NOTE TO USERS

ELUCIDATION OF LIFESTYLE PREDICTORS OF GESTATIONAL DIABETES MELLITUS IN PAKISTANI WOMEN

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ABSTRACT

As women who experience Gestational Diabetes Mellitus (GDM) are at considerably greater risk of developing type 2 diabetes in life, prevention of GDM is particularly important. The objectives of this research were to identify lifestyle predictors associated with GDM in a developing country and to validate a physical activity questionnaire for assessing total energy expenditure in a Pakistani population.

A prospective cohort study of 750 South Asian women recruited early in gestation was conducted in Karachi, Pakistan. Eligibility criteria included South Asian origin and ≤ 18 weeks gestation. Data on physical activity, diet, socio-demographic covariates, weight, height and body composition were obtained at recruitment and women were followed to assess GDM status at ≥ 26 weeks of gestation.

Logistic regression analysis of data from 611 women to assess the impact of age, body fat percentage, height, family history of diabetes, parity, level of education, rate of weight gain during pregnancy, and daily energy expenditure on the development of GDM was undertaken. The risk of GDM increased with increasing maternal age (yr), OR 1.13 (CI 1.06 - 1.21), body fat (%), OR 1.07 (CI 1.03 - 1.13), and decreased with daily energy expenditure (100 kcal), OR 0.89 (CI 0.79 - 0.99). Replacing body fat (%) with pre-gravid BMI provided similar results. Using a nested case (n=49) control (n=98) study design, conditional logistic regression analysis was conducted to assess the association between total energy, macronutrient and fiber intake and GDM. The risk of GDM decreased with

increasing amounts of protein as a percentage of total energy intake, OR 0.75 (CI 0.60 - 0.95).

The Monitoring trends and determinants of cardiovascular disease Optional Study of Physical Activity (MOSPA) questionnaire was assessed against a Caltrac accelerometer (n=50). Subjects wore a caltrac accelerometer for 5 consecutive days. A correlation of 0.51 ($P < 0.01$) was found between MOSPA questionnaire and Caltrac accelerometer values.

Advanced maternal age and body fat (%) predicted increased risk for GDM while physical activity was protective. Hence, prevention strategies should target increasing physical activity, sufficient to alter body composition, in this South Asian population.

RÉSUMÉ

Les femmes atteintes d'un diabète gestationnel (DG) sont beaucoup plus disposées à développer un diabète de type II. La prévention du DG se révèle donc particulièrement importante. Les objectifs de cette étude étaient donc d'identifier les facteurs du mode de vie associés à la prédiction du DG dans les pays en voie de développement et de valider un questionnaire d'activité physique estimant les besoins énergétiques totaux d'une population Pakistanaises.

Une étude longitudinale de femmes enceintes (n=750) fut conduite à Karachi, Pakistan. Les critères d'éligibilité incluaient d'etre originaire d'Asie du sud et une gestation de $\leq$ 18 semaines. Les données sur l'activité physique, le régime, les facteurs socio-économiques, le poids, la taille et la composition corporelle, furent mesurés à la clinique. Le diagnostique de DG fut mesuré à 26 semaines de gestation.

Une analyse par régression logistique (n=611) fut conduite pour déterminer l'impact de l'âge, le pourcentage de graisse, la taille, les antécédents familiaux de diabète, la parité, le niveau d'éducation, le taux du gain de poids durant la grossesse et la dépense énergétique journalière, sur le développement du DG. Le risque de DG augmenta avec un âge maternel croissant (ans) OR 1.13 (IC 1.06-1.21), le pourcentage de gras OR 1.07 (IC 1.03 – 1.13), et avec une dépense énergétique décroissante (100 kcal) OR 0.89 (IC 0.79- 0.99). Remplacer le pourcentage de gras par l'IMC prégravide produisit des résultats similaires. En utilisant une étude de cas (n=49) témoin (n=98) imbriqué, une analyse de régression logistique conditionnelle fut conduite pour évaluer l'association

entre l'apport alimentaire en fibres et de macronutriments et le DG. Le risque de DG fut réduit avec un pourcentage croissant d'énergie totale provenant de protéines, OR 0.75 (IC 0.60-0.95).

Le questionnaire d'activité physique de l'étude Monitoring trends of cardiovascular disease Optional Study of Physical Activity (MOSPA) fut évalué contre un accéléromètre caltrac (n=50). Les sujets portèrent l'accéléromètre caltrac pendant 5 jours consécutifs. Une corrélation de 0.51 ($p<0.01$) fut notée entre le questionnaire MOSPA et les données de l'accéléromètre caltrac.

Un âge maternel avancé et un pourcentage de gras prédisent un risque de DG accru, tandis que l'activité physique a un effet protecteur. C'est pourquoi des stratégies de prévention du DG devraient promouvoir une plus grande activité physique suffisamment intense pour modifier la composition corporelle dans cette population d'Asie du sud.

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STATEMENT OF ORIGINALITY

The objectives of this study and the data presented in this thesis represent an original research work. This is the first study conducted in South Asia exploring lifestyle predictors of GDM. It is also one of the very few studies that have assessed body composition and physical activity in relation with GDM in general.

Furthermore, Monitoring trends and determinants of cardiovascular disease Optional Study of Physical Activity (MOSPA) questionnaire was validated in a developing country for the first time. It is one of the few studies that have validated physical activity questionnaires in developing countries.

The doctoral candidate was responsible for the design, implementation, and analysis of this study. Dr. Katherine Gray-Donald, the thesis supervisor, worked with the student in developing the study design for this project. The candidate went to Pakistan for a year to implement the study. The implementation process included development of a food frequency questionnaire, selection and training of research officers for data collection, and conducting baseline data on first hundred subjects. The data analyses were conducted by the candidate under the guidance of Drs. Gray-Donald and Roger Cue. Dr. Gray-Donald also helped in editorial revisions of both of the manuscripts.

CONTRIBUTION OF AUTHORS

The manuscript presented in chapter 4 will be submitted to Medicine and Science in Sports and Exercise. The doctoral candidate was the primary author for the manuscript. She collected data, performed all statistical analyses and made all major data interpretations. Dr. Katherine Gray-Donald provided consultation for statistical analyses and data interpretation. She also provided editorial revisions for the manuscript. Dr. Rahat Qureshi provided assistance with implementing the study and data collection at the antenatal clinics, Dr. Salma Badruddin helped in implementing the study and provided editorial support. Dr. Ghazala Rafique was the principal investigator for the research project and provided assistance in data collection.

The manuscript presented in chapter 5 will be submitted to Diabetes Care. The doctoral candidate was the primary author for the manuscript. She collected data, performed all statistical analyses and made all major data interpretations. Dr. Katherine Gray-Donald provided consultation for statistical analyses and data interpretation. She also provided editorial revisions for the manuscript. Dr. Cue helped in conducting conditional logistic regression analysis using a SAS macro and helped in interpretation of results of the principal components analysis as well as the logistic regression analysis that was carried out for the cohort study. Dr. Rahat Qureshi provided assistance with implementing the study and data collection at the antenatal clinics, Dr. Salma Badruddin helped in the management of the study particularly in implementing the study and developing the software for the FFQ. Dr. Ghazala Rafique was the principal investigator for the research project and provided assistance in data collection.

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CHAPTER 1. INTRODUCTION

The developing countries of the world are facing a dual burden of disease. High prevalence rates of malnutrition and infectious disease as well as high rates of non-communicable diseases are found simultaneously with geographic variations in the transition from high prevalence of under nutrition and infectious diseases to non-communicable diseases (Yusuf et al. 2001). Type 2 diabetes is a non-communicable disease that is increasing worldwide with high prevalence rates now being reported for developing countries as well (Shera et al. 1995, 1999). Moreover, the low and middle income countries contributed 73% to total global mortality associated with diabetes in 1998 (Yusuf et al. 2001). It has been estimated that by the year 2030 approximately 366 million people will have diabetes. Furthermore, most of these people will be inhabitants of the developing countries and will be relatively young compared to the age group of people that have type 2 diabetes in the developed world (Wild et al. 2004).

Gestational diabetes mellitus is defined as abnormal glucose tolerance diagnosed during pregnancy (Anonymous 2004). Gestational diabetes mellitus is associated with serious immediate as well as long term consequences for the offspring as well as the mother. Women with a history of GDM are at a greater risk of developing type 2 diabetes compared to women that did not have GDM during a pregnancy (Ben-Haroush et al. 2004). Over a 10-15 year time period, 35-42% women who have had GDM develop type 2 diabetes compared to none of the women without GDM (Albareda et al. 2003; Linne et al. 2002). The population attributable risk of type 2 diabetes after GDM in a previous

pregnancy is estimated to be 30 percent (Cheung et al. 2003). Furthermore, GDM and type 2 diabetes share several common modifiable and non-modifiable risk factors including obesity, physical activity and dietary fat intake, smoking and certain drugs (Dornhorst et al. 1998). Therefore, understanding the different lifestyle factors associated with the development of GDM in developing countries will help in formulating prevention strategies for GDM which can potentially prevent the development of type 2 diabetes in a substantial proportion of the population. Hence prevention of GDM would also help in the prevention of type 2 diabetes. In addition, by being very aware of the causes of GDM and type 2 diabetes, one can also potentially intervene during and after pregnancy to reduce the future risk of type 2 diabetes.

A detailed review of the prevalence of GDM in South Asia and the consequences of this condition, risk factors for GDM, and assessment of physical activity in free living human subjects are presented in chapter 2. In brief, the lifestyle associated risk factors for GDM that can be modified include obesity (Metzger et al. 1998), rate of weight gain during pregnancy (Kieffer et al. 2001), body composition (McCarty et al. 2004), diet (Saldana et al. 2004; Moses et al. 1997; Zhang et al. 2004) and physical activity (Dempsey et al. 2004). The last part of the second chapter discusses various aspects of measuring physical activity including strengths and limitations of different methods used, and the validation of a self-reported physical activity questionnaires against motion sensors. In brief, motion sensors, specifically accelerometers have been found to be valid tools for assessing physical activity in free living human populations (Chen et al. 2003). Several self reported physical activity questionnaires designed for general populations

(Richardson et al. 1994; Sobngwi et al. 2001), for subjects in specific age groups (McMurray et al. 1988), as well as among those with different diseases, have been validated against motion accelerometers (Johansen et al. 2001).

In general, the prevalence of type 2 diabetes is high in Pakistan. In a population based survey 16.2% men and 11.7% women had diabetes in Pakistan (Shera et al. 1995). Another study conducted in three villages of Pakistan found a prevalence of 9.2% in men and 11.6% in women (Shera et al. 1999). A comparison of the prevalence of diabetes in urban versus rural populations of Pakistan reported a crude prevalence of 11.1% in men and 10.6% in women in urban areas versus 10.3% and 4.8% respectively in men and women in a rural area, suggesting lower rates in the rural population (Shera et al. 1999). These estimates within Pakistan are very similar and higher than in most settings in the West with the exception of aboriginal population.

In contrast to NIDDM, rates of GDM among Pakistani women in Pakistan appear to be low. In two studies conducted in Pakistan, the prevalence of GDM was found to be about 3%, which is comparable to prevalence in western countries (Akhter et al. 1996; Khan et al. 1991). While in a third study the prevalence ranged from 0.6% in low risk women to 12% in high risk women depending on the clinical risk group (Samad et al. 1996). However, multiethnic prevalence studies of GDM in other settings have found that South Asians have the highest prevalence of GDM compared to all other ethnic groups living in the developed world (Yue et al. 1996; Beischer et al.1991).

Lifestyle associated risk factors of GDM have not been explored in a rigorous manner in any developing country. The overall aim of this study was to assess the association of lifestyle risk factors with the development of GDM in Pakistan. The lifestyle associated risk factors that were studied included pre-gravid BMI, body composition, diet, physical activity, and rate of weight gain during pregnancy. With regards to physical activity it is important to measure whether imprecision of the self-reported exercise questionnaire might be the reason activity may not relate to GDM.

The specific objectives of this thesis were:

1. To determine predictors of GDM among Pakistani women, and in particular, the potentially modifiable risks posed by pre-gravid BMI, body composition, rate of weight gain (prior to GDM diagnosis), self reported physical activity and dietary intake (specifically total energy, macronutrients and fiber intake).

2. To validate self-reported physical activity against an objective physical activity measurement using accelerometers, i.e. Caltrac accelerometers, in a subset of women.

The study design for the overall thesis is presented in chapter 3. The study was a prospective cohort study involving 750 subjects recruited at antenatal clinics at Aga Khan

University Hospital (AKUH). Of these, 612 subjects completed the study (82% follow-up rate) and 49 of the 612 (8%) developed GDM. Information on all predictors of interest was collected at the time of recruitment ($\leq$ 18 weeks of gestation), prior to diagnosis of GDM, by conducting a face to face interview with each subject. A nested case control approach was used for analyzing dietary intake data given some unanticipated difficulties with data coding which led to a serious delay. Two age matched controls for each case were selected from the cohort study in a systematic manner. The study designed to validate a self-reported physical activity questionnaire was conducted on a subset (n=50) of women attending the antenatal clinics at the hospital. The subjects for this study were mostly (n=32) from the cohort study. Each subject wore an accelerometer for five consecutive days and responded to a self-reported physical activity questionnaire. The agreement with the questionnaire used in the cohort is documented.

Chapter 4 is a manuscript addressing the validation of the self-reported physical activity questionnaire, while chapter 5 is a manuscript that describes the findings on the impact of lifestyle predictors of GDM in Pakistani women. An overall conclusion of this research is presented in chapter 6.

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CHAPTER 2. LITERATURE REVIEW

2.1. Introduction

Over the past few decades, the prevalence of chronic diseases namely, diabetes, cardiovascular disease, stroke and cancers have increased in the developing countries of the world. These countries were thought to be immune to the development of chronic diseases in the past compared to the Western or more developed nations of the world. Researchers are interested in examining the risk factors that have lead to such increases in the prevalence of chronic disease. GDM is one of the chronic diseases that deserves attention in this context as it is closely related to type 2 diabetes. Moreover, the prevalence of GDM is indicative of the prevalence of type 2 diabetes in the country where chronic diseases are rising sharply (King 1998). The objective of this literature review is to provide information on the prevalence and risk factors of gestational diabetes mellitus in developing countries. A better understanding of these risk factors will help policy makers and health scientists develop prevention programs for curtailing the rise in the incidence of gestational diabetes in the regions.

This review is divided into several sections, first a definition of GDM and issues related to different criteria for defining GDM will be discussed. Second, prevalence of gestational diabetes in south Asia will be presented. The following section of this review is devoted to the consequences associated with the development of GDM for the mother. Fourth, the risk factors of gestational diabetes will be discussed. These risk factors can be divided into modifiable and non-modifiable risk factors. The modifiable predictors of

gestational diabetes are of special interest in this review as policy makers and health scientists can incorporate them into prevention programs. The modifiable risk factors include pregravid BMI, body composition i.e. amount of fat mass, fat free mass, and body fat percentage, rate of weight gain during pregnancy, diet and physical activity. The last section of this review will describe various approaches for assessing physical activity in human subjects and report the outcome of studies that have validated self reports of physical activity.

2.2. Definition of gestational diabetes mellitus

Gestational diabetes mellitus is defined as "any degree of glucose intolerance with onset or first recognition during pregnancy" (Metzger et al. 1998). This definition includes both women treated with insulin as well as those treated by diet alone. Also there is a possibility that some of these women may have had diabetes prior to entering pregnancy but were not diagnosed earlier (Anonymous 2004).

Gestational diabetes is diagnosed by conducting a series of tests on individuals. Women who have a fasting plasma blood glucose level >126mg/dl (7.0 mmol/l) or a value over 200mg/dl (11.1 mmol/l) on a random blood glucose test that can be confirmed on a subsequent day do not need to undergo any further investigation for GDM detection (Anonymous 2004). However, in the absence of such high levels of hyperglycemia,

women need to go through a more elaborate testing procedure to ascertain their GDM status.

Diabetes in pregnancy in the majority of the population is detected by following either a one step or a two step approach. The one step approach involves conducting an oral glucose tolerance test (OGTT) without prior screening. The two step procedure involves performing an initial screen, glucose challenge test (GCT), by measuring the plasma or serum glucose concentrations, one hour after a 50 gram oral glucose load. Subjects who have a value above a certain cutoff on a GCT undergo the (OGTT). Different cutoffs have been selected for the GCT in order to identify the maximum number of GDM subjects without making the entire pregnant population go through an OGTT. These differences are based on the sensitivity and specificity of the cutoffs. It has been concluded that a cut off of 140 mg/dl (7.8 mmol/l) has a sensitivity of 80% and a cutoff of 130mg/dl (7.2 mmol/l) improves the sensitivity to 90%. In both of these methods, the diagnosis of GDM is based on the OGTT and not on the raised values of a GCT.

In case of a raised GCT (when a two step approach is used), an OGTT is conducted shortly after the GCT, for diagnosing GDM. This test is conducted after 3 days of unrestricted carbohydrate (CHO) diet and unlimited physical activity. The OGTT glucose load could be either 75 (2 hours OGTT) or 100 grams (3 hours OGTT). Blood is drawn at fasting and then every hour for the 3 hour test and fasting followed by one blood

drawn at 2 hours post load for the 2 hour test. The World Health Orgranisation (WHO) recommends the 2 hour 75 gram test for the sake of uniformity with the protocol for diagnosis of diabetes mellitus. Subjects who fall into the impaired glucose tolerance group (IGT) are also labeled as GDM patients (WHO Report, 1999). The three hour test advocated by the American Diabetes Association involves drawing of blood every one hour. Two values out of the four have to be raised in order to determine a person's GDM status on a three hour test. The different tests with their respective cutoffs are presented in Table 2.1. In general, the Canadian Diabetes Association has similar guidelines for diagnosis of GDM as those of the American Diabetes Association (Meltzer et al. 1998).

The benefits and limitations of a three hour test versus a two hour test have been examined in various research studies. American Diabetes Association guidelines suggest that either one of the two tests can be used (Anonymous 2004). A study comparing the two tests (Weiss et al. 1998) found no differences in the 1 hour blood glucose values for GDM cases on a 75 grams test versus the 100 grams test, but the values were different for controls for fasting as well as at 2 hours (n=60). One major limitation of this study is the diagnostic criteria chosen to identify GDM cases for comparison with controls was a 100 gram one hour, one value test that may not have truly reflected the endocrine status of the subjects. The authors of this paper argued that the WHO criteria should be preferred over the American Diabetes Association criteria and recommended the addition of glucose testing at 1 hour in the WHO test as it is associated with fetal outcomes such as macrosomia.

There are also differences of opinion about the cutoff points for detection of GDM in a 100 gram test. The original 100 gram test was suggested by O Sullivan and Mahan in 1964 and values above 2 SD were considered abnormal. Later on, owing to differences in the blood fraction being analysed (plasma versus whole blood), the National Diabetes Data Group (NDDG) suggested different cutoffs, for diagnosis of GDM. In the last two decades, enzymatic analytical procedures have replaced the chemical method used previously. Therefore, Carpenter and Coustan (1982) have suggested even lower values. The current recommendations of ADA are based on the thresholds suggested by Carpenter and Coustan (Anonymous 2004). In an attempt to estimate differences in the prevalence of GDM using NDDG vs. Carpenter and Coustan criteria, 4260 women underwent a 100 gram OGTT after an abnormal GCT in a universal screening setup. Based on the differences in cutoffs 50% more women were diagnosed as having GDM by the Carpenter and Coustan criteria compared to the NDDG cutoffs ($P < 0.001$) (Ferrara et al. 2002).

Even mild glucose intolerance is associated with adverse fetal and maternal outcomes. The Toronto Tri-hospital GDM study observed that women who did not fulfill the NDDG criteria for diagnosis of GDM also had adverse fetal and maternal consequences (Sermer et al. 1998). Similarly, Danish women with risk factors for GDM, yet who did not meet the GDM diagnosis criteria had a graded increase in the rate of maternal as well as fetal complications with increasing glucose intolerance levels (Jensen et al. 2001). The risk factors that these women had were family history of diabetes, past obstetric history, pregravid obesity and age over 35 years. In a comparison of GDM

normal and borderline subjects for the development of macrosomia (>4000 g) and cesarean delivery, the untreated borderline GDM group had increased rates of macrosomia (28.7% vs. 13.7%, P <0.001) and cesarean delivery (29.6% vs. 20.2%, P 0.02) compared to the normal glycemic status women. Macrosomia lead to greater probability of cesarean delivery in women with borderline glucose status (45.5% vs. 23.5%, P 0.03) compared to normal glycemic status women (Naylor et al. 1996).

These studies indicate that even slight increase in maternal glucose levels during pregnancy is associated with adverse consequences for both the mother as well as the fetus. Perhaps, glucose intolerance should be considered as a continuous phenomena rather than a categorical outcome for improving the health outcome for the mother as well as the fetus.

2.3. Prevalence of gestational diabetes mellitus in South Asia

All studies that have examined the prevalence of GDM in South Asia are hospital based studies moreover there are considerable differences in the reported prevalence of gestational diabetes mellitus (GDM) across regions in South Asia (Table 2.2.). There could be several reasons for these differences which are as follows: dissimilarity in the diagnostic criteria used for diagnosing GDM, the type of study site (large tertiary care hospitals often get more complicated referrals such as patients with poor medical history

compared to small antenatal clinics) and the socio-economic background of the study population.

A gap in the current literature on prevalence of gestational diabetes in South Asia exists as very few studies (Ramachandaran et al. 1994, 1998) have tried to examine time trends in the prevalence of GDM. More prevalence studies would help elucidate the association between nutrition transition and gestational diabetes in the region.

Unfortunately, literature is available only for India, Pakistan and Sri Lanka which makes it difficult to assess the situation in the entire South Asian region. However, given similar ethnic background and nutrition transition rate in the region, one could believe that the prevalence of gestational diabetes would be similar in the entire region.

2.4. Consequences of gestational diabetes mellitus for the mother

GDM leads to the development of overt diabetes later in life in the mother. Several studies have investigated this association in numerous populations. In a follow-up in a Danish population 39.9% women who had mild form of GDM (treated by diet alone) developed type 2 diabetes in 9.8 years (Lauenborg et al. 2004). Furthermore multivariate analysis revealed that the odds of developing type 2 diabetes were 2.9 (CI 1.5 – 5.9) after diagnosis of GDM before 24 weeks of gestation. The other significant predictors in this

model were pre-pregnancy BMI, family history of diabetes, fasting plasma glucose at the time of GDM diagnosis and IGT post-partum.

In a review of several studies assessing the rate of conversion to type 2 diabetes mellitus in subjects with GDM during a pregnancy, 2.6 – 70% cumulative incidence rates of type 2 diabetes were reported. The authors found that the lowest rates were from studies that had the shortest follow-up period or studied non-Hispanic white populations (Kim et al. 2002). An analysis adjusted for length of follow-up showed fewer differences in the cumulative incidence due to ethnicity. Furthermore, it was observed that the highest increment in the development of GDM took place in the first five years after index pregnancy and then increased more slowly. However, one limitation of this review is that all the studies reviewed were on non-white populations which limit the external validity of the findings (Kim et al. 2002). Furthermore, none of the studies reviewed had a control group hence it is very difficult to assess whether the rate of development of type 2 diabetes in subjects who had had GDM in a pregnancy was higher than the rate that would be observed for women without GDM.

In a better designed study which had a control group as well, subjects were followed for a period of 11 years, the cumulative incidence for type 2 diabetes and abnormal glucose tolerance was 13.8 and 42.2 % respectively in women who had had GDM and 0 and 2.8% respectively in subjects without GDM ($P < 0.05$) (Albareda et al. 2003). Likewise in another investigation with a control group and a follow-up at 15 years

35% women developed type 2 diabetes from those exposed while none of the subjects in the control group developed diabetes (P <0.001) (Linne et al. 2002). These studies indicate the risk of developing diabetes is considerably higher in women diagnosed with GDM than in women who did not develop GDM. Estimates of population attributable risk (PAR) for developing diabetes after GDM suggest that somewhere between 10 – 31% (PAR 0.10 – 0.30, CI 0.06 – 0.41) of the women that develop diabetes would have experienced GDM (Cheung et al. 2003). One could argue that the population rates would be somewhat lower because all women do not undergo a pregnancy, however in developing countries where the fertility rates are high, one could believe that these rates would not be significantly lower. Furthermore, another limitation of this study is that the PAR has been estimated based on studies conducted in developed nations of the world. In order to get a more accurate PAR for developing countries which host different ethnic populations than the developed world, PAR will have to be estimated based on studies conducted in developing countries. Nevertheless these figures can be used as a ballpark for emphasizing the need for prevention programs.

Hence it is quite obvious that a substantial proportion of women diagnosed as having GDM develop overt diabetes in a short period of time after the index pregnancy. Owing to this association between diabetes and GDM prevention strategies need to be developed. This will help in reducing the number of women who develop type 2 diabetes later in life.

Not only does GDM lead to a greater risk of developing type 2 diabetes later in life but it also shares similar risk factors. The risk factors associated with the development of type 2 diabetes in subjects with GDM can be divided into non-modifiable and modifiable risk factors. The non-modifiable risk factors include ethnicity, pre-pregnancy weight, age, family history of diabetes, parity and level of hyperglycemia in pre-pregnancy and immediately post-partum. The modifiable risk factors include persistent obesity, future weight gain, subsequent pregnancies, levels of physical activity and dietary fat, smoking and certain drugs (Dornhorst et al. 1998).

2.5. Risk factors of gestational diabetes mellitus

This section discusses the non-modifiable and modifiable risk factors of GDM. The non-modifiable risk factors reviewed include age, ethnicity, height, and historical predictors namely, family history of diabetes and past obstetric history. The modifiable risk factors that will be discussed in this review are obesity, rate of weight gain during pregnancy, body composition, diet and physical activity. This section of the review begins with a discussion of the non-modifiable risk-factors and then will discuss the modifiable risk factors of GDM.

2.5.1. Non-modifiable risk factors

I. Age

Women over the age of 35 years are at higher risk of developing GDM compared to younger women in all populations. Evidence for this stems from several studies (Table 2.3). Large, prospective, Caucasian population studies report a relative risk (RR) of 2.38 (CI 1.38 – 4.12) for women over 40 compared to between 25 – 29 years (Solomon et al. 1997). Similar results have been found for multiethnic studies (Berkowitz et al. 1992) RR of 6.88 (CI 3.42 – 13.81) for women over 40 years of age compared to women less than 20 years old.

Likewise, a study conducted in China (n=111563), found women who were <19 years of age (P <0.01) were less likely to develop GDM (Xiong et al. 2001). This analysis was adjusted for parity, maternal weight, smoking and poor pregnancy outcomes. Similar results have also been reported by a study conducted in Turkey (Caliskan et al. 2004).

Furthermore, American as well as Canadian screening guidelines for GDM advice that all pregnant women over 25 years of age should undergo a glucose challenge test in order to rule out the possibility of having GDM (Anonymous 2004; Meltzer et al. 1998).

II. Ethnicity

The American Diabetes Association's guidelines for screening for gestational diabetes suggest all non-Caucasian women to be screened for GDM regardless of the presence or absence of any other risk factors (Anonymous 2004).

Compared to the Caucasian population, Black and Hispanic groups (Dooley et al. 1991) were found to be at a greater risk, RR 1.81 and 2.45 respectively, of developing GDM (RR adjusted for age and pre-gravid ideal body weight percentage). Unfortunately, the study did not have sufficient power to include oriental race in the ethnicity model despite the fact that the highest prevalence of GDM was reported in this group 10.5% compared to 2.7% in Caucasian population. Compared to a Caucasian Dutch population ($n > 24,000$) people from other countries namely Suriname, Turkey, and Morocco were found to be at a higher risk of having GDM ($P < 0.01$) (Weijers et al. 1998). Similar results were also found for the age and sex adjusted prevalence for type 2 diabetes in the area.

Compared to the Caucasian population, in a retrospective study (n=11205), subjects of Indian origin had the highest prevalence of GDM (RR 11.3, 6.8 – 18.8) followed by South East Asians (RR 7.6, 4.1 – 14.1), Caribbean blacks (RR 3.1, 1.8 – 5.5) and a miscellaneous group including Arabic peoples (RR 5.9, 3.5 – 9.9). These relative risks were adjusted for age, BMI and parity (Dornhorst et al. 1992).

II.a. Interaction of ethnicity with obesity

In Canada, the aboriginal population has been found to have a higher prevalence of GDM compared with non-aboriginal population. In a study comparing the effect of ethnicity on the prevalence, risk factors and outcomes of gestational diabetes Aboriginal women who were overweight (BMI $\geq$ 27) had a greater risk of developing GDM compared to non-aboriginal overweight women odds ratio (OR) 8.56 (CI 2.66 – 27.55) vs. 1.41 (CI 0.71 – 2.78), respectively (Dyck et al. 2002). Similar findings have also been reported in a study conducted in the Cree population in James Bay area in which aboriginal women at a healthy weight were no more likely to develop GDM (Rodrigues et al. 1999). The authors of this paper suggest several reasons for higher prevalence rate of GDM in aboriginal population namely, differences in lifestyle i.e. diet, physical activity, body fat deposition and genetics.

These studies show that even after controlling for other confounding factors such as age, BMI and parity, ethnic origin of women remains a significant predictor of GDM.

III. Historical predictors of diabetes mellitus: Family history of diabetes and past obstetric history

Family history of diabetes is a strong predictor of GDM in all studies reviewed (Table 2.2). However, the question that remains unanswered is whether family history of diabetes is a surrogate marker for sharing common lifestyle practices such as poor diet

and low physical activity, or does family history of diabetes per se lead to an increased risk of developing GDM? Examining offspring-parent pairs for physical activity behaviour found that the between pair variation for physical activity was more than the within pair activity (Simonen et al. 2002) indicating familial grouping of risk factors.

Past obstetric history is a less meaningful risk factor of GDM as women undergoing their first pregnancy cannot be evaluated for their risk based on this risk factor. However, for women with a past obstetric history, cesarean section, fetal malformations, hydramnios and neonatal death are significantly associated with the development of GDM (Table 2.2).

Contrary to the general belief, multi-parity was not found to be a predictor of GDM. It seems that owing to the high correlation between parity and maternal age, these studies were not able to demonstrate an effect of parity over and above that of age.

IV. Height

Recently, there has been a growing interest in understanding the association between height and the development of GDM. In a multiethnic study, European and South Asian women with GDM were found to be 2.4 and 3 cm shorter respectively, than controls from the same ethnic communities after adjusting for age (Kousta et al. 2000).

Although not significant, the Afro-Caribbean women seemed to follow the same trend as the other two ethnic communities. The authors argued that GDM and attainment of adult height have a similar biological explanation which is related to fetal origins of chronic disease. Likewise, in a study conducted on a Korean population (n=1890), short height was found to be a predictor of GDM, ($P < 0.0001$) (Jang et al. 1998). The other predictors were age, pre-pregnancy BMI, parental history of diabetes and weight gain. However, a limitation of these studies is that they do not provide information on the socio economic status of the populations, family lifestyle or diet during pregnancy which could have been confounders in these cases.

Shorter adult height was related to one abnormal glucose value ($P < 0.05$), GDM ($P < 0.05$) and type 2 diabetes ($P < 0.01$) in a Greek population even after controlling for age, weight and SES as assessed by high school certification (Anastasiou et al. 1998). Additionally, insulin resistance was inversely associated with height ($P < 0.05$) suggesting a role of insulin in attainment of height. One could argue that the study did not accurately assess SES status, as one might expect considerable homogeneity in this kind of categorization for SES in a Greek population.

In contrast to this, in a Hungarian investigation, no association was found between stature and GDM (Tabak et al. 2002). The authors felt that there is a publication bias in connection with height as a predictor of a disease outcome.

One could argue that differences in height per se may not lead to differences in GDM status; rather it could be serving as surrogate marker of fetal health and nourishment state as well as for nutrition during early years of life. These factors in turn could be related with the socio-economic status, in particular, in food insecure households such as those found in South Asia.

2.5.2. Modifiable risk factors of gestational diabetes mellitus

I. Maternal obesity

There is sufficient evidence to conclude with confidence that maternal obesity is a predictor of GDM. All diabetes consultation groups recommend that women who are obese should be considered at higher risk of developing GDM (Anonymous 2004; Metzger, 1998).

The association between maternal obesity and GDM holds for women in all age groups. An examination of risk factors of GDM in adolescent pregnancy (< 19 years) (Khine et al.1999) found BMI > 27 to be associated with the development of GDM, the other risk factor investigated in this study was ethnicity. A limitation of this study is that data on other predictors of GDM were not collected.

I.a. Explanation

Several research studies have tried to understand the role of adipose tissue in increasing the risk of GDM. Adiponectin and leptin are two hormones that have been investigated. A brief discussion of the two follows.

Adiponectin is a protein hormone secreted by adipocytes, it regulates lipids and glucose metabolism. Adipose tissue plays an important role in insulin resistance in the human body in particular, during GDM. A negative correlation exists between serum adiponectin levels and other markers of insulin resistance i.e. leptin, tumor necrosis factor alpha, C peptide concentrations as well as BMI (Cseh et al. 2004).

High levels of adiponectin are considered protective against the development of type 2 diabetes and coronary artery disease. There is an inverse association between plasma adiponectin concentrations and diabetes and coronary artery disease outcomes. Lower adiponectin plasma levels measured in early pregnancy (< 6.4 μg/ml) were found to lead to a 4.6 fold (CI 1.8 – 11.6) increased risk for GDM (William et al. 2004). This analysis adjusted for maternal age, family history of diabetes and pre-pregnancy BMI. It has been suggested that adiponectin could be used as a screening tool for type 2 diabetes as it has been considered a risk factor for the development of type 2 diabetes later in life. (Retnakaran et al. 2004; Cseh et al. 2004).

On the other hand, some studies suggest that low adiponectin levels could be associated with obesity and may not be related to GDM. A study inspecting women with different pre-pregnancy BMI levels, showed differences in serum adiponectin levels of women with BMI under 25 vs. BMI over 25 ($P < 0.01$), these differences remained significant upon further stratification of women into GDM and control group for BMI < 25 but not BMI $\geq$ 25 (Ranheim et al. 2004).

Another adipocyte derived hormone that has been investigated for its association with gestational diabetes is leptin. Higher concentrations of serum leptin levels (measured at 13 week of gestation) were associated with a 4 fold greater risk of developing GDM even after adjustment for maternal adiposity, parity and family history of diabetes (Qiu et al. 2004). Similar results were found in another study (Kautzky-Willer et al. 2001). Furthermore the investigation showed that plasma leptin levels remained high in women who had gestational diabetes 8 weeks postpartum compared to other groups ($P < 0.05$).

II. Rate of weight gain during pregnancy

Rate of weight gain up to 28 weeks of gestation was found to be an independent predictor of GDM in a prospective study conducted in Latino and African American population residing in the USA with higher weight gain observed in women who developed GDM. The other risk factors associated with the development of GDM in this study, were ethnicity (being Latino), age, family history of diabetes, and body mass index

(Kieffer et al. 2001). This study indicated that rate of weight gain predicts GDM independently of the effect of age, ethnicity, family history of diabetes and BMI.

Several studies indicate that rate of weight gain is associated with pregravid BMI status, with obese women gaining less weight compared to lean women (Okereke et al. 2004; Ehrenberg et al. 2004); this makes assessment of rate of weight gain as a predictor of GDM a difficult task.

III. Body composition

A convincing review of the several techniques available for assessing body composition of women during pregnancy and how that relates to perinatal outcomes suggested that body composition measures are more sensitive predictors of several perinatal outcomes including GDM than maternal obesity (McCarty et al. 2004).

In a case-control study (n=52) conducted to understand the relationship between gestational diabetes and deposition of fat mass in pregnancy, it was observed that pregravid BMI was associated with differences in body composition with lean women gaining more body fat (%) compared to overweight/obese women (BMI > 25) and the glycemic status did not seem to be associated with these differences (Ehrenberg et al. 2003). While, in a prospective study examining differences in body composition in obese

normal glycemic status vs. obese women with GDM (pregravid body fat > 25%), no differences were observed in the fat mass, fat free mass, body fat % as well as weight assessed prior to pregnancy as well as in late pregnancy (36 weeks of gestation) (Okereke et al. 2004).

However in another study changes in body fat percentage, without changes in body weight, have been reported to be positively associated with changes in the Blood HB A1C levels in diabetic subjects (Sohmiya et al. 2004). Furthermore, increased amount of visceral fat and total fat volume have been associated with increased insulin resistance in men suggesting a role of body fat in the development of impaired glucose tolerance as well as type 2 diabetes (Banerji et al. 1999), while muscle mass helps in the uptake of blood glucose (Rigalleau et al. 2003).

IV. Body fat distribution

Central obesity is linked with increased levels of insulin resistance not only in obese but also in normal weight women (Carey et al. 1996). This means that the place where fat is stored is strongly associated with the development of insulin resistance regardless of BMI. In a secondary analysis of the CARDIA study (Zhang et al. 1995) it was found that waist hip ratio was a better predictor of GDM (P value for trend 0.02) than BMI (P >0.05). Another significant risk factor in this study was family history of

diabetes. The major limitation of this study however is that GDM status was self reported by the subjects.

Despite the strong evidence that waist to hip ratio is a significant predictor of GDM, its clinical significance is questionable as often women in developing countries register for antenatal care late in pregnancy when waist to hip ratio may not be a valid indicator of body fat accumulation owing to body changes related to pregnancy.

V. Diet

V.a. Macronutrients

There is considerable information on manipulating macronutrients for management of GDM; however, role of macronutrients in the development of GDM remains unclear. In a prospective cohort study, assessing the effect of carbohydrates and fat intake during the first three months of pregnancy on the development of glucose intolerance later in the pregnancy the authors found that women with GDM had lower percentage of energy from carbohydrates and higher percentage of energy from fat compared to women with normal glucose status. Furthermore, adding 100 more kcal from carbohydrates decreased the risk of GDM (RR 0.9, CI 0.85 – 0.98) while substituting fat (1% substitution) for carbohydrates increased the risk for developing GDM (RR 1.1, CI 1.02 – 1.10) after adjusting for age, BMI, and race (Saldana et al. 2004). However no information was provided about the fiber intake, it is possible that fiber was included in

the carbohydrate category in which case the protective effect of carbohydrates would partly be related to fiber intake.

In contrast, in a case control study (controls matched for age, gestational age and height), no differences were found in total energy (kcal), % energy from carbohydrates, fat, protein or fiber intake (g) of women who had GDM vs. controls (Wang et al. 2000). However, further analysis revealed that women with GDM (n=56) consumed less polyunsaturated fat (% of total kcal) and more saturated fat (% of total fat), compared to women without GDM as well as subjects with impaired glucose tolerance. Furthermore, after matching for BMI, monounsaturated fat intake (% of kcal) was lower in subjects with GDM compared to other groups. However, the leading question of this study which was to explore relationship between macronutrients, energy and fiber intake and GDM, was not found to be significantly different for women with vs. without GDM, further stratified analysis of non-significant main effects is questionable.

In a third study in this area, assessing the role of dietary fat in the development of GDM, the total amount of energy provided by fat was higher in the GDM group and no differences in the proportion of energy contributed by mono, poly and saturated fatty acids were observed (Moses et al. 1997).

Conclusive evidence regarding the relationship of macronutrients and GDM is not available, perhaps large cohort studies investigating the relation of diet and GDM will be able to elucidate the role of diet in the development of GDM.

V.b. Micronutrients

In a case control study (Zhang et al. 2004) assessing dietary intake of vitamin C by a semi-quantitative questionnaire, vitamin C intake was found to be lower in women with GDM compared to women without GDM (OR 3.7 CI 1.7 – 8.2). Likewise, a study assessed plasma ascorbic acid levels in women around 13 weeks of gestation and observed an inverse relationship between plasma ascorbic acid levels and the development of GDM (RR 3.1 CI 1.0 – 9.7). Furthermore, dietary intake < 70 mg of vitamin C per day seemed to be associated with a greater risk of GDM (RR 1.8, CI 0.8 – 4.4) compared to women who met the dietary recommendations of vitamin C (Zhang et al. 2004). Confounders such as maternal age, pre-pregnancy weight, parity, family history of diabetes, and household income were statistically controlled while some potential confounders such as antioxidants or fiber that are often found in the same foods as vitamin C were not adjusted in the analysis. It is possible that some of the beneficial effect attributed to vitamin C could have been due to these other factors present in food.

VI. Physical Activity

Despite literature on the relationship of physical activity and development of chronic diseases such as type 2 diabetes and cardiovascular disease (FAO Report 2003), there is little evidence concerning physical inactivity as a predictor of gestational diabetes.

In a prospective cohort study that recruited ≤ 16 week pregnant women (n=909) (Dempsey et al. 2004), information was gathered on physical activity using a self reported questionnaire for the year prior to pregnancy as well as the week prior to the interview as a surrogate for activity during pregnancy. In general, physically active women who performed any recreational activity during both the time periods were at a reduced risk of developing GDM (RR 0.31, CI 0.12 – 0.79). However, in a separate analysis of the intensity of physical activity and its relation with the development of GDM, recreational physical activity during the year prior to pregnancy lowered the risk of developing GDM compared to inactive women (RR 0.44, CI 0.21 – 0.91). However, further stratified analysis revealed that this association was only significant when ≥ 4.2 hours or ≥ 21.1 MET scores /week were spent in physical activity. These results were adjusted for age, race, parity, and pre-gravid BMI. Recreational physical activity during pregnancy did not prevent GDM after adjusting for confounders despite the impact of physical activity in the previous year.

Similarly, The Nurse's Health Study (Solomon et al. 1997) examined pre-gravid predictors of gestational diabetes. These predictors included age, weight, height, family history of diabetes, smoking habits, and ethnicity as well as physical activity. Physical activity levels were assessed by a questionnaire. Additionally, information was gathered about walking habits of women which involved frequency/week, intensity as well as the speed of walking. Physical activity, reported as metabolic equivalent (MET) scores was not found to be associated with a risk reduction in GDM.

In contrast, in an observational study (Dye et al. 1997) a protective role of physical activity, assessed by a self-reported physical activity questionnaire, was observed in subjects who had a BMI greater than 33 but not among those with a BMI lower than 33.

Social acceptance of physical activity as a means of improving health outcomes is important in order for it to have a significant impact on the health of people. In a qualitative analysis (Kieffer et al. 2002) of pregnant and post partum women's perspectives on physical activity and its association with diabetes and health, it was interesting to note that women did not see a lack of physical activity as being related with the development of diabetes. Only diet and inheritance were considered to be related to the development of diabetes by this group of women. Furthermore, women reported lack of knowledge, partner support, safety, family responsibilities, lack of friends to exercise

with, and physical complaints as issues perceived as barriers in being active during and after a pregnancy.

Although the evidence for preventive role of physical activity, based on observational studies seems to be less obvious, several trials have examined physical activity as a means to manage hyperglycemia in GDM women. In a review on the role of exercise in gestational diabetes (Artal et al. 2003) it has been suggested that all women including those with very low levels of physical activity can also perform some physical activity for management of gestational diabetes. The nature of exercise performed would vary from person to person and as yet there isn't a general guideline that could be given to all patients. Furthermore, all women with gestational diabetes involved in some kind of physical activity will have to be monitored for blood glucose and fetal health more rigorously.

Both aerobic and resistance exercise have been found to lead to a reduction in blood glucose values in patients with GDM. In a study (Brankston et al. 2004) assessing the effect of resistance exercise on requirement vs. no requirement of insulin for the management of gestational diabetes (n=32) subjects were randomised to receive a dietary intervention alone or a diet and exercise intervention. The exercise intervention included 30 minutes of circuit training 3 days per week and dietary intervention involved 40% carbohydrate, 20% protein and 40% fat at 25 – 30 kcal/kg pre-gravid body weight/day. They found the number of subjects who required insulin in the two arms of the

intervention trial were similar, however, the diet plus exercise group subjects required less insulin and it was initiated later in pregnancy than the diet alone group. This suggests that resistance exercise aids in the management of gestational diabetes.

There is a need for well conducted studies that could provide conclusive evidence on the role of physical activity in the prevention of GDM. However, the selection of an appropriate instrument that can measure physical activity accurately is of paramount importance in order to assess associations with disease outcomes. The following section reviews some of the instruments available for assessing physical activity in humans.

2.6. Measuring Physical activity

One of the risk factors of chronic disease is lack of physical activity. Therefore, measuring physical activity has become important in epidemiological studies that are designed for assessing the current levels, adherence to programs, role of physical activity in predicting disease and health outcomes and for evaluating effectiveness of intervention programs related to physical activity (Sirard et al. 2001). Accurately assessing physical activity is a challenging task in free living human populations. This task can be accomplished if the researcher is clear on the purpose of assessment. For example, research assessing the benefits of physical activity in osteoporosis will examine long term activity, while an investigation of benefits of physical activity for cardiovascular disease

subjects will explore fitness levels associated with physical activity (Freedson et al. 2000; Kriska et al. 1997).

Typically activity is being assessed based on self reported questionnaires. These reports can be either in the form of structured questionnaires or diaries. However these are liable to subjective bias and recall errors (Freedson et al. 2000), also questionnaires are not suitable for certain sub-populations such as young children where a structured questionnaire may not be able to assess all modes of activity in which a child engages. Although direct observation of the subject's physical activity should be conducted, in most cases it is not feasible. However, some techniques have been developed that are being used in field settings for direct estimation of physical activity as well as for validation of various self reported questionnaires. These are collectively considered as objective measures of physical activity in contrast to the questionnaires which are prone to subjective bias.

In this section, first various objective measures that have been used for measuring physical activity will be presented with an elaborate review of motion sensors as means of measuring physical activity. In recent years motion sensors have been used quite extensively for the assessment of physical activity and this section will focus primarily on the validity of motion sensors compared to gold standard procedures. Secondly, self reported physical activity questionnaires will be discussed. Several physical activity questionnaires have been validated against motion sensors, in particular against

accelerometers, this review will discuss some of the questionnaires that have been validated by accelerometers.

2.6.1. Objective measures of physical activity

These include calorimetry (direct and indirect), doubly labeled water techniques, measurement of heart rate and different motion sensors (pedometers and accelerometers).

I. Calorimetry

Physical activity leads to expenditure of energy by the body, which can be measured as heat that is emitted by the body. The amount of heat produced by an individual is calculated by measuring the rise in the temperature of water surrounding a chamber in which the subject stays. By measuring the temperature of the water surrounding the chamber (calorimeter) before and after the study, the number of kcal expended can be determined. This is taken as a gold standard technique for validating other instruments that measure physical activity but is not used often because of the expense and complexities associated with it (Westerterp et al. 1999). Another reason is that conditions in the chamber may be quite artificial and physical activity carried out in the chamber may not accurately depict the types of activities carried out in free living conditions.

II. Indirect calorimetry

In this technique, instead of measuring energy expenditure by the amount of heat that the body produces, oxygen uptake and carbon dioxide output are assessed. Several studies have made use of indirect calorimetry for measurement of energy expenditure (Coss-Bu et al. 1998). However a limited number of activities can be measured by this technique. Machines such as a stationary bicycle or treadmill are used for assessing oxygen uptake and carbon dioxide output.

III. Doubly labeled water technique

This technique is often considered the gold standard for measurement of physical activity in free living individuals. The subject is administered isotopes of oxygen and hydrogen and body fluids are measured later which provides an estimate of CO_2 use. Measured CO_2 production can be converted to energy expenditure, using specific equations and making assumptions such as hydration level.

Several validation studies have used doubly labeled water for validating physical activity questionnaires and reported good correlation between the questionnaires and doubly labeled water estimates of energy expenditure (Kupard et al. 1997; Philippaerts et al. 1999), while in another study (Bratteby et al. 1998) the questionnaire was found to underreport physical activity compared to doubly labeled water energy expenditure estimates, in particular, in subjects who were overweight.

Use of doubly labeled water as a means of estimating energy expenditure per se as well as for validation studies is quite limited due to the prohibitively high cost of isotopes that are being used. Hence it is not feasible for use in large epidemiological studies for assessment of physical activity.

IV. Heart rate measurement

Heart rate and maximum oxygen consumption (Vo_2) are closely related and can be used as indicators of Vo_2 to assess physical activity levels. Heart rate monitors consist of a chest strap transmitter and a small receiver watch. These watches can store data for 5.5 days (Polar Electro, Tampere, Finland) to 44 days (Minimitter, Sun river, Oregon).

However, factors such as high ambient temperature, humidity, and emotional stress can lead to an increase in the heart rate without leading to an increase in Vo_2 and cause error in the assessment of physical activity. Furthermore, the relative size of the exercising muscle affects the heart rate yet the Vo_2 remains the same. Also fatigue and hydration affect heart rate (Basset et al. 2000). In large studies it can be difficult to use heart rate monitors since individuals have different physical activity exposure and gender differences also exhibit different heart rates to the same Vo_2. Another problem is that heart rate remains elevated after an exercise even after Vo2 has returned to base line. This error can lead to over estimation of energy expenditure (Freedson et al. 2000).

V. Motion sensors

As the name implies, motion sensors are instruments that detect the movement of the body. Currently there are two main types of motion sensors that are being used in human research; pedometers and accelerometers.

V.a. Pedometers

Pedometers record the total number of steps taken or distance walked by an individual. If data on body weight is keyed in some pedometers can estimate energy expenditure as well. However, this energy expenditure can be a true estimate of a person's daily energy expenditure only if walking is that individual's major component of physical activity (Freedson et al. 2000). This may not be the case in several populations where occupational work leads to significant energy expenditure. On the other hand, in sedentary populations where energy expenditure is limited, they can adequately assess physical activity at a population level. Pedometers have also been used for motivating populations to increase physical activity and goal setting in physical activity programs (Tudor-Locke et al. 2004; Jakicic et al. 2003). Currently, a national Canadian program, organized by the Canadian Institute of Health Research is underway that encourages the use of pedometers to motivate Canadians to increase physical activity (Anonymous 2004).

In a study assessing the validity of pedometers against doubly labeled water in free living subjects (n=17) it was found that the pedometer underreported energy expenditure for sedentary activities that involved only upper body movement while provided accurate results for higher energy expenditure related activities (Tharion et al. 2004). The authors felt that energy expenditure related to upper body movement was underestimated by the pedometer.

In a systematic review of the convergent validity of pedometers when compared to accelerometers (Tudor-Locke et al. 2002) energy expenditure estimated by the pedometers correlated with uniaxial accelerometers r = 0.86 (pooled median r), time in observed activity (median r = 0.82), however reduced accuracy was observed during slow walking. Slower speed of walking has not been picked well in other validation studies as well (Le Masurier et al. 2003).

V.b. Accelerometers

These are non-intrusive instruments attached to the limbs and measure acceleration of the trunk or limbs. The accelerometer works on the principle that acceleration is directly proportional to muscular force and therefore is related to energy expenditure. An advantage of accelerometers over pedometers is that they have large memory capacity and measure the amount as well as the intensity of the physical activity. Two different types of accelerometers are being used for assessment of physical activity,

the uniaxial accelerometers (Caltrac, Muscle Dynamics Fitness Network, Torrence) measure energy expenditure in vertical plane while triaxial accelerometers measure energy expenditure in vertical, mediolateral and horizontal planes (Tritrac – R3 D accelerometer, Hemokinetics, Madison).

In a validation of a triaxial motion sensor (Tracmor) against doubly labeled water correlation of 0.58 was observed between the two techniques (Bouten et al. 1996). Similarly, in a validation study conducted on an adult Japanese population (n=79) total energy expenditure as well as physical activity related energy expenditure measured by an accelerometer was validated against calorimetry, a correlation of 0.93 and 0.57 was observed, respectively. However both the energy expenditure estimates from the accelerometer were lower (8 – 9%) from the direct calorimetry (Kumahara et al. 2004).

In a study comparing two accelerometers (Actiwatch and Actical) to direct calorimetry in children (7 – 18 years), it was found that the accelerometers were able to differentiate between sedentary, light, moderate and vigorous activities well in groups (positive predictive value 81, 68, 72 and 74% , respectively for Actical) (Puyau et al. 2004).

Although the accelerometers correlate with other objective measures of physical activity, they are unable to detect differences in grades of treadmill. In a study using both

Computer Science Application accelerometer and Caltrac accelerometer to assess physical activity during treadmill walking and running at three different grades, both accelerometers significantly correlated with energy expenditure measured by calorimetry ($r = 0.66 - 0.82$), relative Vo2 max ($r = 0.77 - 0.89$), heart rate ($r = 0.66 - 0.80$), tread mill speed ($r = 0.82 - 0.92$) and with each other ($r = 0.77 - 0.82$) but not with treadmill grade (Melanson et al. 1995).

Accelerometers seem to pickup motion related to vehicle transport as motion associated with body movement and can over estimate physical activity (Le Masurier 2003; Bouten 1996). However this error did not lead to misclassification of subjects in relation to physical activity behaviour in this particular study (Le Masurier 2003).

VI. Self-reported physical activity questionnaires

Studies that have been conducted on large populations have mostly used questionnaires to assess physical activity. According to Kriska et al. (1997) the main advantages of using questionnaires over objective means of physical activity assessment are as follows:

- Since a questionnaire assesses physical activity conducted in the past, it does not lead to changes in the physical activity routine of the subjects that may be associated with more objective measures of physical activity.

- Compared to objective measures of physical activity, the questionnaires are not expensive instruments to purchase.
- The questionnaire can be designed to meet the requirements for the particular population under study
- Questionnaires can be reliable as well as valid.

VI.a. Time frame

Some questionnaires may inquire about the physical activity pattern over the entire life, whereas some ask about the past year (Minnesota Physical activity questionnaire, Cardia physical activity history, University of Minnesota, USA), month (Behavioural risk factor surveillance (CDC, USA), week (Seven day physical activity record, San Diego State University, USA) or even a day (Framingham physical activity index, Boston University USA). A year's questionnaire usually tries to measure physical activity carried out by a person habitually; the shorter duration questionnaires focus more on the type and nature of activity.

The major advantage of short time frame questionnaires over long reference period questionnaires is the minimization of recall bias and they can also be validated by objective measures. But the disadvantage is that the short time period selected may not reflect a person's typical physical activity pattern and may lead to misinterpretation of a person's physical activity status. Usually, long time frame questionnaires are used when a

relationship between physical activity and chronic disease is under investigation. Chronic diseases are related to long term sedentary lifestyle rather than a short duration of physical inactivity.

VI.b. Domains of physical activity

In a study examining the construct validity of a physical activity questionnaire in the Netherlands, work related activity, sports and leisure time activities other than sports were the three loading factors for habitual physical activity assessment respectively (Baecke et al. 1982). In contrast, studies done in South East Asia suggest (Tudor-Locke et al. 2003) that often the major contributor to EE are everyday tasks and walking to work/school rather than the leisure time activity, observed in the West. These studies indicate that in order to assess physical accurately, several domains of physical activity should be assessed rather than collecting information only on leisure time physical activity. These domains would be occupation, leisure, household and transportation related activity.

VI.c. Scoring physical activity data

They are 2 methods for analyzing data gathered for physical activity. One is the simple approach which analyses the time spent in physical activity multiplied by the frequency of the activity.

Another method takes the intensity of the activity into account in addition to the duration of the session and the frequency. It is obtained by multiplying the duration of physical activity by the intensity of the activity, which is described as the metabolic cost or metabolic equivalents (MET) of the activity. One MET represents the metabolic rate of an individual at rest and is approximately taken to be 1 kcal/kg/h. The total energy expenditure of an individual over a week can be calculated if the subject's body weight is known. In most cases these MET values are taken from the work of Ainsworth et al. (1993).

There are a few limitations to this method. It assumes that all individuals perform a similar activity in the same manner and hence use the same amount of energy. This may not be true as different individuals have different training levels and may perform similar activities for the same duration at different energy expenditure levels. This equation also assumes that the increase in energy levels above BMR is the same for all individuals.

2.7. Validation of self-reported physical activity questionnaires against accelerometers

Table 2.4. describes several studies that have used accelerometers for assessing the validity of self reported physical activity questionnaires. All correlations presented were significant; they ranged from 0.23 to 0.78. Several of these questionnaires have been validated in the general population while some have been validated in sick individuals

where physical activity can be limited, as well as in special sub populations such as young children.

In the general population the International Physical Activity Questionnaire (IPAQ) and Sub -Saharan Africa Activity Questionnaire (SSAAQ) have been validated in large studies that also included subjects from developing countries. The International Physical Activity Questionnaire has been validated in 12 countries that include developed as well as developing nations of the world (Craig et al. 2003). South Africa, Brazil and Guatemala were the developing countries in this study. Several samples were collected from Guatemala and South Africa based on urban or rural residency of participants and have been analysed separately. The Computer Science and Applications Inc. (CSA) accelerometer was used in this study for validation. Participants wore the machine for 7 days. Two versions of the International Physical Activity Questionnaire were administered, long and short. The long questionnaire reported 5 constructs, time spent in occupational, transport, household, and leisure related physical activities as well as total time spent sitting per week but this was a separate item and was not summed in the other 4 constructs to get a physical activity score. On the other hand, the short questionnaire assessed walking, moderate and vigorous activities and time spent sitting per week. Total MET min per week was the final outcome used from the questionnaires and accelerometer counts were used as the criteria for validation. For the long questionnaire the pooled correlation was 0.33 and for the short questionnaire and accelerometer was 0.30. The sub Saharan Africa Activity questionnaire (SSAAQ) (Sobngwi et al. 2001) was validated by 24 hour data from Caltrac accelerometers as well as heart rates monitors in

rural and urban populations. Correlations with the motion sensors were analysed only in the rural population and were 0.74 for females and 0.60 for male population. The Caltrac correlated only with the occupational, and leisure time activity in both genders while walking to work or leisure only in the female population.

Comparing 4 different measures of energy expenditure, a questionnaire, a tria-axial accelerometer, a uniaxial accelerometer and a pedometer showed that all motion sensors had a good (> 0.80) correlation amongst themselves. However, the mean energy expenditure reported by the questionnaire was (9.7 kcal/kg/day vs. 7.4 kcal/kg/day for a triaxial accelerometer) significantly higher than all the motion sensors (Leenders et al. 2000). This difference could be attributed to social desirability bias associated with the use of self reported data on physical activity. The results of this work cannot be generalized as only women were recruited into this study.

Accelerometers have also been used for validating questionnaires in sick populations where mobility may be quite limited (McDermott et al. 2000; Johansen et al. 2001). Several questionnaires were evaluated simultaneously against a triaxial accelerometer (Johansen et al. 2001) and were found to have correlations ranging from 0.49 for medical outcomes study Short Form 36 items (SF36) health survey to 0.78 for Human Activity Profile (HAP) maximum activity score questionnaires. The authors have suggested that they can all be used for assessing physical activity in individuals with limited physical activity owing to disease conditions.

Children and elderly populations pose a challenge in terms of collection of physical activity data. A structured questionnaire may not be able to assess all the activities that a child performs in a day. Short term questionnaires in young populations may not reflect a child's typical day's physical activity. Hence validation of questionnaires designed for these populations is quite important. Some of the questionnaires that have been developed to assess physical activity in these populations have been validated against accelerometers and seem to have a reasonable validity (McMurray et al. 1998).

2.8. Conclusion

The preceding review summarized and critiqued contemporary findings in the literature related to prevalence and determinants of GDM. It was noticed that very few studies have examined the prevalence and time trends of GDM in South Asia. Furthermore there is no follow-up reporting the development of diabetes in women with GDM residing in South Asia. However given the reports from elsewhere it is probably to assume that between 10-30% women who develop diabetes could have had GDM in the years preceding development of overt diabetes. Owing to this high rate of development of diabetes in women with GDM, the risk factors for GDM need to be explored in order to prevent development of GDM. These risk factors can be divided into modifiable and non-modifiable risk factors. Age, ethnicity, family history of diabetes, poor obstetric history and height are considered the non-modifiable predictors of GDM. Of these, poor obstetric history seems to have less clinical significance as past obstetric history is not

available for many women. The modifiable predictors of GDM include maternal obesity, body composition including proportion of fat and waist hip ratio, rate of weight gain during pregnancy, diet and physical activity. There is sufficient evidence to conclude that maternal obesity is a significant predictor of GDM. Waist hip ratio also seems to be a sensitive predictor for GDM; however, its clinical significance for identifying subjects during pregnancy in a less developed country set up is questionable.

Measurement of physical activity poses special challenges. Most of the objective means of collecting data on physical activity may not be feasible for use in large epidemiologic studies and mostly data are collected by self-reported physical activity questionnaires. The validity of these questionnaires has been evaluated against the objective measures with varying success. Motion sensors seem to have gained great importance in recent years in this connection. There is a need to assess the validity of physical activity questionnaires in different settings as physical activity is an important predictor of many chronic conditions.

Table 2.1. Oral Gluocse Tolerance Test (OGTT) Criteria for Diagnosis of GDM

	American Diabetes Association*	**American Diabetes Association***	**WHO IGT**	**WHO Diabetes**
Glucose load for Oral Glucose Tolerance Test, g	100	75	75	75
Glucose Level Fasting (mg/dl)/(mmol/l)	95/5.3	95/5.3	NA	140/7.8
1 Hour	180/10.0	180/10.0	NA	NA
2 Hour	155/8.6	155/8.6	140/7.8	200/11.1
3 Hour	140/7.8	NA	NA	NA

* May be conducted as a primary test or after a Glucose challenge test

Ref: Adapted from Jovanovic et al. (2001)

Table 2.2. Prevalence of Gestational Diabetes Mellitus in South Asia

Place of Study	Sample Size	GDM Diagnosis Criteria	GDM Prevalence (%)	Study Site	SES*
Karachi, Pakistan Javiad et al. (1992)	2230	Modified O' Sullivan and Mahan	3.5	Tertiary care hospital	Mixed
Karachi, Pakistan Khan et al. (1991)	1267	Modified O' Sullivan and Mahan	3.20	Regional obstetric centre	Mixed
Madras City, India Ramachandaran et al. (1994)	944	O' Sullivan and Mahan	0.56	Tertiary care hospital	Mixed
Karachi, Pakistan Akhter et al. (1996)	6830	WHO	3.30	Tertiary care hospital	High
Karachi, Pakistan Samad et al. (1996)	4497	O' Sullivan and Mahan	5.00	Tertiary care hospital	Low
Colombo, Sri Lanka Siribaddana et al. (1998)	721	WHO	5.50	Tertiary care hospital	Unknown
Madras, India Ramachandaran et al. (1998)	1033	O' Sullivan and Mahan	0.86	Tertiary care hospital	Mixed
Colombo, Sri Lanka Wagaarachchi et al. (2001)	1004	WHO	4.08	Tertiary care hospital	Unknown

* SES = Socio-economic status

Table 2.3. Non- Modifiable Predictors of GDM

Author	Population & Study Design	Risk Factors Examined			
		Age	Ethnicity	Family history of diabetes	Past obstetric history
Baliutavicience (2002)	Case control 147 cases, 300 controls Lithuania	NS	-	<0.001	Previous fetal malformations (0.002) Hydramnios <0.001 Macrosomia NS
Di Cianni (2003)	7 year Retrospective Cohort n = 3950 Italy	<0.001	-	0.0017	Parity NS
Xiong X (2001)	Retrospective Cohort n = 111563 Canada	>35 y age OR 2.34 (2.13-2.58) 19 y age protected from GDM OR 0.35 (0.27-0.44)	-	-	Neonatal death OR 1.19 (1.06-1.34) Cesarean section OR 1.18(1.11-1.25) Multiparity NS Premature delivery NS
Solomon (1997)	Prospective Cohort n = 14613 Nurses health study USA	RR 2.24 (1.26-3.98) for women ≥40 y age compared to 25-29 y age	Asian RR 2.32 (1.52 - 3.54) vs. Caucasian	RR 1.68 (1.26 - 2.04)	-

(-) not tested; NS = non-significant

2.4. Description of Self-Reported Physical Activity Questionnaires Validated by Accelerometers

Name of the Questionnaire	Population	Time frame of recall	Validation Method	Correlation Coefficient
Section 1: Questionnaires used in the general population				
Minnesota Leisure Time Physical Activity Questionnaire (MLPAQ) Richardson et al. (1994)	n = 78 30-59 y age USA	1 year	MLPAQ- Caltrac accelerometer MLPAQ -VO2 MLPAQ-% Body Fat	0.23 0.47 0.24
Sub-Saharan Africa Physical Activity Questionnaire (SSAAQ) Sobngwi et al. (2001)	n = 98 19-68 y age Urban ad rural population Cameroon	1 day	SSAAQ- Caltrac accelerometer (rural only) SSAAQ – heart rate monitors Urban and rural	0.74 (female) 0.60 (male) 0.41-0.59
International Physical Activity Questionnaire (IPAQ) Craig et al. (2003)	n = 744 18-65 y age 12 countries	7 days	IPAQ (long questionnaire) – CSA* accelerometer IPAQ (long questionnaire) – CSA accelerometer	0.33 0.30
CARDIA Physical Activity History (CPAH) Jacobs et al. (1993)	n = 78 20-59 y age USA	1 year	CPAH- Caltrac accelerometer CPAH -VO_2 CPAH-Body fat CPAH-Four week history questionnaire	0.31 0.63 0.35 0.54

Section 2: Physical activity questionnaires for diseased populations				
Leisure Physical Activity Questionnaire (LPAQ) The Stanford 7 day Qhysical Activity Recall Questionnaire (PARQ) McDermott et al. (2000)	n = 41 Peripheral arterial disease patients and controls	7 day	LPAQ - accelerometer PARQ- accelerometer	0.42 0.35
Stanford 7 day Physical Activity Recall Questionnaire (PARQ) The Physical Activity Scale for the Elderly (PASE) Human Activity Profile (HAP) Medical outcomes study Short Form 36 items questionnaire (SF-36) Johansen et al. (2001)	n = 39 End stage renal disease	7 day	PARQ- TriTrac accelerometer PASE – TriTrac accelerometer HAP – TriTrac accelerometer SF36- TriTrac accelerometer (physical component score) (physical functioning scale)	0.59 0.66 0.78 0.49 0.58
Section 3: Questionnaire for special sub-population				
Computerized Activity Recall (CAR) McMurray et al. (1998)	n = 45 11.8 ± 1 y mean age	one day	CAR – TriTrac accelerometer	0.51

*CSA = Computer Science and Application Inc.

2.9. References

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CHAPTER 3. RESEARCH DESIGN AND METHODS

This chapter is divided into several sections. The first section gives a general overview of the study. The second section states the set-up for field work; the third explains the development and use of various tools and instruments in this study. The fourth section describes data validation and analysis decisions and procedures. The final section explains the methodology of the validation of the physical activity questionnaire study.

3.1. General Overview

This study was envisioned as a hospital-based, multi-centre, cohort study to be carried out in Karachi, Pakistan. A cohort of pregnant women was identified at their earliest antenatal visit to the hospital ($\leq$ 18 weeks) to examine predictors of GDM. The exclusion criteria included women who were known to have diabetes, were not South Asian in origin or were more than 18 weeks of gestational age. Informed consent was obtained from all subjects. Women who consented to participate in the study underwent a short interview, anthropometric measurements (including body composition assessment) and at $\geq$ 26 weeks of gestation, blood work was conducted to establish the presence or absence of GDM from screening and confirmatory tests. During the interview, data related to dietary intake as measured by a food frequency recall, self-reported physical activity and socio-demographic indicators were collected. A subset of women were selected to validate the exercise report using Caltrac accelerometers. The study was approved by the ethical review board of McGill University, Canada, it was also approved and funded by the Aga Khan University, Pakistan.

3.2. Set-up in Pakistan

a. Collaboration in Pakistan

In order to carry out the research work in Pakistan, the Dean of the Faculty of Health Sciences at Aga Khan University (AKU), Karachi, Pakistan was contacted. Through him research collaboration was sought at AKU and the proposal was submitted to their research council. A chronological description of the activities carried out by Romaina Iqbal in connection with field work is presented in Table 3.1.

b. Hospital sites

Two hospitals were identified for this study, the Aga Khan University Hospital (AKUH) represented the private sector hospital and Sobhraj Maternity Hospital (SMH) was selected to represent public sector hospital in Karachi. This was done to ensure a broad spectrum of levels of the exposure variables and to enhance the external validity of the work.

Unfortunately, 6 months after the initiation of the study, it was observed that the loss to follow-up of subjects at SMH was higher than anticipated. Subjects did not return for blood testing as physicians did not insist on a GCT. A decision was taken to involve another public sector hospital into the study that served a similar population as SMH and was geographically located in the same area as SMH. Lady Dufferin Hospital (LDH) was

selected for the research work as it fulfilled the selection criteria. Moreover LDH has an AKUH blood work collection point that facilitated the logistics of blood work required for the study.

When all efforts to improve follow-up rate at SMH failed, recruitment at SMH was stopped after recruiting 140 participants and LDH became the sole hospital for recruiting subjects of low socio-economic status. Although the follow-up rate at LDH was better than SMH, it was still lower than what was desired. Furthermore it was observed that there was a selection bias in the women who were undergoing blood work at LDH, as women who were considered at high risk had presented themselves more for blood work compared to women without apparent risk factors. Therefore it was decided that data from the two hospitals (SMH and LDH) would not be used for the analysis of predictors of gestational diabetes work. This decision limited the external validity of the results of the study and has also lead to a considerable loss in the variability of predictor variables.

3.3. Data collection instruments

The predictor variables that were assessed in this investigation were modifiable predictors associated with lifestyle behaviours. These included pre-gravid BMI, rate of weight gain during pregnancy, body composition, diet and physical activity. The outcome variable of interest for this investigation was development of GDM. A description of the predictor and dependent variables follows.

a. Pre-gravid BMI

Pre-gravid BMI refers to BMI of a woman prior to pregnancy. An assessment of weight prior to pregnancy would be the most ideal variable to use for computing pre-gravid BMI for any investigation. However, this is difficult to obtain in a developing country because of lack of/or poorly maintained health records. Furthermore, in instances where health records are available, and often times weight in the past 6 months prior to current pregnancy is accepted as pre-gravid weight, one could argue that this would only be valid if the weight of the subject did not change during the 6 months.

In this study, weight at the time of recruitment into the study (≤18 weeks of gestation) has been considered as a surrogate for pre-gravid weight. This assumes that changes in weight status of the individual will not be significant in this period of time. For subjects with complete follow-up, the mean gestational age at the time of recruitment was 11.20 ± 3.66 weeks. Weight at the antenatal clinics at AKUH is assessed as a routine procedure at every antenatal visit by a trained nurse using a triple beam balance. This weight is then recorded on each patient's medical record. Weight was recorded from the medical records for each subject who consented to participate in our study.

b. Height

Height was measured to the nearest cm by a trained nurse at the clinic at the time of the first recruitment visit using a stadiometer.

c. Rate of weight gain during pregnancy

This variable was computed using weight at the time of recruitment as the initial weight and weight recorded closest to the time of the Glucose Challenge Test (GCT) as the final weight. The specific equation that was developed for computing this rate is as following:

Rate of weight gain (during pregnancy) = final weight- weight at the time of recruitment/ gestational age at the time of final weight- gestational age at the time of recruitment

The reason why gestational age was taken into consideration is that different people were followed for different periods of time and at somewhat different times during pregnancy. Not adjusting for gestational age would have lead to significant bias in data interpretation. Even controlling in this manner is not perfect as the period of time covered could vary although all women were recruited before 18 weeks gestation and the GDM test and measurement of weight were after 26 weeks gestation.

d. Body composition analysis

Body composition analysis was conducted using the Tanita Body composition analyzer TBF 215, (Tanita Corp. Tokyo Japan). This is a non-invasive instrument that works on the principle of foot to foot bio-electrical impedance. Bioelectrical impedance

indicates the resistance that the body generates to flow of a small current that passes from one electrode, located in the foot, to the other. The conductivity of the current varies from tissue to tissue in a human body. This allows the machine to estimate the fat mass, fat free mass, total body water and fat percentage of a subject. Utter et al. (1999) found a good correlation (r = 0.78) between leg to leg bioelectrical impedance and underwater weighing in women for measuring fat free mass. Body fat percentage, fat mass and fat free mass were assessed by the scale based on age, gender, weight and height of each subject that was keyed into the machine before the subject was requested to stand on the scale.

e. Physical activity

Energy expenditure related to physical activity was assessed by a self- report of all voluntary activities. For this purpose Monica Optional Study of Physical Activity (MOSPA) questionnaire, developed by Centre of Disease Control (CDC) was used (Jones et al. 1997 cited in ed. Kriska and Casperson 1997). The MOSPA questionnaire is an adjunct to the WHO Monitoring Trends and Determinants of Cardiovascular Disease (MONICA) study being conducted in several European countries to assess the risk factors of cardiovascular disease. This questionnaire measures time and energy spent in a range of physical activities including occupational work, transport related activities, household chores as well as leisure time activity over a one year period. The energy expenditure is calculated in metabolic equivalents (MET) and was converted to energy expenditure in kcal for a day as the final output. The MET scores for each activity were obtained from

the MOSPA MET intensity codes developed by CDC, these codes correspond with the Compendium of Physical Activities MET scores developed by Ainsworth (Ainsworth et al. 1993).

The questionnaire was translated into Urdu (the national language of Pakistan). The translated questionnaire was reviewed by several members of the research team to ensure that the translations were appropriate and was pilot tested prior to administration. Although, the questionnaire was always done in Urdu, the English statements were retained in the questionnaire.

f. Food frequency questionnaire (FFQ)

The dietary analysis was focused towards macronutrient, fiber and total energy intake of subjects. In order to assess intake a semi-quantitative food frequency questionnaire was developed in Pakistan by Romaina Iqbal with the past year as the reference period. This questionnaire was developed by conducting 30, 24-hour dietary recall interviews: 15 at AKUH and 15 at SMH. The objective of conducting these recalls was to generate a list of food items commonly consumed by adult women in Karachi, Pakistan. Owing to seasonal variations in the consumption of foods, several food items that were not reported by the subjects but are commonly consumed in other seasons in Karachi, were also added to the list. These food items were taken from other FFQ that were in use for research purposes at AKUH.

The total number of food items in the FFQ was 85. These food items were grouped into 11 categories, for example fruits or dairy products to cue the respondent in answering the questions. The format of the questionnaire was similar to another FFQ being developed for a study in Pakistan assessing antenatal risk factors of malnutrition in the mother as well as the off- spring. There was a blank food item row as well in the questionnaire under each of the 11 general headings. The purpose of having a blank row was to fill in any food item that was consumed by the subject but was not on the list of food items.

Food models were prepared for some food items to help the subjects in assessing portion sizes of respective food items. The questionnaire was developed in the Urdu language and then pilot tested at both the hospital sites.

For conversion of food intake into nutrient values, a food composition table for the nutrients of interest was developed for each food item on the list by Romaina Iqbal. This list was developed by using several resources (Food Composition Table for Pakistan, Ministry of Planning and Development Government of Pakistan 2001; Nutritive Value of Indian Foods, Gopalan et al. 1991; The composition and Nutrient content of Foods Commonly consumed by South Asians in the UK, Judd et al. 2000; USDA food composition data, US Department of Agriculture 2004; and FAO Food Composition Table for the Near East, FAO and USDA 2004) with preference given to Pakistani resource where possible. The food composition table had a total of 101 food items; this

included the 85 food items on the list and 16 other food items mentioned by the subjects. These 16 food items included other food items that were not on the list.

A software program was developed using SAS (version 8.2) to merge the food composition file and dietary intake file in order to obtain the nutrient consumption per person per day. A nested case control approach was adopted for analysis of dietary data using conditional logistic regression to predict the importance of macronutrients in the development of GDM.

g. Maternal and socio-demographic variables

Information pertaining to the ethnic origin, level of education and family history of diabetes was obtained from each subject by means of a structured questionnaire. Subjects defined as having a positive family history of diabetes were those who reported any one of the following as having diabetes: parents, siblings or aunts and uncles. Grandparents were not included in this classification as there might have been a bias associated with the age of the grandparents and whether or not the information was known. Education had 8 levels ranging from no education to post graduate education. The questionnaire also had questions on smoking status, betel nut chewing and tobacco consumption (Appendix 2).

A pro forma was developed to collect information on maternal characteristics from the medical charts of each subject as well as record information on anthropometric predictors of GDM. Medical charts were reviewed for subject's age, past obstetric history, gestational age and height at the time of recruitment while anthropometric measures as well as body composition analysis was noted down on the pro forma from assessment conducted at the time of the interview (Appendix 3).

h. Gestational diabetes mellitus status (Dependent variable)

Gestational diabetes was diagnosed by using a two step approach that involved conducting a 75 gm, 2 hour glucose challenge test (GCT) and in case of a GCT value ≥140mg/dl (7.8 mmol/l) subjects underwent a 100 gm, 3 hours oral glucose tolerance test (OGTT) within one week after the GCT. Blood was drawn at fasting and then every hour for the 3-hour test. Two values out of the four tests have to be raised in order to consider a person as having GDM according to the American Diabetes Association (Anonymous 2004) on this test. Subjects who had one value above the normal cut off were also included as GDM cases in this analysis. This definition is broader than the American Diabetes Association's definition for identifying GDM subjects yet it is more stringent than the WHO definition (WHO Report 1997) whereby subjects that fall in the impaired glucose tolerance category are also labeled as GDM cases. A break up of the respective categories in which cases fell is given in Table 3.2. The cutoffs used for diagnosis of GDM are the ones suggested by the American Diabetes Association (Anonymous 2004). These cutoffs are based on the work of Carpenter and Coustan that suggest that lower

cutoffs should be used for enzymatic analysis of blood glucose levels. Blood glucose levels were analysed by an enzymatic process involving peroxidase/ Glucose oxidase as the reactants. The machine used for blood glucose analysis was Synchron (Backmann Coulter, USA). All blood work analysis was conducted at AKUH pathology laboratories, this laboratory has an ISO 9001 certification and there was no reason to doubt the validity of the results. This laboratory has several collection points all over the city with trained personnel that executed GCT and OGTT in cases where the subjects found it difficult to visit the main hospital for blood work.

Initially, it was decided that each subject would undergo 2 GCTs, one at 18 weeks of gestation and the second test, after 26 weeks of gestation as most of the obstetricians at AKUH recommend two tests for their patients. However, this policy was not found feasible and only 247 subjects underwent 2 GCTs. All subjects underwent a GCT after 26 weeks except if they had an early diagnosis of GDM. A few subjects that did not have raised glucose values at 26 weeks underwent another GCT upon the attending obstetrician's request. Subjects who did not undergo a GCT or did not undergo an OGTT after a raised GCT were excluded from the analysis.

Blood work results were available to the research officer through an internal computer information program that was accessed through the antenatal clinic. In cases where GDM was confirmed (n=49) the respective attending obstetrician was notified by the research officer. In some cases the subjects were referred to the endocrinology clinic

and an internal system was developed between the two clinics to provide participants of the study further treatment.

3.4. Data entry, validation and analysis

A data entry program was developed by the computer division in the faculty of health sciences for inputting all the data collected. Initial data entry was supervised to ensure that the program was adequate for data entry. Another objective of this supervision was to ensure that data entry person understood how to enter the questionnaire adequately.

In February, 2004 data were sent to McGill University, Canada and hard copies of the data followed later. Upon data validation in June 2004, it was observed that the data entered did not match the data on the questionnaires at all. This led to a decision of a nested case control analysis of the study in the interest of time and finances. Data for the cases along with 2 age matched controls were entered, conditional logistic regression analysis was run for all variables.

In November 2004, the collaborators at AKUH sent re-entered data for AKUH. These data were validated, cleaned and analysed using logistic regression analysis for all variables except dietary intake data. But dietary data codes were not clear from AKUH

collaborators and to be certain the data that were entered by Romaina Iqbal for FFQ were used. Dietary predictors of GDM were analysed on a subset of the cohort study participants using a nested case-control study design. Each case was matched with two controls (± 1 year of age). However, two cases were matched to controls with more than one year of age difference. Results from both of these analyses are presented in the second manuscript in this dissertation.

Salient characteristics of the entire study population (n=750) were examined by using descriptive statistics procedures such as mean, standard deviations and frequency of distribution for categorical variables and used students t-tests and chi-square tests for assessing differences between those who completed the study versus those who were lost during follow-up. Univariate analysis was carried out for subjects with gestational diabetes and those with normal glycemic status, using a level of $P < 0.05$ as statistically significant, to assess differences in predictor variables and covariates that included level of education, gestational age at recruitment, parity and family history of diabetes.

Principal components analysis was conducted to choose the most appropriate variables and to avoid co-linearity in the logistic regression analysis. An eigen value above 1 was used as a cut off for identifying components. This analysis revealed that there were 5 components with eigen values over 1 that explained 78.26% of the total variance in the sample. Varimax rotations were used to aid in data interpretation. The five rotated components in descending order of importance were body composition, maternal

age and parity, level of education, family history of diabetes, and daily energy expenditure with height. The communalities were high (> 0.85) for variables within a component, but we chose to use the variables per se for further statistical analysis rather than the rotated components for the ease in data interpretation. However, this analysis helped in the selection of one variable from each component. For example, in the case of the body composition variable that loaded high on BMI, fat percentage, fat mass, fat free mass and total body water, fat percentage was used in one model of logistic regression and BMI was used in another model and all the other variables in the component were not included in the logistic regression analysis. The selection of variables that were included in the logistic regression model was based on a review of current literature.

Logistic regression analysis was used to assess the associations between the lifestyle predictors and the development of GDM. The lifestyle predictors that were examined were body mass index/ fat percentage, physical activity (kcal/day), and rate of weight gain (kg) per week. The covariates included family history of diabetes, level of education and parity. We used backward elimination procedure using maximum likelihood ratio for the selection of models. Maternal age (years) was forced in all models.

Difference in dietary predictors of GDM between cases vs. controls were first analysed by univariate tests (n=147). Significant differences were observed between protein and carbohydrate intake (% of energy) between the two groups. Further association between dietary intake and GDM was assessed by a conditional logistic

regression analysis that matched each case to its respective controls. Based on a priori knowledge obtained from the logistic regression analysis carried out for the cohort study, body fat percentage, physical activity were forced into the model along with protein/ carbohydrates (% of energy).

Statistical Analysis Software (SAS) macro Mcstrat (Vierkant et al. 1999) was used for conditional logistic regression analysis and SAS version 8.2 (SAS institute, Cary, North Carolina, 2001) was used for all analyses.

3.5. Validation of a self-reported physical activity questionnaire

Most of the subjects who consented to participate in this study were participants of the cohort study as well. The inclusion criteria were women attending an antenatal clinic at the Aga Khan University (AKU), Pakistan and who were $\leq$ 24 weeks pregnant and were willing to wear a Caltrac accelerometer for 5 days as well as answer two activity questionnaires. A total of 65 subjects consented to participate in the study. Of this group, 2 withdrew because of family concerns about the safety of Caltrac, 2 lost their pregnancy; 11 did not complete the protocol (could not be reached, did not wear Caltrac regularly, battery failure etc).

Subjects were asked to wear a Caltrac accelerometer at all times for five consecutive days (including at least one weekend day when possible). The apparatus was not worn while sleeping or bathing. None of the subjects were involved in any water sport activities. On the completion of the study, i.e. 120 hours, participants were contacted by the telephone and asked to report the reading on the Caltrac lithium screen. At this time subjects also completed a 5 day physical activity questionnaire over the telephone. Most of the subjects (n=35) recruited for this validation study had provided information on physical activity long term (LT) questionnaire, before beginning this study. For subjects (n=15) who had not done so, information on LT questionnaire was collected by telephone after the Caltrac monitoring period.

a. Questionnaires

The original MOSPA (LT) questionnaire as well as a modified version of LT was administered to the subjects over the telephone. The modified version (ST) captured activity during the five days during which the validation was done. It was developed by changing the reference times for LT which were "during the last year".

b. Accelerometer

The accelerometer used in this study was the Caltrac accelerometer (Muscle Dynamics Fitness Network California, USA). It is a uniaxial motion sensor that can detect body movement and convert it into counts or kilocalories of energy expenditure

using individual data on weight, height, age and sex. This equipment has been previously used as a direct measure of physical activity (Weston 1997; Richardson 2001). It is worn on the waist and captures movement of the lower body.

c. Body composition measures

As an indirect means of assessing the validity of the questionnaire, body composition was also measured using the Tanita Body composition analyser TBF 300 GS, (Tanita Corp., Tokyo, Japan). This information was only available for subjects (n=35) who participated in the cohort study two others as well.

d. Statistical methods

The Energy Expenditure (EE) for physical activity data from both the questionnaires as well as the Caltrac were not normally distributed therefore non-parametric tests were used to examine correlations among the EE variables and body composition measures. Repeated measures analysis using Greenhouse-Geisser adjustments for violations of spherecity were carried out to estimate differences between the three energy expenditures measures. For post-hoc analysis Bonferroni corrections were used. Data were analysed using SAS version 8.2 statistical software (SAS institute Inc, Cary NC, 2001).

3.1. Chronological Description of the Main Activities Carried out in Pakistan by Romaina Iqbal

Date	Purpose of the visit	Description of activities carried out during the visit
First Visit 20th Dec. 2001 to 16th Jan. 2002	Strengthen collaboration and help submit the research protocol for grant funding	1. Met all the GDM study team members 2. Submission of research protocol* to AKU Research Council * The protocol had been developed at McGill University, Canada under the supervision of Dr. Gray-Donald.
Second Visit 21st June 2002 to 24th Nov. 2002	Set up the study	1. Wrote ethics protocol for AKU research council and secured certification in the first week of July. 2. Hired research assistants for AKUH (Aga Khan University Hospital) as well as Sobhraj Maternity Hospital (SMH). 3. Subsequent to ethical approval, ordered research instruments. 4. Trained research officers for both hospitals. 5. Developed and adapted questionnaires for use in Pakistan, pilot tested all questionnaires and subsequently requested printing of questionnaires. Also incentive slips were printed. 6. Initiated data collection. 7. Developed action plan and circulated it to all the study investigators. This plan outlined the role of investigators in data entry, spot checking, data validation etc. This plan was later used as the job description for the research coordinator. 8. Interviews conducted for hiring a new research officer for SMH.
26 Oct. AKUH and 28th Oct. SMH		
12th Nov.		
20th Nov.		

Third Visit 08 April 2003 to 02 October 2003 First week of June June/July	1. Improve the recruitment and follow-up at LDH and SBH 2. Conduct physical activity questionnaire validation study 3. Initiate data entry	1. Conducted an intensive campaign at SMH to improve follow up. 2. Subject recruitment stopped in June at SMH. 3. Met with all key members at Lady Dufferin Hospital (LDH). 4. Initiated monthly meeting with physicians at LDH. 5. Validation study started. This study ended in the first week of October 2003. 6. Interviewed and selected additional research officers for LDH 7. Supervised the development of a data entry program and ensured that the program was working.

Table 3.2. Description of blood work outcomes

Definition	Frequency
Total GCT	612
Impaired GCT	99
Total OGTT	84
Refusals for OGTT/inappropriate testing	15*
Impaired OGTT (one raised value)	18
GDM case (two raised values)	31
Total number of cases	49

* These subjects were not included in the analysis

Note: GCT = Gluocose Challenge Test
OGTT = Oral Gluocse Tolerance Test

3.6. References

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4.1. ABSTRACT

Precise measurements of activity at a population level are important for monitoring trends and evaluating health promotion strategies. As few studies have assessed the measurement of physical activity in developing countries. The aims of this study were to measure physical activity levels and to validate the MOSPA questionnaire which was developed for the WHO-MONICA study sites

The MOSPA questionnaire (LT) assesses energy expenditure related to physical activity (employment, household work, transportation, and leisure time) over a one year period. An adapted short term (ST) 5 day questionnaire was developed to assess convergent validity. Questionnaire data were compared with energy expenditure estimates from a Caltrac accelerometer and with body composition measures (height, weight and bioelectrical impedance) in 50 women from Aga Khan University (AKU) hospital antenatal clinic.

Subjects were aged 25.95 ± 3.84 years and were16.14 ± 6.74 weeks pregnant. Their average weight was 58.84 ± 10.72 Kg. The average energy expenditure/day assessed by the Caltrac accelerometer, was 223.8 kcal and by MOSPA LT questionnaire it was 403.5 kcal. The questionnaires and Caltrac data were reasonably well correlated: $r = 0.51$ and $r = 0.60$ ($P < 0.01$) for LT and ST questionnaires, respectively. Energy expenditure from questionnaire data was not correlated with body composition measures.

The low average energy expenditure values indicate that urban Pakistani women are very inactive early in their pregnancies and they do not report greater activity during a period prior to and including pregnancy. The MOSPA questionnaire is useful in assessing physical activity levels in a sedentary population over a one year period.

KEY WORDS

Sedentary

Developing country

Accelerometer

Female

Self-report

4.2. INTRODUCTION

Physical inactivity, diet and other risk factors contribute significantly to the global burden of chronic diseases such as obesity, diabetes, heart disease, stroke, and breast and colon cancer (WHO Report 2004). Over one million deaths annually can be attributed to physical inactivity alone on a worldwide basis (WHO Report 2004). In the developing world, urban areas have higher prevalence rates of chronic diseases than rural areas (Shera et al. 1999). One of the reasons suggested for this higher prevalence in the urban areas is a sedentary life-style characterized by less physically demanding work (FAO 2003; Singh et al. 1995). There are a growing number of studies monitoring differences in physical activity across regions and changes over time (Hayes et al. 2002; CDC 2001), however, there are few published studies validating measures of self-reported physical activity in developing countries.

Several review papers (Melanson et al. 1996; Sallis et al. 2000) address the reliability and validity of self-reported physical activity questionnaires, however, most of these validation studies were carried out in industrialized country settings where physical activity patterns may be quite different from those in developing countries in terms of leisure activities, transportation and type of work. Three self-report measures validated in developing countries could be found. The sub-Saharan Africa Activity Questionnaire (SSAAQ) conducted in Cameroon showed good agreement with accelerometer measures ($r = 0.60$-0.74) in an active young population (Sobngwi et al. 2001). The International Physical Activity Questionnaire (IPAQ), validated against accelerometers, in 12 countries including South Africa and Guatemala in urban as well as rural populations showed similar agreement in developing countries (Craig et al. 2003). The Indian Physical

Activity Questionnaire was validated using energy balance, i.e. reported energy intake vs. energy expenditure, and showed weak overall correlations r = 0.30 on average with their questionnaire (Bharathi et al. 2001).

This study was undertaken to validate a self-reported physical activity questionnaire in a sedentary, urban living population in a developing country, Pakistan. The specific objectives of our study were to describe physical activity levels among women living in Pakistan and to assess the validity of a WHO administered physical activity questionnaire using Caltrac accelerometers (Muscle Dynamics, Torrance, CA) and body composition measures.

4.3. METHODS

This study is part of a larger investigation of the predictors of gestational diabetes in South Asian women. A sub-sample from the main cohort was invited to participate in this study. The inclusion criteria were women attending an antenatal clinic at Aga Khan University (AKU) Hospital, Pakistan who were $\leq$ 24 weeks pregnant. A total of 65 subjects consented to participate in the study. Of this group, 2 withdrew because of family concerns about the safety of Caltrac, 2 lost their pregnancy; 11 did not complete the protocol (could not be reached, did not wear Caltrac regularly, battery failure etc). The study was approved by the ethical review boards of AKU, Pakistan and McGill University, Canada. Informed consent was obtained from all study participants.

Subjects were asked to wear a Caltrac accelerometer at all times for five consecutive days. The apparatus was not worn while sleeping or bathing. None of the

subjects were involved in any water sport activities. On completion of the study, i.e. 120 hours, participants were contacted by the telephone and asked to report the reading on the Caltrac lithium screen. At this time subjects also completed a 5 day physical activity questionnaire. Most of the subjects (n=35) recruited for this validation study had provided information on physical activity long term (LT), before beginning this study. For subjects (n=15) who had not done so, the LT questionnaire was conducted by telephone after the Caltrac monitoring period.

a. Questionnaire

The physical activity questionnaire used for this study was the MONICA Optional Study of Physical Activity (MOSPA) questionnaire (Jones et al. 1997 cited in ed. Kriska and Casperson 1997) developed by the Centers for Disease Control, USA (CDC). This questionnaire captures physical activity for a period of one year. A modified version to capture activity during the five days during which the validation was done was adapted for this study by changing the reference times. In this paper, the one year questionnaire is referred to as the long term questionnaire (LT) and the adapted questionnaire to measure concurrent activity during the five days on which the subjects wore the Caltrac machine as the short term questionnaire (ST).

The MOSPA questionnaire is an adjunct to the WHO Monitoring Trends and Determinants of Cardiovascular Disease (MONICA) study being conducted in several European countries to assess the risk factors of CVD. This questionnaire measures time and energy spent in a range of physical activities including occupational work, transport

related activities, household chores as well as leisure time activity over a one year period. The energy expenditure is calculated in metabolic equivalent (MET) scores and can be converted to energy expenditure in kcal/week as the final output. This was obtained by multiplying the MET scores for each activity by the duration of the activity. The MET scores for each activity were obtained from the MOSPA MET intensity codes developed by CDC, these codes correspond with the Compendium of Physical Activities developed by Ainsworth et al. (1993). Daily energy expenditure (kcal/day) was obtained by dividing the weekly MET scores by 7. The questionnaires (five day and 1 year reference period) were translated into Urdu (the national language of Pakistan). The translated questionnaires were reviewed by members of the research team to ensure that the translations were appropriate. The questionnaires were pilot tested prior to administration.

b. Accelerometer

The accelerometer used in this study was the Caltrac accelerometer (Muscle Dynamics Fitness Network, California, USA). It is a uniaxial motion sensor that can detect body movement and convert it into counts that represents frequency of movement or energy expenditure (kcal), using individual data on weight, height, age and sex. This equipment has been previously used as a direct measure of physical activity for validation of self reported measures (Weston et al. 1997; Richardson et al. 2001). It is worn on the waist and captures movement of the lower body.

c. Body composition measures

As an indirect means of assessing the validity of the questionnaire, body composition was measured using the Tanita Body composition analyzer TBF 300 GS, (Tanita Corp., Tokyo, Japan). The body composition analyzer works on the principle of bio-electrical impedance which measures the flow of a small current through the body, (foot-to-foot in this case) and different tissues of the body conduct the current differently. Taking into consideration the age, gender, weight and height of each subject, total body water, fat mass, fat percentage and fat free mass were calculated. These measures were available for 37 of the 50 women enrolled.

d. Statistical methods

The Energy Expenditure (EE) from both the questionnaires and the Caltrac readings were not normally distributed thus non-parametric tests were used to examine correlations among the EE and body composition measures. Repeated measures analysis using Greenhouse-Geisser adjustments for violations of sphericity was carried out to estimate differences between the three energy expenditure measures (LT and ST questionnaires and Caltrac). For post-hoc analysis, Bonferroni corrections were used. Data were analyzed using SAS version 8.2 statistical software (SAS institute Inc., Cary NC, 2001).

4.4. RESULTS

Fifty subjects completed the study. The women were on average 25.95 ± 3.84 years of age with a BMI of 23.20 ± 4.30 kg/m^2 and fat percentage of 26.48 ± 7.23. Forty

percent of the subjects were university educated (Table 4.1). During the course of the study, 8 of the subjects forgot to wear the Caltrac at some point. These lapses averaged 52.5 ± 37.7 minutes (mean ± SD) over the entire study period of five days. Energy expenditure (EE) as measured by Caltrac was not different between subjects who forgot to wear Caltrac versus the subjects reporting complete adherence to the protocol.

In order to measure the extent to which individual measures of physical activity from MOSPA questionnaires agree with the criterion measure, a correlation matrix for the direct measure of physical activity i.e. the Caltrac activity EE score as well as the indirect measures i.e. the body composition measures is provided (Table 4.2). Both the questionnaires, LT and ST, were positively correlated with the Caltrac physical activity values ($r = 0.51$ and 0.60, respectively). None of the body composition scores correlated with any of the three measures of EE with the exception of the BMI and the Caltrac values. Since body weight is part of both the calculation of EE estimated by the Caltrac and BMI, some correlation is to be expected.

The mean EE from activity from the MOSPA LT was 403.45 ± 530.09 kcal/d. The mean for ST questionnaires was 305.75 ± 369.75 kcal/ day. The Caltrac estimated less activity at 223.80 ± 93.78 kcal/day. The ST questionnaire was not different from the Caltrac energy estimates, however the Caltrac energy estimate and the LT questionnaires (activity in past year) were different from each other ($P < 0.05$) in repeated measures ANOVA.

The MOSPA questionnaire measures reported physical activity in 4 broad categories; work, household chores, leisure and transportation. Based on the analysis of the MOSPA (LT), 16 women (32%) were involved in some kind of occupational work and the average EE calculated for work from the questionnaire was 865.87 kcal/ day. This resulted from work related activity of 5.72 hours/ day. Other reported activities, such as household chores or leisure time activities, done by more women, provided much lower levels of energy expenditure and were done for much shorter periods of time (Table 4.3).

Owing to the high EE reported on the questionnaire by the women who worked outside the home and the possibility that this factor had an important impact on the correlations found, a stratified analysis was done to examine the working and the non-working women with respect to the agreement of Caltrac readings to the MOSPA (LT and ST). For the employed women (n=16) MOSPA ST correlated with the Caltrac readings r = 0.62 ($P < 0.05$) but MOSPA (LT) was not significantly correlated with Caltrac, r = 0.45 ($P > 0.05$) but the statistical power is low in this small subset. In the non-working group (n=34) both MOSPA (LT and ST) correlated with Caltrac, r = 0.47, $P < 0.005$ and r = 0.60, $P < 0.001$, respectively.

On examination of the subset of working women, a total energy expenditure of 1077.87 kcal/day was reported on the LT questionnaire, but the total daily Caltrac value was only 262.92 kcal. This overestimation was similar in the ST questionnaire. This is a large over estimation by the MOSPA with regards to EE. In contrast, among those not employed the MOSPA (LT) did not capture all activities as the MOSPA (LT) reported a total expenditure of only 86.07 kcal/day whereas the Caltrac recorded 205.38 kcal/day (P

<0.001). Findings for the ST questionnaire were similar. MOSPA thus tends to overestimate work activity and underestimate other activity (mainly household) in this setting.

The MOSPA questionnaire also has a self-rating question for physical activity assessment with 4 categories; 1 indicating the least and 4 the most physical activity. The figure shows the self categorization ratings from the MOSPA (LT) versus the Caltrac physical activity scores for subjects in each category. None of the subjects reported being involved in very vigorous activity and only one person reported moderate physical activity while 32 subjects reported no activity and 17 thought that they were involved in light activity on most of the week days. A comparison between groups 1 and 2 (no activity and light activity) showed a 100.05 kcal difference (P <0.001) by the Caltrac measure.

4.5. DISCUSSION

Despite very low levels of physical activity in this population of young women, the total EE from the ST and LT questionnaires correlated reasonably well with the Caltrac confirming that the questionnaires can assess physical activity levels in even a sedentary urban population. The MOSPA questionnaire is easy to administer and gives a valid measure of activity levels overall, however, questionnaire items to detect work related activities overestimated activity and some low energy expenditure activities by women such as caring for self and others are not picked up by the questionnaire.

The absolute EE values, using both the questionnaires as well as the Caltrac, reflect a very sedentary population. Similarly low levels of physical activity have also been found in a study conducted in Filipino youth where the mean EE as measured by the Caltrac was 271 kcal ± 105.4 kcal/ day (Tudor-Locke et al. 2003). In a cross sectional survey conducted in urban India, 49.5% of the population did not engage in any leisure time physical activity as assessed by an interview and another 5.7% performed physical activity irregularly, indicating that the level of leisure time related physical activity is very low in urban, populations in the region (Bhasin et al. 2001). Leisure activity represented a small portion of the activity in our sample as well.

Certain limitations to our validation study need to be recognized. The women studied were on average 16 weeks pregnant which may limit the ability to generalize these results. However, the ST questionnaire reflects their actual activities at the time of the Caltrac measure and the LT questionnaire reflected their usual activities in the last year.

The mean EE, based on LT and ST questionnaires is higher than that from the Caltrac accelerometer; several studies have reported similar findings when using Caltrac accelerometers (Sallis et al. 2000). This may be because uniaxial Caltrac cannot measure movement in the horizontal plane or because of overestimation of activity on the questionnaire by the subject or the assumptions of the MET scores used to assess total energy expenditure. This overestimation seems to be pronounced for the work related activities in this questionnaire.

In the only study to date validating the MOSPA questionnaire, the criterion measures used were BMI, body composition, and peak oxygen uptake values on an exercise test (Royekens et al. 1998). The subjects of their study were physical activity instructors or former athletes. A positive correlation of r = 0.53 was observed between the questionnaire and lean body mass. In contrast our study indicated there were no significant correlations between LT and body composition measures. We speculate that the reason for this lack of correlation is that our study population, as a whole, was not active enough to develop differences in body composition related to activity. The lack of association with biological parameters in our study is unlikely due to a lack of statistical power as our sample size offered power of 0.80 to detect a significant correlation of r = 0.38 as statistically significant.

In a study examining the construct validity of a physical activity questionnaire in the Netherlands, work related activities, sports activities and leisure time activities (other than sports) were the three loading factors for habitual physical activity assessment (Baecke et al. 1982). In contrast, studies done in South East Asia suggest that often the major contributor to EE are everyday tasks and walking to work/school rather than the leisure time activity, observed in the West (Tudor-Locke et al. 2003). Our study also confirms this finding, as there was a 30% difference based on the Caltrac values between those working outside the home vs. not employed, but the values for energy expenditure were low in both groups. One of the probable reasons the questionnaire EE under reported activity for women involved in household work is its inability to assess particular elements such as care giving activities for the elderly and/or child care. Similar

findings have also been reported in a Canadian Aboriginal population study where housework was the principal physical activity reported (Kriska et al. 2001).

In a review of seven different types of self-reported activity measures used in industrialized countries, it was observed that questionnaires that recalled activity for a shorter duration, such as past week, had validity correlations of 0.5 with Caltrac accelerometers compared to correlations ranging between 0.14 and 0.36 for longer term, physical activity questionnaires (Sallis et al. 2000). Although our findings follow the same pattern, the correlations found among our sample of Pakistani women were higher than the correlations reported in the literature on adult participants. Although the correlation of the ST physical activity questionnaire is higher than the LT questionnaire, we do not suggest the use of the ST questionnaire to measure physical activity because of a lack of consistency in activity over weeks, variations due to seasonality, acute illness or other reasons for variability over time as have been reported by others (Kriska et al. 1990).

Comparing our findings to other reports of physical activity questionnaires which were validated using accelerometers in developing countries, we found similar correlations. The IPAQ (Craig et al. 2003) conducted in 14 countries including 2 developing countries, South Africa and Guatemala reported correlations of 0.46 and 0.61 respectively in these two countries for their urban population and these were far higher correlations than in the industrialized nations participating in the study. Similarly in a validation study in sub-Saharan Africa (Sobngwi et al. 2001) correlations of 0.60 and 0.74 for females and males respectively were observed in a very active population.

The last item in the MOSPA LT questionnaire is a global question asking subjects to categorize themselves into 4 categories. We feel that the subjects are quite cognizant of their generally low levels of physical activity as they accurately classified themselves as being sedentary. The difference in Caltrac values between the two lowest levels of activity was significant. Such self-reporting scales are not, however, always successful.

We have shown that overall energy expenditure levels are very low in our population which could be a significant predictor of rising chronic disease prevalence in the region. We have demonstrated that MOSPA physical activity questionnaire is able to assess physical activity levels adequately in a sedentary population. As the questionnaire tends to overestimate activity related to work, and not capture some household movement, some refinements in this assessment measure may enhance the precision of the questionnaire.

4.6. ACKNOWLEDGEMENTS

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TABLE 4.1. Description of Pregnant Pakistani Women Enrolled in the Validation Study (n=50)

Characteristics	Mean	SD
Weight(kg)	58.84	10.72
Height(cm)	159.45	6.38
BMI (kg/m^2)	23.20	4.30
Age (years)	25.95	3.84
Gestational Age (weeks) at the time of Caltrac study	16.14	6.74
Fat (%)*	26.48	7.23
Fat Mass (kg)*	15.74	6.65
Fat Free Mass (kg)*	41.30	3.14
Educational status (% university graduates)	40	-
Employment status (% employed)	32	-

* Data available for 37 subjects

TABLE 4.2. Spearman's Rank Order Correlations for Physical Activity Measures From Questionnaires with Accelerometer Readings and Body Composition Measures

	CALTRAC ACCELEROMETER AND BODY COMPOSITION MEASURES				
MOSPA QUESTIONNAIRE	**Caltrac Activity (kcal)**	**Body Fat (%)[a]**	**Fat Mass (kg)[a]**	**Fat Free Mass (kg)[a]**	**BMI (kg/m^2)[a]**
STQ Questionnaire (kcal)	0.60**	0.19	0.24	0.09	0.19
LTQ Questionnaire (kcal)	0.51**	0.15	0.14	0.17	0.25
Caltrac Values Caltrac activity (kcal)	-	0.03	0.06	0.20	0.38**

** $P < 0.001$ level

a. data available for 37 subjects

TABLE 4.3. A Break Down of Average Energy Expenditure and Time Spent in Various Activities for Pakistani Women

ACTIVITIES	N Reporting activity	EE (kcal)/ day		Time (Minutes)/day	
		Mean	SD	Mean	SD
Work	16	865.87	397.09	343.84	121.21
Transportation	17	35.78	15.45	8.94	3.91
Household chores	24	123.49	123.00	56.88	45.25
Leisure time activities	31	88.59	124.20	25.65	23.60
Total Activity	50	403.45	530.09	127.26	174.14

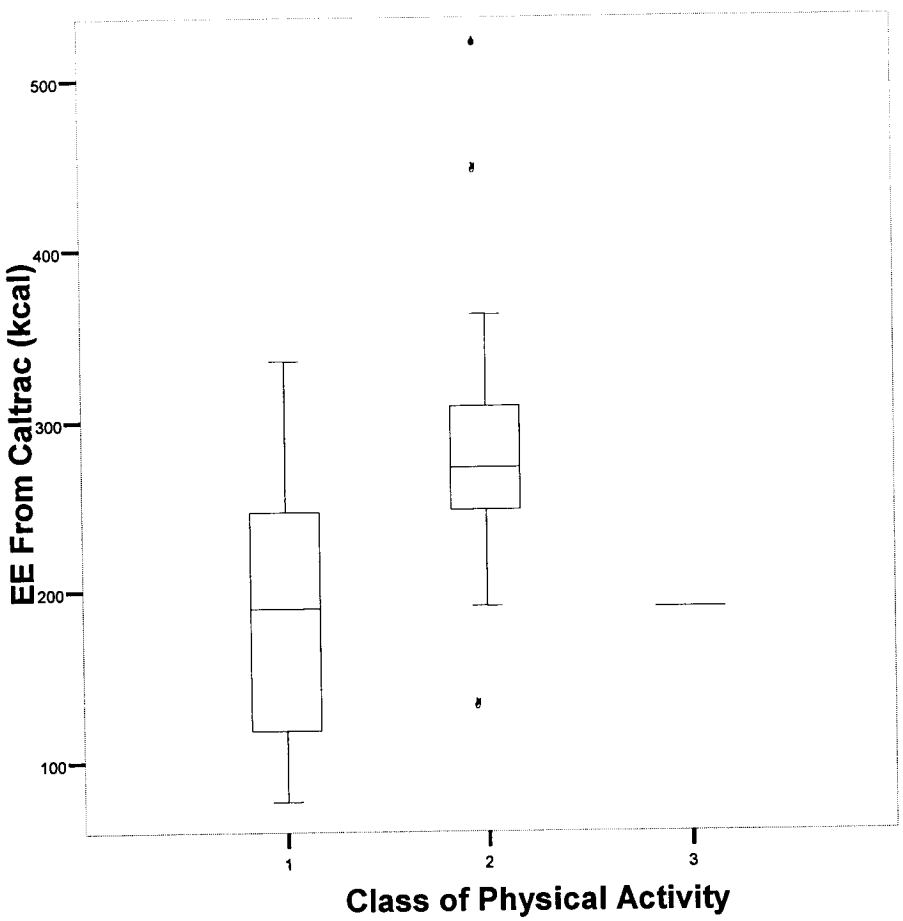

Figure 4.0 Self-Categorization of Pakistani Women into Different Self-Reported Physical Activity Levels

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LINK STATEMENT

One of the risk factors of chronic disease is lack of physical activity. Therefore, measuring physical activity has become important in epidemiological studies that are designed for the association of physical activity with chronic disease outcome. Accurately assessing physical activity in free living humans is a challenging task

With regards to physical activity it was important to measure whether imprecision of the self-reported exercise questionnaire might be the reason activity may not relate to GDM. The first manuscript in this thesis describes the results of a validation study that was conducted to assess the accuracy of the Monica Optional Study of Physical Activity (MOSPA) physical activity questionnaire. The study indicated that MOSPA could adequately assess physical activity in a Pakistani sedentary population. The correlation with an accelerometer worn for 5 days was 0.60 in comparison with a short term activity assessment and 0.51 for a year long physical activity assessment measurement. As this measure reflects activity reasonably well in a very sedentary population where there is little sports activities to differentiate people, one can have confidence that should activity at low levels be important to disease prevention, it will have a good chance of being detected in a large cohort study.

The following manuscript reports the outcome of the prospective cohort study that assessed lifestyle predictors of GDM. The predictors investigated were pre-gravid BMI, body composition, rate of weight gain during pregnancy, diet and physical activity. Physical activity was assessed by the MOSPA physical activity questionnaire.

5.1. ABSTRACT

As women who experience Gestational Diabetes Mellitus (GDM) are at greater risk of developing type 2 diabetes later in life, prevention of GDM is particularly important. The objective of this study was to identify lifestyle predictors of GDM in a developing country. Predictors included pre-gravid BMI, body composition, rate of weight gain during pregnancy, energy expenditure for physical activity (EE), and dietary intake.

This prospective cohort study, conducted at the Aga Khan University (AKU) Hospital antenatal clinic in Karachi, Pakistan, involved 611 South Asian women ≤ 18 weeks gestation. Weight, height and body composition (body fat %) were measured and data on reported energy expenditure (EE), diet, and socio-economic covariates were collected at baseline and a glucose screen was done at ≥ 26 weeks.

At recruitment, mean age was 26.4 ± 4.3 y, gestational age 11.2 ± 3.7 weeks, BMI 23.2 ± 4.2 kg/m^2 and body fat % 27.9 ± 8.1. Predictors of GDM were assessed using logistic regression analysis. Independent variables were age, body fat %, height, rate of weight gain during pregnancy, family history of diabetes, parity, level of education, and EE. The risk of GDM increased with increasing maternal age, OR 1.13 (CI 1.06-1.21), body fat, % OR 1.07 (CI 1.03 – 1.13), and decreased with EE (100 kcal), OR 0.89 (CI 0.79 - 0.99). Using a nested case (n=49) control (n=98) study design, conditional logistic regression analysis was conducted to assess the association between macronutrient, total

energy and fiber intake and GDM. The risk of GDM decreased with increasing protein (% energy) in the diet OR 0.75 (CI 0.60- 0.95).

Increase in maternal age and body fat % independently predicted an increase in the risk of GDM while increased EE was protective. Hence, prevention strategies should involve decreasing body fat, increasing daily physical activity and consuming a balanced diet.

KEY WORDS

Risk factors

Lifestyle

Body composition

Sedentary

Nutrition transition

5.2. INTRODUCTION

The World Health Organization estimates that approximately 300 million people will develop diabetes by 2025, a number far above the 150 million today. The rise in prevalence will take place mainly in the developing countries of the world, affecting people in their productive years (45-64) as compared to an older (65+) age group in the West (WHO Report 2002). Gestational diabetes mellitus (GDM) is defined as glucose intolerance that is first recognized during a pregnancy (Anonymous 2003). GDM is closely associated with type 2 diabetes (Ben-Haroush et al. 2004); between 10 and 31 percent of parous women with type 2 diabetes have had GDM earlier in life (Cheung et al. 2003). In one prospective study over a 15 year period, 35% of the women with GDM vs. none in the control group developed type 2 diabetes (Linne et al. 2002), whereas in another study, 48% of the subjects developed diabetes 7 years after a GDM pregnancy (Kjos et al. 1998). These follow-up studies indicate that women with GDM are at high risk of developing Type 2 diabetes. In addition to the adverse consequences for the mother, GDM is associated with poor pregnancy outcomes (Persson et al. 1998) and adverse long-term health consequences for the offspring, including obesity and development of diabetes in adolescence or young adulthood (Lindsay et al. 2000).

In developed countries a number of risk factors for GDM have been studied. Pregravid weight has been found to be a predictor of GDM in several studies (Metzger et al. 1998; Khine et al. 1999), but studies of weight gain during pregnancy have shown inconsistent effects (Kieffer et al. 2001). In terms of diet, higher carbohydrate diets (% of energy) have been associated with a reduced the risk of GDM (Saldana et al. 2004).Two studies have examined the association of physical activity with GDM; one was limited to

recreational physical activity (Dempsey et al. 2004) and the other failed to show a reduction in the risk of GDM (Solomon et al. 1997). Body composition has only been studied by waist circumference during pregnancy (Zhang et al. 1995), but this has obvious limitations.

With ongoing nutrition transition and the dramatic shifts in chronic disease morbidity (Popkin et al. 2002) in developing countries, it is important to study modifiable predictors of GDM. We studied the modifiable predictors of GDM with a view to understand how to prevent the development of GDM. The objective of this study was to investigate the impact of pre-gravid BMI, body composition (body fat %), rate of weight gain during pregnancy, diet and physical activity on developing GDM in South Asian women.

5.3. RESEARCH DESIGN AND METHODS

a. General overview

A prospective, cohort study of women (n=750) attending antenatal clinics at Aga Khan University Hospital in Karachi, Pakistan was conducted between October 2002 and May 2004. Women eligible for inclusion were of South Asian origin, ≤18 weeks of gestation and did not have diabetes mellitus. At the time of recruitment, participants answered questions on potentially modifiable lifestyle predictors of GDM (diet, physical activity), as well as on maternal health and socio-demographic variables. Anthropometric variables including, weight, height and body composition were also measured at this time. Rate of weight gain during pregnancy was also analysed based on weight measurement at

the time of recruitment. The outcome variable, gestational diabetes was defined by the results of blood work done after ≥ 26 weeks of gestation by a two step procedure. Informed consent was obtained from each participant. The ethics review boards of McGill University, Canada and Aga Khan University, Pakistan approved the study protocol and informed consent was obtained from all subjects.

b. Baseline measurements

Information pertaining to the ethnic origin, level of education, and family history of diabetes was obtained from each subject by means of a structured questionnaire. Subjects with parents, siblings, aunts or uncles who had diabetes were classified as having a positive family history of diabetes. Education was measured using 8 levels ranging from no formal education to post graduate education. Current smoking status, betel nut chewing and tobacco consumption were also reported. Medical charts were reviewed for subject's age (years), parity, and gestational age (weeks) at the time of recruitment.

Weight was measured by a nurse using a triple beam balance. Height (to the nearest cm) was measured by a stadiometer attached to the triple beam balance. Body mass index was calculated as weight at the time of recruitment in kg/height in m^2. This measure was used as a surrogate for pre-gravid BMI. A variable estimating rate of weight gain during pregnancy was computed from weight at the time of recruitment as the initial weight and weight at the time of the glucose challenge test (GCT) as the follow-up weight. This value was then divided by the number of weeks for which the subject was followed to arrive at rate of weight gain per week. Body composition measures were

obtained at recruitment by using a foot to foot bio-electrical impedance scale (Tanita Body Composition Analyzer TBF 215, Tanita Corp. Tokyo Japan). Body fat percentage, fat mass (kg) and fat free mass (kg) and total body water (kg) were assessed based on the age, gender, weight and height of each subject by body composition analyzer. Foot to foot bio-electrical impedance scales have been validated in human populations (Cox-Reijven et al. 2002; Utter et al. 1999).

Information on physical activity was gathered by an interviewer administered physical activity questionnaire, the World Health Organization's Monitoring Trends and Determinants of Cardiovascular Disease (MONICA) Optional Study of Physical Activity (MOSPA) instrument, developed by the Centers for Disease Control (CDC) to assess the risk factors of cardiovascular disease (Jones 1997, cited in ed. Kirska and Casperson 1997). This questionnaire measures time and energy spent in a range of physical activities including occupational work, transportation, household chores as well as leisure time activity over a one year period. The energy expenditure was calculated in metabolic equivalent (MET) scores and converted to energy expenditure in kcal/day for each subject. We found a good correlation $r = 0.51$ ($P < 0.01$) between the physical activity questionnaire and Caltrac accelerometers in a sub sample ($n=50$) of this population indicating that the questionnaire had good validity for assessing physical activity in our study population (Iqbal et al. under review).

A food frequency questionnaire (FFQ) was developed to assess macronutrient (fat, carbohydrates, and protein), total energy (kcal) and fiber intake. This 85 item FFQ was developed in Pakistan and was based on foods recalled on thirty 24-hour food recalls

from women attending antenatal clinics in Karachi. The FFQ was designed to collect information on how much and how often each food item on the list was consumed. Depending on the type of food item, different amount categories were defined for different food items, with small, medium and large being the most frequently used categories. Three frequency categories (times per week, month or year) were specified. Owing to the seasonal variation in the consumption of foods in Pakistan, three categories (summer, winter, both) were defined for the season of the year in which the food item was consumed. We developed a food composition grid for all of the items on the FFQ using several food composition tables used in the region (Food Composition Table for Pakistan, 2001; Nutritive Value of Indian Foods, 1991; The Composition and Nutrient Content of Foods Commonly Consumed by South Asians in the UK, 2000, USDA Food Composition Tables, accessed online 2004, and FAO Food Composition Table for the Near East, accessed online 2004). Preference was given to the Pakistani food composition table where possible. These data were only analysed for a subset of the study population due to the time intensive nature of entering the data.

c. Outcome variable

All subjects underwent a 2- hour, 75-gram, glucose challenge test at ≥ 26 weeks of gestation, although there were some subjects identified as having GDM earlier by a test conducted earlier in the pregnancy. In individuals with a GCT value > 140 mg/dl (7.8 mmol/l), a 3-hour, 100 gram oral glucose tolerance test (OGTT) was conducted. Cutoff values suggested by the American Diabetes Association were used; values of 95mg/dl (5.3 mmol/l) (fasting), 180 mg/dl (10.0 mmol/l) (1hr), 155 mg/dl (8.6 mmol/l) (2 hr) and 140 mg/dl (7.8 mmol/l) (3hr) were used to identify subjects with GDM (Anonymous

2003). Subjects with either one or two raised values on the OGTT were grouped together for this analysis. However, glucose intolerance may be considered as a continuous outcome as even slight dysglycemia is associated with adverse consequences (Sermer et al. 1998). Our definition was broader than the American Diabetes Association's (Anonymous 2003) classification of GDM (two raised values), but more stringent than the WHO suggestion of identifying subjects with impaired OGTT, with one raised value >140 mg/dl (7.8 mmol/l) at 2 hours (based on a 75 gram glucose load test) as having GDM (WHO Report, 1997). Blood glucose levels were analysed by an enzymatic process involving peroxidase/glucose oxidase as the reactants on Synchron LX Systems (Beckmann and Coulter, CA, USA). All blood work was carried out at the Aga Khan University (AKU) Hospital.

d. Statistical analysis

We examined the salient characteristics of the entire study population using descriptive statistics and used students t-tests and chi-square tests for assessing differences between subjects with gestational diabetes and those with normal glycemic status using a level of $P < 0.05$ as statistically significant.

Principal components analysis was conducted to choose the most appropriate variables for the logistic regression analysis in order to understand the underlying constructs as well as to avoid co-linearity in the variables used in regression analysis. An eigen value above 1 was used as a cut off for identifying components. This analysis revealed that there were 5 components with eigen values over 1 that explained 78.26% of the total variance in the sample. Varimax rotations were used to aid in data interpretation.

The five rotated components in descending order of importance were body composition, maternal age and parity, level of education, family history of diabetes, and daily energy expenditure which grouped with height. The communalities were high (> 0.85) for variables within a factor, but we chose to use measured variables from each factor for further statistical analysis rather than the rotated components for ease in data interpretation.

We used logistic regression analysis to assess the associations between lifestyle predictors and the development of GDM. The selection of predictors that were included in the model was based on a review of current literature. The lifestyle predictors that were examined were body mass index, body fat percentage, physical activity (kcal/day), and rate of weight gain (kg) per week. Smoking was not included as few (0.2%) reported smoking during pregnancy. Daily energy expenditure for physical activity was truncated at 1200 kcal/day as some women (n=6) clearly over-reported number of working days as well as hours. The covariates included family history of diabetes, level of education, height and parity. We used a backward elimination procedure using maximum likelihood ratio for the selection of models. Maternal age (years) was forced into all models because of its well known relationship with GDM.

e. Dietary analysis

The association of diet with GDM was analyzed in a subset of subjects from the entire cohort using a nested case control study design. The 49 GDM cases were age matched ± 1 year to 2 controls from the main cohort. Total sample size for this analysis

was 147 subjects. A SAS program was created to convert dietary intake data into kcal of energy, grams of macronutrients, and grams of fiber for each subject/day. Initially, univariate analyses were performed on diet (grams of carbohydrate, proteins, fats and fiber, kcal of energy, and percent of energy contributed by the macronutrients). Based on the results of the entire cohort's logistic regression analysis, we deliberately included body fat percentage, physical activity (kcal/day) and protein (% energy) into a conditional logistic regression analysis. Hazard ratios were used for assessing the significance of the model at $P < 0.05$. This analysis was carried out using a SAS macro (Vierkant et al. 1999) for conditional logistic regression. All analysis was carried out on SAS version 8.2 (SAS institute, Cary, North Carolina, 2001).

5.4. RESULTS

A total of 750 women were recruited between Oct. 2002 and Nov. 2003 and the follow-up was completed by May 2004. Of these, 612 completed the study and 138 (18.5%) were lost to follow-up. Of these 138 women who were lost to follow-up, 66 discontinued antenatal care at AKU hospital, 41 had an abortion or their pregnancy was terminated, 9 refused a GCT and 14 refused an OGTT after a raised GCT, 3 were known diabetics prior to pregnancy, data were missing for another 3, 1 underwent inappropriate testing and 1 withdrew participation.

Descriptive statistics for those who completed the study as well as those who were lost to follow-up are presented in Table 5.1. Participants included in this analysis were taller and had a lower BMI but were otherwise similar to the subjects who were lost to follow-up.

Of the 612 subjects who completed the study, 8% (n=49) were diagnosed as having GDM based on the criteria mentioned above. Of these, 31 had two raised values and 18 had one blood value above the cut-off. Table 5.2 presents a univariate comparison between subjects who developed GDM versus those who did not. Subjects who were diagnosed as having gestational diabetes were older (29.39± 4.67 vs. 26.26± 4.26 years), heavier (BMI 25.1± 3.78 vs. 23.0± 4.15) and had more body fat (%) (32.21±6.42 vs. 27.38 ± 7.82%). This translates into a 4.83 body fat % difference between the two groups and a 2.1 unit difference in the BMI. The daily energy expenditure (kcal) was not different between the two groups in this analysis.

Results of multiple logistic regression analysis showed that maternal age odds ratio (OR) 1.13 (1.06 – 1.21), body fat percentage OR 1.07 (CI 1.03 – 1.13) daily energy expenditure per day OR 0.89 (CI 0.79 – 0.99) for 100 kcal difference were significant predictors of GDM. This model also included family history of diabetes, level of education, parity, rate of weight gain during pregnancy and height, which were not found to be related to the development of GDM. In a second model we replaced body fat percentage by BMI and found that this model predicted GDM as well. Both the models are presented in Table 5.3. Categorical variables and quadratic terms were also computed for daily energy expenditure, age, body fat percentage to assess their association with GDM but as they did not add further precision to the model they were not used in the final analysis.

Dietary predictors of GDM were analysed in a subset of subjects from the cohort study. In a bivariate analysis, carbohydrate and protein intake as a percentage of total energy were found to be significantly different in GDM cases vs. controls (Table 5.4). The GDM cases had higher carbohydrate and lower protein intake (% energy) compared to subjects who did not develop GDM. Using a conditional logistic regression analysis procedure and based on a priori knowledge obtained from the main cohort analysis, we deliberately included body fat percentage, physical activity (kcal/day) and protein as a proportion of total energy intake into the model. Similar to the cohort analysis, in the nested-case control analysis, we found that increased body fat percentage predicted the development of GDM OR 1.08 (CI 1.01 – 1.15) but with the reduced statistical power, EE was not a significant predictor and thus dropped from the final model. A higher contribution of protein to energy intake was protective of developing GDM (OR 0.75, CI 0.60 – 0.95), but in a similar model, replacing carbohydrate for protein (% energy), carbohydrate (% energy) was not found to be a predictor of GDM (data not shown). These dietary variables were tested separately so as to avoid colinearity in the conditional logistic regression analysis.

5.5. CONCLUSIONS

This study was conducted to understand the role of lifestyle predictors in the development of GDM in South Asian women residing in Pakistan. The two modifiable factors predicting GDM were body fat percentage, and low physical activity. Replacing body fat percentage by BMI (kg/m^2), in a similar model, led to comparable results with this measure of body fatness. In addition, using a nested case control approach, the

proportion of energy contributed by dietary protein had a protective effect while carbohydrate, fat, fiber or total energy intake were not found to be related to GDM.

We have shown that subjects who had higher levels of body fat percentage at the beginning of their pregnancy were at a greater risk of developing GDM. Changes in body fat percentage, without changes in body weight, have been reported to be positively associated with changes in the Blood HB A1C levels in diabetic subjects (Sohmiya et al. 2004). Increased amount of visceral fat and total fat volume have been associated with increased insulin resistance in Indian men suggesting a role of body fat in the development of impaired glucose tolerance as well as type 2 diabetes in the Indian population (Banerji et al. 1999), while muscle mass helps in the uptake of blood glucose (Rigalleau et al. 2003). Several studies have investigated the effect of sedentarism on body composition and reported low levels of fat free mass in inactive subjects (Kyle et al. 2002).

The overall daily physical activity scores were extremely low in this population, however, similar results have also been reported in a cross sectional survey conducted in urban India, in which 49.5% of the population did not engage in any leisure time physical activity as assessed by an interview and another 5.7% performed physical activity irregularly, indicating that the level of leisure time related physical activities is very low in urban, affluent populations in the region (Bhasin et al. 2001). In addition, sedentary lifestyle is a risk factor for central obesity in Indian women (Singh et al. 1998).

Despite the low general physical activity level in our population, higher levels of physical activity had a protective effect against the development of GDM. This has also been shown by a study conducted in a western population (Dempsey et al. 2004) wherein recreational physical activity alone was measured, whereas we examined several domains of physical activity including occupational, household, leisure time and transportation related physical activity. In contrast, another investigation (Solomon et al. 1997) did not show an association between GDM and physical activity in nurses. However, the authors felt that there could have been errors related to self reporting of physical activity in their study. Several prevention trials in the developed as well as developing countries have indicated that increasing physical activity substantially reduces the risk of developing type 2 diabetes (Mark et al. 2003; Laaksonen et al. 2005; Ramachandaran et al. 1998).

Our study found that BMI predicted GDM in a similar manner to body fat percentage. In an investigation comparing Asian Indians to African Americans and Caucasians, it was found that the same BMI value is associated with higher levels of body fat percentage in South Asians compared to the other two ethnic groups (Banerji et al. 1999). Lower BMI cutoffs for diabetes prevention (type 2) have been suggested (males 22 kg/m^2 and females $23kg/m^2$) for the South Asian population (Vikram et al. 2003). A limitation of our study is that there were too few cases to establish a robust BMI cutoff for risk of GDM in this setting.

We observed a protective effect of dietary protein (% energy). To our knowledge, we are the first to report such an association. It is possible that higher protein intake was related to good dietary practices such as intake of pulses and legumes that are high in

fiber which have been shown to have a protective role in the development of type 2 diabetes (Salmeron et al. 1997; Schulze et al. 2004). Dietary fiber per se was not related to GDM in our study. In an Indian investigation of diet and risk of ischemic heart disease, meat that included chicken as well (OR 0.57, 95% CI 0.33 – 0.98) as well as fish (OR 0.72 95% CI 0.47 – 1.09) had a protective effect (Rastogi et al. 2004) indicating that specific foods or nutrients such as protein may play a role in preventing GDM. Our analysis is limited to nutrient analysis consequently we cannot comment about the dietary sources of protein in our population. It is likely that foods high in protein such as (fish) were consumed by our subjects that are high in polyunsaturated fatty acids and would therefore some of the saturated fat intake. In a case control study it was found that women who developed GDM consumed less polyunsaturated fat and higher amounts of saturated fat (% total fat intake) (Wang et al. 2000). Likewise in another investigation higher total fat intake as well as fat (% of energy) was associated with increased risk of GDM (Saldana et al. 2004).

This is the first study of its nature conducted in South Asian women to assess the association between lifestyle predictors and GDM. This was a prospective cohort study in which data on predictors was collected before the outcome was known. This reduces both recall bias and interviewer bias during data collection. However a limitation of this work is that all that data were collected at Aga Khan University hospital which primarily serves the affluent population of the city. This could have limited our ability to clearly assess the impact of some lifestyle factors such as diet due to a lack of sufficient variability in the data.

This study indicates that potentially modifiable lifestyle factors such as physical activity, body fat percentage or BMI are associated with the development of GDM. Prevention strategies for GDM need to be developed in a country like Pakistan where the prevalence of type 2 diabetes is high (Shera et al. 1999, 1999). The focus of these efforts should be towards increasing physical activity in women and decreasing fat stores in those with a high percentage body fat.

5.6. ACKNOWLEDGEMENTS

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Table 5.1. Baseline Characteristics of Study Participants Lost To Follow-Up vs. Those With Complete Follow-Up Data in Karachi, Pakistan

	Subjects with complete follow-up (n=612)		Subjects lost during follow-up (n=138)		P value*
	Mean	SD	Mean	SD	
Maternal Age (years)	26.42	4.38	27.14	4.95	0.087
Gestational age @ recruitment (weeks)	11.20	3.66	10.68	3.76	0.131
Pregravid weight (kg)	58.62	10.46	60.48	12.44	0.070
Height (cm)	159.00	5.51	157.80	5.04	0.020
BMI (kg/m^2)	23.21	4.15	24.30	4.90	0.008
Body Fat (%)	27.85	8.09	29.16	8.74	0.092
Fat Free Mass (kg)	41.43	3.76	41.60	4.91	0.643
Level of education (% university graduates)	53.1		60.0		0.132
Family history of diabetes (%)	49.8		47.1		0.538
Parity (% nulliparous)	54.1		53.6		0.146

*P values are based on t-test for continuous variables and chi-square test for categorical variables

Table 5.2. Univariate Comparison of Subjects With vs. Without GDM in Pakistan

	GDM (n=49)		No GDM (n=563)		P value*
	Mean	SD	Mean	SD	
Maternal age (years)	29.39	4.67	26.26	4.26	<0.001
Gestational age @recruitment (weeks)	10.86	3.55	11.25	3.67	0.475
Pregravid weight (kg)	62.73	9.12	58.30	10.50	0.004
Height (cm)	158.18	5.51	159.07	5.51	0.279
BMI (kg/m^2)	25.10	3.78	23.00	4.15	<0.001
Body Fat (%)	32.21	6.42	27.38	7.82	<0.001
Fat mass (kg)	20.74	6.49	16.78	7.54	<0.001
Fat free mass (kg)	41.98	2.96	41.39	3.82	0.290
Rate of weight gain/ week (kg)	0.46	0.23	0.48	0.29	0.620
Physical activity expenditure (kcal/day)	180.0	273.0	235. 0	315.	0.237
Level of education (% university graduates)	55.10		52.93		0.869
Positive family history (percentage)	63.27		48.85		0.053
Parity (% nulliparous)	44.90		54.90		0.110

*P values are based on t-test for continuous variables and chi-square test for categorical variables

Table 5.3. Logistic Regression Models Of Predictors of GDM in South Asian Women (n=611)

	Model 1[a]		**Model 2[a,b]**	
Variables	OR (95% CI)	P value	OR (95% CI)	P value
Maternal Age[c]	1.13 (1.06-1.21)	<0.001	1.15 (1.08-1.23)	<0.001
Body Fat%[c]	1.07 (1.03-1.13)	0.003	NA[d]	
BMI[c]	NA[d]		1.09 (1.01 – 1.17)	0.021
Physical Activity[c]	0.89 (0.79- 0.99)	0.049	0.89 (0.79-0.99)	0.049

a. Models 1 and 2 also included family history of diabetes, level of education, parity, height and rate of weight gain during pregnancy which were not found to be significant predictors.
b. In model 2 fat % was replaced by BMI
c.OR for age, body fat% and BMI are for one unit increase and for physical activity are for a 100 kcal increase.
d.NA= not applicable

Table 5.4. Comparison of Macronutrient Intake of Subjects with vs. without GDM in Pakistan*

Variables	GDM (n=49) Mean	SD	Non-GDM (n=98) Mean	SD	P value
Fat (g)	71.29	27.55	70.77	27.94	0.92
Carbohydrates (g)	327.83	109.19	203.71	102.19	0.06
Protein (g)	76.04	20.49	75.34	23.98	0.86
Energy (kcal)	2205.88	673.43	2067.16	670.35	0.24
Fat (% energy)	28.95	5.61	30.61	5.38	0.08
Proteins (% energy)	14.03	1.74	14.70	1.80	0.03
Carbohydrates (% energy)	59.33	6.35	56.86	6.61	0.03
Fiber (g)	14.82	5.57	13.68	6.69	0.31

* These results are based on a nested case-control study design (n=147)

5.7. REFERENCES

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CHAPTER 6. CONCLUSION AND SUMMARY

It has been projected that by 2020 non-communicable diseases such as diabetes, cardiovascular diseases, cancers and respiratory diseases collectively will account for 70% of the world's global burden of disease. Moreover, the majority of the chronic disease morbidity and associated disability as well as mortality is taking place in the developing world (Wild et al. 2004). Hence the developing world is facing a dual burden of disease, high prevalence rates of malnutrition and infectious diseases as well as high rates of non- communicable diseases are found simultaneously (Yusuf et al. 2001). High rates of non-communicable diseases in the developing world are hampering the socio-economic development of these countries (WHO Report 2004).

This study focused on modifiable predictors associated with lifestyle behaviour risk factors of GDM i.e. body mass index, body composition, rate of weight gain during pregnancy, physical inactivity, and diet in Pakistani population. Women who developed GDM had higher levels of body fat percentage/BMI compared to women without GDM. Also, physical inactivity was found to be an independent predictor of GDM in this population (presented as the second manuscript in this thesis). Several studies have reported increased BMI as a predictor of GDM and type 2 diabetes. Reducing BMI through change in lifestyle could prevent the development of GDM in this population. This change could include increasing physical activity as well as consuming a balanced diet. A recent American study reports that the magnitude of the association between BMI and type 2 diabetes mellitus is greater than that of physical activity and type 2 diabetes mellitus (Weinstein et al. 2004).

Findings of this study indicated that, in general, Pakistani women living in an urban area have low levels of physical activity. Similar findings on sedentary lifestyle in South Asians and its association with chronic disease outcome such as cardiovascular disease or diabetes have been reported by others (Misra et al. 2004, Bhasin et al. 2000). Physical inactivity can be considered a predisposing risk factor for the development of GDM because of its role in glucose metabolism as well as by having negative impact on body composition of subjects. Sedentarism is associated with reduction in fat free mass index and increase in fat mass index (Kyle et al. 2004) and has been suggested to be a predisposing risk factor for cardiovascular disease influencing other more direct risk factors such as hypertension (Yusuf et al. 2001).

Physical activity, in this research project, was assessed by the Monitoring trends and determinants in cardiovascular disease Optional Study of Physical Activity Questionnaire (MOSPA) (Jones 1997 cited in ed. Kriska and Casperson 1997). This questionnaire was validated against Caltrac accelerometer in a subset of the study population. The first manuscript in this thesis presents the results of validating the questionnaire against accelerometers. Overall good correlation was observed between the questionnaire and accelerometer output despite low energy expenditure. Hence, the questionnaire was able to assess physical activity adequately in this population. This holds promise for measuring physical activity in a number of settings and may advance research into the role of even light exercise in different chronic conditions.

are several reasons for declining physical activity rates globally. Mechanization, robotics and computerization have changed the nature of physical activity associated with work and only a very small proportion of the population is now involved in physically exerting professions (Popkin et al. 2002). Even in rural parts of the world the use of machinery to till the land, for instance, has taken away the need of manually ploughing the land and this consequently leads to a decrease in energy expenditure associated with farming. Household and other chores have also become less physically demanding. It is believed that physical activity has declined in developing countries such as India owing to decrease in occupational work hours, mechanization, use of motor cars and leisure time being devoted to less physically demanding activities such as watching television (Shetty 2002). The number of television sets owned in all countries in Asia has increased (Popkin et al. 2002). TV viewing displaces the time that people spend in more physically demanding activities. Television watching has been associated with obesity, high serum cholesterol levels, higher smoking rates and lower fitness levels in a 26 year long prospective cohort study of children and adolescents (Hancox et al. 2004).

The "built" environment of the neighbourhood also affects the amount of time spent in physical activity, particularly walking (Saleans et al. 2003). Sidewalks, safety from crime, attractiveness of the area, residential density, automobile traffic are factors that can influence walking habits (Giles-Corti et al. 2003; Saleans et al. 2003). In contrast with developed countries, in a developing country such as Pakistan fewer sidewalks, and a worse perceived crime record, and less safe driving habits may also have contributed to less walking for leisure in the urban population. Another reason for low physical activity

in this study could be the sultry conditions (heat and humidity) found in equatorial cities that can make walking, for example, uncomfortable (Jauregui et al. 1991).

Nutrition transition is said to be a "change in the diet from a traditional, indigenous, rural, high-fiber diet low fat diet that is eaten by poor people to a western type of diet rich in animal fat and low in fiber" (Vorster et al. 1999). This definition is narrow as some traditional diets are very high in fat, in some settings where animal products are mostly consumed, but it is the physical activity that likely saves these people from chronic diseases. Overall, the macronutrient intake of the entire study population met the WHO recommendations for prevention of chronic diseases (WHO Report 1990) except for fiber intake. Similar findings have also been reported for Asian Indian immigrants in the USA (Jonnalagadda et al. 2002). One may speculate that low intake of dietary fiber is an indication of nutrition transition that is taking place globally (Popkin et al. 2002). However, differences in dietary fiber intake were not observed between women who developed GDM vs. those who did not. This may have been the case because of the low variation in the intake of fiber among the women studied.

Furthermore, in the univariate analysis, it was observed that both carbohydrates (% energy) and proteins (% energy) were significantly different in the cases and controls and fat intake (% energy) was not significant. A multivariate analysis was required as the macronutrients could have been predictors of obesity. In the multivariate anlysis only protein (% energy) was found to be a significant predictor of GDM.

Increasing the consumption of protein (% energy) had a protective effect against development of GDM. In an Indian investigation high biological value protein food items such as meats (including beef and chicken) and fish were found to have a protective effect against development of ischemic heart disease (Rastogi et al, 2004). This might have been the case due to better fatty acid profile of fish. High poly unsaturated fatty acid diets have been shown to have a protective effect against development of GDM (Wang al. 2000) Since this is a micronutrient analysis, one cannot comment about specific high protein food items that could potentially impart a beneficial effect. Furthermore the biological cause and effect association for the relationship of high protein foods having a protective role in the development of GDM is quite weak. Therefore consumption of a balanced diet is recommended for this population.

Subjects who develop GDM are at a greater risk of developing type 2 diabetes mellitus later in life in comparison to women who do not develop GDM (Kim et al. 2002, Albareda et al. 2003), so that the diagnosis of GDM can be considered an early warning for the development of type 2 diabetes mellitus (Ben-Haroush et al. 2004). Therefore prevention of GDM would help in preventing the development of type 2 diabetes in a large segment of the Pakistani population. This study indicates that advancing age and higher levels of body fat (%)/BMI are independent risk factors for developing GDM while increasing physical activity can help in reducing the risk of GDM. Diet and physical activity interventions have shown to lead to significant reduction in the incidence of type 2 diabetes in subjects with impaired glucose tolerance. Both the Finnish diabetes prevention study (Uusitupa et al. 2000) as well as the Diabetes Prevention Project (Mark et al. 2003) observed a 58% reduction in the incidence of type 2 diabetes compared to

controls over a 4-6 years period. However, in both of these studies it is difficult to tease out the effect of physical activity from diet as the intervention arm included dietary modification as well. In another trial with 3 intervention arms, physical activity, diet and diet and physical activity together, similar reduction in the incidence of type 2 diabetes was observed for all the intervention groups (41-46%) compared to controls (Pan et al. 1997). This study indicates that physical activity alone versus physical activity and diet together had similar impact in reducing the incidence of type 2 diabetes. The role of physical activity over and above reduction in BMI and changes in body composition is not clear since the diabetes prevention project as well as the Finnish diabetes prevention study aimed to reduce weight of subjects. A recent American study, however, reports that magnitude of the association between BMI and type 2 diabetes mellitus is far greater than that of physical activity and type 2 diabetes mellitus (Weinstein et al. 2004). After adjustment for BMI the association between physical activity and type 2 diabetes incidence weakened in an aboriginal investigation as well (Kriska et al. 2003). Regardless of the unclear, independent association of increased physical activity and type 2 diabetes, there remains sufficient evidence suggesting a preventive role of physical activity in the relation with type 2 diabetes.

A substantial proportion of the cohort (8%) was found to have GDM at the time of follow-up. This prevalence rate of GDM is higher than similar studies conducted in the past that reported 3.2 and 5.0 percent prevalence of GDM in hospital based studies (Khan et al. 1991; Samad et al. 1996). This high rate of GDM warrants attention in preventing eventual diabetes in these women through lifestyle changes as these women are developing diabetes at a considerably younger age than women without GDM. In a

follow-up of women with GDM vs. without GDM, at 15 years 35% women developed type 2 diabetes in the GDM group while none of the women in non-GDM group developed diabetes ($P<0.001$) (Linne et al. 2002).This translates into a third of the women developing type 2 diabetes at a very young age and at a time when they are raising teenage children. Type 2 diabetes can no longer be considered a disease that afflicts only the elderly populations as women with GDM are also likely to develop it if necessary preventive measures are not adopted.

The prospective nature of this research made it a stronger study on the role of lifestyle predictors in the development of GDM. Furthermore, validation of the MOSPA physical activity questionnaire reinforced the validity of this questionnaire for assessing physical activity in the Pakistani population. The findings clearly indicated that increasing age, body fat percentage increased the odds of GDM while increased physical activity was associated with a reduction in the odds of GDM. On the basis of these findings, one could recommend an increase in physical activity levels to ensure a reduction in the development of GDM in Pakistani women. Owing to increased mechanization at work and sedentary behaviour increase in physical activity should be advocated at a lifestyle level that would incorporate all domains of life i.e. occupation, transportation, household and leisure activity rather than focusing solely on leisure time/ recreational activity because for many individuals increasing or adopting some form of recreational physical activity may not be a feasible option (Levine et al. 2002; Peters et al. 2002).

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APPENDICES

1. Ethics certificate
2. Questionnaire used for face to face interview
3. Pro forma for chart review and anthropometric information

Appendix 1: Ethics certificate

Appendix 2: Questionnaire used for face to face interview

GDM STUDY AKU

Socio Demographic questionnaire سوالنامہ برائے ذاتی معلومات

Name of the respondent:_____ Husband's name: _____

Medical record Number: _____ Study Number: _____

Lanuage of the interview: _____ 1 (Urdu) 2(English) 3(Sindhi) 4(Other)

Date of the interview: _____ Name of the inerviewer : _____

Time at the beginning of the interview: _____ Name of the hospital: _____

Place of residence: _____

Answers	Skip to	Coding category	Questions	Q. No. & Category
		Sindh 1 Baluchitan 2 Punjab 3 NWFP 4 Other.1 دیگر	آپ کس صوبے میں پیدا ہوئی تھیں؟ In what Province were you born?	نسلی پس منظر **Ethnic background** Q1
		1.سندھی Sindhi 2.اردو Urdu 3.بلوچی Balochi .4 Punjabi .5 پشتو Pushto 6. ہندکو Hindko 7. دیگر Others	آپکی مادری زبان کونسی ہے؟ what is your mother tongue?	Q.2
(b) (a)		مقام 1. پاکستان Pakistan 2.بیرون ملک Foreign درجہ 1.پرائمری اسکول Primary 2.ثانوی Secondary 3.اعلیٰ ثانوی HigherSec 4.تیکنیکی تعلیم technical 5. گریجویشن graduate 6.پوسٹ گریجویشن Post graduate 7. مسجد/مدرسہ Mosque 8.ان پڑھ uneducated 9.دیگر others	آپ نے کہاں تعلیم حاصل کی ہے؟ آپ نے کس درجہ تک تعلیم حاصل کی ہے؟	تعلیمی قابلیت **level of education** (a) Q.3 (b)Q.3

		yes .1 ہاں	کیا آپ سگریٹ/ بیڑی پیتی ہیں؟	تمباکو نوشی
	If No, skip to Q.5	No .2 نہیں	Do you smoke in any	(a)Q4
			form (cigarette, beri)	
			اگر ہاں تو دن میں کتنے سگریٹ پیتی	
			ہیں؟	(b)Q4
		5 .1	If yes, how many berri	
		5-10 .2	/cigarettes/day?	
		+10 .3		
		yes .1 ہاں	کیا آپ تمباکو کھاتی ہیں؟	(a)Q5
	If No, skip to Q.6	No .2 نہیں	Do you have tobacco	
			in any form?	
		in Paan .1 پان میں	کس طرح ؟	(b)Q5
		Tobacco .2 خالی تمباکو	in what form?	
		Others .3 دیگر		
		< 5/day.1	اگر ہاں تو کتنا؟	(c) Q5
		5-10 /day .2	If yes, how much?	
		10+ .3		
		yes .1 ہاں	کیا آپ پان کھاتی ہیں؟	(a) Q6
	If no, skip to Q.7	No .2 نہیں	Do you eat paan?	
			اگر ہاں تو کتنا؟	(b) Q6
		<5/day.1	If yes, how much?	
		5-10/day .2		
		+10/day .3		

				خاندان میں ذیابیطس کا رجحان
		1. ہاں yes	(a) کیا آپکے قریبی رشتداروں میں	**Family history of**
	If no end the	2. نہیں No	کسی کو ذیابیطس ہے؟	**diabetes**
	sociodemographic		Does anyone in your	Q.7 (a)
	questionnaire	1. والد father	family have diabetes?	
		2. والدہ Mother		
		3. بہن، بھائی Siblings	(b)۔اگر ہاں تو آپکا ان سے کیا رشتہ	Q.7 (b)
		4. چچا، ماموں Uncles/Aunties	ہے؟	
		/خالہ، پھوپھی	) If yes, can you please	
		6. دیگر Others	describe your	
			relationship with each	
			one of them?	

AKU GDM Study

سوال نامہ برائے جسمانی ورزش

Answers	Skip to	Coding categories	Questions	Q. No. & Category
				جسمانی ورزش
		1. زیرتعلیم Student	آپکی آج کل مصروفیات کیا ہیں؟ Please	Q1
	if 4 or 6 then	2. گھرداری housewife	indicate the category that best	
	skip to:	3. بیروزگاری unemployed	describes your current situation:	
	Q.12	4. برسرروزگار employed		
		5. دیگر others		
		6. جسمانی/ ذہنی		
		معزوری disabled		
	If 2 then skip	1. ہاں	Are you also? کیا آپ ملازمت بھی کرتی ہیں	Q.2
	to:	2. نہیں	employed?	
	Q.12			

Q3	آپ کا تعلق کس پیشے سے ہے؟ What is your occupation?	1. پیشہ ور اور تیکنیکی کام Prof & technical worker 2. پرائیوٹ گھریلو کام Private household workers 3. منیجر، آفیسر Managers officers 4. گھریلو کام کے علاوہ کوئی اور کام Service workers except household work 5. کلرک clerk 6. کھیتی باڑی farmers 7. ہاتھ کا کام Craftwork 8. سیل sales 9 گھریلو خاتون House wife 10. دیگر others		
Q.4	ایک معمول کے ہفتے میں آپ کتنے گھنٹے ملازمت کرتی ہیں؟ How many hours do you work during a typical week?	Time in Minutes		
Q.5	ایک معمول کے ہفتے میں آپ کتنے دن ملازمت کرتی ہیں؟ How many days do you work during a typical week?	7. سات دن 6. ۶ دن 5. ۵ دن 4. ۴ دن 3. ۳ دن 2. ۲ دن 1. ۱ دن		

		Time in Minutes	ایک معمول کے دن ملازمت کے دوران آپ کتنے گھنٹے بیٹھ کر گزارتی ھیں؟ On a typical day at work, how much time do you spend sitting? کتنے گھنٹے کھڑے ہو کر گزارتی ھیں؟ and standing? (وہ وقت جو کام پر پہنچنے اور واپس جانے میں صرف ہو اور جو بھاری چیزیں اٹھانے میں خرچ ہو وہ شامل نہ کریں) Do not include time spent going to and from work.Do not include time spent lifting or carrying moderately heavy objects or very heavy objects.)	(a)Q.6 (b) Q.6
		Time in Minutes	ایک معمول کے دن کام کے دوران آپ چلنے میں کتنا وقت خرچ کرتی ہیں؟ On a typical day at work, how much time do you spend walking (Do not include time spent going to and from work, do not include time spent lifting or carrying moderately heavy objects or very heavy objects.)	Q.7
		Time in Minutes	ایک معمول کے دن کام کے دوران آپ بھاری چیزیں (۵-۱۰کلو) وزن اٹھانے میں کتنا وقت خرچ کرتی ہیں؟ On a typical day at work, approximately how much time do you spend actually spend lifting or carrying moderately heavy objects (about 5-10 kg) or doing activities of a similar effort?	Q.8
		Time in Minutes	ایک معمول کے دن کام کے دوران آپ بہت بھاری چیزیں (۱۰+ کلو) وزن اٹھانے میں کتنا وقت خرچ کرتی ہیں؟ On a typical day at work, approximately how much time do you actually spend lifting or carrying very heavy objects (10+ kg) or doing activities of a similar effort?	Q.9

Q.10	ایک معمول کے دن کام کے دوران، آپ کتنا وقت محنت طلب کام میں صرف کرتی ہیں؟ (مثلاً جھاڑو پونچھا، کپڑے دھونے، جھاڑ پونچھ) On a typical day at work, how much time do you spend doing moderately vigorous or very vigorous chores like sweeping, vacuuming, washing clothes, scrubbing floors, etc. ?			
Q.11	جب آپ یہ کام کرتی ہیں تو آپکی سانس کی رفتار یا گہرائی میں کیا فرق پڑتا ہے؟ When you do these chores, what usually happens to the rate or depth of your breathing ?	1. کوئی تبدیلی نہیں آتی 2. معمولی سی بڑھ جاتی ہے 3. کافی بڑھ جاتی ہے 4. بہت زیادہ بڑھ جاتی ہے		
Q.12	کام، اسکول اور خریداری کے لیے جانے اور واپسی میں آپکا کتنا وقت پیدل چلنے میں صرف ہوتا ہے؟ Going to and from work, school or shopping, how much time do you spend walking each day?	Time in Minutes	ملازمت، اسکول اور خریداری کے لیے ٹرانسپورٹ Transportation to and from work, school and shopping	
Q.13	عام طور پر ہفتے میں آپ کتنا وقت چہل قدمی میں صرف کرتی ہیں؟ During an average week, how many hours do you spend walking? (وہ وقت جو برائے کام، اسکول یا شاپنگ میں صرف ہو وہ شامل نہ کریں) (Do not include time spent at work, or going to and from work, school or shopping.)	Time in Minutes	چہل قدمی برائے تفریح یا ورزش **Walking during leisure- time or for pleasure or exercise**	
Q.14	چہل قدمی کے دوران آپکی سانس کے رفتار اور گہرائی میں کیا فرق پڑتا ہے؟ When you are walking, what usually happens to the rate or depth of your breathing?	1. کوئی تبدیلی نہیں آتی 2. معمولی سی بڑھ جاتی ہے 3. کافی بڑھ جاتی ہے 4. بہت زیادہ بڑھ جاتی ہے		

		Time in Minutes	عموماً روزانہ آپ کتنا وقت محنت طلب کام میں صرف کرتی ہیں؟ (مثلاً جھاڑو پونچھا، کپڑے دھونے، جھاڑ پونچھ) On the average, how much time do you spend every day doing moderately vigorous or very vigorous chores at home such as sweeping, vacuuming, washing clothes, scrubbing floors, etc. ?	گھریلو کام **House work** Q.15
		1. کوئی تبدیلی نہیں آتی 2. معمولی سی بڑھ جاتی ہے 3. کافی بڑھ جاتی ہے 4. بہت زیادہ بڑھ جاتی ہے	جب آپ یہ کام کرتی ہیں تو آپکی سانس کی رفتار یا گہرائی میں کیا فرق پڑتا ہے؟ When you do these chores, what usually happens to the rate or depth of your breathing?	Q.16
	If No skip to Q No. 29	1. yes 2. No	پچھلے بارہ مہینوں کے دوران کم از کم ۱۲ مرتبہ آپ نے کسی کھیل یا ورزش وغیرہ میں حصہ لیا ہے؟ During the last 12 months, did you play any sports or do any exercises such as.... (مثلاً TableTennis, Badminton, Running, Aerobics, Jogging)	خالی اوقات، کھیل، کھیلوں کی تربیت اور ورزش **Leisure- time sport, sport training or exercise** Q.17
		Aerobic exercises.1 2.باغبانی gardening 3.ڈوڑنا یا تیز تیز چلنا (Jogging/running) 4. Tennis/ Badminton 5.دیگر Others	آپ نے کونسے کھیل یا ورزش یا تفریح کو سب سے زیادہ پسند کیا؟ (ایک کا انتخاب کیجیے) What sport or exercise did you do most frequently?	Q.18
		Months	پچھلے ایک سال کے دوران آپ نے یہ کھیل/ورزش یا تفریح کتنے مہینوں تک جاری رکھی؟ During the past year, in how many months did you do this sport or exercise?	Q.19

Q.20	جن مہینوں میں آپ نے یہ کھیل/ورزش کی ان میں ہفتے میں کتنی مرتبہ آپ نے اس میں حصہ لیا؟ In the months that you did this sport how many times per week did you usually do it?	0. ایک مرتبہ سے کم 1. ایک مرتبہ 2. دو مرتبہ 3. تین مرتبہ 4. چار مرتبہ 5. پانچ مرتبہ 6. چھ مرتبہ 7. سات یا سات سے زیادہ مرتبہ		
Q.21	اس کھیل یا ورزش میں ایک مرتبہ میں عموماً آپ کتنا وقت صرف کرتی ہیں؟ When you did this sport or exercise, how much time did you usually spend for each session?	Time in Minutes		
Q.22	جن مہینوں میں آپ نے اس کھیل یا ورزش میں حصہ لیا، آپکی سانس کے رفتار یا گہرائی میں کیا فرق پڑا؟ In the months when you did this sport or exercise, what usually happened to the rate or depth of your breathing?	1. کوئی تبدیلی نہیں آتی 2. معمولی سی بڑھ جاتی ہے 3. کافی بڑھ جاتی ہے 4. بہت زیادہ بڑھ جاتی ہے		
Q.23	پچھلے بارہ مہینوں کے دوران کم از کم ۱۲ مرتبہ آپ نے کسی اور کھیل یا ورزش وغیرہ میں حصہ لیا ہے؟ During the past 12 months did you play any other sport or do any other exercise at least 12 times?	1. ہاں yes 2. نہیں No	If no, go to Q.29	
Q.24	آپ نے کونسے کھیل یا ورزش یا تفریح کو سب سے زیادہ پسند کیا؟ (ایک کا انتخاب کیجیئے) What sport or exercise was it? (Chose one from the list.)	1. Aerobic exercises 2. باغبانی 3. ڈوڑنا یا تیز تیز چلنا (Jogging/running) 4. Tennis/ Badminton 5. دیگر		
Q.25	پچھلے ایک سال کے دوران آپ نے یہ کھیل/ورزش یا تفریح کتنے مہینوں تک جاری رکھی؟ During the past year, in how many months did you do this sport or exercise?	Months		

Q.26	جن مہینوں میں آپ نے یہ کھیل/ورزش کی ان میں ہفتے میں کتنی مرتبہ آپ نے اس میں حصہ لیا؟ In the months that you did this sport how many times per week did you usually do it?	0. ایک مرتبہ سے کم 1. ایک مرتبہ 2. دو مرتبہ 3. تین مرتبہ 4. چار مرتبہ 5. پانچ مرتبہ 6. چھ مرتبہ 7. سات یا سات سے زیادہ مرتبہ		
Q.27	اس کھیل یا ورزش میں ایک مرتبہ میں عموماً آپ کتنا وقت صرف کرتی ہیں؟ When you did this sport or exercise, how much time did you usually spend for each session?	Time in Minutes		
Q.28	جن مہینوں میں آپ نے اس کھیل یا ورزش میں حصہ لیا، آپکی سانس کے رفتار یا گہرائی میں کیا فرق پڑا؟ In the months when you did this sport or exercise, what usually happened to the rate or depth of your breathing?	1. کوئی تبدیلی نہیں آتی 2. معمولی سی بڑھ جاتی ہے 3. کافی بڑھ جاتی ہے 4. بہت زیادہ بڑھ جاتی ہے		
Q.29	پچھلے ۱۲ مہینوں سے قبل کیا آپ نے کسی کھیل یا ورزش میں حصہ لیا؟ Prior to the past 12 months, did you play any sports or do any exercises such as ..... for exercise or pleasure at least 12 times in one year (مثلاً Table Tennis, Badminton, Running, Aerobics, Jogging)	1. ہاں Yes 2. نہیں No	If no, go to Q. 32	
Q.30	پچھلے سال سے قبل آپ نے کونسے کھیل یا ورزش یا تفریح کو سب سے زیادہ پسند کیا؟ (ایک کا انتخاب کیجیے) What was the recent physical activity that you did on a regular basis prior to this last year? (Chose one from the list.)	1. Aerobic exercises 2. باغبانی 3. ڈوڑنا یا تیز تیز چلنا (Jogging/running) 4. Tennis/ Badminton 5. دیگر		

Q.31	یہ کھیل/ تفریح آپ نے کتنے عرصے پہلے بند کردی تھی؟ How many years ago did you stop this sport?	Years		
محنت طلب کام Q.32	مندرجہ ذیل میں سے کونسا جملہ آپکی موجودہ ہفتہ وار جسمانی ورزش (جسمیں ملازمت سے منسلک کام شامل نہیں) کو ظاہر کرتا ہے؟ برائے مہربانی کام کے لئے ٹرانسپورٹ، کھیل اور دیگر جسمانی حرکت مثلاً باغبانی، aerobics کو مدنظر رکھیے۔ Which of the following four activities best describe your present activity outside your job? Please consider transportation to and from work, sporting activity and other physical effort during your leisure time, like gardening.	0. کوئی جسمانی کام نہیں 1. بہت ہلکی پھلکی جسمانی حرکت 2. ایک یا دو مرتبہ کم از کم ۲۰ منٹ کے لیے سخت جسمانی حرکت 3. ۳ یا ۳ سے زیادہ مرتبہ کم از کم ۲۰ منٹ کے لیے سخت جسمانی حرکت	سخت جسمانی حرکت وہ ہے کہ جسمیں سانس پھولنے لگے، دل کی رفتار تیز ہوجائے اور پسینہ آئے	
Q.33 گھریلو آمدنی Household income	آپکی ماہوار گھریلو آمدنی کتنی ہے؟ What is your monthly household income?	Amount in Rupees		

Food Frequency Questionnaire
for gestational diabetes study

Subject's name:_____
MR#:_____
Name of the interviewer:_____
انٹرویو کرنے والے کا نام

Food item کھانے کی اقسام	Sizes S/M/L	Amount	How often? Never	Month	Week	Day	Season All	Summer	Winter	Office Use Code		Amount	
On average, over the last year, did you consume cereals? Which ones and how often?													
Chapati without oil سادی روٹی													
Chapati with oil روٹی گھی/تیل کے ساتھ													
Tandoori naan تندور کی روٹی													
Paratha پراٹھا													
Sheermaal/ Taftan شیرمال/تافتان													
Puree پوری													
Bread ڈبل روٹی													
Rusk پاپے													
Boiled Rice اُبلے ہوئے چاول													
Bolied rice with oil اُبلے ہوئے چاول تیل کے ساتھ													
Biryani/Pulao/ Fried rice بریانی/پلاؤ/فرائڈ رائس													
Kitchree کھچڑی													
Cooked cereals (corn flakes, porridge) کارن فلیکس/دلیہ													
Others دیگر													

Food item	Sizes S/M/L	Amount	Never	Month	Week	Day	All	Summer	Winter	Code		Amount	
In average, over the last year, did you consume raw vegetables? Which ones and how often?													
Carrots, radish, beetroot گاجر، مولی، چقندر													
Tomato, cucumber ٹماٹر / کھیرا													
Others (specify) دیگر													
On average over the last year did you consume cooked vegetables? Which ones and how often?													
Potato آلو													
Cauliflower, cabbage گوبھی، پتہ گوبھی													
Torai, lokkee, Kaddu, Tinda ٹنڈا، بیگن egg plant لوکی، کدو، توری،													
Raddish, مولی carrots, گاجر beetroot, turnip شلجم، چقندر													
GLV (Spinach, mustard, cholai etc.) سرسوں کا ساگ پالک اور چولائی وغیرہ													
Okra, Bitter gourd, yam بھنڈی، کریلے، اروی													
String beans, green beans, Guar پھلیاں، گوار وغیرہ													
Peas مٹر													
Others specify دیگر													
On average over the last year did you consume meat, fish, poultry, eggs? Which ones and how often?													
Mutton/beef curry گائے / بکرے کا سالن													
Mutton/beef Qorma گائے / بکرے کا قورمہ													

Food item	Sizes S/M/L	Amount	Never	Month	Week	Day	All	Summer	Winter	Code		Amount	
Lamb curry بھنڑ کا													
Lamb Qorma سالن بھیڑ کا قورمہ													
Minced meat/ قیمہ، کباب kofte کوفتے													
Chicken curry مرغی کا سالن													
Chicken Qorma مرغی کا قورمہ													
Fish Fry/curry مچھلی تلی ہوئی/سالن													
Any curry without meat کوئی بھی سالن گوشت کے													
Shell fish (Shrimp, crab. Lobster, etc) Fried جھینگے، کیکڑے وغیرہ													
Liver/kidneys کلیجی/گردے													
Brain مغز													
Katacut کٹا کٹ													
Paya پائے													
Nihari نہاری													
Haleem حلیم													
Eggs fried/ Omelet/ curry انڈے/فرائی/آملیٹ/													
Eggs Boiled ابلے													
KFC/ Mac burger KFC برگر													
Chicken Broast/ Fry چکن بروسٹ													
Chicken Tikka (BBQ) چکن تکہ													
Chowmein چاؤمن													
Pizza پیزا													
Seekh Kebab/ boti (BBQ) سیخ کباب/بوٹی													

Food item	Sizes S/M/L	Amount	Never	Month	Week	Day	All	Summer	Winter	Code		Amount	
On average over the past year did you consume daal /lobia /chaana? Which ones and how often?													
Legumes (daal)													
Chickpeas چنے													
Lobia لوبیا													
Others (specify) دیگر													
On average over the last year did you consume dairy products? Which ones and how often?													
Whole milk دودھ													
Yogurt دہی													
Lassi with sugar لسی (شکر والی)													
Lassi with salt													
Others دیگر													
On average over the last year did you consume fruits? Which ones and how often?													
Watermelon تربوز Cantaloupe خربوزہ													
Bananas کیلا													
Papaya پپیتا													
Plum, mango, آم orange, apple, کینو apricot, peach آڑو Grapes انگور سیب، آلو بخارہ													
Pomegranate انار custard apple, شریفہ، بیر bair													
Dates کھجور													
Guava امرود													
Other fruits دیگر													
On average over the past year did you consume fruit juices? If yes, which ones?													
Orange/ کینو lemonade/ لیموں grapefruit/ گریپ فروٹ apple سیب													
Frost/ Nestle ڈبے کا													
Others دیگر													
On average over the past year did you consume sweets/desserts/ miscellaneous items? Which ones and how often?													
Mithai/ Halwa													

Food item	Sizes S/M/L	Amount	Never	Month	Week	Day	All	Summer	Winter	Code		Amount	
Kheer/Firni/ sheer/ custard													
Zarda (sweet rice) میٹھے چاول													
Vermicelli سویاں													
Ice cream آئسکریم (Igloo, Polka, walls) اگلو، پولکا، والز													
Kulfi, Peshawari ice cream, faluda													
Biscuits بسکٹ (Packets) ڈبے والے													
Biscuits بسکٹ (bakery) بیکری کے													
Cakes, brownie													
Cakes with cream, Pastry													
Chocolates, toffee													
Honey شہد													
Butter/ Margarine مکھن مارجرین													
Others specify دیگر													
On average over the past year did you consume salty snacks? Which ones and how often?													
Samosa / Pakora/Patties سموسے													
Corn بھٹے													
Sweet potato شکرقندی													
Nimco/ chips													
French fries/Pizza small بیکری والا پیزا													
Nuts and seeds مونگ پھلی													
Others (specify) دیگر													
On average over the past year did you consume beverages? Which ones and how often?													
Regular soft drinks ٹھنڈی بوتل													
Tea with sugar چائے شکر کے ساتھ													

Food item	Sizes S/M/L	Amount	Never	Month	Week	Day	All	Summer	Winter	Code		Amount	
Sherbet e.g. Rooh Afza, Tang شربت													
Others (specify) دیگر													

Questions

Q.1 How many liters of oil/month is consumed by your household? _____
آپ کے گھر میں ایک مہینے میں کتنے لیٹرز تیل استعمال ہوتا ہے؟

Q.2 How many liters of ghee/ month is consumed by your household? _____
آپ کے گھر میں ایک مہینے میں کتنے لیٹرز گھی استعمال ہوتا ہے؟

Q.3 How many people eat from the same kitchen? _____
آپ کے گھر میں کل کتنے افراد ہیں؟

Q.4. a) On average over the past year, how many times did you eat out? _____
عموماً پچھلے ایک سال میں کتنی دفعہ کھانا باہر کھایا؟

i) Dinners/weddings _____ ii) Restaurants _____
دعوت/شادی iii) Working luncheons _____ کام کے دوران ہوٹلز

b) What dishes did you have most often?
کون کون سے کھانے زیادہ کھائے گئے؟
1. _____ 2. _____ 3. _____

Q.5 Was your intake different last year from the previous year? Yes____ No_____
کیا آپ کے کھانوں میں پچھلے سال اور اس سے پچھلے سال کوئی فرق آیا؟

Appendix 3: Pro forma for chart review and anthropometric information

AKU GDM Study

Form for chart review and anthropometric variables

MR. No:_____ Date:_____

Name: _____ Husband's Name:_____

Study# :_____ Ph #:_____

Research officer:_____

Blood work:

GCT 1 Value: Date:_____

GCT 2 value: Date: _____

OGTT 1: Date:_____

OGTT 2: Date:_____

Anthropometric:

Weight (Kg) 1:_____ Date:_____

Weight (Kg) 2:_____ Date:_____

Height (m): _____

Body composition analysis I:(please attach the print out as well)

Date _____

1. Fat%: _____
2. Fat Mass: _____
3. Fat Free mass (FFM): _____
4. Total Body Water (TBW): _____

Body composition analysis II:(please attach the print out as well)

Date of the II analysis: _____