1	18.61 ± 6.04	19.68 ± 5.92	20.55 ± 6.03	0.111
Perceived Stress Score T1				
Low (Score≤13)	24.7	16.3	13.3	0.160
Moderate (Score 14-26)	68.5	73.2	71.4	
High (Score≥27)	6.8	10.5	15.3	
Mean Perceived Stress Score T2	20.26 ± 5.62	20.46 ± 6.45	22.17 ± 6.57	0.060
Perceived Stress Score T2				
Low (Score≤13)	14.8	16.7	11.2	0.125
Moderate (Score 14-26)	75.4	66.9	64.0	
High (Score≥27)	9.8	16.4	24.7	
Mean Perceived Stress Score T3	20.13 ± 6.29	21.43 ± 6.98	21.92 ± 7.14	0.283
Perceived Stress Score T3				
Low (Score≤13)	19.7	15.1	12.5	0.343
Moderate (Score 14-26)	65.6	62.6	59.1	
High (Score≥27)	14.8	22.3	28.4	

Mean Edinburgh Depression Scale T1	9.15±5.00	9.73±4.91	9.18±5.49	0.465
Edinburgh Depression Scale T1				
Non-Depressed (Score <10)	52.1	51.0	54.6	0.809
Depressed (Score≥10)	47.9	49.0	45.4	
Mean Edinburgh Depression Scale T2	10.38±4.34	9.67±4.80	10.00±5.60	0.523
Edinburgh Depression Scale T2				
Non-Depressed (Score <10)	31.7	44.7	45.5	0.149
Depressed (Score≥10)	68.3	55.3	54.5	
Mean Edinburgh Depression Scale T3	10.65±5.09	9.41±4.94	9.63±5.88	0.216
Edinburgh Depression Scale T3				
Non-Depressed (Score <10)	38.3	48.6	48.3	0.326
Depressed (Score≥10)	61.7	51.4	51.7	
Sleep Score T1				
Bad Sleep (Score≥5)	57.5	50.6	57.1	0.323
Good Sleep (Score<5)	42.5	49.4	42.9	
Sleep Score T2				
Bad Sleep (Score≥5)	75.0^{A}	73.8^{A}	86.5^{B}	**0.038***
Good Sleep (Score<5)	25.0	26.2	13.5	
Sleep Score T3				
Bad Sleep (Score≥5)	83.3	82.3	88.6	0.350
Good Sleep (Score<5)	16.7	17.7	11.4	
Pulse Pressure T1, mm Hg	25.69±18.17 ^{A}	21.04±18.28 ^{A}	15.23±19.08 ^{B}	**0.002***
Pulse Pressure T2, mm Hg	25.15±17.36 ^{A}	20.50±17.53 ^{AB}	16.44±20.95 ^{B}	**0.016***
Pulse Pressure T3, mm Hg	27.74±20.57 ^{A}	21.16±18.86 ^{B}	15.99±19.02 ^{C}	**0.001***
MAP T1, mm Hg	132.86±12.86 ^{A}	130.02±12.67 ^{A}	126.78±14.42 ^{B}	**0.016***
MAP T2, mm Hg	133.25±14.80	131.79±12.08	129.05±14.25	0.104
MAP T3, mmHg	140.31±18.24 ^{A}	134.06±12.52 ^{B}	135.67±12.70 ^{AB}	**0.002***
Mean GWG T1, Kg	1.29±2.49	1.55±4.19	3.02±5.66	**0.011***
Mean GWG T2, Kg	4.29±3.00	5.43±3.62	5.52±2.74	0.059
Mean GWG T3, Kg	6.22±3.3.69	7.10±3.78	7.64±3.85	0.100
Adherence to the LMeD T1	16.6±4.2	17.5±3.9	18.0±3.0	0.205
Adherence to the LMeD T2	16.5±4.2 ^{A}	18.5±3.9 ^{B}	18.0±4.9 ^{AB}	**0.033***
Adherence to the LMeD T3	16.5±4.9 ^{A}	18.8±4.4 ^{B}	18.2±5.2 ^{AB}	**0.038***

Values are means ± standard deviation (SD) if normally distributed, median (min-max) if not normally distributed, or percentages (%) if binary, unless otherwise specified. One way ANOVA was conducted to test means across SGA, AGA and LGA. [a] Sedentary was defined as engaging in physical activity for less than 1-2 times/week for <20 min duration, active was defined as having greater than 1-2 times/week for >20 min duration. *Indicates significant associations between percentages across trimesters followed by post hoc Tukey's test. Abbreviations: FBG, fasting blood glucose, IGT, impaired glucose tolerance, T1, trimester 1, T2, trimester 2, T3, trimester 3, MAP, mean arterial pressure, GWG, gestational weight gain, LMeD, Lebanese Mediterranean diet

Table 5-5. Dietary Characteristics of Mothers Delivering SGA, AGA and LGA infants

Food Groups (# of Servings/d)	**SGA Mean±SD**	**AGA Mean±SD**	**LGA Mean±SD**	**p**
		Trimester 1		
Burghol, 1 cup	0.16±0.38	0.12±0.21	0.11±0.18	0.208
Dried Fruits, 1 ex	0.18±0.32	0.17±0.42	0.19±0.62	0.935
Legumes, 1 cup	0.27±0.41	0.24±0.27	0.28±0.44	0.392
Olive oil, 1 tsp	1.08±0.86	1.03±0.79	1.15±1.01	0.372
Eggs, 1 large	0.26±0.35^{A}	0.31±0.39^{A}	0.45±0.66^{B}	**0.007***
Starchy Vegetables, 1 cup	0.37±0.36	0.42±0.51	0.35±0.38	0.338
Dairy Products, 1 serv	2.14±1.57	2.44±1.63	2.16±1.26	0.125
Fruits, 1 piece	2.30±1.57	2.47±1.90	2.43±1.71	0.749
Vegetables, 1 cup	1.77±1.18	1.76±1.15	1.96±1.28	0.323
		Trimester 2		
Burghol, 1 cup	0.13±0.37	0.14±0.20	0.13±0.19	0.947
Dried Fruits, 1 ex	0.18±0.32	0.17±0.42	0.19±0.62	0.935
Legumes, 1 cup	0.23±0.40	0.28±0.35	0.29±0.31	0.470
Olive Oil, 1 tsp	0.90±0.93^{A}	1.06±0.79^{B}	1.28±1.13A^{B}	0.016*
Eggs, 1 large	0.20±0.33^{A}	0.35±0.47^{B}	0.48±0.64^{C}	**0.001***
Starchy Vegetables, 1 cup	0.33±0.42	0.37±0.37	0.34±0.36	0.668
Dairy products, 1 serv	1.07±1.23^{A}	1.65±1.29^{B}	1.52±1.21^{B}	0.001*
Fruits, 1 piece	1.97±1.59	2.43±1.81	2.31±1.63	0.114
Vegetables, 1 cup	1.46±1.33^{A}	1.94±1.39^{B}	2.07±1.62^{B}	**0.013***
		Trimester 3		
Burghol, 1 cup	0.14±0.39	0.13±0.19	0.11±0.18	0.714
[2] Dried Fruits, 1 ex	0.15±0.27	0.19±0.43	0.22±0.62	0.579
Legumes, 1 cup	0.23±0.41	0.26±0.27	0.27±0.31	0.580

Olive Oil, 1 tsp	1.03±1.12[A]	1.33±0.95[A]	1.51±1.25[B]	**0.009***
Eggs, 1 large	0.17±0.34[A]	0.35±0.43[B]	0.54±0.70[C]	**0.000***
Starchy Vegetables, 1 cup	0.27±0.31	0.33±0.37	0.29±0.35	0.311
[2] Dairy Products, 1 serv	1.00±1.33[A]	1.62±1.34[B]	1.40±1.21[B]	**0.001***
Fruits, 1 piece	1.98±1.70	2.20±1.52	1.92±1.37	0.182
Vegetables, 1 cup	1.28±1.25[A]	1.69±1.18[B]	1.71±1.35[B]	**0.025***

Sample size= 618. Values are means ± standard deviation (SD) if normally distributed, median (min, max, interquartile range) if not normally distributed, or percentages (%) if binary. [1]Food group intake was reported as the daily average number of servings consumed for each food group of the MeD. [2] 1 exchange (ex) for dried fruits (2tbsp raisins or cranberries, 2 pieces dates, 4 pieces apricots), and dairy products (1 cup milk or yogurt, 1 slice cheese or 2 tbsp labneh). *Indicates significant associations using McNemar test for proportions followed by post hoc Tukey's test. Abbreviations: tsp, teaspoon

Table 5-6. Linear Regression Describing Determinants of Infant Birth Weight-for-Gestational Age (%) In Pregnant Women in Lebanon (N=618)

Birth Weight for GA	**Unadjusted Model**			**Adjusted Model**		
	B	**SE**	**p**	**B**	**SE**	**p**
				Model 1-Maternal Characteristics		
Smoking T1, No/Yes	-6.011	9.183	0.513	-	-	NS
Smoking T2, No/Yes	-9.742	9.188	0.290	-	-	NS
Smoking T3, No/Yes	17.903	11.139	0.109	-	-	NS
Parity, #	3.683	1.112	**0.001***	3.935	0.018	**0.015**
Infant Sex, M=0/ F=1	-9.299	2.584	**0.000***	-9.208	0.042	**0.002**
Maternal Height (m)	32.332	20.890	0.122	-	-	NS
Family Hx DM (No, Yes)	0.009	0.051	0.863	-	-	NS
Hx Macrosomia (No, Yes)	19.054	7.045	**0.007***	19.686	7.032	**0.001**
Total GWG, kg	0.937	0.229	**0.000***	0.951	0.003	**0.000**
Pre-pregnancy BMI, kg/m^2	0.799	0.298	**0.007***	0.750	0.295	**0.011**
				Model 2-Maternal Health Factors		
Parity, #	3.495	1.160	**0.003***	3.701	1.104	**0.001**
Infant Sex, M=0/F=1	-10.706	2.644	**0.000 ***	-9.841	2.540	**0.000**
Hx Macrosomia (No, Yes)	21.067	7.165	**0.003***	19.736	7.014	**0.005**
Total GWG, Kg	0.983	0.234	**0.000***	0.960	0.225	**0.000**
Pre-pregnancy BMI, kg/m^2	0.825	0.308	**0.008***	0.713	0.291	**0.015**
GDM, No/ Yes	1.201	3.201	0.366	-	-	NS
FBG≥100 mg/dl T1	-0.049	0.072	0.500	-	-	NS
FBG≥100 mg/dl T3	-0.004	0.054	0.947	-	-	NS
MAP T1, mm Hg	-0.002	0.002	0.467	-	-	NS
MAP T2, mm Hg	0.001	0.002	0.712	-	-	NS
MAP T3, mm Hg	-0.001	0.002	0.753	-	-	NS
Pulse Pressure T1, mm Hg	-0.001	0.003	0.662	-	-	NS
Pulse Pressure T2, mm Hg	0.413	0.188	**0.029***	0.397	0.152	**0.009**
Pulse Pressure T3, mm Hg	-0.369	0.165	0.026*	-0.491	0.144	**0.001**
PSQI T1	-0.004	0.007	0.618	-	-	NS
PSQI T2	1.819	0.625	**0.004***	1.169	0.380	**0.002**
PSQI T3	0.009	0.009	0.365	-	-	NS
Adherence to the LMeD T1	0.015	0.038	0.702	-	-	NS
Adherence to the LMeD T2	-0.017	0.042	0.683	-	-	NS
Adherence to the LMeD T3	-0.006	0.044	0.890	-	-	NS
				Model 3- Individual Food Groups		
Parity, #	--	--	--	4.017	1.096	**0.000**
Infant Sex, M=0/F=1	--	--	--	-8.990	2.525	**0.000**
Hx Macrosomia, No=0/Yes=1	--	--	--	15.466	6.574	**0.019**
Total GWG, Kg	--	--	--	0.765	0.216	**0.000**
PSQI T2	--	--	--	1.088	0.379	**0.004**
Olive Oil T3, Serving/day	--	--	--	2.898	1.279	**0.024**
Parity, #	--	--	--	3.934	1.095	**0.000**
Infant Sex, M=0/F=1	--	--	--	-9.169	2.513	**0.000**
Hx Macrosomia, No=0/Yes=1	--	--	--	16.186	6.518	**0.013**

Total GWG, Kg	--	--	--	3.934	1.095	**0.000**
PSQI T2	--	--	--	1.171	0.379	**0.002**
Dairy Products T1, Serving/day	--	--	--	-3.132	0.955	**0.001**
Dairy Products T2, Serving/day	--	--	--	2.656	1.201	**0.027**
Parity, #	--	--	--	3.738	1.102	**0.001**
Infant Sex, M=0/F=1	--	--	--	-9.119	2.518	**0.000**
Hx Macrosomia, No=/Yes=1	--	--	--	13.814	6.621	**0.037**
Total GWG, Kg	--	--	--	0.733	0.216	**0.001**
PSQI T2	--	--	--	1.131	0.378	**0.003**
Eggs T3, Serving/day	--	--	--	7.279	2.587	**0.005**

Model 1: The following covariates were entered: smoking T1, T2, T3, total GWG, pre-pregnancy BMI, parity, infant sex, maternal height in meters, family history of diabetes and previous macrosomia. Model 2: The significant variables after adjustment in model 1 were entered in model 2 with the following covariates: GDM, FBG≥100 mg/dl T1 and T3, pulse pressure at T1, T2 and T3, PSQI at T1, T2 and T3, and adherence to the MeD at T1, T2, and T3. Model 3 contains the significant variables from model 2 after adjustment and the significant food groups. Adjustment was done using the stepwise model. *Indicates significant associations. - Indicates non-significant associations. -- Values were not reported as unadjusted. Abbreviations: GWG, gestational weight gain, GDM, gestational diabetes mellitus, FBG, fasting blood glucose, MAP, mean arterial pressure, PSQI, Pittsburgh Sleep Quality Index, LMeD, Lebanese Mediterranean diet, NS, non-significant.

Table 5-7. Linear Regression Describing Determinants of AGA Infants in Pregnant Women in Lebanon (N=447)

	Unadjusted Model			Adjusted Model		
AGA	**B**	**SE**	**p**	**B**	**SE**	**p**
				Model 1-Maternal Characteristics		
Smoking T1, No/Yes	-2.891	7.446	0.698	-	-	NS
Smoking T2, No, Yes	-10.017	7.452	0.180	-	-	NS
Smoking T3, No, Yes	12.845	9.192	0.163	-	-	NS
Parity, #	2.924	1.191	**0.015***	3.220	1.160	**0.006**
Infant sex, M=0/F=1	-4.378	2.327	0.061	-	-	NS
Maternal Height (m)	8.991	19.670	0.648	-	-	NS
Family Hx DM, No/Yes	0.831	2.767	0.764	-	-	NS
Hx Macrosomia, No/Yes	2.247	8.200	0.784	-	-	NS
Total GWG, Kg	0.336	0.215	0.118	-	-	NS
Pre-Pregnancy BMI, kg/m^2	0.302	0.283	0.285	-	-	NS
				Model 2-Maternal Health Factors		
Parity, #	3.338	1.272	**0.009***	3.291	1.156	**0.005**
FBG≥100 T1, mg/dl	2.270	4.064	0.577	-	-	NS
FBG≥100 T3, mg/dl	2.189	2.976	0.462	-	-	NS
GDM, No/Yes	-7.008	6.291	0.266	-	-	NS
MAP T1, mm Hg	0.020	0.127	0.872	-	-	NS
MAP T2, mm Hg	0.068	0.146	0.644	-	-	NS
MAP T3, mm Hg	-0.020	0.121	0.870	-	-	NS
Pulse Pressure T1, mm Hg	-0.103	0.169	0.543	-	-	NS
Pulse Pressure T2, mm Hg	0.223	0.205	0.279	-	-	NS
Pulse Pressure T3, mm Hg	-0.062	0.146	0.670	-	-	NS
PSQI T1, mm Hg	-0.227	0.405	0.575	-	-	NS
PSQI T2, mm Hg	1.462	0.584	**0.013***	0.674	0.336	**0.045**
PSQI T3, mm Hg	-0.818	0.523	0.118	-	-	NS
Adherence to the LMeD T1	-3.652	2.158	0.091	-	-	NS
Adherence to the LMeD T2	0.065	2.297	0.977	-	-	NS
Adherence to the LMeD T3	3.443	2.455	0.161	-	-	NS
				Model 3- Individual Food Groups		
Parity, #	--	--	--	3.726	1.168	**0.002**
Dried Fruits T3, Serving/day	--	--	--	6.324	2.564	**0.014**
Adherence to the LMeD T1	--	--	--	-3.807	1.843	**0.040**
Parity, #	--	--	--	3.293	1.150	**0.004**
Dairy Products T1, Serving/day	--	--	--	-1.892	0.690	**0.006**

Model 1: The following covariates were entered: smoking T3, total GWG, pre-pregnancy BMI, parity, infant sex, maternal height in meters and family history of diabetes and previous macrosomia. Model 2: The significant variable after adjustment in model 1 was entered in model 2 with the following covariates: GDM, FBG≥100 mg/dl T1 and T3, pulse pressure at T1, T2 and T3, PSQI at T1, T2 and T3, and adherence to the LMeD at T1, T2, and T3. Model 3 contains the significant variables from model 2 after adjustment and the significant food groups. Adjustment was done using the Stepwise Model. *Indicates significant associations. – Indicates non-significant associations. – Values were not reported in the unadjusted model. Abbreviations: GWG, gestational weight gain, GDM, gestational diabetes mellitus, FBG, fasting blood glucose, MAP, mean arterial pressure, PSQI, Pittsburgh Sleep Quality Index, LMeD, Lebanese Mediterranean diet, NS, non-significant.

Table 5-8. Multiple Logistic Regression Describing Likelihood of SGA to AGA Infants in Pregnant Women in Lebanon (N=520)

	Unadjusted Model			Adjusted Model		
SGA	**OR**	**CI**	**p**	**OR**	**CI**	**p**
			[1] **Model 1-Maternal Characteristics**			
Parity, #	1.103	0.760-1.600	0.606	-	-	NS
Smoking T1, No/Yes	0.627	0.060-6.353	0.696	-	-	NS
Smoking T2, No/Yes	0.107	0.004-3.523	0.212	-	-	NS
Smoking T3, No/Yes	6.747	0.144-225.818	0.326	-	-	NS
Total GWG, kg	0.894	0.329-0.781	**0.001***	0.511	0.337-0.774	**0.002**
Pre-Pregnancy BMI, kg/m^2	0.109	0.657-1.895	0.686	-	-	NS
Infant sex, M=0/F=1	1.438	0.734-2.674	0.272	-	-	NS
Maternal Height (m)	6.090	0.024-1411.08	0.523	-	-	NS
Family Hx DM, No/Yes	0.874	0.371-2.085	0.761	-	-	NS
FBG≥100 mg/dl	0.793	0.334-1.949	0.607	-	-	NS
GDM, No/Yes	1.613	0.321-10.242	0.591	-	-	NS
MAP T1, mm Hg	0.994	0.963-1.030	0.715	-	-	NS
MAP T2, mm Hg	0.966	0.933-1.004	0.064	0.958	0.928-0.990	**0.009**
MAP T3, mm Hg	1.047	1.015-1.078	**0.004***	1.045	1.017-1.073	**0.001**
Pulse Pressure T1, mm Hg	0.993	0.951-1.042	0.756	-	-	NS
Pulse Pressure T2, mm Hg	0.978	0.927-1.033	0.447	-	-	NS
Pulse Pressure T3, mm Hg	1.039	1.002-1.076	**0.037***	**-**	**-**	**NS**
PSQI T1	1.023	0.915-1.129	0.667	-	-	NS
PSQI T2	1.048	0.922-1.199	0.489	-	-	NS
PSQI T3	0.987	0.864-1.123	0.847	-	-	NS
Adherence to the LMeD T1	1.205	0.661-2.258	0.554	-	-	NS
Adherence to the LMeD T2	0.771	0.377-1.361	0.434	-	-	NS
Adherence to the LMeD T3	1.001	0.536-2.088	0.998	-	-	NS
			Model 2- Individual Food Groups			
Total GWG, Kg	0.430	0.267-0.695	**0.001***	0.483	0.315-0.740	**0.001**
MAP T2, mm Hg	0.948	0.909-0.988	**0.012***	0.956	0.925-0.987	**0.007**
MAP T3, mm Hg	1.047	1.012-1.084	**0.009***	1.049	1.020-1.079	**0.001**
Burghol T1, Serving/day	16.329	1.440-185.213	**0.024***	3.130	1.145-8.560	**0.026**

Model 1: The following covariates were entered family history of diabetes, smoking at T1, T2 and T3, total GWG, pre-pregnancy BMI, infant sex, maternal height in meters, FBG≥100 mg/dl, GDM, MAP at T1, T2 and T3, pulse pressure at T1, T2 and T3, PSQI at T1, T2 and T3, and adherence to the LMeD at T1, T2 and T3. Model 2: The significant variables in model 1 after adjustment were entered along with individual food groups. Only significant food group models were represented. Adjustment was done using Forward Wald. *Indicates significant associations. – Indicates non-significant associations. Abbreviations: GWG, gestational weight gain, GDM, gestational diabetes mellitus, FBG, fasting blood glucose, MAP, mean arterial pressure, PSQI, Pittsburgh Sleep Quality Index, LMeD, Lebanese Mediterranean diet, NS, non-significant

Table 5-9. Multiple Logistic Regression Describing Likelihood of LGA to AGA Infants in Pregnant Women in Lebanon (N=458)

	Unadjusted Model			Adjusted Model		
LGA	**OR**	**CI**	**p**	**OR**	**CI**	**p**
			[1] **Model 1-Maternal Characteristics**			
Parity, #	1.369	1.077-1.740	**0.010***	1.452	1.165-1.811	**0.001**
Smoking T1, No/Yes	0.459	0.049-4.277	0.494	-	-	NS
Smoking T2, No/Yes	0.366	0.028-4.699	0.440	-	-	NS
Smoking T3, No/Yes	5.809	0.231-146.243	0.285	-	-	NS
Infant sex, M=0/F=1	0.340	0.173-0.670	**0.002***	0.314	0.166-0.594	**0.000**
Maternal Height, m	51.173	0.414-6455.58	0.109	-	-	NS
Family Hx DM, No/Yes	0.489	0.218-1.098	0.083	0.456	0.215-0.968	**0.041**
Hx Macrosomia, No/Yes	8.482	2.533-28.407	**0.001***	6.447	2.145-19.376	**0.001**
Total GWG, Kg	1.220	0.877-1.817	0.290	-	-	NS
Pre-pregnancy BMI, Kg/m^2	1.080	0.735-1.587	0.695	-	-	NS
FBG≥100, mg/dl	0.736	0.419-1.672	0.396	-	-	NS
GDM, No/Yes	1.687	0.509-6.164	0.411	-	-	NS
MAP T1, mm Hg	0.972	0.946-1.000	0.051	-	-	NS
MAP T2, mm Hg	0.972	0.947-1.005	0.069	-	-	NS
MAP T3, mm Hg	1.039	1.007-1.072	**0.016***	**-**	**-**	**NS**
Pulse Pressure T1, mm Hg	0.976	0.931-1.014	0.272	0.977	0.961-0.994	**0.007**
Pulse Pressure T2, mm Hg	1.017	0.982-1.060	0.425	-	-	NS
Pulse Pressure T3, mm Hg	0.995	0.955-1.035	0.801	-	-	NS
PSQI T1	1.022	0.937-1.121	0.646	-	-	NS
PSQI T2	1.036	0.920-1.164	0.563	-	-	NS
PSQI T3	1.045	0.937-1.171	0.443	1.081	1.000-1.167	**0.049**
Adherence to the LMeD T1	1.524	0.852-2.380	0.117	-	-	NS
Adherence to the LMeD T2	0.624	0.387-1.119	0.086	-	-	NS
Adherence to the LMeD T3	1.070	0.639-1.923	0.811	-	-	NS
			Model 2-Individual Food Groups			
Parity, #	1.367	1.074-1.740	**0.011***	1.498	1.208-1.859	**0.000**
Infant sex, M=0/F=1	0.327	0.165-0.650	**0.001***	0.352	0.187-0.663	**0.001**
Hx Macrosomia, No/Yes	8.321	2.433-28.460	**0.001***	6.145	2.231-16.928	**0.000**
MAP T3, mm Hg	1.036	1.004-1.069	**0.028***	-	-	NS
Olive oil T2, Serving/day	1.327	0.802-2.194	0.271	1.447	1.094-1.913	**0.010**

Model 1: The following covariates were entered family history of diabetes, previous macrosomia, smoking at T1, T2 and T3, total GWG, pre-pregnancy BMI, infant sex, maternal height in meters, FBG≥100 mg/dl, GDM, MAP at T1, T2 and T3, pulse pressure at T1, T2 and T3, PSQI at T1, T2 and T3, and adherence to the LMeD at T1, T2 and T3. Model 2: The significant variables in model 1 after adjustment were entered along with individual food groups. Only significant food group models were represented. Adjustment was done using the Forward Wald. *Indicates significant associations. – Indicates non-significant associations. Abbreviations: GWG, gestational weight gain, GDM, gestational diabetes mellitus, FBG, fasting blood glucose, MAP, mean arterial pressure, PSQI, Pittsburgh Sleep Quality Index, LMeD, Lebanese Mediterranean diet, NS, non-significant

Chapter VI

General Discussion

6.1 Novel Findings

This dissertation studied the association between the LMeD, psychosocial factors as well as socio-demographic, medical and weight factors at three different time points during pregnancy on blood pressure measurements including MAP, as well as on diagnosis of GDM and IGT, and on infant outcomes including birth of SGA, AGA and LGA infants. This allowed us to investigate the exposure in relation to the outcome measured per trimester and to specifically answer the following questions: Whether adherence to the LMeD is associated with each of eMAP, IGT, GDM, SGA, AGA and LGA, and whether other factors including medical, psychosocial and weight variables are associated with the outcomes.

The three studies in this dissertation have contributed several novel observations to the literature. First, the findings demonstrated that although the prevalence of elevated SBP and DBP was low in all trimesters (<4%), eMAP emerged as important with more than 40% of women having eMAP in the 2^{nd} and 3^{rd} trimester, which has been associated with the emergence of HDPs during pregnancy (Gonzalez-Fernandez et al., 2020). Moreover, even though GDM diagnosis was low (5.6%) compared to other Mediterranean countries (8-32%) (Karamanos et al., 2014), the prevalence of IGT was high in T1 (12.4%) and T3 (26.5%) which was comparable to Lebanon's IGT prevalence of 26% in the general population (Savona-Ventura et al., 2014). In addition, the incidence of SGA at 13% and LGA at 16% was identified among a national sample of pregnant women that was lacking in the different regions of Lebanon. SGA prevalence is comparable to global estimates of developed countries (Lee et al., 2017; Osuchukwu & Reed,

2023) and LGA prevalence is comparable to global and LMIC estimates (Falcão et al., 2021; Hocquette et al., 2021). Second, our data suggests that specific elements of the LMeD including olive oil, dried fruits, burghol, legumes and vegetables may be more important to protect against adverse pregnancy outcomes than the overall adherence to the LMeD. A specific recommendation of 1 tsp olive oil/day and ≥0.3 servings/day of dried fruits was identified for lowering eMAP risk. In contrast, no specific recommendations can be inferred with regards to the daily number of servings that should be consumed from burghol, legumes, olive oil and vegetables to decrease IGT and LGA risk. However, these findings provide the initial evidence for further investigations to identify the optimal daily consumption of specific food groups of the LMeD through randomized clinical trials and larger cohort studies.

Important Features of Study Design and Analyses

National Cohort Study in Pregnant Women

This was the first investigation in Lebanon to design a national prospective cohort study on pregnant women in partnership with Lebanese American University and Notre Dame University-Louaize in collaboration with McGill University. The two universities in Lebanon implemented the study and provided training to their Senior and/or Masters students for data collection and data entry. This allowed us to engage well-trained individuals to assist in the recruitment and execution of the study across all the regions of Lebanon.

Moreover, the program directors at the two universities supervised the students' work and oversaw the implementation of the study design. First, a simple random sampling was conducted using SPSS across 732 clinics across the different regions of Lebanon, and a total of 20 clinics were selected. Different students were assigned to specific clinics in the various regions to recruit an average of 30 participants per clinic, administer the questionnaires and collect medical information from chart reviews. This work allowed undergraduate and graduate students to translate theoretical course material into practical work after extensive training that was led by the program directors and the principal investigator.

Hierarchical Modeling

Recognizing that several maternal factors had previously been associated with our major outcomes including HDPs, GDM, IGT and infant birth outcomes, we designed a study to assess these factors using the hierarchical modelling approach. This approach was unique because it tested the associations between the variables using three subgroups or levels of maternal characteristics on our principal outcomes MAP, IGT, GDM and SGA, LGA. In level 1, maternal factors including socio-demographic data (place of residence, occupation), weight gain and pre-pregnancy BMI, psychosocial factors and medical history were entered since prior evidence demonstrated consistent associations with each of the major outcomes including HDPs (Luger & Kight, 2022), eMAP (Wright et al., 2015), GDM (Karasneh et al., 2021), IGT (Nicolosi et al., 2020), and birth of SGA, and LGA (Ögge et al., 2022). Education was not assessed because more than 75% of the women were college educated nor was household income used since more than 25% either did not know or did not want to disclose this information. Household income provided sufficient amount of missing data to drop sample size in the regression below N=570. In level 2, adherence to the LMeD (main exposure variable) which was assessed using the index developed by Naja et al. (2015) for the Lebanese pregnant population was entered to study its association with each of the major outcomes. Significant variables in level one were retained in level 2. In level 3, individual food groups of the LMeD were entered to explore the distinct association of specific food elements on each of the study outcomes as they were shown in the literature to modify the risk of adverse pregnancy outcomes (Assaf-Balut et al., 2017; Martínez-Galiano et al., 2018; Zhao et al., 2021).

Upon adding LMeD and food groups in the 2nd and 3rd layer, we were able to identify 1st layer associations that became either non-significant, or associations that became weaker or stronger which supports our hypothesis that pregnancy risk factors are multi-factorial. In study II and III, the same hierarchical modeling approach was applied however some maternal characteristics were entered or removed depending on their significance with the outcome or exposure in the bivariate analyses.

The novelty of this approach is that it uncovered associations that may have not been identified in traditional logistic regression approach. For instance, place of residence was identified as a significant predictor of eMAP along with pre-pregnancy BMI, olive oil, dried fruits, and adherence to the LMeD. On the other hand, GWG, burghol, legumes and vegetable were associated with IGT, and MAP also predicted GDM risk. MAP and burghol were associated with SGA risk, and olive oil in addition to parity and previous macrosomia were associated with LGA risk.

Place of Residence

MAP significantly varied across the different regions of Lebanon, and place of residence, however it was not associated with IGT, GDM, SGA and LGA risk. Living in Beirut was associated with eMAP across all trimesters compared to South Lebanon, whereas living in Mount Lebanon showed a greater risk of eMAP only in the 1st trimester compared to South Lebanon. This may arise because each governorate has unique and specific socio-demographic characteristics and culture. For instance, Beirut is a governorate and the capital of Lebanon and is considered the most important region in Lebanon because of its political, economic, cultural and social activity. Mount Lebanon has the greatest population density among the governorates and has mostly urban regions. It includes the highest percentage of industrial establishments in Lebanon and most of these establishments service the food industries sector.

Moreover, people residing in Beirut and Mount Lebanon are more likely to follow a more Western diet than those living in other governorates (Hwalla et al., 2021; Nasreddine et al., 2006). This was supported in the analysis where a significant difference was found for the adherence to the LMeD among the different regions in Lebanon where Beirut had the least adherence in all trimesters. Bekaa on the other hand consists of three districts Zahle (urban), Rachaya and West Bekaa, the latter being mostly rural areas. Akkar is Lebanon's poorest region and has the country's highest illiteracy rate and suffers from lack of basic infrastructure and services. Furthermore, the highest food insecurity has been reported among Akkar and Baalbeck hermel residents (part of Bekaa) (Hoteit & Al Jawaldeh, 2021). South Lebanon on the other hand has few mixed rural areas concentrated around 3 main cities with a majority of natural areas and agricultural lands. A low adherence to the LMeD was also identified in South Lebanon compared to the other governorates in the three trimesters. In general, the overall assessment showed that pregnant women in Lebanon had an average LMeD score of 17.4 (range between 9-27) which allowed us to assess low and high adherence in the Lebanese population of pregnant women.

Pre-pregnancy BMI and Gestational Weight Gain

Pre-pregnancy, approximately 33% of the women were overweight or obese, but pre-pregnancy BMI was not associated with IGT, GDM and infant birth outcomes SGA, and AGA. In our study, which is the first in the Middle East to assess predictors of eMAP, we observed a significant association between higher pre-pregnancy BMI and eMAP in trimester 2 and 3. This is in contrast to previous studies that explored associations between pre-pregnancy BMI and HDPs (Hinkosa et al., 2020; Ren et al., 2018; Shubham Prasad, 2022; Zhao et al., 2021).

In this study the majority of the women exceeded weight gain recommendations in all trimesters particularly among normal and overweight women who had the greatest weight gain compared to other pre-pregnancy BMI categories. Furthermore, all women who exceeded weight gain were at higher risk of having adverse pregnancy outcomes. Obese women also had high GWG in the 2nd and 3rd trimester. Lowering weight gain was most important in the second and third trimester to reduce risk of developing GDM and IGT, while higher total GWG decreased SGA risk and increased infant birth weight for gestational age.

Adherence to LMeD

Studies on associations between MeD and pregnancy outcomes are lacking in the Middle East, especially Lebanon. A study by Karam et al. (2006) reported that 60.8% of adults had a low adherence to the MeD in the general population, while no study evaluated adherence among pregnant females or women of child-bearing age in Lebanon. Our study was the first national study in Lebanon among pregnant women of different regions that assessed the adherence to the Lebanese MeD using an index developed by Naja et al. 2015 revealing that a medium adherence among pregnant women.

Association between LMeD and MAP

Previous research in Mediterranean countries reported associations between MeD and HDPs including gestational hypertension, pre-eclampsia and elevated SBP and/or DBP among pregnant women but neglected MAP which is an important indicator of early risk of HDPs (Assaf-Balut et al., 2019; Di Renzo et al., 2022; Savitri et al., 2016; Zaragoza-Martí et al., 2022). However, LMeD was not associated with other BP measurements including SBP and/or DBP due to their low prevalence (<4%) in the population. Our results highlight the importance of adherence to LMeD in the 2nd trimester as it was associated with lower MAP and birth of AGA infants.

The MeD diet may contribute to improved oxidative stress and placental endothelial cell function as seen in previous cohort studies (García-Montero et al., 2023; Minhas et al., 2022) and randomized controlled trials (Assaf-Balut et al., 2017; García-Montero et al., 2023; Shannon et al., 2020). The MeD can also lower cardiovascular disease (CVD) risk factors such as overweight, dyslipidemia, inflammation, high blood glucose levels, and diabetes (Benhammou et al., 2016; Bonaccio et al., 2013). Despite that LMeD decreased eMAP risk in the 2nd trimester, it did not lower eMAP in the 1st and 3rd trimester which suggests that adherence to this diet may not prevent the oxidative stress which may be associated with a high pre-pregnancy BMI. Others have shown an association between pre-pregnancy BMI and MAP (Guedes-Martins et al., 2015;

Omaña-Guzmán et al., 2021). During pregnancy in particular, endothelial dysfunction can occur in normotensive women, and maternal obesity can augment the physiologic and metabolic changes that occur during pregnancy leading to higher BP including MAP (Ramsay et al., 2002).

Adherence to the LMeD and IGT/GDM

Adherence to the LMeD did not differ among pregnant women with IGT or normal FBG and was not associated with decreasing IGT risk in any trimester, but other factors were including higher stress and higher GWG which may have implications for clinical practice. Additionally, although various studies demonstrated an association between MeD and GDM, our findings showed that LMeD did not protect against GDM risk, but that other factors were including family history of diabetes, high GWG and MAP.

Association between LMeD and Infant Birth Outcomes

Adherence to LMeD was higher among women who delivered AGA infants compared to SGA and LGA infants. In contrast, adherence did not decrease the odds of SGA or LGA which suggests that other factors are contributing to this risk. For instance, high MAP and high burghol intake increased the likelihood of SGA, and greater parity and previous macrosomia increased the likelihood of LGA among the study population. In contrast to our study, previous research demonstrated an association between adherence to the MeD and lower SGA risk (Assaf-Balut et al., 2019; Díaz-López et al., 2022; Martínez-Galiano et al., 2018; Yisahak et al., 2021) and higher infant birth weight (Parlapani et al., 2019; Timmermans et al., 2012). This reinforces that the LMeD supplies essential nutrients which are important to the fetus and hence can improve their growth (Yisahak et al., 2021). Based on our study findings, LMeD was associated with delivering normal birth weight infants, but did not decrease SGA or LGA risk.

From these observations, we can infer that adhering to LMeD might not be sufficient alone to lower risk of eMAP, IGT, GDM, and birth of SGA and LGA infants in the presence of maternal risk factors including high GWG, overweight and obesity, medical history, health and psychosocial factors.

Food Groups of LMeD

Food Groups and MAP

Several components of the MeD can ameliorate maternal risk factors and are associated with improving pregnancy outcomes (Zaragoza-Martí et al., 2022). In our study, intake of LMeD food groups protected against specific maternal-fetal outcomes. For instance, 1 Tsp olive oil in T1 and ≥0.3 cups of dried fruits in T2 decreased eMAP risk. The high content of mono-unsaturated fatty acids (anti-inflammatory) in olive oil and anti-oxidant polyphenols in dried fruits was shown to protect against oxidative stress (Schwingshackl et al., 2015). Furthermore, a previous study demonstrated that olive oil decreased the risk of cardiovascular diseases including high BP in pregnant women (Assaf-Ballut et al., 2017). In our study, consumption of olive oil within the 2^{nd} tertile (1 Tsp) lowered the risk of eMAP in the 1st trimester which suggests an optimal daily consumption of 1 Tsp olive oil. In addition, consumption of dried fruits within the third tertile (≥0.3 servings/day) in the 2nd trimester was associated with lower eMAP risk, since dried fruits can limit the oxidative stress for the placenta which could be related to a low BP (Assaf-Ballut et al., 2019).

Food Groups and IGT

Burghol and legumes in T1 increased IGT risk while vegetables in T3 decreased IGT risk. Burghol (a type of cracked wheat) and legumes are high sources of carbohydrates that may lead to impaired glycemia especially during pregnancy (Dorheim et al., 2012). Although it is recommended that women diagnosed with GDM or elevated BG to consume complex carbohydrates including legumes and whole grains, however the total amount of carbohydrate should not exceed 40-45% of their total caloric intake (Pinzón et al., 2012) and foods with high glycemic load including burghol can negatively affect glycemia (Dorheim et al., 2012; Timmermans et al., 2012). Therefore, it is important to educate patients on the type and amount of carbohydrate foods that should be consumed during pregnancy to protect against impaired fasting blood glucose.

In addition, even though the majority of women had a high GWG in the 3rd trimester, vegetable intake lowered the risk of impaired FBG in T3. Vegetable foods are low in carbohydrate and rich in antioxidants, fibers and low in saturated fats which can reduce inflammation and improve glycemia (Abalos et al., 2014). A daily vegetable consumption of ≥2 cups may be beneficial which was reported in women having a healthy glucose tolerance test, while those in the IGT group were consuming an average of 1.7 cups per day.

Food Groups and SGA/LGA

With respect to infant birth outcomes, high olive oil in T2 increased LGA risk. Even though olive oil can protect against placental oxidation and enhance fetal growth leading to higher infant birth weight (Assaf-Balut et al., 2017), but the greater risk of LGA may have been confounded by the presence of other maternal factors among these women including previous macrosomia and family history of diabetes. On the other hand, burghol in T1 was shown to increase the odds of SGA infants. To further explore the relationship between burghol and SGA, we compared protein intake across the three groups: SGA, AGA and LGA. Our exploration revealed that total protein intake did not differ between women who delivered SGA, AGA and LGA.

Psychosocial Factors

Perceived stress and sleep quality were significantly different across trimesters and worsened in trimester 3 compared to trimester 1. This was also seen in other studies where stress and sleep quality deteriorated as pregnancy progressed (Tang et al., 2021). However, associations in the present study were only seen in trimester 1. For instance, in T1, poor sleep quality was associated with eMAP, and high perceived stress was associated with IGT. This can be explained given that poor sleep and high stress can increase cortisol levels, promote inflammation, and lead to insulin resistance (OuYang et al., 2021). A similar study by Tang et al. (2021) also reported first trimester poor sleep being linked to higher BP in pregnancy. OuYang et al., 2021 reported that stress diagnosed early in pregnancy suggests a previous history of stress and anxiety and is associated with increased GDM risk. This indicates that early counseling is necessary to screen for the presence of psychosocial factors including stress and poor sleep among pregnant women as they may be important targets for intervention. Additionally, these women should be educated on techniques to reduce stress and improve sleep quality. Early screening is also recommended for women with high risk factors such as family history of diabetes, previous macrosomia, elevated SBP and/or DBP, eMAP, and high pre-pregnancy BMI.

6.2 Strengths and Limitations

Strengths

Cohort studies are strong study designs as they allow the development of the outcome over a period of time, however they are also prone to loss-to-follow up. However, in the present study we added 20% to the original sample size initially to control for loss-to-follow up which was less <6%. Moreover, each of the questionnaires used including PSQI, EPDS, PSS, and adherence to the LMeD have been previously validated in either a Lebanese or Arabic pregnant population which allows the direct comparison of our results to other studies. The LMeD is a valid tool that has been developed based on previous factor analysis done on a national sample of Lebanese adults. Among 30 food groups, 9 food groups repeatedly loaded high on this pattern (Naja et al., 2011). Correlation between LMeD and 5 other European indices that are used for pregnancy was done to assess for the validity of this tool, and the findings demonstrated a good correlation between them using Kappa statistics and percent agreement between scores' tertile distribution (Naja et al., 2015).

Limitations

Several limitations need to be acknowledged. All questionnaire data in the current study were obtained by maternal self-reporting, which may be subject to misreporting and recall bias. Moreover, given that the validated LMeD tool assessed the specific consumption of the Lebanese population and includes food groups relevant to their traditional diet and can be used for pregnant women, this makes the study findings only relevant to the Lebanese or Middle Eastern population rather than other Mediterranean countries. The LMeD index also does not assess consumption of food items such as sweets, pizza, burgers, French fries, sandwiches, total amount of processed food intake and total caloric intake although they might have a contribution on certain risk factors and outcomes such as obesity, GDM, high BP and infant birth outcomes. Furthermore, pre-pregnancy nutrition was not assessed in this study even though previous literature demonstrated that it is a dominant predictor of pregnancy outcomes (Brown et al., 2001; Zaragoza-Martí et al., 2022).

With respect to maternal variables that were collected, PA was not included in the final analyses since more than 90% of the women were sedentary and there was no variability between the two groups (sedentary and active). Moreover, we were unable to collect food security from all women which did not allow to assess its relationship with dietary intake, BMI and weight gain during pregnancy. A previous study in Lebanon identified a high prevalence of food insecurity of mothers from urban Lebanese household; it has been reported that mothers from food insecure households had a high risk of inadequate dietary intake and obesity (Jomaa et al., 2016). Level of income was not used in the analyses as well since more than 30% of the women did not know or did not want to disclose this information.

Despite the strong study design, however causality cannot be proven in cohort studies. The associations that were reported are important targets for potential interventions in clinical settings to screen for women with risk factors and counsel them on dietary and behavioral changes. Moreover, these associations serve as the basis for the development of randomized controlled trials that may be conducted to establish causality and directionality.

Finally, a lower percentage of women were recruited from rural areas given the small population density and low number of obstetric clinics found in these regions compared to urban ones. Future studies should focus on rural areas which may further our understanding on the observed associations and differences.

6.3 Recommendations for Future Research

The findings of this study provide several possibilities for future work. Research has found that dietary quality in pregnancy is poor and may even decrease over the course of pregnancy (Juul et al., 2021), which was observed in this study with a greater percentage of low adherence in the 3rd trimester compared to early pregnancy. In Lebanon, a recent study showed that the majority of pregnant women adhered to a Neo-Mediterranean diet that is classified by consumption of mainly proteins from lean meat sources, such as poultry and fish, eggs, and dairy, as well as fruits, vegetables, legumes and seeds (Papazian et al., 2022). A more recent study also aimed at developing national dietary and lifestyle guidelines specific to Lebanese pregnant women which will be established in 2024 while taking into consideration scientific evidence and long-term health consequences (Naja et al., 2021). These guidelines consisted of 12 themes including GWG, diet diversity (incorporation of the LMeD as the principal diet), supplementation of folic acid, iron, omega 3 fatty acids, vitamin D and calcium, limiting harmful foods, alcohol and smoking, addressing food safety, hydration, physical activity, breastfeeding, religious fasting, well-being and nutrition resilience. Their objective is to incorporate these guidelines during prenatal counseling (Naja et al., 2021). Based on our findings, we can contribute to formulation of these recommendations.

Upcoming research could also explore dietary patterns across Lebanese pregnant women to see if a Neo-Mediterranean diet can improve maternal-infant outcomes more than a traditional LMeD. Given that the Neo Mediterranean diet includes lean meat sources that were lacking in the LMeD, we could assess whether consuming the meat, fish and poultry food groups is associated with lowering or increasing risk of adverse pregnancy outcomes versus the traditional LMeD that includes only eggs and dairy products. The association between ultra-processed food intake and pregnancy outcomes which was demonstrated in several studies (Paula et al., 2022; Puig-Vallverdú et al., 2022) is an important target to assess in future studies as well.

It is also worthy to note that our population has a low prevalence of HDPs and GDM which may be confounded by specific socio-demographic factors including high education level and possibly a good compliance to the LMeD which may have contributed to lowering their overall risk. This also suggests that these women may be having a good adherence to the LMeD before pregnancy as well. A recent body of evidence has highlighted the importance of pre-pregnancy optimal nutrition as a target to improve pregnancy outcomes, however these studies are scarce in the Middle East and the majority of studies were done in high income countries (Wirawan et al., 2023). Therefore, maternal pre-pregnancy diet in relation to developing HDPs, GDM, IGT, and SGA, LGA should also be explored in future research.

6.4 Conclusion

In conclusion, adherence to LMeD may be recommended to lower eMAP during pregnancy and for the birth of AGA infants, but LMeD was not associated with decreasing IGT, GDM, and SGA or LGA risk. From our study given that the women were complying to the LMeD, this may have contributed to the low prevalence of SBP, DBP, HDPs and GDM in the population. Moreover, intakes of LMeD food groups protected against specific maternal-fetal outcomes: Dried fruits in T2 and olive oil in T1 decreased eMAP risk. Olive oil in T2 increased LGA risk. Burghol and legumes in T1 increased IGT risk and vegetables in T3 decreased IGT risk.

However, adhering to LMeD and its specific components might not be sufficient alone to lower risk of pregnancy outcomes. For instance, weight gain was most important in the second and third trimester to lower risk of developing GDM and IGT, while higher total GWG decreased SGA risk. Moreover, early screening is recommended for women with risk factors such as family history of diabetes, previous macrosomia, elevated SBP and/or DBP, eMAP, and high pre-pregnancy BMI. Finally, women with high stress and poor sleep should be counselled early during pregnancy on stress reduction and improving sleep quality.

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Appendices

Questionnaire

This study aims to evaluate the impact of dietary intake as well as psychosocial factors and physical activity during pregnancy on maternal and infant outcomes. This study is being conducted in various obstetric clinics in Lebanon by students from Notre Dame University, Lebanese American University and McGill University.
This questionnaire is divided into seven parts. It explores your socio-demographic characteristics, stress, sleep, depression, diet, physical activity, and advice on diet and lifestyle during pregnancy. Participation in this research is entirely voluntary and withdrawal can be made without any penalty. Information collected during this study is kept confidential and anonymous. The average time to complete the questionnaire is 15 minutes.
Thank you for taking your time in completing this questionnaire.

Please choose the choice (s) that best matches you answer unless otherwise indicated

ID # __________________ Clinic: _________________

A) SOCIO-DEMOGRAPHIC CHARACTERISTICS

A1- Age in years ____________

A2- Highest level of education completed?
1. Less than Brevet
2. Brevet
3. High school
4. BSc. degree
5. Masters degree and beyond

A3- What was your pre-pregnancy weight? ______________________

A4- What is your current height (in cm)? ______________________

A5-Where do you live?
1. Mount Lebanon
2. Beirut
3. Akkar
4. Bekaa
5. North Lebanon
6. South Lebanon

7. Nabatiyeh

A6- Current monthly household income in Lebanese pounds

1. <1,000,000 LBP
2. 1,000,000-3,000,000 LBP
3. >3,000,000 LBP
4. No answer
5. Does not know

A7- What is your current occupation

1. Homemaker
2. Employee part time
3. Employee full time
4. Self-employed
5. Student

B) PERCEIVED STRESS SCALE

The questions in this scale ask you about your feelings and thoughts during the last month. In each case, you will be asked to indicate by circling how often you felt or thought a certain way.

0= Never 1= Almost Never 2= Sometimes 3= Fairly Often 4= Very Often

	Questions	**0**	**1**	**2**	**3**	**4**
1	In the last month, how often have you been upset because of something that happened unexpectedly?					
2	In the last month, how often have you felt that you were unable to control the important things in your life?					
3	In the last month, how often have you felt nervous and “stressed”?					
4	In the last month, how often have you felt confident about your ability to handle your personal problems?					
5	In the last month, how often you felt that things were going your way?					
6	In the last month, how often have you found that you could not cope with all the things that you had to do?					
7	In the last month, how often have you been able to control irritations in your life?					
8	In the last month how often have you felt that you were on the top of things?					
9	In the last month, how often have you been angered because of things that happened that were outside of your control?					
10	In the last month, how often have you felt difficulties were pilling up so high that you could not overcome them?					

C) THE PITTSBURGH SLEEP QUALITY INDEX (PSQI)

Instructions: The following questions relate to usual sleeping habits during the past month only. Your answers should indicate the most accurate reply for the majority of days and nights in the past month. Please answer all questions. During the past month,

1. When have you usually gone to bed? __________

2. How long (in minutes) has it taken to fall asleep each night? ________

3. When have you usually gotten up in the morning? _________

4. How many hours of actual sleep do you get at night? (This may be different that the amount of time you spend in bed) ___________

5. During the past month, how often have you had trouble sleeping because you…	Not during the past month (0)	Less than once per week (1)	Once or twice a week (2)	Three or + times/week (3)
a. Cannot get to sleep within 30 minutes				
b. Wake up in the middle of the night or early in the morning				
c. Have to get up to use the bathroom				
d. Cannot breathe comfortably				
e. Cough or snore loudly				
f. Feel too cold				
g. Feel too hot				
h. Have bad dreams				
i. Have pain				
j. Other reason (s), please describe, including how often you have had trouble sleeping because of this reason (s):				
6. During the past month, how often have you taken medicine (prescribed or "over the counter") to help you sleep?				
7. During the past month, how often have you had trouble staying awake while driving, eating meals, or engaging in social activities?				
8. During the past month, how much of a problem has it been for you to keep up enthusiasm to get things done?				
	Very good (0)	Fairly good (1)	Fairly bad (2)	Very bad (3)

9. During the past month, how would you rate your sleep quality overall?				

D) EDINBURG PERINATAL/POSTNATAL DEPRESSION SCALE (EPDS)

For use between 28-32 weeks in all pregnancies. Please mark next to the answer which comes closest to how you felt in the past 7 days- not just how you feel today

In the past 7 days:

	0. As much as I would always do	1. Not quite so much now	2. Definitely not so much now	3. Not at all
1. I have been able to laugh and see the funny side of things				
2. I have looked forward with enjoyment to things				
3. I have blamed myself unnecessarily when things go wrong				
4. I have been anxious or worried for no good reason				
5. I have felt scared or panicky for no good reason				
6. Things have been getting on top of me				
7. I have been so unhappy that I have had difficulty sleeping				
8. I have felt sad or miserable				
9. I have been so unhappy that I have been crying				
10. The thought of harming myself has occurred to me				

Score

E) FOOD FREQUENCY QUESTIONNAIRE

Think about your eating patterns during the past year while answering this questionnaire. Please indicate your usual intake of each of the following food items per Day, Week, or Month. <u>For example:</u> Apple. If you consume 3 apples daily, write 3 in the "Day" column, if you think you average 3 apples a week over the year, write 3 in the "Week" column. However, if you rarely consume a food, let's say once or twice a year, then tick below "Rarely/Never".
Please be precise as much as you can.
Remember! The accuracy of the study results depends on the accuracy of your answers.

Food item	Serving size	Day	Week	Month	Rarely / Never
Example: Apple	1 item		3		
Bread and Cereals					
1. White bread (1 slice)	1 slice (30g) Or ½ baguette or 3 toast				
2. Brown or whole wheat bread	1 slice Or ½ baguette Or 3 toast				
3. Breakfast cereals, regular/ bran	1 cup				
4. Rice, white, cooked	1 cup				
5. Pasta, plain, cooked	1 cup				
6. Wheat, whole, cooked / Bulgur	1 cup				
Dairy products					
7. Low-fat milk (2% fat)	1 cup				
8. Whole fat milk	1 cup				
9. Fat free / low fat yogurt	1 cup				
10. Whole fat yogurt	1 cup				
11. Cheese regular	1 slice (30g)				
12. Cheese low fat	1 slice (30g)				
13. Labneh	2 Tbsp				
Fruits & Juices					
14. Citrus Orange (1 item) / Grapefruit (1/2 item)	1 serving				
15. Deep Yellow or orange(Peach, plums, etc..)	1 item				
16. strawberry	1 cup				
17. grapes	1 cup				
18. Others: Banana, medium /Apple, fresh, small	1 item				
19. Dried fruits: raisins (2 Tbsp), dates (2), apricots (4)	1 serving				
20. Fresh fruit juice	1 cup				
21. Fruit drinks: canned/bottled	1 cup				
Vegetables					
22. Salad – green: lettuce, celery, green peppers, cucumber	1 cup				
23. Dark green or deep yellow vegetables (e.g.: spinach, hindbeh,, carrots , …)	1 cup				

24. Tomatoes, fresh, medium	1 item				
25. Corn / green peas, cooked	1 cup				
26. potato, baked / boiled / mashed	1 item				
27. Squash, summer (kussa), Eggplant /cooked	1 cup				
28. Cauliflower/ Cabbage/ broccoli	1 cup				
Meat & Alternates	**Serving size**	**Day**	**Week**	**Month**	**Rarely / Never**
29. Legumes: lentils, broad beans, chickpeas, etc., cooked	1 cup (200 grams)				
30. Nuts and seeds: peanuts, almonds, sunflower seeds, etc.	1 cup (150 grams)				
31. Red Meat	1 item (3 oz.) 90 grams				
32. Poultry	1 item (3 oz.) 90 grams				
33. Fish, (including Tuna)	1 serving (3 oz.) 90 grams				
34. Eggs, whole, large	1 item (50 grams)				
35. Organ Meats(Liver, kidneys, brain)	1 cup (90 grams)				
36. Luncheon meats: Mortadell, Jambon, salami, turkey, etc.	1 slice (20g)				
37. Sausages, makanek, hot dogs	1 item (30g)				
Fats and oils					
38. Oil: corn / sunflower / soy/olive	1 Tbsp				
39. Olives	1 item				
40. Butter/ghee	1 Tbsp				
41. Mayonnaise	1 Tbsp				
Sweets &Desserts					
42. Cake, Cookies ,Donut, muffin, croissant	1 item				
43. Ice cream	1 cup				
44. Chocolate bar	1 item				
45. Sugar, , honey, jam, molasses	1 Tbsp				
46. Arabic sweets, baklawa, maamoul, Knefeh	1 item (40g)				
Beverages					
47. Soft drinks, regular (1 can = 1½ cup)	1½ cup (11 fl. oz)				
48. Soft drinks, diet (1 can = 1½ cup)	1½ cup (11 fl. oz)				
49. Turkish coffee (1 small cup = ¼ cup)	¼ cup (2 fl oz)				
50. Coffee/Nescafe or tea	1 cup				
51. Hot chocolate or cocoa	1 cup				
52. Beer, regular (1 can = 1½ cup)	1½ cup				
53. Wine: red, white, or blush	½ cup (4 fl. oz)				
54. Liquor: whiskey, vodka, gin, rum	1/6 cup (1.5 fl oz.)				
Miscellaneous					
55. Manaeesh, zaatar, cheese	1 large				
56. French fries	1 cup				
57. Chips: potato, corn, tortilla	1 cup				
58. Falafel sandwich, medium	1 item				
59. Chawarma sandwich, medium	1 item				
60. Burgers(Beef, chicken, fish)	1 item				
61. Pizza	1 slice				

Are there any other foods not mentioned above that you usually eat at least once per week?

Other foods that you usually eat at least once /week	Usual serving size	Servings/week

F) ADVICE ON DIET AND LIFESTYLE DURING PREGNANCY

1) Do you receive counseling during pregnancy on any of the following? If yes, please mark all relevant choices. If no, go to part G.

Weight gain	Smoking	Diet	Physical activity	Alcohol

2) From whom do you receive advice and what did they tell you? (Please mark all relevant choices and describe the advice that you received)

	Doctors	Dietitians	Mother /mother in law	Father / father in law	Husband	Friend	Sister	Website / social media	Other, specify
Source									
Advice									

3) Do you receive specific counseling on eliminating or reducing certain food items?

a) Yes, specify food items ____

b) No

4) Do you receive specific counseling on introducing or increasing certain food items?

a) Yes, specify food items ____

b) No

G) Physical activity Habits during the last month

1) List only regular fitness/recreational activities

____

Intensity

Heavy
Medium
Light

Frequency (times/week)
1-2 2-4 4+
___ ___ ___
___ ___ ___
___ ___ ___

Time (minutes/day)
<20 20-40 40+
___ ___ ___
___ ___ ___
___ ___ ___

2) Does your regular occupation (job/home) activity involve: Y N

Heavy lifting?

Frequent walking/ stair climbing?

Occasional walking (> once/hr)

Prolonged standing?

Mainly sitting?

Normal daily activity?

3) Do you currently smoke tobacco?

a) Cigarette

b) Waterpipe

4) Do you consume alcohol?

<u>Score:</u>

Levels of recreational physical activity	**Physical activity index**	**Frequency (times/week)**	**Time (minutes)**
Sedentary/inactive	0	<1-2	<20
Active	1	1-2	=20
	1	>2	<20
Fit	2	>2	>20

H) FOOD INSECURITY

Please select the best answer

1-This food that we bought just didn't last, and we didn't have money to get more.	○ Often true ○ Sometimes true ○ Never true ○ Don't know/Refused
2-We couldn't afford to eat balanced meals.	○ Often true ○ Sometimes true ○ Never true ○ Don't know/Refused
3- In the last 4 months, did (you/you or other adults in your household) ever cut the size of your meals or skip meals because there wasn't enough money for food?	○ Yes ○ No
[Ask only if #3 = YES] 4-How often did this happen—almost every month, some months but not every month, or in only 1 or 2 months?	○ Almost every month ○ Some months but not every month ○ Only 1 or 2 months ○ Don't know/Refused
5-In the last 4 months, did you ever eat less than you felt you should because there wasn't enough money to buy food?	○ Yes ○ No
6- In the last 4 months, were you ever hungry but didn't eat because you couldn't afford enough food due to COVID related issues?	○ Yes ○ No

Parity C	
Previous miscarriage C	☐ Yes ☐ No
Previous GDM C	☐ Yes ☐ No
Previous gestational hypertension C	☐ Yes ☐ No
Family history of diabetes C	☐ Yes ☐ No
Previous ceasarian delivery C	☐ Yes ☐ No
Previous macrosomia C	☐ Yes ☐ No
Multiple gestation C	☐ Yes ☐ No
Weight in kg (first trimester) C	
Weight in kg (second trimester) C	
Weight in kg (third trimester) C	
Weight in kg after delivery H	
Height in cm C	
Structural malformation/ chromosomal anomalies/ TORCH infection C	☐ Yes ☐ No
Second trimester ultrasound measurements C	Fetal weight: Fetal height: Abdominal circumference: Head circumference:
Anemia C	☐ Yes ☐ No
General maternal health status during pregnancy (infections, bed rest, COVID) C	
Vitamin/mineral supplement brand name and dosage C	
Gestational diabetes C	☐ Yes ☐ No
Systolic blood pressure <140 or >140 C	1st trimester: 2nd trimester:

	3rd trimester:
Diastolic blood pressure <90 or >90 C	1st trimester: 2nd trimester: 3rd trimester:
Pre-eclampsia C or H	☐ Yes ☐ No
Maternal delivery location C or H	
Maternal delivery type (caesarian or vaginal) H	
Maternal delivery complications (specify): Shoulder dystocia, baby resipiratory distress, hypoglycemia or hyperbilirubinemi, NICU admission, PPH, stillbirth, abruption, eclampsia or seizures, HELLP syndrome, or other specify H	
Gestational age at delivery	
Infant sex C or H	
Infant birth weight H	
Infant birth height H	
Infant birth head circumference H	
Infant abdominal circumference H	
Apgar Score at 1 and 5 min H	
Last estimated fetal weight EFW (HC/AC) Specify gestational age of ultrasound C	

Medical Chart Data Extraction Form

ID#: ________ Clinic: _____________ Doctor's Name: ____________