DETERMINANTS OF SMALL-FOR-GESTATIONAL-AGE: A CASE STUDY IN A CONFLICT-ZONE IN COLOMBIA

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Abstract

Since the introduction of Millennium Development Goals in early 2000s, maternal and child health has been the priority for public and global health interventions in developing nations. However, the early identification of risk factors is challenging in communities experiencing a history of conflict-related displacement. This study assessed associations of symphysis-fundal height (SFH), sonography-detected fetal weight (FW) and amniotic fluid index (AFI) with sociodemographic characteristics, conflict-related stresses, food security and diet quality, clinical biomarkers, and medication and supplements in high-risk pregnancies (n=61) from a post-conflict area in Colombia. Results showed that although 72% of the population was food secure, there were instances of mild (10%), moderate (8%) and severe (10%) food insecurity in the region. Consumption of dairy products increased the odds of SFH <10th percentile (P=0.02), however the presence of nuts and avocados in the diet lowered the odds of low SFH (P=0.04). Considering psychosocial determinants, maternal experience of conflict-related stress was associated with low AFI (P=0.04) and maternal depression was borderline significantly associated with lower fetal weight (P=0.05). Prescribed calcium (P=0.03), and prophylactic iron (P=0.04) but not multivitamin-mineral supplementation, were associated with higher mean SFH Z-scores whereas low diastolic blood pressure (DBP) was significantly associated with SFH < 10th percentile (P=0.04). Of all the environmental factors studied, the presence of cats was associated low mean SFH Z-scores (P=0.02), possibly because they are carriers of infections that could interfere with fetal growth. Due to collinearity, the final overall model was run separately with respect to iron and calcium supplement intake, however the iron model was better at explaining the total variability in SFH in the population (46%) than the calcium model (44%). The factors that contributed to low SFH Z-scores were physical activity (P=0.006), anemia (P=0.03) and history of displacement (P=0.003). Conversely, the factors contributing to better SFH Z-scores were DBP (P=0.01) and high hematocrit (P=0.01). Our findings show SFH as an antenatal screening tool responds to a range of physical, environmental and psychosocial factors affecting maternal-fetal health. Therefore, our findings would suggest that antenatal care interventions could use SFH as a low cost and low technology method for monitoring fetal growth and surveillance of high-risk pregnancies.

Résumé

Depuis la présentation des objectifs du millénaire pour le développement, au début des années 2000, la santé des mères et des enfants a été la priorité des interventions de santé publique dans les pays en développement.Cependant, l'identification précoces des facteurs de risque dans les communautés déplacés en situation de conflit, est un véritable défi.Cette étude a évalué les associations entre la hauteur utérine (H.U.), le poids fœtal (P.F.) mesuré par l'échographie et l'index de liquide amniotique (I.L.A.) avec les caractéristiques socio-démographiques, le stress post-traumatique dans les conflits, les apports alimentaires, la qualité du régime alimentaire, les biomarqueurs, les médicaments et les suppléments chez les grossesses à risque (n=61) dans des zones post-conflictuelles de Colombie. Les résultats ont montré que même si 72% de la population était en suffisance alimentaire, il y avait des cas légers (10%), modérés (8%) et sévères (10%) de carence alimentaire dans la région.La consommation de produits laitiers augmentait le taux de H.U.<10ème percentile (P=0.02).Cependant, la présence de noix et d'avocats dans la nourriture abaissait le rapport de vraisemblance de la H.U. (P=0.04).En considérant, les déterminants psycho-sociaux, l'expérience maternelle du stress post-traumatique lié au conflit a été associée à un I.L.A. faible (P=0.04) et la dépression maternelle était marginalement associée avec un faible poids fœtal (P=0.05).La prescription de calcium (P=0.03) et le fer en prophylaxie (P=0.04) mais pas la supplémentation de multivitamines et minéraux, a été associée à une valeur centrée réduite plus haut de la H.U. alors qu'une faible pression diastolique (P.D) était significativement associée à la H.U. < 10ème percentile(P=0.04).Parmi tous les facteurs environnementaux étudiés, la présence de chats était associée à des valeurs centrée réduite de la H.U. basses (P=0.02), probablement par ce qu'ils sont porteurs d'infections qui peuvent interférer avec la croissance fœtale.En raison de la colinéarité, le modèle final global a été réalisé séparément en ce qui concerne la prise de supplément en fer et en calcium. Cependant le modèle du fer était meilleur pour expliquer la variabilité totale de la H.U. dans la population (46%) par rapport au modèle du calcium (44%).Les facteurs qui ont contribué au faible valeur centrée réduite de la H.U. étaient l'activité physique (P=0.006), l'anémie (P=0.03) et les antécédents de déplacement (P=0.003).Inversement, les facteurs contribuant à une meilleure valeur centrée réduite de la H.U. étaient la pression diastolique (P.D.) et une hématocrite élevée (P=0.01).Nos résultats montrent que la H.U. comme un outil de dépistage anténatal répond à une gamme de facteurs physiques, environnementaux et psychosociaux affectant la santé maternelle et fœtale.Par conséquent, il est suggéré que les interventions de soins prénatals utilisent la H.U. comme une méthode peu coûteuse et d'application simple pour surveiller la croissance fœtale et les grossesses à haut risque.

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Contribution to knowledge

Antenatal care in developing regions of the world is unable to achieve its full potential due to lack of early diagnosis of risk factors affecting pregnancy. In my study I evaluated the role of symphysis-fundal height as an antenatal screening tool in diagnosing determinants of small-for-gestational-age in a conflict zone. Symphysis-fundal height was more effective in detecting the rate of SGA in the population than traditionally used fetal weight measurements. Symphysis-fundal height as an antenatal screening tool was able to identify intervention strategies that included interventions for hypertensive disorders of pregnancy, dietary elements like low-fat dairy, iron and multiple micronutrient supplementation and surprisingly to presence of cats in the household having an impact on SFH. This study has established symphysis-fundal height as a simple, accessible and cost-effective antenatal screening for detection of small-for-gestational-age.

Contribution of authors

This thesis was written under the supervision of my supervisor Dr. Kristine G Koski and co-supervisor Dr. Julián Herrera along with constant support from Dr. Doris Gonzalez, a PhD Candidate in Dr. Koski's laboratory. They provided guidance on the design of the research, data analysis and interpretation and presentation of results. I was responsible for data entry and analysis and the preparation and writing of thesis.

List of abbreviations

AA- Amino Acid

ACC-Antenatal Care Coverage

BMI- Body mass index

BV- Bacterial Vaginosis

CRH- Corticotropin Releasing Hormone

DASH- Diet Approach to Stop Hypertension

DBP- Diastolic Blood Pressure

DHA- docosahexaenoic acid

eMAP- elevated Mean Arterial Pressure

EPA- eicosapentaenoic acid

FA- Folic Acid

FGR- Fetal Growth Restriction

GWG- Gestational Weight Gain

HDP- Hypertensive disorders of pregnancy

HPA axis- Hypothalamus-pituitary adrenalin axis

HSD11B2 enzyme - 11β-hydroxysteroid dehydrogenase type 2

IFA- Iron folic acid

IUGR- Intrauterine Growth Restriction

LBW- Low Birth Weight

LMIC's- Low- Middle Income Countries

LMP- date of Last Menstrual Period

MAP- Mean Arterial Pressure

MMN- Multiple micronutrient

MUFAs- Mono-unsaturated fatty acids

PAPP-A- Pregnancy associated plasma protein- A

PCR- Polymerase Chain Reaction

PP- Pulse Pressure

PUFA's- Poly-unsaturated fatty acids

PTH- Parathyroid hormone

RMNCH- Reproductive, Maternal and Child Health

SBP- Systolic Blood Pressure

SD- Standard Deviation

SFA- Saturated fatty acid

SGA- Small-for-gestational-age

SFH- Symphysis- fundal height

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Chapter I – Introduction

1 Antenatal Care in Developing Nations

Since the introduction of Millennium Development Goals in the 2000's, maternal and child health has been the priority for public and global health interventions in developing nations that bear the brunt of the highest maternal and child mortality and morbidity. One of the primary determining factors is the quality of the antenatal care in these nations (Manzi et al., 2018). The goal of antenatal care is the prevention and early treatment of pregnancy complications through systematic assessments, women's education on positive behaviors, gestational age assessment, screening for fetal development and early detection of mother and baby abnormalities (Manzi et al., 2018). However, antenatal care in developing nations may not be able to realize its full potential due to lack of early diagnosis of danger signs affecting pregnancy or fetal growth, therefore, leading to delayed referral to emergency obstetric care (Manzi et al., 2018). Apart from health workforce shortage in these areas, the lack of proper screening equipment may be a limiting factor also (Manzi et al., 2018) and apart from lack of reliable and comparable data about the predictivity of conventional risk factors affecting maternal or child health, the quality of antenatal screening in resource constraint nations is often questioned. In a study assessing the quality of prenatal care in Nigeria, it was inferred from a sample of 330 pregnancies that the quality of screening for risk factors during pregnancy was poor (Prual et al., 2000). Others have concluded that implementation of essential obstetric care of quality is a critical tool in improving antenatal care in resource-limited nations (Prual et al., 2000). In this study, I will be examining the role of symphysis-fundal height (SFH) as a cost useful and accessible antenatal screening tool for assessment of fetal growth and detection of small-for-gestational age (SGA) in resource constraint nations where obstetric care through ultrasounds may not be feasible. Under such circumstances, SFH has been found to be more acceptable as an antenatal screening tool (Wanyonyi et al., 2018).

Fetal growth restriction (FGR) refers to poor growth and development of fetus in the mother's womb during pregnancy, with profound implications on the subsequent health during childhood and adulthood and a higher risk of mortality and morbidity (Portella and Silveira, 2014). Fetal growth impairment has also been associated with altered feeding behaviour and food preferences during lifetime and has been found to be at associated with a higher risk of developing obesity, type 2 diabetes, cardiovascular diseases and metabolic syndrome during adulthood (Portella and Silveira, 2014). It is the most important determinant of infant mortality in the context of developing nations (Portella and Silveira, 2014). As a major public health problem, FGR affects 32.4 million newborns in low and middle-income countries (Accrombessi et al., 2018). It has been associated with a number of chronic maternal conditions (such as infections, hypertension, diabetes and obesity), exposures (such as tobacco smoke and drugs), and malnutrition (Portella and Silveira, 2014). In the context of nations undergoing a rapid nutrition transition (a condition wherein individuals, households and populations experience the co-existence of both underweight and overweight or the "double burden of malnutrition"), fetal growth restricted children can be simultaneously growth-restricted and overweight, thereby increasing the burden of double malnutrition at an individual level (Portella and Silveira, 2014). The problem of FGR is dependent on the context of developing or developed nations. In developing nations, the risk factors associated to FGR are more closely related to poverty and chronic maternal malnutrition whereas in developed and industrialised countries the risk factors are more closely related to medical complications in pregnancy (Escamilla et al., 1992).

In 2010, globally 32.4 million babies were born SGA and 27% of these births occurred in low-middle income Countries (LMIC's), (Black, 2015). The burden of FGR is concentrated mainly in Asia which accounts for about 75% of all the affected cases; Africa and Latin America account for 20% and 5% of the cases respectively (Murki and Sharma, 2014).

2 The scope of the topic

Clinicians have traditionally relied on the date of last-menstrual period, abdominal palpation along with SFH to detect high risk pregnancies in the absence of obstetric ultrasound services (Wanyonyi et al., 2018). SFH may be used as a determinant of proper fetal growth and amniotic fluid development during pregnancy and usually implemented from 20 weeks of gestation onwards (Robert et al., 2012). The limitation with this practice is that the distance of the anatomical landmark from the pubic symphysis is quite variable depending upon the individual body type (Robert et al., 2012). Maternal factors that can influence SFH measurements include maternal obesity, abnormal fetal lie, multiple gestations, large pelvic masses, e.g., fibroids, and fetal head engagement and body mass index (BMI) (Wanyonyi et al., 2018). For instance, amongst rural women in Mozambique, BMI > 27 and <19 gave 1cm higher and 1cm lower SFH readings and nulliparous women had 0.5 cm lower SFH growth curve than multiparous women (Challis et al., 2002).The sensitivity of SFH to detect SGA babies is reported between 56-86% from observational studies and is an essential tool in antenatal care especially in resource-constrained nations (Robert et al., 2012).

Early detection and management of risk factors affecting maternal and fetal health remain a challenge for any health intervention aiming at reducing perinatal mortality and morbidity in resource-limited nations due to their limited access to obstetric ultrasound services. Under such circumstances, the majority of antenatal care in these areas rely on simple anthropometric measures such as SFH, date of the last menstrual period (LMP) and the Ballard scores (Pay et al., 2015). The Ballard Maturational Assessment, Ballard Score, or Ballard Scale is a commonly used technique of gestational age assessment (Pay et al., 2015). It assigns a score to various criteria, the sum of all of which is then extrapolated to the gestational age of the fetus. These criteria are divided into physical and neurological criteria. This scoring allows for the estimation of age in the range of 26 weeks-44 weeks (Pay et al., 2015). The New Ballard Score is an extension of the above to include extremely pre-term babies i.e. up to 20 weeks (Pay et al., 2015). SFH method requires less training and fewer resources, but its reliability is often controversial especially when comparing SFH growth charts between different countries. For instance, SFH growth chart developed for rural population in Ethiopia and Nepal, could not be

compared against the Westin's chart for Swedish population because of lower SFH measurements per pregnancy, lack of standards for optimal birthweight and lack of data for fundal height measurements in developing countries (Kiserud, 1986; Ulstein et al., 1988). Moreover, majority of research on SFH has been carried out in hospital-based settings which also limits the application of study results to primary care in a community environment (Pay et al., 2015). In an attempt to facilitate efficient detection of IUGR, several region-specific charts (Westin's and Cardiff's chart) of symphysis-fundal height measurement had been constructed (Westin, 1977; Calvert et al., 1982).

Therefore, it was recommended that for SFH to increase its scope and application to antenatal care at a much larger scale, uniformity in the use of this technique was needed with an international call for better growth curve formulas integrating specific maternal and neonatal characteristics, racial and ethnic factors associated with a population was required (Hoorsan et al., 2018; Mongelli, 2018). In 2016, a multicentre and multiethnic study of 8 geographically different countries around the word developed standards for SFH that could be applied to the general population, known as the intergrowth-21 project (Papageorghiou et al., 2016). It is this newly developed chart that is being used in this thesis.

3 The context of IUGR in Latin America

A review of causes and consequences of IUGR in the context of Latin America where 2.8 million newborns were born with IUGR in 1985 concluded that body proportions at birth are an important risk factor associated with FGR (Escamilla et al., 1992). The primary factors associated to the risk of FGR in Latin America include depleted mother's nutritional reserves, like high parity, a short birth interval, breast-feeding a prior infant during pregnancy, and, low maternal weight gain (Escamilla et al., 1992). Although smoking during pregnancy was not a common habit associated to women in reproductive age in the marginal zones of Latin-America or other developing countries, it was observed that these women were continuously getting exposed to high-concentrations of carbon monoxide being produced by makeshift wood and coal stoves used inside poorly ventilated dwellings (Escamilla et al., 1992). Hence, stove smoke was

concluded to be an important determinant of FGR in the context of Latin America and other developing countries (Escamilla et al., 1992).

4 The context of the Colombian conflict

Colombia has been experiencing armed conflict and violence for the past 50 to 60yrs (1964-present) leading to a disturbed social and political conditions along with widespread displacement of population (McEniry et al., 2018). Between 1958 and 2012 this conflict had generated the world's second largest population of Internally Displaced Person's (IDP). Colombia witnessed the largest displacement of population in the Latin American region (McEniry et al., 2018) and though in the Americas the rate of IDP's had dropped by 23%, the newest displacement occurred in Colombia (Albuja, 2014) where nearly 10% of the country's population had been displaced by violence (over 6 million people) (Morales, 2018).

Displacement is of recognized international importance and such displaced individuals experience adverse economic and health conditions including poor nutrition, (Morales, 2018). The majority of the victims of the war were females', adolescents, single mothers or widows experiencing forced displacement and sexual and gender-based violence (Rivillas et al., 2018). As a result of war conditions in Colombia, in 2012, National Health Plan 2012-2021 recognised victims of armed conflict as a vulnerable target group especially emphasizing on the need to address the lack of access to basic health care and delivery of health care benefit packages in reproductive and maternal health (Rivillas et al., 2018). Evidence suggested that in context of Colombia there was slower progress in achieving optimal levels of antenatal care, family planning services and skilled birth attendance (Rivillas et al., 2018). The magnitude of inequality displayed a pro-poor inclination until 2005 but showed a substantial change between 2005-2015 with rates of absolute inequalities falling from -14.5 to -4.5 (Rivillas et al., 2018). Therefore, the effects of armed conflict continue now days to threaten reproductive maternal health in Colombia, after a peace agreement signed in November 2016.

5 Study Site and Design

For this cross-sectional study, women were recruited from the catchment area for the University Hospital San José, which is one of the main hospitals in the conflict zone. The participants have been referred from health institutions in Popayan and from different parts of the region to the gyneco-obstetric department at San José Hospital, given evidence of having a high-risk pregnancy (n=61); these risk factors included history of pre-term delivery, gestational diabetes and hypertensive disorders of pregnancy.

6 Hypothesis and Objectives

Hypothesis

Experiences of conflict related displacement and stress during pregnancy are associated with indicators of maternal and fetal health

Objectives

The three fundamental questions are explored in this pilot study:

1. Is the household environment contributing to fetal growth?
2. Does food insecurity and/or diet quality contribute to low symphysis-fundal height or fetal weight?
3. Do maternal experiences of stress associate with pregnancy related indices?

Chapter II – Literature Review

1 History of Symphysis-fundal height

Symphysis-fundal height is a measure of the size of the uterus determined by a tape measurement and Spielberg first described the technique of SFH in German literature in 1891 (Mongelli, 2018). The SFH measurement is taken while a woman is in a supine position and after having emptied her bladder with the help of a non-elastic metric tape (Chasmors). Using a non-elastic metric tape with one hand at the upper border of the symphysis pubis bone, the start of the tape is positioned and thereafter the tape is placed in a straight line over the uterus until reaching the fundus.

Measurements are taken to the nearest complete half centimeter (Papageorghiou et al., 2016). The recorded SFH measurements are then plotted on a curve and compared with the distribution of the reference population. In case of the recorded measurements being lower than the limits which are considered acceptable according to the reference curves, referrals to a high-risk pregnancy unit are made for further investigations of poor fetal growth and well-being (Pay et al., 2015). From 24 weeks of gestation, the SFH measurement in centimeters should correspond to the number of weeks of gestation, with an allowance of a 2-cm difference either way. In the context of developing nations, it is recommended that SFH measurements should form part of the routine Antenatal Care Coverage (ACC) and can aid in estimating gestational age (White et al., 2012), identifying IUGR, multifetal pregnancy, macrosomia and polyhydramnios (Hoorsan et al., 2018).

2 Traditional tools used for estimating Symphysis-fundal height

Traditionally abdominal palpation was used to detect IUGR but due to its low sensitivity and false-positive results the use of this method has not been recommended (Wanyonyi et al., 2018). In an attempt to facilitate efficient detection of IUGR several charts of symphysis-fundal height measurement had been constructed.

2.1 Westin's chart for Symphysis-fundal height

The Westin's chart for SFH was derived from 100 uncomplicated term pregnancies in Sweden in which the birthweights were distributed symmetrically about the mean, showing a graphical representation of increase in SFH with relation to gestational age. It was based on the gravidogram system which helped in supervision of pregnancy by means of graphic comparisons between changes in maternal symphysis-fundus distance, girth, weight and blood pressure, and known normal values. In Westin's study, SF-distance had the smallest coefficient of variation and was therefore selected as an indirect indicator of fetal growth (Westin, 1977). In an analysis of 12,800 fundal height charts, Westin's Chart was able to predict 75% of all infants of birthweights more than 1 Standard Deviation below the mean and 65% of large for gestational age infants (Westin, 1977; Quaranta et al., 1981).

2.2 Cardiff's chart for Symphysis-fundal height

The Cardiff's chart for SFH was derived based on data from 381 ultrasound dated pregnancies within the first 16 weeks of gestation. Amongst all the pregnancies the birthweight was symmetrically distributed around the mean and was between the 10^{th} and the 90^{th} centiles for gestation. SFH measurement below the 10^{th} centile indicate growth retardation. Using data based on the Cardiff's chart the inter and intra observer variation reported in a sample of 12 patients at different stages of gestation was reported to be 6.4 % and 4.6 % respectively indicating the lack of reproducibility of results obtained by this method (Calvert et al., 1982). This chart has been specifically recommended to be used in the context of developing countries and is suitable only in case of low-risk, normal pregnancies (Walraven et al., 1995).

Sensitivity of SFH measurements is contingent upon the older charts which varied according to different ethnic settings. Therefore, different population specific SFH growth curves had been developed and compared with the reference growth curves. Common limitations associated with the Westin's and Cardiff's chart for SFH were their overdependency on locally derived data that used different methods and standards for measuring SFH and different cut off points (3^{rd},5^{th} or 10^{th} centile) to establish abnormal fetal growth. Another limitation was the use of uncorroborated

menstrual dates that can cause artificial flattening of the growth curve at term often attributed to overestimation of gestational age due to faulty dating practices (Westin, 1977; Walraven et al., 1995). However, locally developed SFH growth charts had been found to perform better regarding detecting fetal and maternal abnormalities than generic charts as in the case of Mozambique where the locally generated growth charts were 0-3 cm lower in measurements at the same gestational interval than the reference western charts (Challis et al., 2002).

2.3 Reference symphysis-fundal height chart used in Latin America

Published in 1984 the reference SFH chart presently used in Latin America was recommended by the Brazilian Health Ministry and was developed by the Latin American Centre of Perinatology and Human Development (CLAP) (Fescina et al., 1984; Fescina et al., 2011). The charts were developed from a longitudinal study of normal pregnant women, 1074 pregnancy measures were obtained with which a standard curve of uterine height during pregnancy was built. The sensitivity and specificity of the curves to detect IUGR at 10^{th} percentile was 92% and 52% respectively, whereas for the 25^{th} percentile it was 78% and 69% respectively. Furthermore, for all the pregnant women who delivered within 72 hrs of the last measurement of SFH, the correlation of uterine height to neonatal weight was also studied and these growth charts were further used to predict low neonatal weight according to uterine height at a particular gestational age (Fescina et al., 1984; Fescina et al., 2011).

2.4 Intergrowth-21 Project

It was a multicentre, multiethnic, population-based project conducted between 2009-2014 with the primary aim of studying growth, health, nutrition and neurodevelopment from less than 14 weeks gestation to 2 years of age amongst eight geographically diverse countries (Brazil, China, India, Italy, Kenya, Oman, United Kingdom, and United States). SFH measurements were taken every five weeks after 14^{th} week of gestation from a total population of 59000 women enrolled in the Fetal Growth Longitudinal Study component of this project. The majority of the pregnancies were medium-high risk. The main outcome was to generate standardized SFH measurement norms indicating optimal maternal, fetal and newborn parameters of growth and development. The standards were presented as 3^{rd}, 10^{th}, 50^{th}, 90^{th} and 97^{th} centile curves by gestational age and

sex. All pregnancies complicated by fetal death or congenital abnormalities, previous history of smoking, cases of Malaria, HIV and Cancer were excluded from this study (Papageorghiou et al., 2016).

3 A critical summary of literature examining applications of SFH

Table-1 Summary table of studies on validation of symphysis-fundal height as an antenatal screening tool in developed and developing country context.

Studies not validating use of SFH as an antenatal screening tool	
Author and year	Study location
Persson et al., 1986	Sweden
Nielson, 1998	Systematic-review
Goto, 2013	Meta-analysis
Peter et al., 2015	Systematic-review
Zahran et al., 2015	Turkey
Policiano et al., 2019	Portugal
Studies validating use of SFH as an antenatal screening tool	
Author and year	Study location
Kiserud, 1986	Ethiopia
Ulstein et al., 1988	Nepal
Krishna et al., 1991	India
Medhat et al., 1991	Egypt
Anderrson and Bergstorm, 1995	Rural Africa
Walraven, 1995	Rural Tanzania
Vanneste et al., 2000	Bangladesh
Onah et al., 2002	Nigeria
Imdad et al., 2011	Systematic review
White et al., 2012	Thai-Burmese border
Karl et al., 2015	Rural Papua (New Guinea)
Dias et al., 2016	Sri Lanka
de Sousa Basso et al.,	Brazil
Hoorsan et al., 2018	Iran
Pugh et al., 2018	United States
Rada et al., 2018	Africa
Ricchi et al., 2019	Italy
Unger et al., 2019	Sub-Saharan Africa

A critical review of studies published in Pub-Med between 1986-2018 evaluating the applicability of SFH was done (Table-1). The primary objective associated with this review of literature was to find compelling evidence in favor of the use of SFH as an alternative antenatal screening tool in resource constraint areas where obstetric ultrasound services are not accessible and also to find studies which outline limitations associated with the use of SFH as a tool. Every study was evaluated based on the consistency in reference fundal height method used, specific study objectives and limitations of SFH specific and non-specific to the study environment. The standard reference SFH growth chart used as a comparator against individual study results was the Westin's 1977 standard SFH measurement (Westin, 1977) except a particular study from rural Tanzania where Cardiff Wale's SFH chart specifically designed for developing countries was used (Walraven et al., 1995). More recently, new international standards (Intergrowth-21) for SFH measurement were devised based on the data from an urban population of healthy and well-nourished women from eight countries as a part of the INTERGROWTH-21 Project (Papageorghiou et al., 2016). The majority of the articles in our review were comprised of studies from rural Africa followed by other countries like Bangladesh, India and Nepal, implying that SFH as a method has broad applicability in developing nations (Kiserud, 1986; Ulstein et al., 1988; Krishna et al., 1991) comparing to developed countries (Pugh et al., 2018) where obstetric ultrasound services are still considered as a more reliable tool for predicting adverse maternal and child outcomes during pregnancy (Goto, 2013). Moreover, Goto's meta-analysis of over 46 hospital-based studies in developing countries concluded that SFH is unsuitable for primary screening of low birth weight or small-for-gestational-age (Goto, 2013).

The primary challenge encountered by SFH in context of developing nations is lack of reliable statistical data on growth measurements during pregnancy (Ulstein et al., 1988). The absence of standards for optimal birthweight, weight for gestational age, inefficient reporting of the date of last menstrual period, and standardized SFH growth charts (Kiserud, 1986; Ulstein et al., 1988; Challis et al., 2002; Cutland et al., 2015) are amongst the most common limitations to SFH method. Maternal factors such as increasing BMI and obesity reduce the performance of SFH measurement (White et al., 2012). It is also subject to high inter and intra-observer variation and cannot be reliably measured by different observers in the same pregnancy with sufficient agreement upon small, normal or large fundal height observed which limits its application as an

antenatal screening tool (Mongelli, 2018). Usually, low technology methods like SFH are associated with lesser training and education, however, with increased experience and training interobserver bias can be managed (Challis et al., 2002).

However, because locally derived SFH charts were the most common, this heterogeneity in charts made countrywide comparisons became difficult due to different measurement techniques used and standards used. However, more recently international SFH standards were derived from the eight urban populations of healthy, well-nourished women as a part of the INTERGROWTH-21st Project between 2009-2014 and helped tackle the methodological limitations associated with the use of multiple local SFH growth charts (Papageorghiou et al., 2016).

4 Determinants of fetal growth in developing countries

Major maternal factors influencing fetal growth and development in the country included hypertension, haemorrhage and infections during pregnancy (Bhutta et al., 2013).Out of the various social determinants of maternal and child health in the country, poverty remains the major factor contributing to the issue (Bhutta et al., 2013).There exist huge disparities between and within provinces making it difficult for health and development programs reach the poor and marginalised communities (Bhutta et al., 2013).An evidence-based Reproductive, Maternal and Child Health (RMNCH) intervention along with strategies to overcomes the barrier of poverty and access to healthcare in Pakistan has been shown to reduce maternal and child deaths by 57%. For the sake of better health coverage and access, it has been recommended to generate political will to prioritise pro-poor and integrated RMNCH services with effective implementation of primary care strategies for women and children alongside addressing the key social determinants of health (Bhutta et al., 2013).

4.1 Maternal infections and fetal growth

Maternal exposure to bacteria, viruses and parasite can lead to significant damages to fetus in -utero causing fetal death, organ injury or other sequelae depending upon the pathogen and

multiple factors like timing of exposure, infant demographic variables, maternal factors and genetic or epigenetic determinants (Waldorf and McAdams, 2013). The classic group of teratogenic pathogens and causing impaired fetal and placental development leading to fetal growth retardation are referred to as "TORCH" (*Toxoplasma gondii,* others like *Trepenoma pallidium,* Rubella virus, Cytomegalovirus, Herpes simplex virus) but can also include a much broader group of bacteria, viruses and parasites that can injure the fetus or impact placental development and function such as Parvovirus B19, *Varicella zoster* virus and *Plasmodium falciparum* to name a few. Intrauterine infection triggers an inflammatory response which is believed to be associated with pre-term labor (Waldorf and McAdams, 2013). The greatest burden of maternal infectious diseases remains in low- and middle-income countries (Madrid et al., 2016). In Latin America one of the most endemic pathogens is *Trypanosoma cruzi* which causes Chagas disease, affects 30% of the population and more than 15,000 infants annually (Waldorf and McAdams, 2013). Moreover, infectious disease management in resource-constrained areas is both epidemiologically and ethically challenging because of limited availability of baseline data, quality of standard care compared to international standards, unpredictable changes in disease epidemiology and social-cultural beliefs (Divala et al., 2015).

4.1.1 Congenital Toxoplasmosis

Toxoplasmosis caused by *Toxoplasma gondii* is one of the most widespread parasitic infections worldwide. The parasite has a complex life cycle with multiple forms. The intermediate hosts (a host in which parasite passes one or more asexual stages) such as humans get infected by sporozoites (asexual stage) in the form of oocysts, whereas the sexual stage of the parasite occurs in the intestine of the definitive host (final host) like feline species such as cats. However, the parasite does not need to pass through sexual stages or its definitive host for transmission to other species (Dubey, 2014).

The common routes of transmission of the parasite are being exposed to infected cat feces from a cat shedding oocysts, foodborne (eating raw or undercooked pork, mutton, lamb, beef or mince

meat products), gardening (consuming raw or unwashed fruits and vegetables), contact with soil and poor hygiene practices (Jones et al., 2001).

Higher seroprevalence of *T.gondii* is found in tropical areas where the hot and humid climate favors survival of oocysts like Latin America or sub- Saharan Africa (Jones et al., 2001). About 85% of the women of childbearing age are at a risk of acute infection with *T. gondii. (*Khademi et al., 2019*).* Congenital transmission of toxoplasma (when the parasite is passed transplacentally to the fetus) is associated with shorter length of gestation leading to preterm delivery (Freeman et al., 2005). Severe clinical manifestations of congenital toxoplasmosis are observed in women when infection is acquired during early gestation, but the risk of transmission is increased with gestational age (Khademi et al., 2019).

Recently it has been brought to attention that foodborne transmission of toxoplasma can also occur through contaminated milk and dairy products (Boughattas, 2017). Milk consumption has been linked to infection more than dairy product consumption (Boughattas, 2017). Based on a meta-analysis of 39 peer-reviewed papers it was noted that heterogeneous responses have been observed worldwide with respect to risk assessment of milk consumption and toxoplasmosis occurrence, so no crude conclusions can be drawn (Boughattas, 2017). Specifically, ingestion of any source of raw, unpasteurized milk including breastmilk from an infected mother has been considered as a potential risk factor (Boughattas, 2017). The potential association between milk and toxoplasma transmission was attributed to the presence of tachyzoites in the milk, suckling trauma and, tissue cyst excretion. Smaller concentrations of proteolytic enzymes in the intestines of children favors survival of *T.gondii* forms making congenital toxoplasmosis as an important infectious cause of pregnancy and fetal growth complications (Boughattas, 2017).

4.2 Maternal urogenital infections

Bacterial Vaginosis (BV) is the leading cause of vaginitis amongst both pregnant and non-pregnant women and affects nearly 1 in 3 reproductive-aged women. It is a syndrome wherein the normal vaginal hydrogen peroxide- producing lactobacilli are replaced by a mixed flora with high concentrations of anaerobic bacteria, *Gardnerella vaginalis* and *Mycoplasma hominis*

(Klebanoff et al., 2005). Initially BV was diagnosed using the Amsel's criteria that was based on a wide range of vaginal symptoms like elevated vaginal pH (>4.7), the presence of greyish discharge etc, however this criterion has been replaced by a 'more objective' assay known as the Nugent criteria which is based on the microscopic observation of Gram-stained vaginal secretions (Nasioudis et al., 2017). About 50% of pregnant women worldwide have been found to have BV (Laxmi et al., 2012). Majority of the cases of BV are asymptomatic and remain unreported and untreated. There exists a strong correlation between microbiological environment of the vagina and adverse fetal outcomes. BV has been associated with a wide range of gynaecological conditions and complications of pregnancy such as pelvic inflammatory disease, post-hysterectomy, vaginal-cuff cellulitis, endometritis, amniotic fluid infection, preterm delivery, preterm labor, prelabour rupture of the membrane and spontaneous abortion (Laxmi et al., 2012). It has been postulated that vaginal organisms found in BV first ascend into the choriodecidual space stimulating a maternal and fetal immune response to choriodecidual bacterial colonization resulting in preterm labor and delivery. Under other circumstances, the bacteria might cross the intact chorioamniotic membranes and enter the amniotic fluid, ultimately infecting the fetus. The relative risk of preterm delivery is >2-fold in women with BV, even after controlling for the major risk factors. Moreover, BV in early pregnancy has been established as a stronger risk factor for preterm delivery than BV in later pregnancy, (Leitich et al., 2003). The presence of BV at 28 weeks of gestation has been associated with the greatest risk of spontaneous preterm birth (n=2929, odds ratio 1.84, 95% CI, $p < 0.01$), (Meis et al., 1995). Maternal vitamin D status plays a significant role in development of BV during early pregnancy (<16 weeks of gestation) as it exerts a significant influence on maternal immunity.

The occurrence of BV decreases as maternal vitamin D status improves (Bodnar et al., 2009). Amongst 41 % of 469 women at <16-week gestation diagnosed positive for BV, 52% had serum 25(OH)D concentration <37.5 nmol/L (Bodnar et al., 2009). Vitamin D also contributes to the racial disparity between the occurrence of BV (Bodnar et al., 2009). As vitamin D deficiency is far more common amongst black females than their white counterparts, because of their dark skin pigmentation that prevents adequate cutaneous synthesis of cholecalciferol from casual exposure to sunlight (Bodnar et al., 2009), black women's dietary and supplemental vitamin D intakes fail to meet the national recommendations (Bodnar et al., 2009). It is recommended that

high-risk women (with history of at least one preterm delivery) must be screened for BV and the treatment should include oral dose of metronidazole. Adequate diagnosis and proper handling of BV and other genital diseases during pregnancy is the key to prevent both maternal and fetal complications. Additional factors like socio-demographic conditions and difficult to access health services which are inherent to underdeveloped countries, could also favor a greater prevalence of BV and thereby an increased risk of perinatal complications (Leitich et al., 2003).

4.3 Maternal nutritional determinants and fetal growth

4.3.1 Body mass index

One of the most important risk factors for fetal growth restriction and prematurity in developing countries is low prepregnancy weight or BMI, (Singh et al., 2016). There is evidence from metanalysis of 78 studies (n=1025794) that maternal underweight is associated with an overall increased risk of preterm birth by 29% (RR1.29; 95% CI 1.15-1.46) and that of LBW by 64% (RR 1.64; 95% CI 1.38-1.94). In addition to maternal BMI, increased physical activity performed by women such as farming or gathering water is reported to be linked to incidences of LBW, (Imdad and Bhutta, 2013). However, pre-pregnancy overweight/obesity has also been shown to increase the risk of adverse neonatal outcomes as preterm delivery, both low and high birthweight, (Yu et al., 2013). Evidence from two marginalised and underweight ethnic communities in Nepal showed that increasing BMI and gestational weight gain was strongly associated with the birth weight of newborn. The community with the higher BMI and gestational weight gain (GWG) (BMI=23 and GWG=12.8kg) compared with the community with lower BMI and GWG, (BMI=21 and GWG=10.3kg) showed a higher mean birth weight (3460 grams vs 2960 grams), (Upadhyay et al., 2011). A study exploring the relationship between maternal BMI and neonatal birthweight in North-West Nigeria found significant correlations between the two parameters. Low- first trimester BMI was correlated to the delivery

of LBW neonates (<2500 g), also, obese mothers delivered significantly larger neonates compared to mothers of average weight (r=0.607, P< 0.001).

4.3.2 Maternal Protein status

Maternal protein status during gestation is a key determinant in embryonic survival, growth, and development .The consumption of supplemental nutrition during pregnancy where protein contributes to less than 25% of the energy has been shown to contribute to a reduction in both still-and small-for-gestational-age births to about 31% (Imdad and Bhutta, 2011; Clark, 2016). Moreover, from the Auckland Birthweight Collaborative study it was deduced that traditional diets containing fish, low-fat dairy products, lean meat, fruits and vegetables were associated with a lower risk of IUGR than western diets that predominantly contain refined grains, processed meat and confectionaries (CI-95%, odd ratio-0.86) (Greiger and Clifton, 2014).

Both protein deficiency and protein excess during pregnancy play a vital role in fetal growth and development. Protein deficiency during pregnancy leads to deficiency of specific amino acids (AA) that are crucial for regulating cell metabolism and function and thereby affects fetal growth and development (Herring et al., 2018). For instance, specific amino acids such as L-arginine also recognised as “conditionally essential AA” acts as a precursor for synthesis of molecules with cell signalling and metabolic functions (e.g. nitric oxide, polyamines, and creatine) and improves the rate of embryonic survival when adequately provided through well supplemented diet (Herring et al., 2018). Adequate levels of amino acids are essential for placenta to deliver nutrients to the fetus and a low dietary protein intake results in placental insufficiency and consequently IUGR and other adverse pregnancy outcomes as embryonic losses, low feed efficiency and reduced postnatal growth (Herring et al., 2018). Low maternal dietary protein intake is also associated with greatest abdominal adiposity amongst fetuses regardless of carbohydrate and fat intakes (Herring et al., 2018). However, protein excess also results in IUGR and embryonic death due to amino acid excess leading to ammonia, homocysteine, and H_2S toxicity that are generated as a part of the amino-acid catabolism process (Herring et al., 2018). Strong positive association occurs between birth weight and maternal milk (milk and milk

drinks) and dairy (milk, yogurt, cheese, butter, quark, milk pudding, dairy-based ice cream and cream/creamers) protein consumption as reported by the Generation R Study, Rotterdam, The Netherlands. Maternal consumption of 3 glasses (3×150 ml) of cow's milk per day is associated with greater fetal weight gain during the third trimester (Clark, 2016). However, consumption of protein dairy protein from cheese shows a negative association with birth weight, particularly at highest quintile of consumption and, higher birth weights were found to be particularly linked to the protein component of dairy in the form of milk and not to the fat or carbohydrate (Clark, 2016).

Studies from both developed and developing nations highlight the role of maternal protein status and its effect on fetal growth and development, but protein quality may play a pivotal role. In a cohort of 8,839 women from Southern Scotland, women with a pregnancy associated plasma protein – A (PAPP-A) in the lowest 5th percentile had an increased risk of IUGR (CI-95%, odds ratio-2.9), extremely premature delivery, preeclampsia and still birth (Smith et al., 2002). In developing nations like India, high maternal protein intakes (>70g/d) during pregnancy were positively associated with head, abdominal circumference and femur length of the babies (Borazjani et al., 2013). Therefore, adequate consumption of protein during gestational period is a key determinant in embryonic survival, growth, and development and to overcome harmful consequences of maternal protein malnutrition, dietary supplementation with arginine and glutamine during gestation can fulfil the nutritional requirements of both mother and fetus leading to higher rates of reproductive successes (Herring et al., 2018).

4.3.3 Maternal dietary fat and lipid status

The developing fetus requires substantial amount of fatty acids to support rapid cellular growth and activity which is dependent on maternal fatty acid intake, its concentration in the maternal circulation and the extent to which it is transported across the placenta (Herrera and Ortega-Senovilla, 2010). Recent reviews of the association between maternal fatty acid intake and fetal growth shows mixed results and no specific conclusion can be drawn about the role of maternal fatty acid intake and birth outcomes (Table-10). However, studies from developing nations of the

world have led to the assumption that there is an increased risk of SGA with consumption of high SFA diets, but diets in other areas of the world are very different in composition to the standard western style diet. For instance, Indian diets are comprised of mainly cereals, pulses with milk and vegetable oil being the major source of fat (Mani et al., 2016).

Much attention has been payed to abnormal lipid levels during pregnancy leading to complications like preeclampsia. Recent reviews suggest that dysregulation of maternal and placental lipid metabolism is involved in the pathogenesis of this condition (dos Santos and Couto, 2018; Wojcik-Baszko et al., 2018). However, link to dysregulation in maternal lipid profiles and gestational diabetes has also been made. A study evaluating lipid profile changes during gestation in pregnancies confirmed that the risk of preeclampsia and/or gestational diabetes increased with the levels of triglycerides from 7.2% in low triglyceride group to 19.8% in the group with high triglycerides (Wiznitzer et al., 2009). There is scarce literature on the role of maternal lipid concentrations on anthropometric birth outcomes amongst undernourished mothers in low-and-middle income countries. As per the Pune Maternal Nutritional Study in Pune, India, maternal total cholesterol levels at 18 and 28 weeks of gestation were significantly related to birth size and risk of preterm birth. One Standard Deviation (SD) higher maternal cholesterol and triglyceride concentrations at 28 weeks of gestations were associated with 54 grams and 36 grams higher birthweights respectively ($P<0.05$) (Kulkarni et al., 2013). An observational cohort study from India (n=1838) reports that higher intake of saturated fatty acids (SFA) and n-3 Poly-unsaturated fatty acids (PUFA) during early stages of pregnancy reduce the incidence of SGA and low birthweight in Indian population (Mani et al., 2016).

4.3.4 Maternal Multiple micronutrient supplementation

Multiple micronutrient (MMN) deficiencies co-exist among women of reproductive age and such deficiency conditions are exacerbated during pregnancy as it is a state of increased metabolic requirements (Neggers and Goldenberg, 2003). Not only developing but also in developed nations women of childbearing age do not meet the recommended dietary intake for micronutrients, particularly, zinc, folate, calcium and iron (Neggers and Goldenberg, 2003). A possible mechanism supporting the significance of micronutrients in management of adverse

pregnancy outcomes is the role it plays in partially mediating plasma volume expansion during pregnancy (low plasma volume and low BMI is a risk factor for adverse pregnancy outcomes), (Neggers and Goldenberg, 2003). In developing countries, where MMN deficiencies are more common, MMN supplementation (defined as administration of three or more micronutrients) or increasing consumption of micronutrient rich foods has shown a reduction in the rate of IUGR in women with low pre-pregnancy BMI (Neggers ang Goldenberg, 2003; Huybregts et al., 2009). Zinc, calcium and magnesium supplementation has been associated with improved pregnancy outcomes. Vitamin A supplementation has led to reduced maternal mortality and increased birthweight. Vitamin C deficiency has been linked to risk of preterm delivery (Neggers and Goldenberg, 2003). A systematic review of 14 randomized controlled trials concluded that MMN supplementation during pregnancy was more effective in reducing the rate of SGA at birth by 9 % in fixed effects model and 12% in random effects model, when compared to the standard iron-folic acid (IFA) supplementation (Haider etal., 2011). Another review observed that the birthweight of infants was on average 53 grams greater in the intervention group (mother on MMN supplementation) in comparison to control group (on IFA supplementation alone). It also suggested that MMN supplementation increases length of gestation, but no conclusive evidence could be drawn regarding its association to preterm birth (Ramakrishnan et al., 2012). Recently it has been recommended to replace iron and folic acid supplementation and integrate MMN supplements with iron and folic acid for pregnant women in low-middle income Countries to reduce the incidence of low birthweight and SGA and improve overall maternal health and fetal growth and development (Haider and Bhutta, 2017; Bourassa et al., 2019).

However, there is also other side to the coin wherein a number of studies have shown no beneficial effects of MMN supplementation on pregnancy outcomes. Information is lacking on optimal formulation of MMN supplementation for pregnant women and in most situations MMN deficiencies co-exist with dietary inadequacies (Allen, 2005). Data from developing countries are fragmentary and inconclusive and very few randomized controlled trials are available which found limited benefits of MMN supplementation on pregnancy outcomes (Gernand et al., 2015; Lawande et al., 2018), therefore, till date no conclusions can be made on the benefitting effects of MMN supplements on maternal and fetal health over and above iron-only supplementation (Ramakrishnan et al., 2003; Allen, 2005).

4.3.5 Iron Supplementation

Additional absorption of iron is required during pregnancy to support fetal growth. In developing countries iron deficiency is one of the leading micronutrient deficiencies amongst pregnant women (Hovdenak and Haram, 2012).). On an average 56% of pregnant women in developing countries are suffering from iron deficiency anemic (Hovdenak and Haram, 2012).). The maternal daily iron requirements increase from approximately 1 to 2.5mg/d in early pregnancy to 6.5 mg/d in the third trimester. Fe- deficiency leads to maternal and fetal stress as it increases corticotropin- releasing hormone, cortisol production and induces oxidative damage to fetal erythrocytes, thereby inhibiting fetal growth, (Hovdenak and Haram, 2012). Severe maternal anemia i.e. hemoglobin <80g/L has been associated with preterm delivery, low birth weight and IUGR, (Steer, 2000). Data from low-income countries suggest that the risk of having a low-birth weight infant is 3 times higher in mothers with iron deficiency anemia, (Allen, 2000). The nature of association between preterm birth and maternal anemia is U-shaped where both low and high hemoglobin concentrations (>145g/L) has been associated with higher rates of preterm deliveries. The mechanism linking maternal anemia to poor pregnancy outcomes is the failure in expansion of maternal plasma volume adequately and thereby diminished adequate placental profusion resulting in growth restriction in the developing fetus (Scholl, 2000). Maternal anemia diagnosed before mid-pregnancy has been associated with a greater risk of preterm birth and this association is not significant after third trimester of pregnancy, (Scholl, 2000).

4.3.6 Maternal Folic Acid

Folate is a key micronutrient essential for the rapid proliferation of cells, which is crucial for adequate fetal growth and development, in addition to the healthy development of the placenta and maternal adaptation to pregnancy (i.e., increased maternal blood volume) (McGee et al.,

2018). Folate is vital for the growth of the spine, brain, and skull of the fetus, especially throughout the first 4 weeks of pregnancy (McGee et al., 2018).

Pregnant women are recommended to eat folate-rich foods and take a supplement containing 400µg of Folic acid (FA) (additional to the folate content in the diet) starting from 2 months before to 3 months after conception, however, globally folate intake amongst women is found between 13% and 63% below recommendations in pregnancy (Scholl et al., 2000). Low folate intake from diets and supplements are associated with maternal characteristics reflecting poor nutritional status, including low energy intake, low rate of gestational weight gain, and a high frequency of iron deficiency anemia at entry to prenatal care (Scholl et al., 2000).

FA deficiency (<400nmol/kg diet) is related to threefold increase in the rate of fetal developmental abnormalities with adverse effects seen at FA plasma level below 5.5 nmol/L (Milman et al., 2016).The primary functions of FA are to protect the newborn from incidences of neural tube defects, additionally, peri conceptional folic acid use is also linked with epigenetic changes in insulin-like growth factor 2 in the child which could influence intrauterine programming of growth and development with consequences for health and disease over a lifetime (Milman et al., 2016). FA supplementation during pregnancy has resulted in higher live birth rates and lower risks of spontaneous abortions and congenital heart defects (Milman et al., 2016), and is also associated with favorable effects on birth weights and Apgar scores of newborns and reduced prevalence of FGR and maternal infections (Tamura et al, 1992). Diets low or enriched in FA induce altered DNA methylation in humans. Folate deficiency during embryogenesis can significantly alter the gene expression and reduce nucleic acid and protein synthesis and therefore can increase the risk of IUGR and other birth weight related complications (Sram et al., 2005; Qian et al., 2016).

A pub-med search for publications including review articles assessing the association between maternal folate status and pregnancy outcomes including keywords such as “Folic Acid” associated with “infant birth weight”, “fetal growth” and “preterm birth” was carried out. Majority of the review studies suggested a positive association (Chen et al., 2014; Gadgil et al., 2014; Moussa et al., 2016; Hovedenak and Haram, 2012) and only one suggested a contrary

association (Dwarkanath et al., 2013). Studies evaluating effect of maternal folate status on variables except preterm birth are few and have reported positive associations. Chen et al., in 2018 reported that placental folate transport capacity is decreased in IUGR and suggest that folate supplementation in the second and third trimester is of particular importance in pregnancies complicated by IUGR. Similarly, folic acid supplementation was associated with reduced risk of infant LBW and SGA and larger prenatal head size but not with prenatal or postnatal head growth (Graaff et al., 2017). However, most of the studies have focussed on the effect of folic acid on fetal growth in mid and later pregnancy and only a few studies have investigated this correlation in early pregnancy (Moussa et al., 2016). According to various studies, low vitamin B12 intake in the presence of high folate intake in the first and second trimesters of pregnancy was associated with a higher risk of SGA (Dwarkanath et al., 2013; Gadgil et al., 2014). Therefore, it is not the independent intake of folate that is the primary factor affecting birth outcome but vitamin B12: folate ratio that plays a pivotal role in determining birth outcomes. Studies suggesting a positive association between maternal folate intake and birth outcomes have shown a skewedness towards preterm birth being the only variable analysed amongst other birth outcomes (Chen et al., 2014). Higher plasma folate concentrations were associated with a longer gestational age (0.12 week per SD increase in folate (CI-95%) and tended to be associated with lower risk of preterm birth (Chen et al., 2014), these results were further verified by other studies as well (Wang et al., 2015; Liu et al., 2016; Chen et al., 2017).

Folate and cobalamin metabolism are intimately related and they both have an effect on adverse pregnancy outcomes through their role in the regulation of 1C metabolic pathways.
Folate acts as a cofactor for essential cellular reactions and regulates cell division and plays a pivotal role in DNA synthesis. It also serves as a substrate for variety of reactions affecting the metabolism of several amino acids, including the transmethylation and transsulfuration pathways (Scholl and Johnson, 2000). Since widespread and sustained cell division is crucial for fetal development the mechanism through which folate deficiency influences fetal growth precisely is by their effect on folate/methionine metabolism in the mother and fetus. Perturbations in the methionine/folate metabolism can have a profound impact on cell function, metabolism, growth and proliferation which in turn will pose a greater impact on the growing embryo and the fetus (Kalhan and Marczewski, 2012). Homocysteine, a sulfur amino acid and a by-product of

methionine metabolism reflects an inadequate folate intake or abnormal folate metabolism. Moreover, higher homocysteine concentrations pose an increased risk to the developing fetus leading to IUGR and other poor pregnancy outcomes (Scholl and Johnson, 2000).

5 Emerging determinants of fetal growth

5.1 Calcium supplementation

Low intake of calcium during pregnancy has been reported in many different parts of the world including Asia, Latin America and Asia. During pregnancy the demand for calcium substantially increases (+300 mg/day) because of its crucial role in fetal bone mineralization which is met by doubling of intestinal absorption and mobilization from the skeleton (Kanagal et al., 2014). In pregnant women, a calcium intake of <600 mg Ca/d results in a negative Ca balance (Kanagal et al., 2014). Low serum calcium during pregnancy is associated with high blood pressure as it stimulates the parathyroid hormone (PTH) and renin release and also induces vasoconstriction by increasing its level in the vascular smooth muscle (Kanagal et al., 2014). An inverse relationship occurs between dietary calcium intake and hypertensive disorders of pregnancy further increasing risk for pre-eclampsia, preterm birth and intrauterine growth retardation, (Kanagal et al., 2014). Calcium supplementation is associated with a risk reduction of 17% for low birth weight (LBW) and preterm birth (RR 0.76; 95% CI 0.60-0.97) (Hovdenak and Haram, 2012; Hofmeyr et al., 2014). Maternal calcium metabolic stress with PTH >62 pg/mL accompanied with very low calcium intake (<60 % of the estimated average requirement) has been associated adverse influence on fetal growth, leading to 2-3-fold increase in the risk of SGA at birth, (Scholl et al., 2014). Maternal calcium is thus found to play an important role in determining fetal birth weight.

5.2 Blood Pressure

Pregnancy-associated hypertension is an important risk factor for maternal and fetal morbidity and mortality (Lu et al., 2018). Pre-pregnancy hypertensive women with poorly controlled blood pressure during the first trimester of pregnancy are at an elevated risk of poor pregnancy outcomes (Lu et al., 2018). Mild-to-moderate pre-existing hypertension (systolic blood pressure (SBP) 140-159 mmHg or diastolic blood pressure (DBP) of 90-99 mmHg) increases the risk of pre-eclampsia, low-birth weight, placental abruption and growth restriction in the fetus (Lu et al., 2018). However, chronic hypertension (>170/110 mmHg) increases the relative risk of pre-eclampsia to 46% which further worsens maternal and fetal risks, (Lu et al., 2018). An increase in blood pressure from the second to the third trimester is associated with an increased risk of adverse birth outcomes. In a population based prospective cohort study (n=8,623), higher third-trimester SBP and DBP were associated with smaller third-trimester fetal head circumference and lower birth weight, and stronger associations were observed in cases of higher DBP and older gestational ages, (Bakker et al., 2011).

A cross-sectional study was conducted between August and December 2010 in the Ngäbe-Buglé indigenous population in western Panama (González-Fernández et al., 2017). The objectives of this study were to determine if maternal infections, inflammation and nutrient defcienceies were associated with the four measures of maternal BP (SBP, DBP, mean arterial pressure (MAP) and pulse pressure (PP) and also which of the four BP measurements were associated with SFH, interpreted using the INTERGROWTH standards. In this population the prevelance of hypertensive disorders of pregnancy (HDP) was reported to be 4.5% (Vigil-De Gracia, Arias et al., 2007),13% of materenal mortality was attributed to HDPs (Sistema de Naciones Unidas and Gobierno de la Republica de Panama, 2009), and 6.7% of institutional deliveries were LBW, (INEC 2010). The results showed that there was a high prevalalence of low BP in the population which may be indicating a decreased plasma volume, due to suspected presence of low protein status and anemia in the presence of normal haematorcrit and high urinary density, (González-Fernández et al., 2017). Moreover, the alternative BP measurements MAP and PP provided critical information about diagnosing mothers at high risk over the traditional SBP and DBP. MAP has also been validated as a risk factor for HDPs, (Cnossen et al., 2008). This study as well reported that MAP was the only BP measurement for which abnormal elevation of 11.3%

women was observed. Overall all blood preassure measurement parameters pointed towards the high prevalence of low BP in the study population and there is a lack of literature on studies that have actually reported fetal outcomes at lower blood pressures. Few studies report that maternal hypotension leads to increased risks of preterm delivery, low-birth weight and other postpartum complications but these results never reached statistical significance, (Ng and Walters, 1992; Grunberger et al., 1979).

Chapter III Methodology

1 Food Security

Food security is defined as “access by all people at all times to enough food, acquired by socially acceptable means, for an active and healthy lifestyle”, (Anderson, 1990). In our study an adapted Colombian household food security survey [CHFSS] was used which included range of questions about adult, child and household food security experiences (Table-3). Use of questionnaires measuring experiences of food insecurity accurately captured and quantified the experiences of food security at household level and was also relatively less expensive, easy to use and applicable to the study setting. The scoring system was based on the Rasch Model where if the individual responded “yes” to the first question and “almost every day” or “on just a few days” to the frequency question, they remained classified as 1. On the other hand, if the respondent answered “yes” to the first and “on only one or two days” to the frequency question, they were reclassified as zero, (Hackett et al., 2008).

The participants, based on their responses to the food security questionnaire (see Annexes) were provided with a food insecurity score which evaluated them based on the presence or absence of food security. Based on the food insecurity score the study population was further classified into “no to mild” and “mild to severe” food insecurity groups.

2 Diet Quality - The Colombian Dietary guidelines for pregnant women

Since 2000 Colombia has developed dietary guidelines for the population under two years of age, over two years of age and for pregnant and nursing mothers. The Colombian Institute of Family Wellbeing (‘Instituto Colombiano De Bienestar Familiar’, ICBF) manages the function of keeping the food guidelines updated. In 2008 the process to update and revise the guidelines for adults began and the final version was published in 2015 and for children under 5 was published in 2018, (FAO, 2018).

In our study we used a healthy eating questionnaire (Table-3) where we asked the participants "how often do you consume?" a list of food groups and scaled the responses.

The Ministry of Health as per the Food Based Dietary Guidelines (FBDG) for Colombia recommends the following-

1. Fruits and vegetables to be included in each meal i.e. 3 times a day
2. Eggs, milk and dairy are recommended to be consumed daily
3. Nuts are recommended to be consumed in small amounts or once a week
4. Legume consumption is recommended to be twice a week
5. Viscera (internal organs in the abdomen as intestine, liver and kidney) is recommended once a week
6. Grains are recommended two times a week
7. It is recommended to avoid consumption of processed and junk foods
8. Physical activity of a minimum of 20-30 minutes per day is recommended

3 Clinical and Laboratory indices

Maternal blood pressure and hematological indices were obtained and evaluated for the study population. The normal ranges for SBP was between 100-140 mmHg and for DBP was between 60-90 mmHg. Low blood pressure was considered when SBP <100 or DBP <60 (Kalabunde, 2012). MAP was estimated using the DBP with the help of the formula DBP + 1/3 (SBP-DBP) (Kuc, Koster et al., 2013). Cut-offs for elevated MAP (eMAP) during pregnancy were : >87 mmHg between 10-18 weeks of gestation, and >86 mmHg after week 34 weeks of gestation (WHEC (Women's Health and Education Center), 2009). Pulse pressure was calculated as the difference between SBP and DBP (Klabunde, 2012). The cut-offs for low pulse pressure were based on means± SD calculated by Thadani et al in a large population of pregnant women (n=576). Cut-offs for Low PP during pregnancy were: <33 mmHg between 7-15 weeks, <35 mmHg between 16-25 weeks, <34 mmHg between 26-38 weeks and <31 mmHg postpartum (Thadani et al., 2001). Anemia was defined as maternal hemoglobin level < 11g/dl (WHO, 2007). Ranges of normal hematocrit during pregnancy were 0.35-0.44 % during the first

trimester, 0.30-0.39 during the second trimester and 0.28-0.40 during the third trimester (Abbassi-Ghanavati et al., 2009).

4 Maternal and fetal anthropometric indices

Maternal symphysis-fundal height was determined on an empty-bladder using a flexible, nonelastic standard measuring tape. The tape measurement was taken from the middle of the upper border of symphysis pubis to the highest point of the uterine fundus. All the measurements were performed when the participant was lying flat on a bed with her legs extended and were rounded to the nearest centimeter. The original database had sonographically estimated fetal weight values but with nine missing observations therefore, fundal height measured was then used to calculate fetal weight based on the Johnson and Tosch Formula: fetal weight (gm)= 155 x (fundal height -12) and all the missing were then substituted with fundal height determined estimated fetal weight (Kumari et al., 2013). Since, the original fetal weight and estimated fetal weight from fundal height were highly correlated (ρ=0.81) we used these values for further analysis. The Intergrowth-21 standards were used to calculate SFH Z-scores and centiles in women with gestational age ≥ 16 weeks. Fetuses below the 10th percentile were classified as SGA (Papageorghiou et al., 2016).

5 Statistical Analysis

All statistical analysis was performed using STATA IC/15.1 (StataCorp, TX, USA). Summary statistics were calculated for all prevalences and scores of severities. T- test was used for continuous and normally distributed variables. Chi-squared or Fisher's exact test was used for binary variables. Kruskal- Wallis test was used for continuous and not normally distributed variables. Depending on the nature of the dependent variable, we selected either linear multiple regression (continuous variables), logistic regression (binomial variables) or ordered logistic regression (ordinal variables). Backwards stepwise process allowed the selection of final independent variables with a cut-off of P<0.15.

The cluster of independent variables initially explored was, 1. Maternal characteristics 2. Clinical and anthropometric indices 3. Pregnancy related outcomes, 4. Maternal infections and medicines in current pregnancy, 5. Food security (Table-7), 6. Diet Quality, 7. Nutritional Supplements, 8. Environmental Factors and Hygiene Characteristics, 9. Conflict related stresses. For each dependent variable (SFH and FW), we ran a series of exploratory univariate analyses examining all independent variables separately. Spearman correlations were run among independent variables, and significantly correlated variables were avoided in the same regression model. We then obtained a final composite model where significant variables from all the exploratory models were entered into the analyses. Results were only reported for those models which explained more than 10% of the variability of the dependent variable and also identified significantly related variables. Final models presented only those variables with $P<0.05$ or $P<0.1$. All the results are presented as mean± SEM or 95% confidence intervals unless otherwise indicated. In all cases the level of significance was set at $p<0.05$.

6 Ethical considerations

The ethical approval for the project was obtained from Scientific Research Ethical Board at the University Hospital San José, in the city of Popayán, Colombia.

Chapter IV Results

1 Maternal and household characteristics

A total of 61 pregnant mothers with a high-risk pregnancy were included in the study. Mean gestational age was 30 wks. and maternal BMI was 28±7 kg/ m^2. There was no evidence of underweight or obesity in the population; 74% followed the recommendation for 20-30 minutes of physical activity per day. Given ongoing monitoring for hypertensive disorders of pregnancy, mother's SBP, DBP and cardiac rates were within the normal ranges. There was no evidence of high blood pressure (>140 mmHg). However about 16% of the population showed prevalence of low diastolic blood pressure (DBP <60 mmHg) which has been linked to intrauterine hypoperfusion leading to low nutrient delivery to the fetus.

Clinical indices revealed no evidence of anemia (Hb <11g/dl) or high hematocrit (>41 (1 trimester), >39 (2 trimester) and >40 (3 trimester)) in the participants reflecting the presence of hemoconcertation. Concerning the individual experiences of stress, about 30% had a history of displacement as a result of war or armed conflict in the region. About 50% had reported difficulty in sleeping and about 40% experienced recall of stressful events and unusual alertness to surroundings. There was evidence of emotional tension (36%) and depressive mood (25%). The three major nutritional supplements consumed were iron (66%), calcium (67%) and folic acid (59%) alongside the standard multivitamins (41%). (Table-2).

2 Environmental factors and food security

Most (80%) had access to aqueduct and good quality water. The majority (89%) had access to toilets. Common pets in the environment were dogs (49%), cats (16%) and hens (26%). Pests were present as flies (27%), mosquitoes (34%), cockroaches (49%) but only 15% of the households reported presence of rodents (mice/rats) (Table-3). The majority (72%) of the households were food secure despite low incomes. Half (52%) of the women were actively

involved in making decisions regarding purchase and consumption of food in the household (Table-3).

3 Diet Quality

The major food groups consumed by the participants were eggs, dairy products and grains and about 67%, 46% and 33% of the participants, respectively, included these three food groups each day (Table-4).

The Colombian Food and Dietary Guidelines encourages more consumption of vegetable source fat over animal source fat. The majority used vegetable source fat for cooking (87%). During pregnancy as per the dietary recommendations, women were encouraged to include fruits and vegetables in every meal. Fewer than a third participants in our study complied with this recommendation (Table-4).

4 Maternal and fetal anthropometries

The linear fit plot distributions of estimated fetal weight versus gestational age and symphysis-fundal height versus gestational age were obtained (Figure-1). The Intergrowth-21 project provides standards for FW detected with sonography from 20 wks. of gestational age, and for SFH from week 16th of pregnancy, therefore only women with sufficient gestational age were used for analyses (n=46 for SFH and n=53 for FW). The number of participants with fetal weight < 10th percentile was 19/46 and those with SFH<10th percentile was 27/53. When the fetal weight and SFH Z- scores histogram population distribution was observed, SFH as a tool identified 58% as SGA whereas those with estimated fetal weight <10th percentile was only 17% SGA (Figure-2). Therefore, SFH displayed a higher prevalence of poor fetal growth in the study population than estimated fetal weight in our study population.

5 Comparison of symphysis-fundal height and fetal weight centiles and Z-scores above and below 10th percentile

Population characteristics for SFH and FW centiles and Z-scores less than and more than or equal to 10th percentile for each growth index (Table-5 and Table-6) were compared with general population characteristics.

5.1 Comparison of symphysis-fundal height and fetal weight centiles in the presence or absence of population characteristics

As per the comparisons based by the two centile groups, SFH <10th centile differed with higher rate of physical activity >30minutes/day (P=0.03), with lower DBP (P=0.04), with lower MAP (P=0.04) and with a higher AFI (0.0009) while FW did not differ by any general population characteristic (Table-5).

5.2 Comparison of symphysis-fundal height and fetal weight Z-scores in the presence or absence of population characteristics

Better SFH Z-scores were associated with treatment of HDP (P=0.04), iron supplementation (P=0.04) and calcium supplementation (P=0.03), anemia (P=0.01), high hematocrit (P=0.04), multivitamin supplementation (P=0.02), presence of cats in the maternal environment (P=0.02) and history of displacement (P=0.01) worsened mean SFH Z-scores. Fetal weight Z-scores were worsened with consumption of grains (P=0.01) and intake of aspirin (P=0.02) (Table-6).

5.2.1 Treatment of Hypertensive Disorders of Pregnancy is associated with SFH Z-scores

Low dose aspirin and calcium supplementation has been successfully used to lower the risk of pre-eclampsia and other hypertensive disorders of pregnancy. Our results show that treatment of HDPs with aspirin and calcium supplementation led to better mean SFH Z-scores (Figure-3).

5.2.2 SFH Z-scores differed with anemia and supplementation

Iron supplement intake lead to better mean SFH Z-scores whereas anemia and multiple micronutrient supplementation worsened mean SFH Z-scores (Figure-4).

5.2.3 SFH Z-scores differed with environmental factors and history of displacement

Of all the environmental characteristics studied in the population, the presence of cats in the maternal environment was associated with lower mean SFH Z-scores and was the only statistically significant difference (Figure-5). History of displacement worsened the mean SFH Z-scores, indicating that it continues to impact mothers in the study population, but interestingly the overall stress score was not associated with SFH Z-scores (Figure-5).

6 Univariate and multivariate regression analysis for SFH

6.1 Univariate logistic regression for symphysis fundal height centiles and general population characteristics

A series of univariate logistic regression models for SFH <10th centile as dependent variable was run with respect to all the population characteristics as independent variables and all associations with P<0.05 were considered statistically significant. Our results showed that only following consumption of dairy as per the recommendation was statistically significantly associated with lower SFH (P=0.04) (Supplementary Table-1).

6.1.1 Controversial dietary recommendation- low-fat milk

The fact that the Colombian Dietary Guidelines did not recommend intake of animal fat compelled us to analyse other sources of fats in the diet. It was observed that out of all the other sources of animal fat in the diet only intake of dairy emerged as having a statistically significant association and quiet surprisingly, the consumption of dairy products increased the odds of low SFH (OR: 1.5±0.26, P=0.02). This was followed by a series of logistic regression models where we combined dairy with other food groups and analysed their association with low SFH. We observed that the models of dairy with eggs, grains or vegetable fat resulted in dairy continuing to have a negative association with SFH but eggs, grains or vegetable fat did not enter the models as statistically significant (Table-7). However, the model that added nuts/avocados to the dairy model revealed that both were associated with SFH (P=0.004). The addition of nuts/avocados to the dairy model did not change the negative impact of dairy on low SFH (OR:1.98±0.47) but the addition of nuts/avocados did decrease the odds of low SFH overall (OR:0.63±0.14).

6.2 Symphysis-fundal height simple linear regression

Simple linear regression of SFH with overall general population characteristics (Supplementary Table-2) was carried out. Associations with P<0.05 and P<0.1 were considered: physical activity (P=0.06), DBP (P=0.01), MAP (0.02), anemia (P=0.02), high hematocrit (P=0.09), AFI (P=0.09), HDP (P=0.08), iron supplementation (P=0.08), calcium supplementation (P=0.07), multivitamins supplements (P=0.04), presence of cats (P=0.05) and history of displacement (P=0.02).

6.2.1 Symphysis-fundal height final multiple regression model

All statistically significant and non-correlated variables were entered into multiple regression model to identify determinants of SFH. Due to collinearity, two separate models were run for iron and calcium supplementation respectively (Table-8). The factors that contributed to low SFH Z-scores in both the models were physical activity, anemia and history of displacement. Conversely, the factors contributing to better SFH Z- scores were DBP and high hematocrit. The calcium model explained 44% of the total variability in the population whereas the iron model explained 46% of the total variability in the population.

6.3 Fetal weight univariate logistic regression

Fetal weight centiles were compared with overall general population characteristics using univariate logistic regression models. Intake of aspirin (P=0.03) and depressive mood (P=0.05) were statistically significantly associated with lower fetal weight (Supplementary Table-3).

6.3.1 Fetal weight final model

A multiple logistic regression was run between fetal weight as the dependent variable and depressive mood and intake of aspirin as independent variables. The overall model explained 24% of the variability in the fetal weight (P=0.006). Both depressive mood (OR: 7.06±6.88, P=0.05) and intake of aspirin (OR: 9.18± 9.04, P=0.02) increased the odds of FW < 10^{th} centile.

7 Amniotic Fluid Index

Conflict related stresses (overall stress score and component stress scores), blood pressure indices and diet quality were compared between AFI ≤ 13 cms and AFI >13 cms. T-test was carried out for normally distributed and continuous variables and chi-squared or fisher's test for binary variables. The overall stress score (P=0.04), recall of stressful events (P=0.02), physical reaction to stress (P=0.05) were statistically significantly associated with AFI (Table-9).

7.1 Simple linear regression of amniotic fluid index and stress components

Linear regression of overall stress score and AFI was carried out and the association was significant between the two groups (AFI <13 cms and AFI > 13 cms) (Table-10). Higher stress score lead to higher AFI (P=0.04). The overall stress score predicted 12% of the variability in the AFI of the population and out of the specific stress components of the overall stress score, recall of stressful events and physical reaction to stress predicted 10% and 15% of the variation in the AFI of the study population respectively. Greater the frequency of recall or physical reaction to stress, higher was the AFI. This particular observation was very novel and requires further investigation with a larger sample size. Since everyone in our population was within the normal ranges for AFI, we cannot comment any further what might explain this difference.

Chapter V Discussion

Major Findings

This study examined the association of experiences of conflict related displacement and stress during pregnancy with poor maternal health and poor fetal growth using symphysis-fundal height as an antenatal screening tool. A secondary objective was to determine how responsive SFH was in relation to household environmental conditions, food insecurity and/or diet quality. Four novel findings emerged

First, SFH displays a higher prevalence (58%) of SGA than fetal weight (17%) as an antenatal screening tool. Symphysis-fundal height < 10^{th} percentile but not fetal weight <10^{th} percentile was associated with higher physical activity < 30 mins/day, lower DBP, lower MAP and lower AFI.

Second, there is evidence of both physiological stress and conflict related stress in the study population as shown by prevalence of hypertensive disorders of pregnancy (13%) and history of displacement (30%). Although the history of displacement could reflect a host of other variables and social conditions that were not included in the models or collected in the study but which can affect the access to resources and protections that being displaced. Displacement is a complex and diverse experience that cannot easily be constricted to a one variable. Given that this high-risk population was being treated with aspirin and calcium supplement for HDPs, 14% had elevated- mean arterial pressure (eMAP) and surprisingly 16% had low diastolic blood pressure.

Third, final models identifying determinants of SFH showed that physical activity, anemia and history of displacement were associated with poorer SFH Z-scores whereas higher hematocrit and DBP were associated with better SFH Z-scores. In these models, iron but not calcium supplementation was associated with better SFH Z-scores.

Fourth, history of displacement in the population lead to poorer mean SFH Z-scores, suggesting that stress was a problem in this context. The overall stress score did not have any impact on SFH or FW, however, it was associated with amniotic fluid index. The overall stress score

predicted 12% of the variability in the AFI. Out of all the component stress scores, recall of stressful events and physical reaction to stress were significant elements and positively predicted 10% and 15% of the variation of AFI respectively.

Collectively these results demonstrate that SFH is associated to multiple factors such as treatment of hypertensive disorders of pregnancy, dietary elements like low-fat dairy, iron and multiple micronutrient supplementation and surprisingly to presence of cats in the household and these factors should be prioritized for intervention among this population. Our study was the first that used intergrowth-21 standards for symphysis-fundal height measurements, and we observed that SFH picked up more variables as determinants of SGA when compared to ultrasonographically determined fetal weight.

1 Calcium supplementation and aspirin associated with better SFH Z-scores

In our study the population was already being monitored for hypertensive disorders of pregnancy. Traditionally low dose aspirin and calcium are offered to women at increased risk of pre-eclampsia and other hypertensive disorders of pregnancy (Helou et al., 2017). As per the meta-analysis of prophylactic effect of aspirin during pregnancy, daily dosage of $\geq$ 100 mg aspirin when initiated $\leq$ 16 weeks of gestation reduces the risk of preterm pre-eclampsia by 10% (Groom and David, 2018; Roberge et al., 2018). The exact mechanism explaining the role of aspirin is unclear, but a recent meta-analysis suggests that aspirin prevents defective-placentation by improving uteroplacental circulation through its antiplatelet aggregation effect and therefore decreases the risk of pre-eclampsia (Zhu et al., 2018).

Calcium plays a vital role in management of HDPs because low calcium intake contributes to elevated blood pressures by stimulation of the parathyroid hormone or renin release which causes vasoconstriction (Tang et al., 2015). Supplementation of calcium also reduces resistance in uterine and systemic vessels and therefore improves circulation (Tang et al., 2015). Calcium supplementation of at least 1 g/day during pregnancy reduces the rate of pre-eclampsia by 40%

(Tang et al., 2015). Our study results were consistent with the generally accepted clinical guideline and we observed that both calcium supplementation and intake of aspirin were associated with better mean SFH Z-scores in women who were previously diagnosed with HDPs. Hence, our study confirms in a population with low-dietary calcium intake, that pregnant mothers diagnosed for HDPs benefit from supplemental calcium and aspirin.

2 Multiple micronutrient supplementation worsened SFH Z-scores

There is limited understanding of the relationship between antenatal micronutrient supplement and in utero growth. Therefore, the current WHO recommendation suggests that "multiple micronutrient supplementation is not recommended for pregnant women to improve maternal and perinatal outcome" (WHO, 2016).

Data from developing countries are fragmentary and inconclusive and very few randomized controlled trials are available which found limited benefits of MMN supplementation on pregnancy outcomes. A randomised control trial from rural Bangladesh reported that MMN supplementation affected length of gestation but not fetal growth (Gernand et al., 2015). In LMICs, improving micronutrient intakes in undernourished mothers increases birthweight but there is little or no evidence on nature or timing during gestation that could have an effect on fetal growth. A maternal nutrition project in India reported that overall a micronutrient-rich supplement did not increase standard ultrasound measures of fetal size and growth at any stage of pregnancy (Lawande et al., 2018).

As per the latest Cochrane review, the effectiveness of MMN supplementation may be compromised due to possible interaction of certain micronutrients leading to impaired absorption also the risk of interaction is larger when nutrients are provided as supplements (Haider and Bhutta 2017). Moreover, the risk of excessive intake of micronutrients (above the tolerable upper intake levels) is higher amongst supplement users than non-supplement users leading to toxicity and consequently compromising on health-promoting effects of MMN (Engle-Stone et al., 2019). For instance, higher intake of folic acid may mask the symptoms megaloblastic

anemia and interfere in the detection of vitamin B12 deficiency which further is a determinant of IUGR (Johnson, 2007).

MMN supplementation in a population fails to achieve its full potential also due to continued consumption of diet inadequate in calories and proteins (Black, 2001). Nutritionist recommended the consumption of low-fat milk during pregnancy in our study population. Low fat milk is expensive and that might have compromised expenditure on other food products thereby leading to low calorie intake. It is possible that consumption of inadequate calories in the diet interfered with the impact of MMN supplementation in the study population and therefore leading to low SFH Z-score.

3 Toxoplasmosis and maternal-foetal interface

In our study mother's exposure to cats lead to poor mean SFH Z-scores. We suggested that this could be due to acquired *Toxoplasma gondii* infection during pregnancy through uptake of cat-shed oocysts (Opsteegh et al., 2014). Other possible routes of transmission could be through consumption of contaminated milk (Boughattas, 2017) or water. About 50% cases of toxoplasma infection in Colombia can be attributed to water as per by a recent meta-analysis (El Bissati et al., 2018). *T.gondii* parasite survives better in hot and humid conditions (Khademi et al., 2019) therefore, the warm and tropical climatic conditions of our study site, Colombia also favors higher prevalence of *T.gondii* infections. *T. gondii* strains are known to infect the placenta and the immunomodulation during pregnancy also contribute to the development of an environment that allows the parasite to escape from the natural immune response of the body thereby increasing the likelihood of congenital transmission through the maternal-foetal interface (Borges et al., 2019).

Prenatal diagnosis of congenital toxoplasmosis has crucial implications on fetal outcomes. It is suggested in literature that treatment instituted within 3 weeks after maternal seroconversion reduces the rate of transmission of toxoplasmosis to the fetus. The most effective means of diagnosing fetal toxoplasmosis is the Polymerase Chain Reaction (PCR) analysis of the amniotic fluid, which has a sensitivity of 87% and specificity of 99% when performed within 5 weeks of

maternal diagnosis when there is maximum risk of fetal toxoplasmosis (de Oliveira Azevedo et al., 2016).

Estimation of the incidence of congenital toxoplasmosis worldwide is challenging since in many countries neither its diagnosis is not mandatory to be reported to public health officials, nor have pre-natal or post-natal screening programmes been implemented (El Bissati et al., 2018). Until 2013 in Colombia, approximately 40% of pregnant women are not screened or provided treatment for toxoplasmosis. Those mothers receiving gestational screening were also inadequately tested as there was only one test for diagnosis (negative IgG). Negative IgG indicates need for further tests and diagnosis and the mother is still at the risk of primary acquisition and vertical transmission to the fetus. It was in 2013 that Colombian Ministry of Health implemented official guidelines for diagnosis and treatment of toxoplasma during pregnancy and monthly testing was considered as most cost-effective for the region (El Bissati et al., 2018).

Currently, no vaccine exists against human *T.gondii* infection and the commonly used pre-natal and post-natal treatments can only reduce the change of congenital transmission but not prevent it (Borges et al, 2019).

Apart from toxoplasmosis, pregnant women are also at risk of certain co-infections that are associated with lower fetal birth weight. A study from Brazil showed that seropositivity for Toxocara spp. was associated with an increased risk of infection by T.gondii (P=0.001) and co-infection by both the parasites was associated with SGA (Santos et al., 2107). Therefore, in order to effectively manage this emerging infectious disease, it is necessary to have educational programs and public health interventions to improve hygiene, reduce risk behaviours and implement robust gestational screening and treatment of acutely infected mothers.

4 Amniotic fluid index associated with overall stress score

Amniotic fluid index (AFI) is a score given to the amount amniotic fluid seen on ultrasonography of a pregnant uterus and is expressed in cm (Phelen et al., 1987). A four-

quadrant technique is used to estimate AFI wherein the deepest, unobstructed, vertical length of each amniotic fluid pocket is measured in each quadrant of the uterus and then added up to others. Normal AFI ranges between 8-18cms, with <5-6 cms considered as oligohydramnios (less than normal amniotic fluid) and >24-25 cms considered as polyhydramnios (more than normal amniotic fluid index). Both conditions are a crucial risk factors for maternal complications and birth defects (Magann et al., 2011). In our study AFI was associated with the overall stress score ($p=0.04$) but as all our participants were within normal ranges of AFI and also due to small sample size (N=33) we could not comment further on what could explain such a difference (higher or lower AFI).

During birth and neonatal period mother and baby are particularly vulnerable to environmental stressors. Exposure to armed conflict increases prenatal stress which has detrimental effects on obstetric outcomes and fetal development (Keasley et al., 2017). However, majority of studies validating the association between maternal stress and infant birth outcomes have been conducted in high-income countries, whereas exposure to violence and depression are more prevalent in LMIC's (Stein et al., 2015). A recent review examining impact of ongoing current conflicts on pregnancy outcomes in Bosnia, Israel, Libya and Iraq suggested a positive relationship between exposure to armed conflict and low birth weight along with increased rates of miscarriage, stillbirth, prematurity and congenital abnormalities in nine out of thirteen total studies included (Keasley et al., 2017). Our results are consistent with literature studying association between prenatal environment in times of stress and birth outcomes thereby it is essential for antenatal care programs to consider environmental stressors while diagnosing high risk pregnancies.

The prenatal hormonal environment is associated with physical development of the fetus and the key mechanism linking maternal stress to FGR is overexposure of the developing fetus to glucocorticoids (Duthie and Reynolds, 2013). Greater fetal glucocorticoid exposure has been a risk factor for low birthweight and shorter gestation at delivery. The underlying biological mechanism states that, maternal hypothalamic-pituitary-adrenal (HPA) axis undergoes dynamic changes during the course of pregnancy, and it is normal for maternal cortisol levels to rise threefold by the 3rd trimester. However, the fetus is protected from high cortisol by the activity of

an enzyme 11β-hydroxysteroid dehydrogenase type 2 (HSD11B2). Due to chronic maternal stress the activity of maternal HPA axis and HSD11B2 is dysregulated and there is greater glucocorticoid exposure to the fetus thereby causing growth restriction and other developmental complications (Duthie and Reynolds, 2013).

Based on a longitudinal study on associations between prenatal stress and infant birth outcomes, maternal cortisol (endocrinological marker of stress and anxiety) was associated with amniotic fluid cortisol and infant gestational age and birthweight. Higher amniotic fluid cortisol levels further predicted decreased birthweight ($p<0.05$) (Baibazarova et al., 2013). These results were further verified in another recent studies wherein chronic maternal stress affected fetoplacental corticotropin-releasing hormone secretion (CRH) and amniotic CRH was negatively associated with fetal size at amniocentesis and preterm birth (La Marca-Ghaemmaghami et al., 2017; Rabiepoor et al., 2019).

This study implies that maternal stress is a determinant of fetal well-being and an important risk factor for preterm birth, infant mortality and low birthweight. The association of the AFI with maternal stress factors further highlights the relevance of mental health of the mother and strategies to promote psychosocial health of the mother should be integrated with antenatal care.

5 Dietary quality and its impact on symphysis-fundal height

Although we found that study participants were 10% mildly, 8% moderately and 10% severely food insecure, 72% of the population was food secure. However, the quality of the diet was an issue as the consumption of dairy products increased the odds of SFH < 10^{th} percentile however, presence of nuts and avocados in the diet lowered the odds of low SFH. We believe that one explanation for the observed association of dairy to low SFH was related to nutritionist in Colombia recommending low-fat milk intake to women in high-risk pregnancies. Low-fat milk is not only more expensive which affects a person's expenditure on other essential foods but also low in calorie and deficient in essential fat that is crucial for a healthy pregnancy. When nuts and avocados were included in the logistic regression model, a decrease in the odds for low SFH was

observed because of its mineral, vitamin and high monounsaturated fatty acid (MUFA) content which substituted for the otherwise low-fat dairy consumption in the population.

Generally, the 3 major food groups included in everyday meals were eggs (67%), dairy (46%) and grains (33%). Nutritionist recommended to consume fruits and vegetables daily and majority of the participants did not follow this recommendation. In our study, 70% of the study population did not comply with Colombian dietary guidelines for consumption of fruits and vegetables. As these women were at high risk of hypertensive disorders of pregnancy, they were recommended to consume low-fat milk. Consumption of vegetable-source fats were encouraged and 87% of the population used vegetable fat over animal or mixed fat.

Diet plays a therapeutic role in management of hypertensive disorders of pregnancy. A recent metanalysis elucidated on the protective effect of legumes, whole grains and fish (due to presence of n-3 fatty acids) against HDPs and adverse birth outcomes (Kibret et al., 2019; Oken et al., 2007). There are several studies that claim greater adherence to the Diet Approach to Stop Hypertension (DASH) (diet which is rich in fruits, vegetables and low-fat dairy but limited in salt, saturated fat and total cholesterol) is associated with reduced risk of hypertension and cardiometabolic risk in non-pregnant population (Endeshaw et al., 2015; Compher et al., 2018; Kahsay et al., 2018). However, elements of DASH may not be applicable for fetal-maternal health unit and following a sodium restricted DASH diet has not been effective in reducing the risk of HDP or other adverse pregnancy outcomes (Asemi et al., 2014; Fulay et al., 2018). There is evidence that restricting sodium in diet during pregnancy leads to reduced plasma volume expansion and fetal growth retardation (Roy-Clavel et al., 1999; van der Maten, 1995) . WHO in 2013 issued a strong dietary recommendation for management of HDPs, it stated that pregnant women should be provided a daily dose of 1.5-2 grams supplemental calcium (especially in populations with lower dietary intake of calcium) after 20 weeks of gestation for prevention of preeclampsia as a part of antenatal care (WHO, 2013). It also so far, the most widely accepted and efficient recommendation for management of HDPs globally and especially in low- and middle-income countries where maternal diet is deficient in calcium (Cormick et al., 2018).

In areas where there is a higher prevalence of maternal undernutrition other dietary recommendations such as balanced protein-energy supplementation and magnesium supplementation has been associated with 30% reduction in risk of SGA (Merialdi et al., 2003; Stevens et al., 2015) A recent metanalysis elucidated on the protective effect of legumes, whole grains and fish (due to presence of n-3 fatty acids) against HDPs and adverse birth outcomes (Kibret et al., 2019; Oken et al., 2007). There is a positive correlation between maternal plasma volume and infant birthweight and restriction of energy and protein in the diet has been shown to restrict plasma volume expansion during pregnancy thereby affecting fetal growth (Rosso and Streeter, 1979). Energy content of protein-energy supplementation is crucial for fetal growth and it is recommended that providing only up to 20% of energy as protein improves fetal growth whereas supplements with too much protein appear to have a deleterious effect on fetal growth like increasing risk of PTB (Liberato et al., 2013). Apart from balanced energy and protein supplementation there is increasing evidence supporting intake of magnesium rich foods such as nuts, seeds, beans and leafy greens and magnesium supplementation in pregnant women as the need for magnesium increases during pregnancy and diets of mothers are usually lacking in magnesium in both developed and developing country context (Dalton et al., 2016).

There is sufficient literature on the risk of HDPs, however on the contrary there are very few studies that have actually studied the effect of hypotension on pregnancy outcomes which was a crucial observation in this study population. In 1992 a study on effects of chronic maternal hypotension on pregnancy outcomes demonstrated in a sample of 134 pregnant women that hypotensive women had significantly increased risk of delivery before the 38th week of delivery, SGA, and other postpartum complications (Ng et al. 1992). Low maternal blood pressure has also been associated with decreased plasma volume due to presence of low protein status and anemia in an indigenous population (González-Fernández et al., 2017).However, a more recent review concluded that no causal relationship between low blood pressure and poor perinatal outcomes can be drawn but is an important confounding factor (Hohmann and Künzel, 2007).

We observed that nuts and avocados had a positive impact on SFH over other food groups. This observation is consistent with maternal Mediterranean-style diet (regular intake of antioxidant, fiber rich fruits and vegetables, lean choice of protein, n-3 fatty acids, whole grains and MUFA

from plant oils) that has been associated with 90% lower risk of preterm delivery (Khouri et al., 2005). It is well known that dietary adaptation to adequate fatty acid status helps in preventing FGR (Meher et al., 2016). Nuts (especially flaxseed and walnut) are a significant source of n-3 fatty acids (docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA)) which have been associated with prolonging gestation and reducing the risk of PTB (Coletta et al., 2010). Furthermore, maternal DHA status in early pregnancy is positively associated with birth weight (Meher et al., 2016). However, in our study the participants were basically consuming only peanuts but majority of them used avocados in soups and other dishes. Avocados comply within the guidelines for Mediterranean- style diet as they contain MUFA, fiber, antioxidants and are low-glycemic (Comerford et al., 2016). Based on a review, avocado contains higher amounts of key nutrients like folate and potassium which is normally under consumed in maternal diet. They are sodium free and do not contain empty calories from added sugars, saturated fats, or alcohol. Moreover, avocados are also a significant source of fiber, MUFA and lipid soluble antioxidants that have been associated with overall improvement in maternal health and birth outcomes (Comerford et al., 2016).

6 Symphysis-fundal height detects higher prevalence of small-for-gestational-age than fetal weight

In our study SFH was able to detect a higher prevalence (58%) of SGA than sonographically estimated fetal weight (17%). Our results are consistent with literature which states that sonographically estimated fetal weight is subject to error ranging between ± 6 to 11% depending on the parameters measured and equation used for estimation of fetal weight and when compared with clinical methods of estimation of fetal weight (SFH), the mean absolute percentage error was higher in ultrasonographic method (Njoku et al., 2014). Ultrasonographic estimated fetal weight assessment is more likely to overestimate fetal weight when infants are SGA because of the absence of consideration of dynamics of amniotic fluid in the ultrasonic fetal weight formula which influences the accuracy of the ultrasonic fetal weight estimation (Ott et al., 1986; Stefanelli and Groom, 2014). Moreover, there is growing evidence that incorporation of maternal characteristics (such as maternal BMI, gestational age, parity, fetal gender etc.) improves the screening efficiency of detection of fetal growth disorders like IUGR, PTB and SGA (Goetzinger

et al., 2013; Curti et al., 2014).This is consistent with our finding that fetal weight did not identify differences between low and normal birthweight in our population and only when we put in SFH we were able to identify a wide range of determinants of poor fetal growth.

The measurement of SFH identifies the maternal amniotic fluid compartment. Dynamic changes in the AFI has definite implications on the growing fetus (Hebbar et al., 2015). Very low values are associated with risk of IUGR and renal anomalies in fetus whereas high values are indicative of fetal gastro-intestinal abnormalities, maternal diabetes mellitus amongst others, therefore it is recommended that regular AFI assessment be offered biweekly to women at risk (Hebbar et al., 2015). However, in our study we had all the participants within normal ranges of AFI but SFH and not estimated FW responded to maternal physical, psychosocial, dietary and environmental determinants of SGA. Changes in amniotic fluid volume reduces performance of intrapartum clinical as well as sonographic estimated fetal weight measures (Barnhard et al., 1996). However, a 2013 study reported that SFH was reasonably able to predict polyhydramnios (high AFI) with a sensitivity ranging from 69-88% in the study population (n=753) (Friere et al., 2013). Our study implies that although ultrasound estimation of fetal weight is a crucial aspect of antenatal care but SFH is more sensitive to both improper fetal growth and amniotic fluid development therefore it responded to general population indices (physical activity, low blood pressure, dairy intake, iron and calcium supplementation, presence of cats in the environment and experiences of conflict-related stresses) when AFI was normal while fetal weight measures did not (Moghaddam Tabrizi and Saraswathi, 2012). This observation is consistent with a study that evaluated relationships between maternal anthropometrics, maternal factors and birth weight as an outcome of these parameters in pregnancy. Fundal height was identified as a significant predictor of IUGR and was associated with maternal factors (maternal age, weight, ethnicity) gestational weight gain and BMI affecting fetal birth weight (Moghaddam Tabrizi and Saraswathi, 2012).

On the other hand, there is a huge discrepancy in literature regarding usefulness and reliability of SFH as an antenatal screening tool with respect to the developed and developing country context (Table-1). Majority of the studies from developing regions of the world support the use of SFH when ultrasound obstetric care is inaccessible and have reported higher sensitivity rates with

respect to prediction of SGA ranging between 56-86% (Robert et al., 2012) whereas studies from developing countries associate SFH with a high false-positive rate of detection of SGA and consider that there is insufficient evidence to support its clinical usefulness over ultrasound. However, in our study despite the small sample size of 61, SFH was able to detect a higher prevalence of SGA in the population (58%), therefore we establish that SFH is an effective, low-cost and low-technology antenatal screening tool in resource-constrained nations that lack access to obstetric ultrasound and trained ultrasonographers. SFH as a screening tool is readily available, non-invasive prenatal intervention that if provided with continuity is capable of providing reassurance of optimal fetal growth and early diagnosis of fetal growth abnormalities in high-risk pregnancies thereby improving overall maternal and fetal wellbeing.

Final Conclusions

In conclusion, this was a pilot study, we have identified possible areas of intervention that could help to improve maternal fetal health in the region

1. Routine use of calcium and aspirin for treatment of hypertensive disorders of pregnancy should be continued.

2. Our study showed dual burden of both HDPs (13%) and low DBP (16%) in the population. Therefore, we suggest expanding diagnosis and treatment of high-risk pregnancies by including MAP and PP measurements over the standard SBP and DBP. Our study showed a 14 % risk of e MAP which is a validated risk factor for HDPs (Cnossen et al., 2008).

3. Iron supplementation should be continued and favored over multiple micronutrient supplementation because our study showed that iron supplementation lead to better mean SFH Z-scores whereas MMN supplementation was associated with poor mean SFH Z- scores. Moreover, in current literature as well there is insufficient evidence to support the role of MMN supplementation and its impact on fetal growth (Lawande et al., 2018).

4. Our study reported that exposure to cats during pregnancy lead to poor mean SFH Z-scores due to risk of congenital toxoplasmosis. Therefore, it is necessary to have educational programs and public health interventions to improve hygiene, reduce risk behaviours and implement robust gestational screening and treatment of toxoplasmosis.

5. In our study the participants were not complying with the fruit and vegetable intake recommended in the Colombian dietary guidelines. They were also recommended to consume low-fat dairy during pregnancy to avoid risk of cardiovascular disorders most likely because they were being treated for HDPs which is not the same as hypertension in the general population. Diets recommended for avoiding risk of hypertension in general population may not be applicable to fetal-maternal unit health. Therefore, implement health and educational policies that promotes healthy diets during pregnancy is recommended.

6. SFH as an antenatal screening tool was more sensitive in detecting the total prevalence of SGA in the population than FW. Therefore, it is recommended to scale up the use SFH as an antenatal screening tool in areas lacking access to obstetric ultrasound services.

Finally, our study showed that maternal-fetal health is affected by a range of physical, environmental and psychosocial factors and SFH as an antenatal screening tool responds to them. Therefore, in order to improve maternal and child health in resource-poor settings where obstetric ultrasound is unavailable antenatal care interventions should be focussed on using SFH as a low cost and low technology method for monitoring fetal growth and identifying IUGR in high-risk pregnancies.

Table-2 Maternal and household characteristics

Maternal characteristics	Means/Percent/Median	Maternal infections	Means/Percent/Median
Age,yrs	27±7	Genital Infections	
Years of education, yrs	11±3	Yes-1	20%
Marital status		Bacterial Vaginosis	
Single and Non-Stable	30%	Yes-1	13%
Stable	71%	**Medicines**	
Physical Activity		Antibiotics	
<30 min/day	87%	Yes-1	23%
>30min/day	13%	Aspirin	
Physical Activity recommended		Yes-1	33%
20-30 mins a day	74%	Thyroid Hormone medication	
Pregnancy related measures		Yes-1	7%
Gestational age	30±7	Anti-hypertension medication	
Amniotic fluid index	13 (4,17)	Yes-1	3%
Household Characteristics		Preterm delivery medicines	
Urban-1	79%	Yes-1	11%
Rural-2	21%	Anti-diabetes medicines	
Pregnancy outcomes		Yes-1	7%
History of		History of displacement	30%
Pre-term Delivery	16%	Stress Questionnaire	
HDP	13%	Recall of stressful events	49%
Pelvic surgery, No	75%	Dreams about stressful events	31%
Gestational Diabetes, No	90%	Physical reaction to events	43%
Anthropometric measures		No interest in events	36%
Weight,kg	69±17	Not feeling loved by people	31%
Height,cm	156±7	Alert more than usual	46%
BMI, kg/m^2	28±7	Difficulty in sleeping	54%
Blood pressure,mmHg		No of hours of sleep	
SBP	104±9	≤5h	21%
SBP>140	0%		
DBP	64±8	>6h	79%
DBP<60	16%		
Mean Arterial Pressure	78±7	Emotional Tension	36%
EMAP[1]	14%	Depressive mood	25%
Pulse Pressure	41±8	Neurovegetative symptoms	10%
Low pulse pressure[2]	19%	Supplements	
Cardiac rate,bpm	78±9	Iron	66%
Hemoglobin, g/dl	13±1	Calcium	67%
Hemoglobin <11 g/dl	5%	Folic Acid	59%
Hematocrit	39±4	Multivitamins[4]	41%
High Hematocrit[3],%	40%		

[1] >87 mmHg (10-18 weeks), >84 mmHg (18-34 weeks), and > 86 mmHg (after week 34)
[2] <33 mmHg (7-15 weeks), <35 (16-25 weeks) and < 34 (26-38 weeks)
[3] >41(1 trimester), >39 (2 trimester), >40 (3 trimester)
[4] Common multivitamin brands were Natele, Viplena, Cestavid, Similac mama, Ensure, Tarritorojo
They included varying compositions of vitamin A, D, E, C, B1, B2, B3, B6, B12, folic acid, iron, calcium, EPA and DHA.

Table-3 Environmental factors and food security in the general population

Environmental factors	**Percentage**	**Food insecurity score**	**Percentage**
Quality of water		No-0	72 %
Well-0	20%	Yes-1	28%
Aquiduct-1	80%	Food insecurity score	
Defecation place		No to mild-0	82%
Other-0	11%	Moderate to severe-1	18%
Toilet-1	89%	Food Security Questionnaire	
Dogs	49%	Monthly Income (minimal salary=approx. 330 CAD)	
Cats	16%	≤1 min.sal	61%
Hens	26%	>1 min.sal	39%
Flies	27%	Women takes decision to buy food	52%
Mosquitoes	34%	Not having sufficient money to buy food	28%
Cockroaches	49%	An adult eats less because of lack of resources	16%
Mice/Rats	15%	Decrease of meals due to lack of resources	7%
Garden intake	34%	Adult skips meals	5%
Boiling water for drinking	51%	Adult complain of hunger	8%
Washing hands before cooking	98%	Adult went to bed hungry	5%
Washing hands after toilet	98%	Bought less food for kids because of lack of resources	8%
		Child complains of hunger	3%
		Child went to bed hungry	2%

Table-4 Summary of frequency of consumption of food groups*

	Everyday	>3 d/wk	1-3 d/wk	1 time/wk	Occasionally	Never
Eggs	67%	23%	3%	3%	2%	2%
Dairy	46%	13%	11%	7%	18%	5%
Grains	33%	28%	18%	8%	7%	6%
Nuts/Avocados	13%	3%	15%	12%	26%	31%
Viscera	3%	4%	13%	13%	26%	41%
Junk food	7%	3%	8%	7%	29%	46%

*Colombian Dietary Guidelines (FAO, 2018)

Majority of the participants failed to consumed fruits and vegetables as per the recommendation. Only 15% at breakfast, 33% at lunch and 28% at dinner.

The nutritionist recommended vegetable source fat and about 87% of the population used vegetable fat and 8% used animal fat, 2% used mixed fat and 3% used no fat.

Table-5 Comparison of population characteristics for symphysis-fundal height and fetal weight less than and more than 10th percentile

Category	Fetal weight <10 percentile	Fetal weight ≥ 10 percentile		Symphysis-fundal height <10 percentile	Symphysis-fundal height ≥ 10 percentile	
n	**8**	**38**		**31**	**22**	
	Mean ± SD or frequency	**Mean ± SD or frequency**	**P value**	**Mean ± SD or frequency**	**Mean ± SD or frequency**	**P value**
Maternal Characteristics						
[1]Maternal age, yrs	32.12±9.70	26.84±6.70	0.0681	27.93±7.15	27.13±7.44	0.6523
[2]Gestational age, wks	27.44±4.48	32.72±4.49	0.009	31.18±5.46	28.02±6.82	0.1081
[1]Education,yrs	9.62±3.58	11.55±3.31	0.0734	11.48±3.28	10.77±3.61	0.4596
[3]Stable marital status	13%	88%	0.182	55%	45%	0.329
[1]Height,cms	155.87±7.27	155.28±5.93	0.8084	154.70±6.17	155.86±6.16	0.5055
[2]Weight,kg	66.62±8.66	72.47±19.25	0.6322	67.58±11.12	71.81±24.25	0.8496
[2]BMI kg/m^2	27.31±3.92	29.39±8.19	0.6955	27.65±4.41	29.10±10.44	0.9352
[3]Physical activity <30 min/day	17%	83%	0.634	53%	47%	0.032
Blood Pressure (mmHg)						
[1]SBP	110±10.71	106±9.58	0.2256	104±11.50	108±5.70	0.1169
[1]DBP	67±7.23	65±7.86	0.5509	63±8.10	67±6.27	0.0402
[1]MAP	81±7.36	78±7.41	0.1710	77±8.13	80±5.41	0.0413
[1] PP	44±9.22	41±8.72	0.2045	41 ±9.90	41 ±5.92	0.4211
[1]Cardiac rate, bpm	77.25±7.45	79.75±8.97	0.2332	78.13±7.32	80.04±9.66	0.2103
[1]Hemoglobin,g/dl	12.96±1.55	12.75±1.19	0.3372	12.74±1.24	12.94±1.13	0.2846
[1]Hematocrit, %	38.22±4.67	38.85±3.88	0.3451	38.32±3.92	39.15±3.92	0.2353
[2]Amniotic fluid index,cm	12.89±2.39	15.47±0.52	0.06	14.45±0.40	17.59±1.04	0.0009
[3]**Household** Urban	16%	84%	0.497	59%)	41%	0.563
Rural	22%	78%		56%	44%	
[3]**Quality of water** Well	29%	71%)	0.352	33%	67%	0.096
Aqueduct	15%	85%		64%	36%	
[3]**Defecation place** Other	0%	100%	0.452	75%	25%	0.445
Toilet	19%	81%		57%	43%	
No of hours of sleep[3] ≤ 5 h	18%	82%	0.626	46%	54%	0.236
>6h	17%	83%		62%	38%	
Monthly Income[3] **(min. salary= 330 CAD 55pprox..)**						
≤1 min. salary	21%	79%	0.366	56%	44%	0.547
>1 min. salary	12%	88%		50%	50%	

[1] T-test for normally distributed and continuous variables
[2] Kruskal-wallis test for continuous and not normally distributed variables
[3] Chi-squared or Fisher's exact test for binary variables

Table-6 Difference in Z-scores by population characteristics for symphysis-fundal height and fetal weight

	FETAL WEIGHT Z-scores			SYMPHYSIS FUNDAL HEIGHT Z-scores		
Condition	**Yes**	**No**	**P**	**Yes**	**No**	**P**
History of	Mean ± SD	Mean ± SD		Mean ± SD	Mean ± SD	
Preterm delivery	0.26±2.31 (N=7)	-0.21±1.23 (N=39)	0.96	-1.76±1.11 (N=9)	1.43±1.17 (N=44)	0.22
HDP	-0.90±1.28 (N=5)	-0.04±1.42 (N=41)	0.18	-0.73±1.14 (N=6)	-1.58±1.13 (N=47)	0.04
Pelvic surgery	-0.52±1.14 (N=10)	-0.03±1.48 (N=36)	0.31	1.29±1.01 (N=14)	1.56±1.20 (N=39)	0.22
Gestational diabetes	0.13±1.14 (N=5)	-0.17±1.46 (N=41)	0.44	-1.02±1.03 (N=5)	-1.54±1.17 (N=48)	0.17
Blood pressure, (mmHg)						
EMAP	-0.49±1.57 (N=8)	-0.09±1.43 (N=36)	0.67	-1.17±1.27 (N=8)	-1.53±1.16 (N=43)	0.21
LOW PP	0.01±1.08 (N=6)	-0.19±1.50 (N=38)	0.58	-1.31±0.94 (N=8)	-1.50±1.22 (N=43)	0.33
Hypotension	-0.69 (N=1)	-0.12±1.43 (N=45)	0.38	-2.9 (N=1)	-1.46±1.15 (N=52)	-
Blood indices						
Anemia	-1.11±2.35 (N=3)	-0.07±1.35 (N=43)	0.51	-3±1.73 (N=3)	-1.40±1.08 (N=49)	0.01
High HCT	-0.25±1.05 (N=18)	-0.04±1.68 (N=25)	0.50	-1.14±1.34 (N=20)	-1.75±1.07 (N=27)	0.04
Maternal infections						
Urinary tract infections	0.41±2.81 (N=6)	-0.22±1.12 (N=40)	0.43	-1.8±1.19 (N=8)	-1.44±1.17 (N=44)	0.21
Other genital infections	-0.7±2.19 (N=4)	-0.08±1.35 (N=42)	0.84	-2.06±0.99 (N=6)	-1.42±1.17 (N=46)	0.10
Food insecurity score	0.06±2.21 (N=13)	-0.22±0.99 (N=33)	0.47	-1.4±1.16 (N=15)	-1.52±1.17 (N=38)	0.35
Food intake from garden	-0.47±1.27 (N=17)	0.05±1.48 (N=29)	0.25	-1.47±1.22 (N=19)	-1.50±1.13 (N=34)	0.46
Diet quality (recommended intake)						
Dairy	-0.46±1.29 (N=26)	0.27±1.49 (N=20)	0.08	-1.59±1.09 (N=26)	-1.39±1.23 (N=27)	0.26
Eggs	-0.08±1.45 (N=32)	-0.26±1.38 (N=14)	0.92	-1.52±1.09 (N=37)	-1.30±1.30 (N=16)	0.22
Nuts/Avocados	-0.35±1.35 (N=24)	-0.09±1.48 (N=22)	0.48	-1.3±1.29 (N=25)	-1.66±1.01 (N=28)	0.12
Grains	-0.43±1.19 (N=36)	0.90±1.74 (N=10)	0.01	-1.62±1.21 (N=41)	-1.02±0.83 (N=12)	0.05
Viscera	-0.12±1.19 (N=15)	-0.14±1.53 (N=31)	0.95	-1.55±1.09 (N=18)	-1.46±1.20 (N=35)	0.39
Processed	-0.16±1.52 (N=38)	-0.02±0.79 (N=8)	0.74	-1.42±1.18 (N=44)	-1.82±0.99 (N=9)	0.17
Fruits and vegetables	-0.52±1.45 (N=13)	0.01±1.40 (N=33)	0.56	-1.72±1.25 (N=14)	-1.40±1.12 (N=39)	0.18
Fat	-0.04±1.43 (N=39)	-0.68±1.33 (N=7)	0.25	-1.58±1.07 (N=45)	-0.97±1.51 (N=8)	0.08
Junk Food	-0.19±1.26 (N=33)	0.0007±1.81 (N=13)	0.79	-1.48±1.19 (N=40)	-1.51±1.10 (N=13)	0.46
Supplements						
Iron	-0.42±1.42 (N=28)	0.31±1.32 (N=18)	0.29	-1.27±1.11 (N=33)	-1.85±1.16 (N=20)	0.04
Calcium	-0.43±1.40 (N=29)	0.36±1.35 (N=17)	0.20	-1.28±1.10 (N=35)	-1.89±1.18 (N=18)	0.03
Folic Acid	-0.29±1.28 (N=24)	0.02±1.57 (N=22)	0.58	-1.38±1.10 (N=29)	-1.62±1.22 (N=24)	0.23
Multivitamins	-0.13±1.77 (N=19)	-0.14±1.14 (N=27)	0.58	1.88±1.03 (N=21)	-1.23±1.17 (N=32)	0.02
Antibiotics	0.59±1.70 (N=9)	-0.31±1.31 (N=37)	0.31	-1.53±1.11 (N=13)	1.48±1.18 (N=40)	0.44
Aspirin	-0.83±1.47 (N=17)	0.26±1.24 (N=29)	0.02	-1.14±1.14 (N=17)	-1.65±1.14 (N=36)	0.06
Thyroid hormone replacement	0.95±0.26 (N=2)	-0.18±1.43 (N=44)	0.08	-1.6±0.63 (N=4)	-1.48±1.19 (N=49)	0.57
Anti-hypertensive drugs	-0.31±1.47 (N=2)	-0.13±1.43 (N=44)	0.87	-1±1.69 (N=2)	-1.51±1.15 (N=51)	0.27

Preterm delivery pharmacological treatment	-0.05±2.01 (N=6)	-0.15±1.34 (N=40)	0.37	-1.51±1.60 (N=6)	-1.48±1.11 (N=47)	0.47
Anti-diabetes	0.63±0.59 (N=3)	-0.19±1.45 (N=43)	0.17	-1.23±0.51 (N=3)	-1.50±1.18 (N=50)	0.34
Pets						
Dogs	-0.13±1.27 (N=23)	-0.14±1.58 (N=23)	0.48	-1.49±1.33 (N=24)	-1.49±1.01 (N=29)	0.50
Cats	-0.48±1.44 (N=9)	-0.05±1.42 (N=37)	0.58	-2.21±1.52 (N=8)	-1.36±1.05 (N=45)	0.02
Hens	-0.67±1.30 (N=14)	0.09±1.42 (N=32)	0.08	-1.21±1.15 (N=14)	-1.59±1.15 (N=39)	0.14
Pests and rodents						
Flies	-0.33±1.23 (N=8)	-0.05±1.46 (N=37)	0.53	-1.90±0.99 (N=12)	1.42±1.15 (N=40)	0.09
Mosquitoes	-0.25±1.28 (N=17)	-0.07±1.51 (N=29)	0.97	-1.31±1.26 (N=19)	-1.59±1.10 (N=34)	0.20
Cockroaches	-0.17±1.61 (N=25)	-0.10±1.18 (N=21)	0.47	-1.56±1.20 (N=27)	-1.41±1.12 (N=26)	0.31
Mice/Rat	-0.04±0.99 (N=5)	-0.15±1.47 (N=41)	0.87	-1.37±1.40 (N=8)	-1.51±1.12 (N=45)	0.37
Hygiene characteristics						
Boiling water for drinking	-0.31±1.11 (N=24)	0.05±1.70 (N=22)	0.34	-1.32±1.25 (N=28)	-1.68±1.02 (N=25)	0.13
Washing hands before cooking	-0.16±1.43 (N=45)	0.88 (N=1)	0.21	-1.47±1.16 (N=52)	-2.6 (N=1)	-
Washing hands after toilet	-0.16±1.43 (N=45)	0.88 (N=1)	0.21	-1.47±1.16 (N=52)	-2.6 (N=1)	-
Conflict related stress						
Recall of stressful events	-0.33±1.36 (N=22)	0.03±1.47 (N=24)	0.52	0.03±1.47 (N=24)	-1.61±1.24 (N=27)	0.21
Dream about stressful events	-0.13±1.01 (N=15)	0.14±1.59 (N=31)	0.91	-1.38±1.21 (N=18)	1.54±1.14 (N=35)	0.31
Physical reaction to stress	-0.14±1.16 (N=20)	-0.13±1.61 (N=26)	0.77	-1.20±1.00 (N=23)	-1.71±1.23 (N=30)	0.05
Lack of interest in daily activities	0.11±1.89 (N=17)	-0.29±1.06 (N=29)	0.34	-1.58±1.21 (N=19)	-1.43±1.11 (N=34)	0.32
Feeling unloved	-0.25±1.51 (N=14)	-0.08±1.40 (N=32)	0.73	-1.47±1.36 (N=17)	-1.50±1.06 (N=36)	0.46
Alert more than usual	-0.003±1.66 (N=20)	-0.24±1.22 (N=26)	0.67	-1.42±1.41 (N=23)	-1.54±0.93 (N=30)	0.35
Difficulty in sleeping	-0.27±1.32 (N=28)	0.07±1.58 (N=18)	0.75	-1.57±1.22 (N=31)	-1.38±1.08 (N=22)	0.28
Emotionally tensed	-0.41±1.43 (N=18)	0.03±1.41 (N=28)	0.49	-1.42±1.26 (N=20)	-1.53±1.10 (N=33)	0.37
Depressive mood	-0.72±1.69 (N=10)	0.02±1.31 (N=36)	0.35	-1.22±1.33 (N=13)	-1.58±1.09 (N=40)	0.16
Neurovegetative symptoms	-0.41±1.95 (N=6)	-0.09±1.35 (N=40)	0.84	-1.35±1.17 (N=6)	-1.51±1.16 (N=47)	0.37
History of displacement	-0.37±1.28 (N=13)	-0.04±1.48 (N=33)	0.50	-2.04±1.21 (N=15)	-1.27±1.07 (N=38)	0.01

Table-7 Multiple logistic regression models for symphysis-fundal height with dairy and other food groups

SFH <10th centile and Dairy models				
Models	**OR±SE**	**P-value**	**95% CI**	**Overall model**
Model-1 Dairy	1.5±0.26	0.02	1.05, 2.09	Psuedo R^2=0.07, P=0.02
Model-2 Dairy	1.57±0.30	0.02	1.07, 2.28	Psuedo R^2=0.08, P=0.04
Eggs	0.79±0.23	NS	0.44,1.41	
Model-3 Dairy	1.49±0.28	0.03	1.03, 2.15	Psuedo R^2=0.07, P=0.06
Grains	0.98±0.19	NS	0.66, 1.46	
Model-4 Dairy	1.48±0.27	0.03	1.05, 2.09	Psuedo R^2=0.07, P=0.06
Vegetable fat	1.35±1.10	NS	0.27, 6.67	
Model-5 Dairy	1.98±0.47	0.004	1.24, 3.16	Psuedo R^2=0.14, P=0.006
Nuts and Avocados	0.63±0.14	0.04	0.40, 0.98	

Table-8 Multiple linear regression for symphysis-fundal height with either calcium or iron supplementation included in the model

	Coef. ± SE	P
Physical activity[a]	-1.22±0.44	0.009
Anemia[a]	-1.20±0.56	0.04
High hct[b]	0.67±0.28	0.02
DBP, mmHg[b]	0.40±0.01	0.01
History of displacement[a]	-0.95±0.31	0.005
Calcium supplement[b]	0.57±0.29	0.05
Adj R^2	0.44	0.0000

	Coef. ± SE	P
Physical activity[a]	-1.26±0.44	0.006
Anemia[a]	-1.21±0.56	0.04
High hct[b]	0.68±0.28	0.02
DBP, mmHg[b]	0.40±0.01	0.01
History of displacement[a]	-0.99±0.31	0.003
Iron supplement[b]	0.62±0.27	0.03
Adj R^2	0.46	0.0000

[a] determinants contributing to low SFH
[b] determinants contributing to high SFH

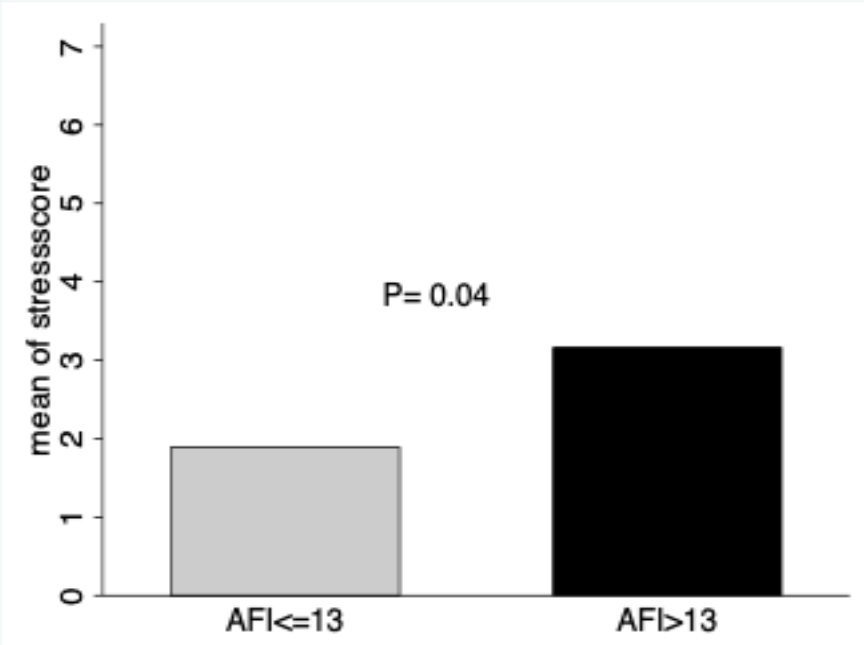
Table-9 Comparing conflict related stresses, blood pressure indices and diet quality with Amniotic fluid index≤ 13 and Amniotic fluid index >13

	All women with AFI ≤ 13 N=9	**All women with AFI >13 N=24**	**P-value**
	Means±SD or frequency	Means±SD or frequency	
Stress score[1]	1.88±1.45	3.17±0.39	0.04
Components of stress score[2]			
1. Recall of stressful events	11%	58%	0.02
2. Stressful dreams	33%	25%	0.47
3. Physical reaction to stress	11%	50%	0.05
4. Lack of interest in events	22%	50%	0.15
5. Not feeling love towards others	22%	29%	0.53
6. Unusual alertness	33%	38%	0.58
7. Difficulty in sleeping	56%	67%	0.42
Biopsychosocial assessment	0.44±0.52	0.42±0.50	0.45
Components [1]			
1.Emotional tension	45%	42%	0.60
2.Depressive mood	0%	25%	0.12
3. Neurovegetative symptoms	0%	17%	0.30
Blood pressure measures[2]			
EMAP	18%	27%	0.42
LOW PP	6%	20%	0.25
Anemia	6%	12%	0.50
High Hematocrit	29%	53%	0.15
Diet Quality[1]			
Dairy	4±1.41	4±1.20	0.48
Eggs	5±0.53	5±0.77	0.39
Nuts/ Avocados	2±1.27	2±1.95	0.67
Grains	4±1	3±1.66	0.10
Viscera	1±1.22	2±1.72	0.61
Processed	1±0.97	1±1.13	0.45
Fruits and Vegetables	2±0.87	2±0.96	0.70
Fat	1±0.50	1±0.20	0.75
Junk food	1±1.01	1±1.63	0.33
Hours of sleep[1]	2±0.60	2±0.88	0.76

[1] T-test for normal and continuously distributed variables
[2] Chi-squared or Fisher's test for binary variables

Table-10 Univariate linear regression model of stressors associated with amniotic fluid index

10A- Statistically significant association between overall stress and amniotic fluid index



10B. Statistically significant associations between amniotic fluid index and component stress scores

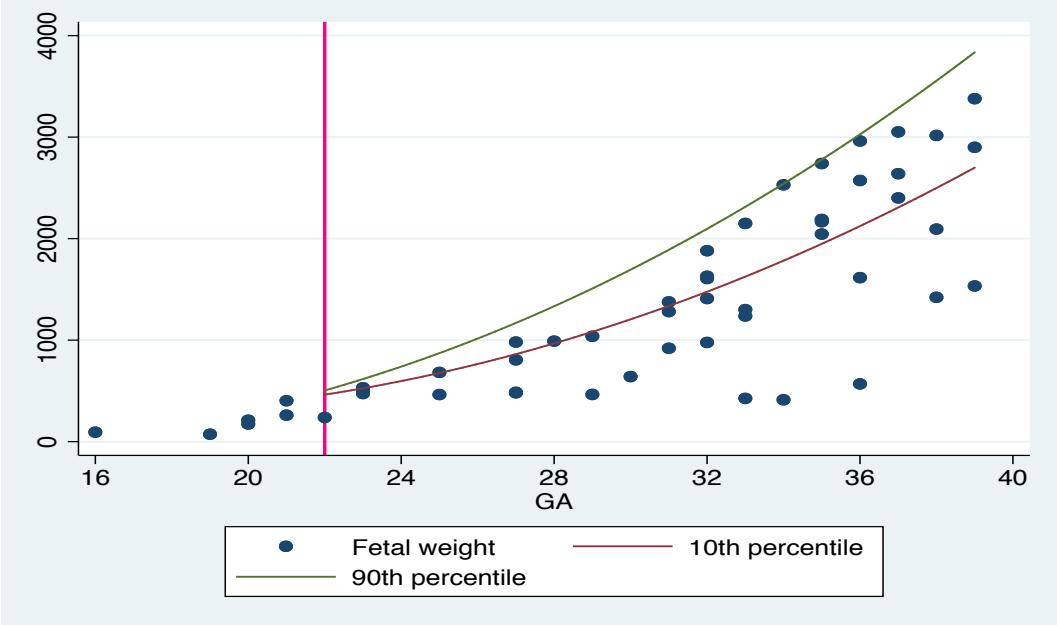
AFI	Coeff± SE	P-value	95% CI	
Stress score	0.66±0.28	0.03	0.90, 1.24	N=33 $F_{1,31}$=5.6 P=0.02 Adj R^2= 0.12
Recall of stressful events	2.27±1.04	0.04	0.14, 4.41	N=33 $F_{1,31}$=4.71 P=0.04 Adj R^2= 0.10
Physical reaction to events	2.66±1.04	0.02	0.54, .4.78	N=33 $F_{1,31}$=6.54 P=0.02 Adj R^2= 0.15

Table-11 Summary table of review articles on maternal fatty acid intake and its association to fetal growth

Author and year	Objectives	Conclusions
Demmelmair and Koletzko, 2014	Review on the importance of long-chain polyunsaturated fatty acids (LC-PUFAs) in the perinatal period	No firm conclusions about the optimal LC-PUFA status of pregnant women or infant birthweight can be drawn.
Kabaran and Besler, 2015	Review of literature to assess role of maternal fatty acids in fetal metabolic programming	Imbalances in fatty acid intake during pregnancy deteriorates fetal metabolic programming. Permanent changes in neuroendocrine function and energy metabolism in the fetus may occur.
Bobiński and Mikulska, 2015	To assess the role of maternal fatty acid metabolism on fetal growth restriction.	Medium-chain fatty acids (MCFAs) play an important role in fetal development and changes in the levels of these acids can be observed in cases of IUGR, premature birth and SGA in pregnancy diet.
Voortman etal., 2015	Systematic review to evaluate the effects of Polyunsaturated fatty acids during pregnancy on cardiometabolic health.	There is insufficient evidence to support the beneficial effects of PUFAs in fetal life.
Saccone etal., 2016	To provide evidence-based recommendations for omega-3 supplementation during pregnancy	Not enough evidence to support routine use of omega-3 supplementation during pregnancy. Omega-3 not associated with prevention of IUGR and/or SGA

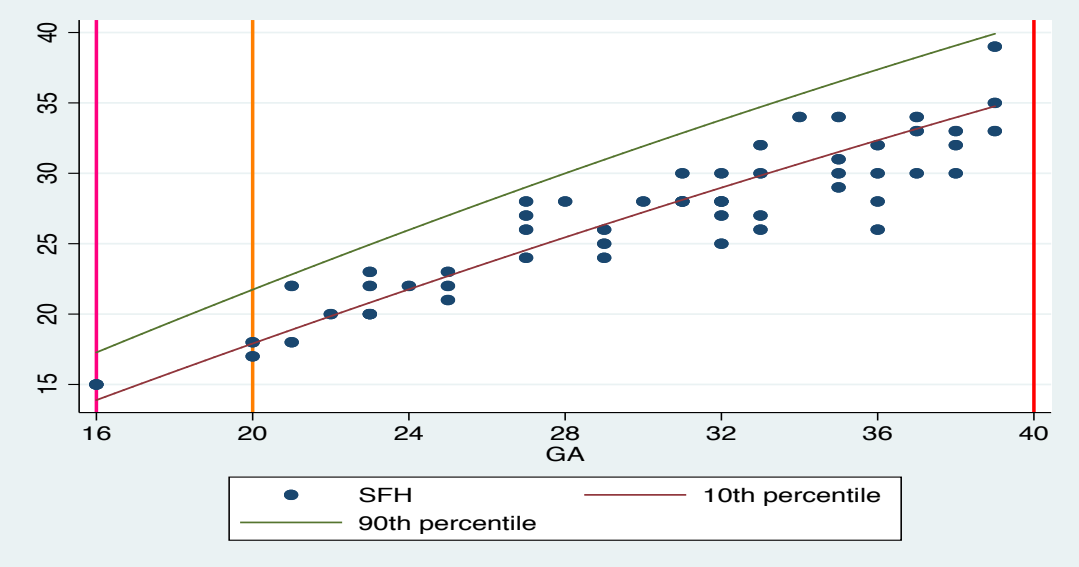
Figure-1 Linear fit plot distribution of Estimated fetal weight and Symphysis-fundal height versus gestational age

1A. Estimated Fetal Weight



Gestational age ≥ 22 weeks was used for estimated fetal weight as per the Intergrowth-21 standards.

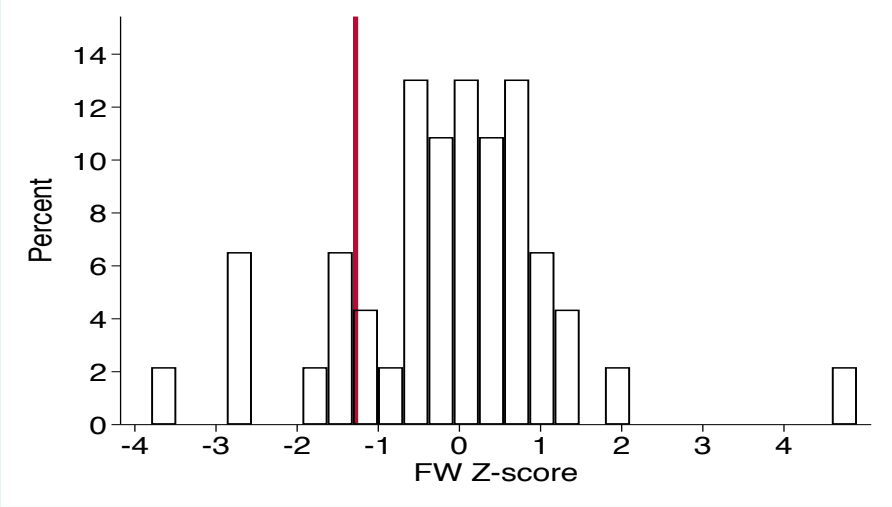
1B. Symphysis-fundal height



Gestational age ≥ 16 weeks was used for symphysis-fundal height as per the intergrowth-21 standards.

Figure-2 Symphysis-fundal height displays higher prevalence of Small-for-gestational-age than Estimated fetal weight

A. Estimated fetal weight Z- score distribution



B. Symphysis-fundal height Z-score distribution

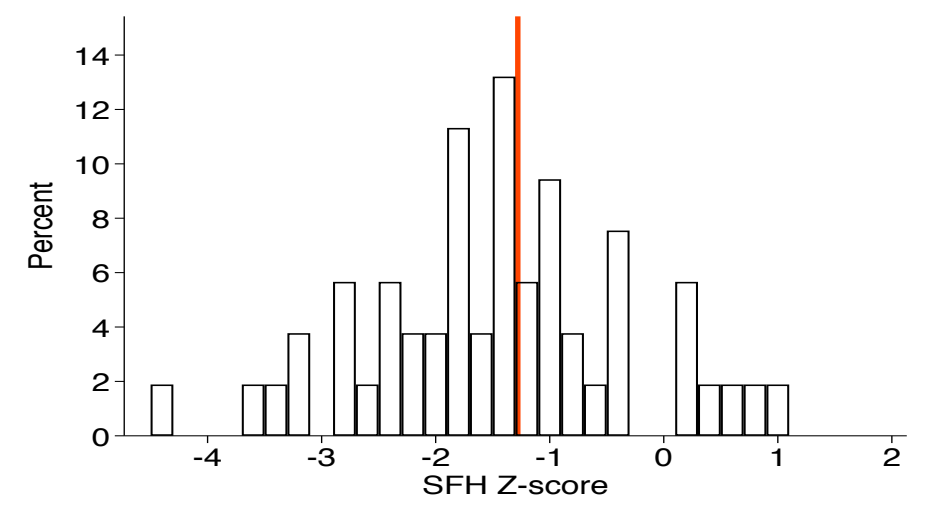


Figure-3 Treatment of hypertensive disorders of pregnancy associated with Symphysis-fundal height Z-score

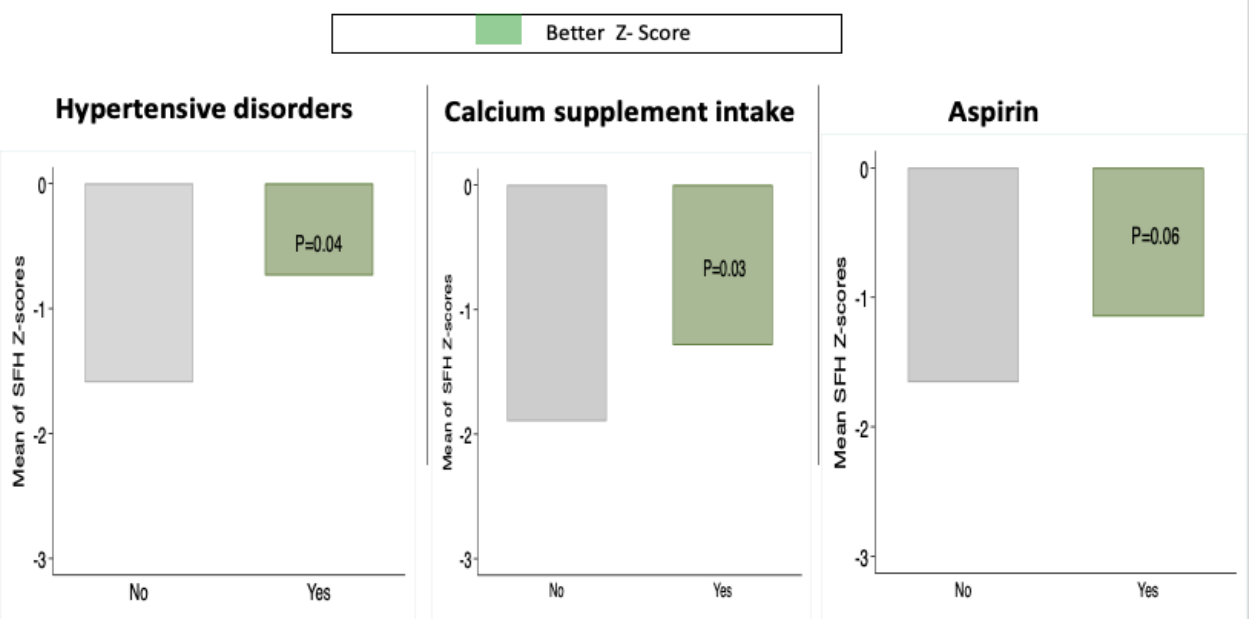


Figure-4 Symphysis-fundal height Z-scores differed with anemia and supplementation

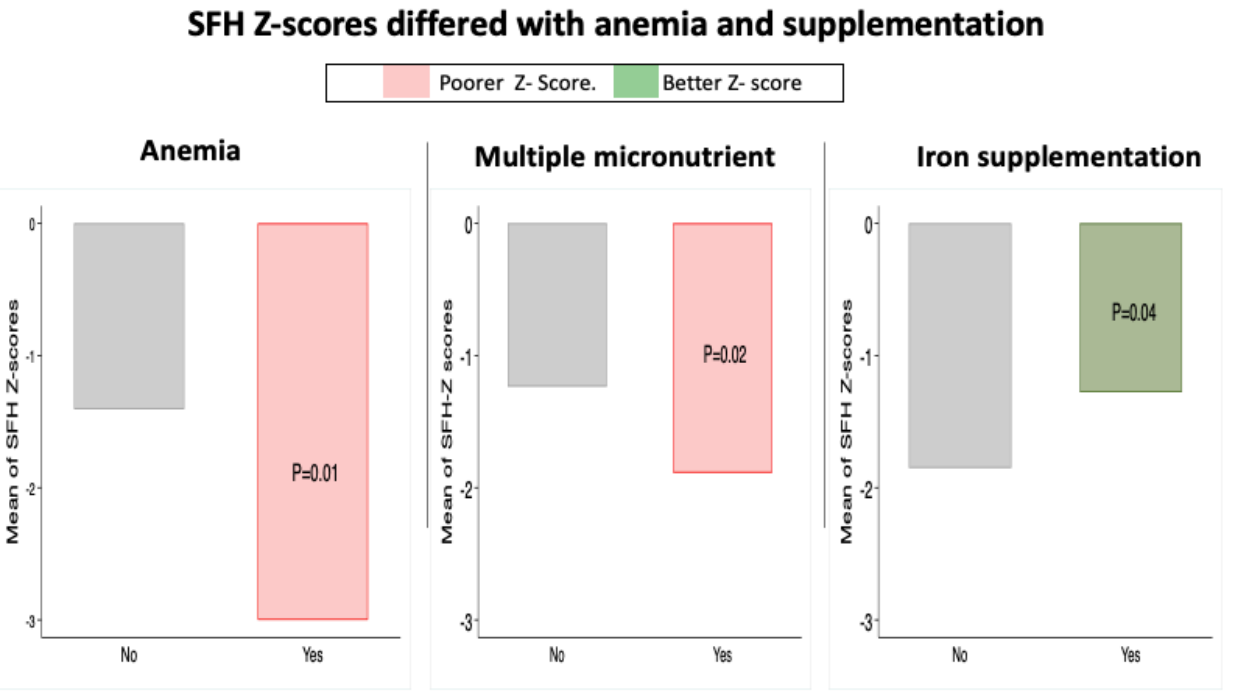
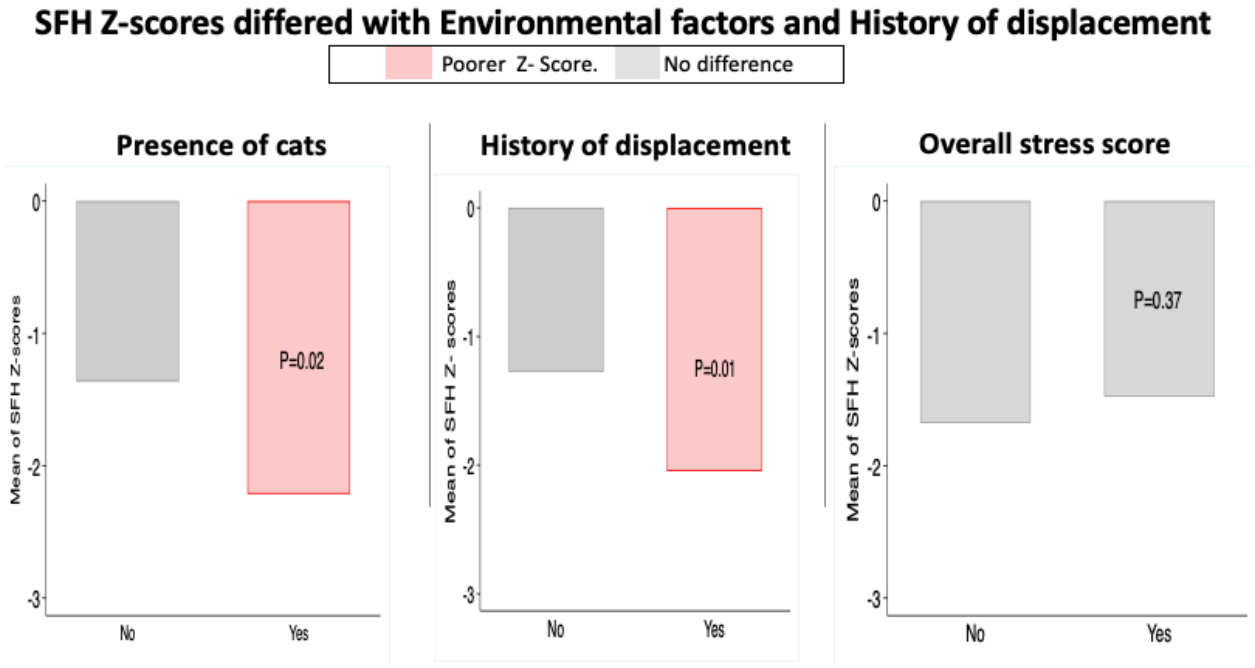


Figure-5 Symphysis-fundal height Z-scores differed with Environmental factors and History of displacement



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Supplementary tables

Table-1 Univariate logistic regression for symphysis-fundal height

SFH < 10 and ≥ 10 percentile	OR±SE	P	95% CI	Overall Model
Maternal Characteristics				
Age, yrs	1.01±0.03	0.69	0.94,1.09	Pseudo R^2= 0.002, P=0.69
Gestational age, wks	1.07±0.05	0.13	0.97, 1.18	Pseudo R^2= 0.04, P=0.12
Years of education	1.06±0.08	0.45	0.90, 1.25	Pseudo R^2= 0.007,P=0.45
Marital Status	0.61±0.39	0.45	0.17, 2.15	Pseudo R^2= 0.008, P=0.44
Height, cms	0.96±0.04	0.49	0.88, 1.06	Pseudo R^2= 0.007, P=0.49
Weight, kg	0.98±0.01	0.40	0.95, 1.02	Pseudo R^2= 0.01, P=0.39
BMI, kg/m^2	0.97±0.04	0.50	0.90, 1.05	Pseudo R^2= 0.007, P=0.48
Physical activity	1	-	-	Pseudo R^2= 0.04, P=0.12
Blood pressure, mmHg				
Systolic blood pressure	0.96±0.03	0.23	0.91, 1.02	Pseudo R^2= 0.02, P=0.22
Diastolic blood pressure	0.93±0.04	0.09	0.86, 1	Pseudo R^2= 0.04, P=0.08
MAP	0.93±0.04	0.09	0.86, 1.01	Pseudo R^2= 0.04, P=0.08
PP	1±0.03	0.84	0.94, 1.08	Pseudo R^2= 0.0006, P=0.83
EMAP	0.75±0.58	0.72	0.16, 3.46	Pseudo R^2= 0.004, P=0.86
Low PP	1.36±1.08	0.70	0.28, 6.46	Pseudo R^2= 0.004, P=0.86
Hypotension	1	-	-	Pseudo R^2= 0.004, P=0.86
Cardiac rate, bpm	0.97±0.03	0.41	0.91, 1.04	Pseudo R^2= 0.009, P=0.41
Hemoglobin, g/dl	0.87±0.21	0.56	0.54, 1.40	Pseudo R^2= 0.005, P=0.55
Anemia	1.45±1.84	0.77	0.12, 17.55	Pseudo R^2= 0.01, P=0.64
Hematocrit, %	0.95±0.07	0.46	0.81, 1.09	Pseudo R^2= 0.008, P=0.46
High Hematocrit	0.59±0.35	0.38	0.18, 1.92	Pseudo R^2= 0.01, P=0.64
Household characteristics	0.87±0.64	0.85	0.20, 3.67	Pseudo R^2= 0.0005, P=0.84
Quality of water	3.5±2.70	0.10	0.76, 15.94	Pseudo R^2= 0.04, P=0.09
Defecation place	0.44±0.53	0.50	0.04, 4.58	Pseudo R^2= 0.007, P=0.47
Number of hours of sleep	1.94±1.25	0.30	0.55, 6.88	Pseudo R^2= 0.01, P=0.30
Monthly income	1.10±0.63	0.86	0.34, 3.42	Pseudo R^2= 0.0004, P=0.86
History of				
Preterm delivery	1.52±1.17	0.58	0.34, 6.87	Pseudo R^2= 0.004, P=0.58
HDP	0.31±0.28	0.20	0.05, 1.87	Pseudo R^2= 0.02, P=0.18
Pelvic surgery	0.93±0.58	0.90	0.27, 3.19	Pseudo R^2= 0.0002, P=0.90
Gestational diabetes	0.44±0.42	0.39	0.07, 2.86	Pseudo R^2= 0.01, P=0.38
Maternal infections in current pregnancy				
Urinary tract infections	1.41±1.29	0.70	0.23, 8.48	Pseudo R^2= 0.002, P=0.70
Other genital infections	1.15±0.91	0.86	0.24, 5.45	Pseudo R^2= 0.0005, P=0.85
Food security				
Food insecurity score	0.76±0.48	0.67	0.23, 2.62	Pseudo R^2= 0.01, P=0.61
Food intake from garden	0.56±0.34	0.34	0.17, 5.84	Pseudo R^2= 0.01, P=0.61
Diet quality				
Dairy	3.39±0.17	0.04	1.07, 10.73	Pseudo R^2= 0.06, P=0.03
Eggs	1.99±1.18	0.24	0.61, 6.41	Pseudo R^2= 0.01, P=0.24
Nuts/ Avocados	0.52±0.29	0.25	0.17, 1.59	Pseudo R^2= 0.01, P=0.25
Grains	1.56±1.03	0.49	0.42, 5.69	Pseudo R^2= 0.006, P=0.49
Viscera	1.46±0.89	0.53	0.44, 4.83	Pseudo R^2= 0.005, P=0.52
Processed	0.54±0.40	0.41	0.12, 2.37	Pseudo R^2= 0.009, P=0.40
Fruits and vegetables	3.01±2.20	0.13	0.72, 12.62	Pseudo R^2= 0.03, P=0.11
Fat	1.5±1.15	0.59	0.33, 6.78	Pseudo R^2= 0.003, P=0.59
Junk Food	1.28±0.82	0.69	0.36, 4.53	Pseudo R^2= 0.002, P=0.69
Supplements				

Iron	0.45±0.27	0.18	0.14, 1.47	Pseudo R^2= 0.02, 0.18
Calcium	0.40±0.25	0.15	0.11, 1.38	Pseudo R^2= 0.03, P=0.14
Folic acid	0.73±0.41	0.59	0.24, 2.22	Pseudo R^2= 0.004, P=0.58
Multivitamins	2.84±1.70	0.08	0.87, 9.19	Pseudo R^2= 0.04, P=0.07
Medicines				
Antibiotics	1.18±0.77	0.79	0.32, 4.25	Pseudo R^2= 0.0009, P=0.79
Aspirin	0.50±0.29	0.24	0.15, 1.61	Pseudo R^2= 0.01, P=0.24
Thyroid hormone replacement	0.68±0.71	0.72	0.08, 5.30	Pseudo R^2= 0.001, P=0.72
Anti-hypertensive drugs	0.7±1	0.80	0.04, 11.83	Pseudo R^2= 0.0008, P=0.80
Preterm delivery pharmacological treatment	0.67±0.58	0.65	0.12, 3.72	Pseudo R^2= 0.002, P=0.65
Anti-diabetes	0.33±0.41	0.38	0.02, 3.92	Pseudo R^2= 0.01, P=0.36
Pets				
Dogs	1.18±0.67	0.75	0.39, 3.59	Pseudo R^2= 0.001, P=0.75
Cats	1.92±1.70	0.46	0.33, 10.96	Pseudo R^2= 0.008, P=0.44
Hens	0.51±0.33	0.30	0.14, 1.82	Pseudo R^2= 0.01, P=0.30
Pests and Rodents				
Flies	2.45±1.81	0.22	0.57, 10.43	Pseudo R^2= 0.02, P=0.20
Mosquitoes	0.49±0.28	0.22	0.15, 1.53	Pseudo R^2= 0.02, P=0.22
Cockroaches	2.77±1.59	0.07	0.89, 8.57	Pseudo R^2= 0.04, P=0.07
Mice/Rat	0.66±0.51	0.59	0.14, 3.01	Pseudo R^2= 0.003, P=0.59
Hygiene Characteristics				
Boiling water for drinking	0.47±0.26	0.18	0.15, 1.44	Pseudo R^2= 0.02, P=0.18
Washing hands before cooking	1	-	-	N=52
Washing hands after toilet	1	-	-	N=52
Conflict related stress				
Recall of stressful events	0.68±0.38	0.50	0.22, 2.05	Pseudo R^2= 0.006, P=0.50
Dream about stressful events	0.35±0.21	0.08	0.10, 1.14	Pseudo R^2= 0.04, P=0.08
Physical reaction to stress	0.32±0.19	0.05	0.10, 1.02	Pseudo R^2= 0.05, P=0.05
Lack of interest in daily activities	1.35±0.79	0.60	0.42, 4.28	Pseudo R^2= 0.003, P=0.60
Feeling unloved	0.50±0.29	0.25	0.15, 1.61	Pseudo R^2= 0.02, P=0.24
Alert more than usual	1.04±0.59	0.94	0.34, 3.16	Pseudo R^2= 0.0001, P=0.94
Difficulty in sleeping	1.51±0.86	0.46	0.49, 4.62	Pseudo R^2= 0.007, P=0.46
Emotionally tensed	1.10±0.63	0.86	0.35, 3.42	Pseudo R^2= 0.0004, P=0.86
Depressive mood	0.77±0.50	0.70	0.22, 2.74	Pseudo R^2= 0.002, P=0.70
Neurovegetative symptoms	0.67±0.58	0.65	0.12, 3.72	Pseudo R^2= 0.002, P=0.65
History of displacement	3.48±2.52	0.08	0.83, 14.44	Pseudo R^2= 0.04, P=0.06

Table-2 Simple linear regression for symphysis-fundal height

	Coef. ± SE	P	95% CI	Overall Model
Maternal Characteristics				
Age, yrs	0.02±0.02	0.31	-0.02,0.06	Adj R^2 = 0.0003, P=0.31
Gestational age, wks	-0.04±0.02	0.06	-0.09,0.003	Adj R^2 = 0.11, P=0.01
Years of education	0.03±0.04	0.52	-0.06,0.12	Adj R^2 = -0.01, P=0.52
Marital Status	0.32±0.35	0.36	-0.38,1.03	Adj R^2 = -0.002, P=0.36
Height, cms	0.009±0.02	0.72	-0.04,0.06	Adj R^2 = -0.017, P=0.72
Weight, kg	0.006±0.009	0.51	-0.012,0.024	Adj R^2 = -0.010, P=0.51
BMI, kg/m^2	0.01±0.21	0.58	-0.03,0.05	Adj R^2 = -0.013, P=0.57
Physical activity	-0.92±0.47	0.06	-1.88,0.04	Adj R^2 = 0.11, P=0.01
Blood pressure, mmHg				
Systolic blood pressure	-0.02±0.01	0.20	-0.01,0.05	Adj R^2 = 0.01, P=0.20
Diastolic blood pressure	0.05±0.02	0.01	0.01,0.09	Adj R^2 = 0.09, P=0.01
MAP	0.04±0.02	0.02	0.006,0.09	Adj R^2 = 0.07, P=0.02
PP	-0.01±0.01	0.46	-0.05,0.02	Adj R^2 = -0.008, P=0.46
EMAP	0.33±0.45	0.47	-0.58,1.25	Adj R^2 = -0.01, P=0.55
Low PP	0.17±0.45	0.70	-0.74,1.10	Adj R^2 = -0.01, P=0.55
Hypotension	-1.36±1.20	0.26	-3.79,1.06	Adj R^2 = -0.01, P=0.55
Cardiac rate, bpm	0.02±0.01	0.27	-0.01,0.06	Adj R^2 = 0.004, P=0.27
Hemoglobin, g/dl	0.26±0.13	0.05	-0.001,0.534	Adj R^2 = 0.05, P=0.05
Anemia	-1.54±0.68	0.02	-2.93,-0.16	Adj R^2 = 0.12, P=0.02
Hematocrit, %	0.07±0.04	0.10	-0.01,0.15	Adj R^2 = 0.03, P=0.10
High Hematocrit	0.58±0.33	0.09	-0.10,1.26	Adj R^2 = 0.12, P=0.02
Amniotic fluid index, cm	0.09±0.05	0.09	-0.01,0.21	Adj R^2 = 0.05, P=0.09
Household characteristics	-0.16±0.41	0.68	-0.99,0.65	Adj R^2 = -0.01, P=0.68
Quality of water	-0.43±0.42	0.31	-1.28,0.41	Adj R^2 = 0.0008, P=0.31
Defecation place	0.78±0.53	0.15	-0.30,1.86	Adj R^2 = 0.02, P=0.15
Number of hours of sleep	-0.45±0.36	0.21	-1.19,0.28	Adj R^2 = 0.01, P=0.21
Monthly income	-0.004±0.33	0.99	-0.67,0.66	Adj R^2 = -0.01, P=0.99
History of				
Preterm delivery	-0.33±0.42	0.44	-1.18,0.52	Adj R^2 = -0.007, P=0.44
HDP	0.85±0.49	0.08	-0.13,1.84	Adj R^2 = 0.03, P=0.08
Pelvic surgery	0.27±0.36	0.45	-0.45,0.99	Adj R^2 = -0.008, P=0.45
Gestational diabetes	0.52±0.54	0.34	-0.57,1.61	Adj R^2 = -0.001, P=0.34
Maternal infections in current pregnancy				
Urinary tract infections	-0.64±0.50	0.20	-1.65,0.37	Adj R^2 = 0.01, P=0.20
Other genital infections	-0.35±0.45	0.43	-1.26,0.54	Adj R^2 = -0.007, P=0.43
Food security				
Food insecurity score	0.14±0.36	0.70	-0.59,0.88	Adj R^2 = -0.03, P=0.92
Food intake from garden	0.05±0.34	0.87	-0.63,0.75	Adj R^2 = -0.03, P=0.92
Diet Quality				
Dairy	-0.20±0.32	0.52	-0.84,0.43	Adj R^2 = -0.01, P=0.52
Eggs	-0.26±0.34	0.44	-0.96,0.43	Adj R^2 = -0.008, P=0.44
Nuts/ Avocados	0.36±0.31	0.25	-0.27,1	Adj R^2 = 0.006, P=0.25
Grains	-0.60±0.37	0.11	-1.35,0.14	Adj R^2 = 0.02, P=0.11
Viscera	-0.08±0.33	0.79	-0.76,0.59	Adj R^2 = -0.01, P=0.79
Processed	0.39±0.42	0.35	-0.45,1.24	Adj R^2 = -0.01, P=0.79
Fruits and vegetables	-0.32±0.36	0.37	-1.04,0.40	Adj R^2 = -0.004, P=0.37
Fat	-0.60±0.44	0.17	-1.49,0.27	Adj R^2 = 0.01, P=0.17
Junk Food	0.03±0.37	0.93	-0.71,0.78	Adj R^2 = -0.01, P=0.93
Supplements				
Iron	0.57±0.32	0.08	-0.07,1.22	Adj R^2 = 0.04, P=0.08
Calcium	0.60±0.32	0.07	-0.05,1.26	Adj R^2 =0.04, P=0.07
Folic acid	0.23±0.32	0.46	-0.41,0.87	Adj R^2 = -0.009, P=0.46
Multivitamins	-0.65±0.31	0.04	-1.28, -0.01	Adj R^2 =0.05, P=0.04
Medicines				
Antibiotics	-0.50±0.37	0.89	-0.80,0.69	Adj R^2 =-0.01, P=0.89
Aspirin	0.50±0.33	0.13	-0.16,1.18	Adj R^2 = 0.02, P=0.13
Thyroid hormone replacement	-0.11±0.60	0.84	-1.33,1.10	Adj R^2 = -0.01, P=0.84

Anti-hypertensive drugs	0.51±0.84	0.54	-1.17,2.19	Adj R^2 = -0.01, P=0.54
Preterm delivery pharmacological treatment	-0.02±0.50	0.95	-1.04,0.99	Adj R^2 = -0.01, P=0.95
Anti-diabetes	0.27±0.69	0.69	-1.12,1.66	Adj R^2 = -0.01, P=0.69
Pets				
Dogs	0.001±0.323	0.99	-0.647, 0.649	Adj R^2 = -0.01, P=0.99
Cats	-0.84±0.43	0.05	-1.71, 0.02	Adj R^2 = 0.05, P=0.05
Hens	0.37±0.36	0.30	-0.34, 1.10	Adj R^2 = 0.001, P=0.29
Pests and Rodents				
Flies	-0.48±0.37	0.19	-1.23, 0.25	Adj R^2 = 0.01, P=0.19
Mosquitoes	0.27±0.33	0.41	-0.39, 0.94	Adj R^2 = -0.006, P=0.41
Cockroaches	-0.15±0.32	0.63	-0.79, 0.49	Adj R^2 = -0.01, P=0.63
Mice/Rat	0.13±0.44	0.75	-0.76, 1.03	Adj R^2 = -0.01, P=0.75
Hygiene Characteristics				
Boiling water for drinking	0.35±0.31	0.27	-0.28, 0.99	Adj R^2 = 0.004, P=0.27
Washing hands before cooking	1.12±1.17	0.34	-1.22, 3.47	Adj R^2 = -0.001, P=0.33
Washing hands after toilet	1.12±1.17	0.34	-1.22, 3.47	Adj R^2 = -0.001, P=0.33
Conflict related stress				
Recall of stressful events	0.25±0.31	0.42	-0.38, 0.89	Adj R^2 = -0.006, P=0.42
Dream about stressful events	0.16±0.33	0.62	-0.51, 0.84	Adj R^2 = -0.01, P=0.62
Physical reaction to stress	0.50±0.31	0.12	-0.13, 1.13	Adj R^2 = 0.02, P=0.11
Lack of interest in daily activities	-0.15±0.33	0.65	-0.82, 0.52	Adj R^2 = -0.01, P=0.65
Feeling unloved	0.03±0.34	0.92	-0.65, 0.72	Adj R^2 = -0.01, P=0.92
Alert more than usual	0.11±0.32	0.71	-0.53, 0.76	Adj R^2 = -0.01, P=0.71
Difficulty in sleeping	-0.18±0.32	0.56	-0.84, 0.46	Adj R^2 = -0.01, P=0.56
Emotionally tensed	0.10±0.33	0.74	-0.55, 0.77	Adj R^2 = -0.01, P=0.74
Depressive mood	0.35±0.37	0.34	-0.38, 1.10	Adj R^2 = -0.001, P=0.34
Neurovegetative symptoms	0.16±0.50	0.75	-0.85, 1.17	Adj R^2 = -0.01, P=0.75
History of displacement	-0.77	0.02	-1.45, -0.09	Adj R^2 = 0.07, P=0.02

Table-3 Univariate logistic regression for fetal weight

Fetal Weight<10 and ≥ 10 percentile	OR±SE	P	95% CI	Overall Model
Maternal Characteristics				
Age, yrs	1.09±0.06	0.08	0.98, 1.24	Pseudo R^2=0.08, P=0.06
Gestational age, wks	0.77±0.07	0.01	0.63, 0.94	Pseudo R^2=0.19, P=0.01
Years of education	0.84±0.09	0.15	0.67, 1.06	Pseudo R^2=0.05, P=0.14
Marital Status	0.35±0.28	0.19	0.07, 1.70	Pseudo R^2=0.03, P=0.20
Height, cms	1.01±0.06	0.80	0.89, 1.15	Pseudo R^2=0.001, P=0.80
Weight, kg	0.96±0.04	0.39	0.89, 1.04	Pseudo R^2=0.02, P=0.31
BMI, kg/m^2	0.93±0.08	0.48	0.78, 1.11	Pseudo R^2=0.02, P=0.40
Physical activity	2.70±3.57	0.45	0.20, 36.21	Pseudo R^2=0.19, P=0.01
Blood pressure, mmHg				
Systolic blood pressure	1.05±0.04	0.23	0.96,1.14	Pseudo R^2=0.04, P=0.22
Diastolic blood pressure	1.03±0.05	0.54	0.93, 1.13	Pseudo R^2=0.009, P=0.54
MAP	1.05±0.05	0.34	0.94, 1.16	Pseudo R^2=0.02, P=0.34
PP	1.03±0.04	0.40	0.94, 1.13	Pseudo R^2=0.02, P=0.39
EMAP	1.60±1.49	0.61	0.26, 9.99	Pseudo R^2=0.006, P=0.88
Low PP	0.86±1.02	0.90	0.09,8.69	Pseudo R^2=0.19, P=0.01
Hypotension	1	-	-	Pseudo R^2=0.19, P=0.01
Cardiac rate, bpm	0.96±0.05	0.46	0.88, 1.06	Pseudo R^2=0.01, P=0.45
Hemoglobin, g/dl	1.14±0.37	0.67	0.61, 2.15	Pseudo R^2=0.004, P=0.66
Anemia	2.86±3.72	0.42	0.22, 36.88	Pseudo R^2=0.02, P=0.75
Hematocrit, %	0.96±0.09	0.68	0.79,1.16	Pseudo R^2=0.004, P=0.68
High Hematocrit	1.09±0.92	0.92	0.21, 5.68	Pseudo R^2=0.02, P=0.75
Household characteristics	1.48±1.35	0.67	0.24, 8.91	Pseudo R^2=0.004, P=0.68
Quality of water	0.45±0.43	0.41	0.07, 2.90	Pseudo R^2=0.002, P=0.42
Defecation place	1	-	-	Pseudo R^2=0.0000
Number of hours of sleep	0.93±0.84	0.94	0.16, 5.45	Pseudo R^2=0.0001, P=0.94
Monthly income	0.51±0.45	0.45	0.91,2.88	Pseudo R^2=0.01, P=0.43
History of				
Preterm delivery	0.76±0.88	0.81	0.08, 7.37	Pseudo R^2=0.001, P=0.81
HDP	3.89±3.94	0.18	0.53, 28.39	Pseudo R^2=0.04, P=0.20
Pelvic surgery	2.66±2.24	0.25	0.51, 13.83	Pseudo R^2=0.03, P=0.26
Gestational diabetes	1.21±1.45	0.87	0.12, 12.57	Pseudo R^2=0.0006, P=0.87
Maternal infections in current pregnancy				
Urinary tract infections	1.67±2.04	0.68	0.15, 18.45	Pseudo R^2=0.004, P=0.69
Other genital infections	0.94±1.10	0.96	0.09, 9.37	Pseudo R^2=0.0001, P=0.96
Food security				
Food insecurity score	3.42±2.83	0.14	0.67, 17.28	Pseudo R^2=0.05, P=0.33
Food intake from garden	1.32±1.12	0.74	0.25, 6.95	Pseudo R^2=0.05, P=0.33
Diet Quality				
Dairy	1.35±1.08	0.71	0.28, 6.47	Pseudo R^2=0.003, P=0.71
Eggs	0.68±0.55	0.63	0.14, 3.34	Pseudo R^2=0.005, P=0.64
Nuts/ Avocados	1.67±1.33	0.52	0.35, 7.98	Pseudo R^2=0.009, P=0.52
Grains	2.17±2.47	0.49	0.23, 20.10	Pseudo R^2=0.01, P=0.46
Viscera	0.64±0.57	0.62	0.11, 3.63	Pseudo R^2=0.006, P=0.61
Processed	1.58±1.81	0.69	0.17, 14.99	Pseudo R^2=0.004, P=0.68
Fruits and vegetables	3.22±2.59	0.15	0.67, 15.56	Pseudo R^2=0.05, P=0.15
Fat	0.45±0.43	0.40	0.07, 2.91	Pseudo R^2=0.02, P=0.42
Junk Food	1.22±1.09	0.82	0.21, 7.01	Pseudo R^2=0.001, P=0.82
Supplements				
Iron	1	-	-	N=28
Calcium	1	-	-	N=29
Folic acid	1.66±1.33	0.52	0.35, 7.98	Pseudo R^2=0.009, P=0.52

Multivitamins	0.83±0.66	0.81	0.17, 3.96	Pseudo R^2=0.001, P=0.81
Medicines				
Antibiotics	1	-	-	N=37
Aspirin	7.36±6.56	0.03	1.28, 42.25	Pseudo R^2=0.14, P=0.02
Thyroid hormone replacement	1	-	-	N=44
Anti-hypertensive drugs	5.29±7.79	0.26	0.29, 94.83	Pseudo R^2=0.03, P=0.28
Preterm delivery pharmacological treatment	0.94±1.10	0.96	0.09, 9.37	Pseudo R^2=0.0001, P=0.96
Anti-diabetes	1	-	-	N=43
Pets				
Dogs	1±0.78	1	0.22, 4.59	Pseudo R^2=0.000, P=1
Cats	1.48±1.35	0.67	0.24, 8.91	Pseudo R^2=0.004, P=0.67
Hens	1.47±1.19	0.63	0.29, 7.25	Pseudo R^2=0.005, P=0.64
Pests and Rodents				
Flies	0.74±0.85	0.79	0.08, 7.15	Pseudo R^2=0.002, P=0.79
Mosquitoes	1.03±0.83	0.97	0.21, 4.97	Pseudo R^2=0.000, P=0.97
Cockroaches	1.5±1.19	0.61	0.31, 7.19	Pseudo R^2=0.006, P=0.61
Mice/Rat	1.21±1.45	0.87	0.12, 12.57	Pseudo R^2=0.0006, P=0.87
Hygiene Characteristics				
Boiling water for drinking	0.9±0.70	0.89	0.19, 4.14	Pseudo R^2=0.0004, P=0.89
Washing hands before cooking	1	-	-	N=45
Washing hands after toilet	1	-	-	N=45
Conflict related stress				
Recall of stressful events	2.06±1.65	0.37	0.43, 9.87	Pseudo R^2=0.02, P=0.36
Dream about stressful events	1.3±1.05	0.75	0.27, 6.35	Pseudo R^2=0.002, P=0.75
Physical reaction to stress	1.38±1.07	0.68	0.29, 6.34	Pseudo R^2=0.004, P=0.68
Lack of interest in daily activities	1.03±0.83	0.97	0.21, 4.97	Pseudo R^2=0.000, P=0.97
Feeling unloved	1.47±1.19	0.63	0.29, 7.25	Pseudo R^2=0.005, P=0.64
Alert more than usual	1.38±1.07	0.68	0.29, 6.34	Pseudo R^2=0.004, P=0.68
Difficulty in sleeping	1.09±0.87	0.92	0.23, 5.24	Pseudo R^2=0.0003, P=0.92
Emotionally tensed	3.21±2.58	0.15	0.66, 15.57	Pseudo R^2=0.05, P=0.14
Depressive mood	5.33±4.46	0.05	1.04, 27.42	Pseudo R^2=0.09, P=0.05
Neurovegetative symptoms	2.83±2.76	0.28	0.42, 19.06	Pseudo R^2=0.02, P=0.30
History of displacement	0.82±0.73	0.82	0.14, 4.69	Pseudo R^2=0.001, P=0.82

Appendix 1 Ethical approval forms

HOSPITAL UNIVERSITARIO SAN JOSE EMPRESA SOCIAL DEL ESTADO POPAYAN *Juntos mejoramos tu salud*	COMITÉ DE ETICA DE LA INVESTIGACION CIENTIFICA	FO-ARH-01 Versión: 02 Página 1 de 1

ACTA DE AVAL: ACTA N° 02

PROYECTO: "ESTADO DE RIESGO BIO-PSICO-SOCIAL, NUTRICIONAL Y DE CRECIMIENTO FETAL EN EMBARAZADAS CAUCANAS ATENDIDAS EN INSTITUCIONES DE SALUD DE COBERTURA EN NIVELES SOCIO-ECONOMICOS MEDIO-BAJO".

Tipo de Estudio: Es un estudio de corte trasversal, piloto o prueba con entrevista e información de historia clínica.
Investigador Principal: Dra. Doris Gonzales. MD, PHD Estudiante de Doctorado de la Escuela de nutrición humana de la Universidad de McGill.
Tutores: Universidad del Cuca, Dr. Jose Enrique Chaguendo MD, Dr. Roberth Alirio Ortiz Martínez MD, MSc.

Código interno [ ] Fecha en que fue solicitado: [02] [03] [2018]

El comité de Ética de la investigación científica del Hospital Universitario San José creado mediante Resolución 0665 del 19 de Octubre de 2011, regido por la Resolución 008430 de 4 de octubre de 1993 del Ministerio de Salud y Seguridad Social por el cual se determinan las normas Éticas, Científicas, Técnicas, Administrativas de la investigación científica de salud en Colombia, la declaración de Helsinki de 1964, el Código de Belmont, el Código de Regulaciones Federales del Instituto Nacional de Salud Norteamericano.

Este comité avala el presente proyecto, previo estudio, análisis del:

- [X] Resumen del proyecto
- [X] Marco teórico
- [X] Objetivos
- [X] Metodología
- [X] Análisis del riesgo
- [X] Operacionalidad de las variables
- [X] Presupuesto
- [X] Instrumentos de recolección de datos
- [X] Formatos y anexos
- [X] Consentimiento Informado
- [X] Manejo de la confidencialidad

Dirección: Carrera 6 No 10N – 142
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Conmutador: 8234508- Extensión: 286
Email etica_medica@hospitalsanjose.gov.co

Beneficio

El proyecto es auspiciado por fondos del programa "Mcburney Latinoamerica" de la universidad de McGill den Montreal, Canadá, la Universidad del cauca y la Universidad del valle, cuyo propósito es averiguar el estado nutricional de las embarazadas de estrato socioeconómico 0 – 3. El estudio es de suma importancia para determinar la nutrición, la obtención de alimentos y el estrés. Mediante análisis estadísticos se determinara la prevalencia de malnutrición o sobrepeso maternos y de fetos pequeños o grandes para la edad gestacional y las asociaciones entre factores sociodemográficos y factores de riesgo Bio-psicosocial entre otros. El estudio ayuda a mejorar la salud materna y fetal de la población caucana vulnerable.

El investigador principal informará al Comité de Ética de la Investigación Científica lo siguiente:

- De cualquier cambio que se presente en el proyecto.
- Cualquier conocimiento nuevo respecto al estudio que pueda afectar la tasa riesgo beneficio para los sujetos de la investigación.
- La suspensión o terminación prematura del proyecto.
- Al finalizar el estudio los investigadores responsables del proyecto deberán presentar un informe de los resultados obtenidos al Hospital Universitario San José, para los efectos pertinentes como publicaciones, acceso bibliográfico u otros.
- Se llevara a cabo por parte del comité seguimiento del desarrollo del proyecto de manera aleatoria.
- Las decisiones significativas tomadas por otro Comité de Ética o autoridades reguladoras para el estudio propuesto y una indicación de la modificación o modificaciones del protocolo realizadas en esa ocasión.

Este aval tendrá vigencia por un año a partir de la fecha de su aprobación, luego de la cual deberá ser revisado y actualizado, se firma en la Ciudad de Popayán al día (09) del mes de Abril de 2018.

Atentamente,

Dra. YOLANDA BOTERO DE CASAS
Coordinadora C.E.I.C
Hospital U. San José

Dr. CESAR GILBERTO ZUÑIGA
Subgerente Científico
Hospital U. San José

Proyectó: Yolanda María Botero de Casas
Elaboró: Yerly pino.
Archivado según TRD: AVALES 2017

Appendix 2 Questionnaire and clinical form for pregnant women

2.1. General information

Service center _____ Code _____

Origin _____ Origin: _____ Occupation _____

Displacement history No____Yes ____ Urban housing_____ rural_____

Years of education: Primary ___ (Can read ☐ No ☐ Yes, you can write ☐ No ☐ Yes)

Higher Secondary _____

Marital status: Single ___, Married ___, Free union __, Widow __, Separated / divorced ___

2.2. Characteristics of the home

The water that your family drinks comes from: Aqueduct ☐ Well ☐ River ☐ Tank ☐ Bottled

Place of defecation: Sanitary ☐ Latrine ☐ Open field ☐ Vegetable garden ☐ Patio ☐

Other___ Which _____

Pets in the house: Pets: ☐ Dog ☐ Cattle ☐ Other _____

Breeding animals: No☐ Yes☐, ☐ Chickens, ☐codornices, ☐cayes, ☐Other _____

For consumption? For sale?

Pests: ☐ Flies ☐ Zancuts ☐ Cockroaches ☐ Rats or rats ☐ Other _____

Home garden: No☐ Yes☐ The products are for consumption.

Hygiene practices

	Never	Sometimes	always
Boil water for consumption			
Performs hand washing before cooking			
Performs hand washing after defecating			

2.3. Medication during the present pregnancy

	No	Yes	Treatment time
Iron			
Folic acid			
Multivitamins			
Antibiotic			
ASA			
Calcium			
Others			

2.4. Food safety

Total monthly income in the home: <1 minimum wage ☐ Minimum wage ☐> 1 minimum wage ☐

At home, who decides what food to buy?

The interviewee ☐ The interviewee and her partner ☐ The couple ☐ Other ☐ (who) _____

In the last month, there was ever a time when at home ...

	Yes	No	Always	Sometimes	Rarely
*A. There was not enough money to buy food?					
B. An adult ate less than he wanted because there was not enough money to buy food?					
C. The normal number of meals was reduced, for example, there was no breakfast, lunch or food because there was no money to buy food?					
D. An adult did not eat breakfast, lunch or food because there was not enough money to buy food?					
E. An adult complained of hunger due to lack of food in the house?					
F. An adult went to bed hungry because there was not enough money to buy food?					
G. Did he buy less food than needed for the children because he could not afford the money?					
H. Did any child eat a smaller portion of food because there was not enough food for everyone?					
I. Did any child complain of hunger due to lack of food in the house?					
J. Did some child go to bed hungry because there was not enough money to buy food?					

** Filter: if the answer is negative, Food Insecurity = 0 is assumed. The interview is not continued.*

Healthy eating questionnaire
A. Scale of food groups
How often do you consume

	Everyday	>3 days/week	1-3 days/week	1 time/week	Ocassionaly	Never
Milk and milk products	5	4	3	2	1	0
Eggs	5	4	3	2	1	0
Nuts, peanuts or avocado	5	4	3	2	1	0
Legumes (grains = peas, lentils, beans, chickpeas ...)	5	4	3	2	1	0
Viscera	5	4	3	2	1	0
Processed or canned meats	0	1	2	3	4	5
Package products, fast foods, soft drinks or artificial juices	0	1	2	3	4	5

A. Directional guide

1. In how many meals does it include whole fruits and vegetables (at least 1 yellow)?
(a) At breakfast
(b) At lunch
(c) To food
(d) In two of the above
(e) In all previous
(f) In none of the above
2. How many minutes of physical activity per day?
(a) 5-15 minutes / day
(b) 20-30 minutes / day
(c) 45-60 minutes / day
(d)> 1 hour / day
3. What type of fat is used for cooking food in the home?
(a) Oil of vegetable origin
(b) Butter of animal origin
(c) Butter
(d) Two of the above
(e) All of the above
(f) None of the above

2.5. Stress evaluation questionnaire

Mark with an X the box that indicates the frequency with which you have been presented with the following discomforts in the last three months.

Malestares	Always	Almost always	Sometimes	Never
1. Repetitive memories, thoughts or unpleasant images of a stressful experience in the past				
2. Repetitive dreams or nightmares of a stressful experience in the past				
3. Physical reactions (tachycardia, difficulty breathing or sweating) when something reminds you of a stressful experience of the past				
4. Loss of interest in things that you used to like to do				
5. Inability to feel love for close people				
6. Always be on alert, or in a state of constant vigilance				
7. Difficulty falling asleep or getting enough sleep				

How many hours do you sleep in the day?
(a) 3 or less
(b) 4-5
(c) 6-8
(d) 9 or more

2.6. Data to be taken from the CLAP sheet or the Clinical History

. Anamnesis and physical examination:

Gestational age due to amenorrhea: _____

Weight_____ Size_____ PA_____ FC_____

Temperature _____ Uterine Height _____

Visit to the dentist: No____ Yes_____ Dental pathology No____ Yes____

b. Laboratories:

Hemoglobin _____ Glicemia _____

Uroanalysis or urine culture indicating urinary infection or asymptomatic bacteriuria:

No____Yes ____

Density (severity) urinary _____

VDRL: Reagent _____ Not reactive _____

Evidence of genital infection: No____Yes ____ Diagnosis _____

Evidence of another infection: No____ Yes____ Which one?

_____

c. Data to be taken from obstetric ultrasound:

Gestational age:_____

Calculation of fetal weight by Hadlock's formula _____

Calculation of growth percentile (Hadlock curve) _____

Amniotic fluid index _____

Fetal presentation_____

Placental pathology No____ Yes ____ Which one? _____

INFORMED CONSENT FORMAT

Status of bio-psycho-social, nutritional and fetal growth risk in pregnant women treated at health institutions with coverage at medium-low socio-economic levels: A pilot cross-sectional study.

McGill University, Universidad del Cauca, Universidad del Valle

Doris González Fernández (McGill University)
Project Coordinator

Pregnant women who attend prenatal care in health care facilities of municipal capitals of Popayán and Cauca belonging to socio-economic strata 0-3 are invited to participate in this pilot research project

Hosted by
McBurney Latin America (McGill University)

This consent form contains two parts

- Part I: Information sheet (to share information about the study with you)
- Part II: Consent certificate (to sign if you choose to participate)

Part I: Information sheet

About us?
We are an inter-institutional research team made up of the Universities of Cauca, Valle and McGill (Canada).

What is the investigation about?
The project wants to find out the nutritional status of pregnant women of socio-economic strata 0-3, if they follow the recommendations of the Ministry of Social Protection in terms of nutrition or if they have difficulties to get food, if they have stress and if they are at risk of Pregnancy is complicated. We also want to know if nutrition and stress are related to the size of the baby in the womb.

What is the study?
This is a pilot study or test, where you will be interviewed only once and asked for authorization to obtain information about your medical history.

Selection of participants
You are cordially invited to be part of this research project because you are pregnant, because you belong to socioeconomic stratum 0-3 and for attending prenatal check-ups at this health institution.

Your participation is voluntary
You can freely choose if you want to be part of the research project. If you do not want or can not be part of the study, all the health services you receive at this health facility will continue as usual. Even if you agree to participate now, you can change your mind at any time and stop participating.

What will be asked?
You will be asked to have access to the information concerning your pregnancy that is on your pregnancy card or your medical record. There will be an interview where you will answer questions about your pregnancy, about the environment in your home, about your diet, if you have difficulty getting food and about your stressful state**.**

Risks and discomforts
The interview will take about half an hour of your time when you come to your prenatal check-up or at a convenient time. No type of examination will be taken. The study does not involve any risk to your health or that of your baby.

Benefits
The benefits of the study will be seen through a better knowledge of the nutritional and stress situation of pregnant women in their community, which will help the health authorities to take measures that help improve the health of mothers and their babies. If you wish, personalized tips to improve your diet will be given at the end of the interview.

Incentives
You will not receive any economic incentives (you will not be given money) for participating in the study. If you encounter serious problems of a nutritional nature, you will be referred to your doctor or to the appropriate health professional to assist you.

Your information is confidential
Only our research group will have access to the information collected through the interview. The information will be stored in a locked drawer in the office of Universidad del Valle.
When we place your information inside our computer, we will not include your name but a code assigned to you. When we explain and / or publish the results of our research, we will not use your name or anything that allows other people to know who you are.

Disclosure of results
The results of the analysis of the study will be delivered to your health entity, who, according to your policies, will decide the best way to give them to know. We will also write about our results, so that other people from other communities can learn from this research.

Right to refuse or withdraw
As stated, your participation is voluntary. You can withdraw from the study at any time if you wish. In that case, your information will be discarded.

Who to contact?
You will be given a copy of this written consent. If you have additional questions, please contact Dr. Doris González at (+57) 312 822 5773. You can also contact Dr. Julián Herrera of Universidad del Valle, telephone 25565621 or Dr. José Chagüendo of Universidad del Valle. Cauca, telephone 8202832-8234508 ext. 173-206.

Part II: Consent certificate

I have been invited to participate in the research about risk factors of pregnancy, the state of nutrition, stress and growth of the baby. I understand that they are going to do an interview where they will ask me about the environment in which I live, my diet and my state of stress. I understand that the risk to me and my pregnancy is minimal and that the interview will take time. I know I will not receive money. I have been given the name and telephone number of researchers who can be contacted easily.

I have read all the information. I have had the opportunity to ask questions. I am satisfied with the answers to all my questions. I am also aware that I can withdraw at any time and this will not affect my medical care in my area in any way. I give voluntary consent to be a part of this study.

Legible name of the participant_____

Signature of the participant _____

Date (Day/month/year _____ c.c _____

If you can not read or write

I have witnessed that the participant's consent form was read exactly and that she has had the opportunity to ask questions. I confirm that the participant has given consent freely.

Legible name of the participant_____ Fingerprint of the participant

Witness signature_____

Date_____ c.c _____

Day/month/year

I have read exactly or witnessed the correct reading of the consent to the participant and she has had the opportunity to ask questions. I confirm that the participant has given consent freely.

Reasonable name of the investigator_____ Investigator's signature_____

Date_____

Day/month/year

A copy of this informed consent has been given to the participant_____(the researcher's initials)