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VITAMIN D DEFICIENCY IN EARLY PREGNANCY, DIET AND PHYSICAL ACTIVITY AND DEVELOPMENT OF GESTATIONAL DIABETES IN EMIRATI WOMEN

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Declaration of Original Work

I, Sharifa Ali Abdulrahman Al Belooshi , the undersigned, a graduate student at the United Arab Emirates University (UAEU), and the author of this dissertation entitled "*Vitamin D Deficiency in Early Pregnancy, Diet and Physical Activity and Development of Gestational Diabetes Mellitus in Emirati Women*", hereby, solemnly declare that this dissertation is my own original research work that has been done and prepared by me under the supervision of Dr. Abderrahim Oulhaj, in the College of Medicine and Health Sciences at UAEU. This work has not previously been presented or published, or formed the basis for the award of any academic degree, diploma or a similar title at this or any other university. Any materials borrowed from other sources (whether published or unpublished) and relied upon or included in my dissertation have been properly cited and acknowledged in accordance with appropriate academic conventions. I further declare that there is no potential conflict of interest with respect to the research, data collection, authorship, presentation and/or publication of this dissertation.

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Abstract

Vitamin D deficiency and Gestational Diabetes Mellitus (GDM) are common health problems among pregnant women in the Middle East region including the United Arab Emirates. However, a few prospective studies have investigated the association between vitamin D deficiency and risk of GDM.

We estimated the incidence of GDM and examined the association of vitamin D status in early pregnancy and the development of GDM in Emirati pregnant women. In addition, we studied the association of diet, low physical activity and other covariates with the risk of GDM.

We conducted a prospective cohort study on Emirati pregnant women who visited eight primary healthcare clinics for antenatal care. A cohort of 563 women was selected that included women aged 18 - 45 years, ≤ 15 weeks pregnant and were free of GDM. The primary exposure was vitamin D deficiency (25(OH)D < 12 ng/ml) and vitamin D insufficiency (25(OH)D = 12 – 20 ng/l) as per Institute of Medicine Criteria. Secondary exposure variables were levels of physical activity (low, moderate and high as per WHO recommendations) and dietary intake. The physical activity was measured by using Global Physical Activity Questionnaire (GPAQ) and dietary intake was determined by using a validated Food Frequency Questionnaire (FFQ). The outcome variable was GDM that was diagnosed by using fasting and 75 g 2-hour postprandial Oral Glucose Tolerance Test (OGTT) in 24 - 28 weeks of gestation. The data on socio-demographic characteristics, personal and family medical history, physical activity, dietary intake, blood pressure and anthropometric indices were collected at baseline. In addition, fasting blood samples were taken to measure fasting blood glucose and 25(OH)D levels. The participants revisited antenatal clinics in their 24 - 28 weeks of gestation for the screening of GDM. The status of GDM was confirmed by reviewing medical records of mothers or by telephonic interview.

Overall, 58.3% of pregnant women had vitamin D deficiency and 26.4% had insufficiency. The overall incidence of GDM was 15.2%. The incidence of GDM was 16% in vitamin D deficient women, 16.1% in vitamin D insufficient women and

10.7% in women with normal vitamin D. Adjusted logistic regression analysis showed that vitamin D concentration (Adjusted Odds Ratio [AOR]: 0.99, 95% Confidence Interval [CI]: 0.95 – 1.02, p = 0.450), vitamin D insufficiency (AOR: 2.11, 95% CI: 0.81 – 5.64, p = 0.101) and deficiency (AOR: 1.94, 95% CI: 0.88 – 5.32, p = 0.118) were not associated with GDM. Low (AOR: 1.09, 95% CI: 0.43 – 2.79, p = 0.850) and moderate (AOR: 0.78, 95% CI: 0.45 – 1.34, p = 0.372) physical activity levels were not significantly associated with increased odds of GDM. The Daily consumption of red meat (AOR: 6.16, 95% CI: 1.31 - 28.92, p = 0.021) and dates (AOR: 1.86, 95% CI: 1.03 - 6.49, p = 0.043), family history of diabetes (AOR: 1.93, 95% CI: 1.02 - 3.62, p = 0.043) and Body Mass index (BMI) before pregnancy (AOR: 1.07, 95% CI: 1.02 - 1.11, p = 0.003) were significantly associated with GDM.

Vitamin D deficiency and physical activity were not associated with GDM, while daily intake of red meat and dates, increasing BMI before pregnancy and positive family history were positively associated with GDM. These findings are congruent with some previous studies in the Middle East region and elsewhere and provide guidelines to health stakeholders and healthcare providers for improving the screening, prevention and management of GDM in Emirati women.

Keywords: Gestational Diabetes (GDM), Vitamin D deficiency, Vitamin D insufficiency, Physical Activity, Diet, Obesity, Family History of Diabetes.

Title and Abstract (in Arabic)

علاقة نقص فيتامين د، التغذية والنشاط الرياضي في المراحل الأولى من الحمل بالإصابة بسكري الحمل عند الإماراتيات

الملخص

يعتبر سكري الحمل حالة مرضية مهمة، حيث تعاني منه الكثير من النساء في دولة الإمارات العربية المتحدة. تشير الدراسات إلى أن نسبة الإصابة بسكري الحمل في دولة الإمارات العربية المتحدة تصل ما بين 7.9% -24.9 %، كما يعتبر سكري الحمل عامل خطورة بالنسبة للأم والجنين حيث أنه يؤدي إلى مضاعفات لكليهما ويعزز الإصابة بالنوع الثاني من السكري.

أثبتت بعض الدراسات أن نقص فيتامين د له دور كبير في الإصابة بسكري الحمل، كما أن العوامل المرتبطة بنمط الحياة كالتغذية والرياضة تلعبان دورا مهما في علاج المرض والسيطرة عليه.

صممت هذه الدراسة لتشمل 563 حامل إماراتية في مدينة رأس الخيمة في دولة الإمارات العربية المتحدة، وللكشف عن وجود علاقة بين نقص فيتامين د وتأثير عوامل نمط الحياة كالتغذية والرياضة، بالإضافة إلى التاريخ العائلي للإصابة بالسكري ومنسب كتلة الجسم وعلاقة هذه العوامل بالإصابة بسكري الحمل.

لم نتمكن من الحصول على علاقة واضحة وقوية بين نقص فيتامين د والنشاط الرياضي للحوامل والإصابة بسكري الحمل، إلا أنه كانت هناك علاقة قوية بين تناول اللحم الأحمر، التمر من الناحية الغذائية و الإصابة بسكري الحمل بالإضافة إلى التاريخ العائلي للإصابة بالسكري ومنسب كتلة الجسم اللذان كانا من العوامل التي لها دور كبير للإصابة بسكري الحمل.

مفاهيم البحث الرئيسية: سكري الحمل، نقص فيتامين د ، التغذية، النشاط الرياضي، التاريخ العائلي للإصابة بالسكري، منسب كتلة الجسم.

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Dedication

To my father's soul

To my beloved mother, brothers and sisters

To my husband and kids

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List of Abbreviations

25(OH)D	25-hydroxyvitamin D
ADA	American Diabetes Association
ACOG	American College Obstetricians and Gynecologists
ADA	American Diabetes Association
ADIPS	Australian Diabetes in Pregnancy Society
AMDHREC	Al Ain Medical District Human Research Ethics Committee
AOR	Adjusted Odds Ratio
BMI	Body Mass Index
C & C	Carpenter & Coustan
CDA	Canadian Diabetes Association
CI	Confidence Interval
CNGOF	French College of Gynecologists and Obstetricians
COR	Crude Odds Ratio
DM	Diabetes Mellitus
DIPSI	Diabetes in Pregnancy Study Group in India
DPSG	Diabetic Pregnancy Study Group
EASD	European Association for the Study of Diabetes
FBG	Fasting Blood Glucose
FIGO	International Federation of Gynecology & Obstetrics
G	Gram
GAD	Glutamic Acid Decarboxylase
GCT	Glucose Challenge Test
GDM	Gestational Diabetes Mellitus

GI	Glycemic Index
GPAQ	Global Physical Activity Questionnaire
HPL	Human Placental Lactogen
HAPO	Hyperglycemia & Adverse Pregnancy Outcomes
HCG	Human Chorionic Gonadotropin
IOM	Institute Of Medicine
JDS	Japan Diabetes Society
OGTT	Oral Glucose Tolerance Test
IOM	Institute Of Medicine
IU	International Unit
IGT	Impaired Glucose Test
IADPSG	International Association of Diabetes and Pregnancy Study Groups
LGA	Low Gestational Age
LGI	Low Glycemic Index
Mg	Milligram
µg	Microgram
MODY	Maturity onset diabetes of the young
NCEP-ATPIII	National Cholesterol Education Program Adult Treatment Panel
NDDG	National Diabetes Data Group
NICE	National Institute for Health and Clinical Excellence
Nmol	Nanomol
NZSSD	New Zealand Society for the Study of Diabetes
OGTT	Oral Glucose Tolerance Test
RAK	Ras Al Khaimah

RAKREC	RAK Research Ethics Committee
SOGC	Society of Obstetricians and Gynecologists of Canada
TNF-a	Tumor Necrosis Factor – alpha
UVB	Ultra Violet B
UAE	United Arab Emirates
USA	United States of America
WHO	World Health Organization

Chapter 1: Introduction

1.1 Overview of Gestational Diabetes Mellitus

Gestational diabetes mellitus (GDM) is a type of diabetes that is developed during pregnancy (ADA, 2015). During pregnancy, various hormones such as human placental lactogen (HPL), estrogen, progesterone and cortisol are produced by the placenta and ovaries to maintain the pregnancy, these hormones can disrupt the uptake of insulin by body cells which could lead to insulin resistance and consequently increase blood glucose concentrations (Reece et al., 2009). This condition can develop at any gestational age; however, the majority of cases are reported after 24 weeks (ADA, 2015).

1.2 Statement of the Problem

Recent data indicates that the burden of GDM has increased by 10 - 100% in various populations during the last two decades (Ferrara et al., 2007; Dabelea et al., 2005). This increase in the burden of GDM is thought to be somewhat responsible for increasing burden of metabolic complications in both mothers and offspring (Ferrara et al., 2007).

As mentioned earlier, vitamin D deficiency and GDM are common conditions in Emirati pregnant women. However, a few studies have examined their association in the region and country. In addition, these studies have various limitations. First, the majority of previous studies used a cross-sectional study design; therefore, temporality of the association between vitamin D and GDM could not be established. Second, findings regarding the direction of association were inconsistent. Last, the

most of studies did not account for confounding factors such as physical activity and diet.

The UAE has experienced a rapid economic growth in recent decades, which has considerably changed physical activity patterns and dietary habits of the people (Ng et al., 2011). Since these life-style risk factors are strongly associated with GDM and vitamin D deficiency, a limited research has explored the role of diet and physical activity in the development of GDM in the region including the UAE.

It is well-established that exercise and dietary interventions can effectively improve the management of type 2 diabetes and GDM (Asemi et al., 2013; Brankston et al., 2004). However, in the UAE, primary focus is on the pharmacological management of GDM, which needs to be shifted to lowering its risk factors.

Prospective epidemiological studies are needed with better study designs and quality to understand the pathophysiology and etiology of GDM and to determine the association between vitamin D and other factors and GDM to decrease the burden and impact of the condition on mothers and their children.

1.3 Relevant Literature

1.3.1 Pathophysiology and Etiology of Gestational Diabetes Mellitus

Insulin resistance is increased in pregnant women three times compared to non-pregnant women. Auto-immune diabetes and β-cell dysfunction may correlated with GDM and glucose intolerance during pregnancy as studies showed that the prevalence of auto-immune markers of type 1 diabetes in women with GDM was

between 0.98 and 14.7% (Baz et al., 2016). This is characterized by circulating immune markers directed against pancreatic islets (anti-islet cell antibodies) or β-cell antigens (such as Glutamic Acid Decarboxylase (GAD), or insulin autoantibodies (Kaaja et al., 2008).

Studies showed that low insulin sensitivity and high insulin resistance during pregnancy is related to pregnancy hormones such as estrogen, and progesterone (influence β-cell function in early pregnancy and increase insulin resistance in late pregnancy, cortisol (decreases glucose tolerance and increase blood glucose), and placental hormones as Human Placental Lactogen, and Prolactin increase during pregnancy to preserve pregnancy (Baz et al., 2016)

It has been showed that Human Chorionic Gonadotropin (HCG) may have no effect on insulin resistance during pregnancy as it increases during the first trimester, the period which is associated with an increase in insulin sensitivity and improvement of glucose tolerance (Palani et al., 2014). Prolactin may have no role on glucose tolerance during pregnancy, as studies demonstrated that there were no significant differences in the level of plasma prolactin among GDM and non-GDM women. HPL has a main role in stimulating insulin-like growth factor (IGF) production to provide more fuel for the fetus in form of glucose and amino acids (Palani et al., 2014).

Studies demonstrated that adiponectin levels (in adipose tissue which controls local storage and distribution of fat by stimulating glucose uptake in muscles), decrease with advancing gestation leading to high glucose levels (Palani et al., 2014).

It has been shown that Tumor Necrosis Factor alpha (TNF-a) may promote insulin resistance as it prohibit the insulin receptor, high level of TNF-a during pregnancy associate with progressive insulin resistance (Baz et al., 2016).

1.3.2 Screening and Diagnosis of Gestational Diabetes Mellitus

The screening of GDM is usually based on Glucose Challenge Test (GCT), while its diagnosis is based on Oral Glucose Tolerance Test (OGTT) (ADA, 2015). In addition, two approaches are usually employed to screen and diagnose GDM. In the two-step approach, 50g GCT is administered to screen women for GDM followed by administering the 100g OGTT to GCT-positive women to diagnose GDM. The one-step approach administers OGTT directly to diagnose GDM (ADA, 2015).

A substantial disagreement exists over the gestational age at which women should be screened for GDM. In 1964, Sullivan and Mahan introduced the Oral Glucose Tolerance Test (OGTT) to diagnose GDM. However, the gestational age was not specified by them. In 1982, Carpenter and Coustan were the first to suggest the gestational age of 24 - 33 weeks for screening of GDM. In 1996, the French College of Gynecologists and Obstetricians (FCNGO) recommended using OGTT in 24 - 28 weeks of gestation in low-risk gestational women. In the same year, the European Association for the Study of Diabetes (EASD) suggested a single step OGTT at 28 weeks of gestation.

In 2000, the American Diabetes Association (ADA) recommended performing the 75 g OGTT at 24 - 28 weeks of gestation. Since 2000, the majority of guidelines have unanimously recommended to administer OGTT at 24 - 28 weeks of gestation to screen for GDM; however, the rationale behind this approach has not been

provided (Liu et al., 2016). Table 1.1 shows the history of OGTT for diagnosis of GDM.

Table 1.1: History of Oral Glucose Tolerance Test for Diagnosis of GDM

Year	Author/Organization	Gestational Age	Major Contribution
1964	O' Sullivan & Mahan	No recommendation	To evaluate the risk of future development of T2D in the mother Introduced OGTT as a diagnostic criterion for GDM
1967	NDDG	No recommendation	Test plasma rather than whole blood to increase reproducibility
1982	Carpenter & Coustan	24 – 33 weeks	Apply the glucose oxidase method rather than the Somogyi-Nelson method to avoid the measurement of other substances
1996	CNGOF	24 – 28 weeks	First to recommend gestational age in low-risk pregnant women
1996	EASD	28 weeks	One step OGTT
2000	ADA	24 – 28 weeks	The cut-off to diagnose GDM was set at 5.3-10.0-8.6 mmol/L in 75 g OGTT
2008	HAPO study	24 – 32 weeks	Focused on perinatal outcomes associated with OGTT value
2010	IADPSG	24 – 28 weeks	Adjusted diagnosis cut-offs
2011	ADA	24 – 28 weeks	
2013	WHO	24 – 28 weeks	
2015	ADA	24 – 28 weeks	

ADA: American Diabetes Association, CNGOF: French College of Gynecologists & Obstetricians, EASD: European Association for the Study of Diabetes, GDM: Gestational Diabetes Mellitus, HAPO: Hyperglycemia & Adverse Pregnancy Outcomes, IADPSG: International Association of Diabetes & Pregnancy Study Groups, NDBG: National Diabetes Data Group, OGTT: Oral Glucose Tolerance Test, WHO: World Health Organization

Source: Adapted from (Liu et al., 2016)

Table 1.2: Comparison of screening and diagnostic criteria of GDM

Advising Body	Year	Screening advise	Screening method (Positive cut-off ≥)	Glucose load-g	Glucose Thresholds (mmol/L)				No. of OGTT values for diagnosis
					Fasting	1hr	2hr	3hr	
NDDG	1979	None	50g GCT (7.8)	100	5.8	10.5	9.2	8.0	2
ADA	2003	All but for those at low risk	50g GCT (7.8)	100	5.3	10.0	8.6	7.8	2
				75	5.3	10.0	8.6	-	2
C & C	1982	None		100	5.3	10.0	8.6	7.8	2
IADPSG	2010	All	75g OGTT	75	5.1	10.0	8.5		
CDA	2003	All	50g GCT (7.8)	75	5.3	10.6	8.9	-	2
CDA	2013		50g GCT (7.8)	75	5.3	10.6	9.0	-	1
SOGC	2002	All except low risk	50g GCT (7.8)	100	5.3	10.0	8.6	7.8	2
				75	5.3	10.0	8.6	-	2
BSD	2014	All	FPG (4.7)	75	5.1	10.0	8.5		1
NICE	2015	Clinical risk	75g OGTT	75	5.6	-	7.8	-	1
EASD	1991	NS	NS	75	5.5 or 6.0			9.0	1
JDS	2013	All	50g GCT (7.8)	75	5.1	10.0	8.5	-	2
DIPSI	2009	-	-	75	-	-	7.8		
ADIPS	2014	All, unless resources limited	75g OGTT	75	5.1	10.0	8.5	-	1
NZSSD	1998	All	50g GCT (7.8) 75g (8.0)	75	5.5	-	9.0	-	1
WHO	2013	All	75g OGTT	75	5.1	10.0	8.5	-	1

ADA: American Diabetes Association, ADIPS: Australian Diabetes in Pregnancy Society, BSD: Brazilian Society of Diabetes, CDA: Canadian Diabetes Association, C & C: Carpenter & Coustan, EASD: European Association for the Study of Diabetes, DIPSI: Diabetes in Pregnancy Study Group in India, FPG: Fasting Plasma Glucose, JDS: Japan Diabetes Society, NDDG: National Diabetes Data Group, NZSSD: New Zealand Society for the Study of Diabetes, NICE: National Institute for Health & Care Excellent, NS: Not specified, SOGC: Society of Obstetricians and Gynecologists of Canada, WHO: World Health Organization

Source: Adapted from (Agarwal et al, 2015)

1.3.3 Epidemiology of Gestational Diabetes Mellitus

1.3.3.1 Worldwide and European Countries

GDM is a common condition that is estimated to affect 1 - 14% of pregnant women (ADA, 2015). According to recent estimates, the burden of both GDM and diabetes is increasing worldwide (Wild et al., 2004; Feig et al., 2008). However, it is difficult to estimate the prevalence of GDM due to the choice and timings of the diagnostic tests and socio-demographic and environmental factors of the population

under study (Bener et al., 2013; Agarwal et al., 2005). In European countries, the prevalence of GDM ranges between 2 and 6%.

In the United States of America (USA) 7% of pregnant women are affected by GDM with more than 200,000 cases every year. In addition, two studies showed that incidence of GDM in multi-ethnic women in the USA increased from 4% in 1991 to 6% in 2002 (Olsen et al., 2016; Buchanan et al., 2012).

1.3.3.2 Asia and Middle Eastern Countries

Research suggests that the burden of GDM is higher in Asian women than European and American women. A study conducted in New York documented that South Asian women (Pakistani, Indian, Sri Lankan) had a higher prevalence of GDM than South East Asian (Malaysian, Thai, Cambodian, Filipino) and East Asian women (Japanese, Chinese, South Korean, Taiwanese) (Savitz et al., 2008). Another study conducted in Australia showed that South Asian women had the highest rate of GDM (69%) of other ethnic groups (Girgis et al., 2012). According to a review, the prevalence of GDM ranged from 3 to 21% in Asian women (Yuen & Wong, 2015). In China and India, GDM is reported to affect 13.9% and 14.3% of women (Alzaim & Wood, 2013).

The burden of GDM in Middle Eastern Countries is reported to be among the highest in the world. In Bahrain, the incidence of GDM has increased from 7.2% in 2002 to 12.5% in 2010 (Rajab et al., 2012). The burden of GDM has been reported as the highest (36.6%) in Saudi Arabia, while it was 16% in Qatar and 12 - 25% in the UAE (Al-Rubeaan et al., 2014; Bener et al., 2011; Agarwal et al., 2010).

1.3.4 Complications of Gestational Diabetes Mellitus

Gestational Diabetes increases the risk of various immediate and long-term complications in pregnant women and their offspring. Some of the major complications are discussed below.

1.3.4.1 Type 2 Diabetes Mellitus

It is well established that women with GDM are at increased risk of developing type 2 Diabetes in later years. A study reported that approximately 10% of women with GDM develop type 2 diabetes soon after the delivery and 20 - 60% develop type 2 diabetes within 5 to 10-year period after the pregnancy (Buchanan et al., 2012). A meta-analysis conducted on Caucasian and mixed population documented that the risk of diabetes was seven fold higher in women with GDM (Bellamy et al., 2009). In another systematic review of twenty eight epidemiological studies, the cumulative incidence of type 2 diabetes among pregnant women was found between 3 and 72% soon after the delivery and 42% after eight years of pregnancy (Kim et al., 2002).

1.3.4.2 Cardiovascular Diseases (CVDs)

Studies have consistently shown a significant relationship between GDM and CVDs. A matched case control study on pregnant women showed that women with GDM were at 51% higher risk of developing CVDs as compared to women without GDM (Fadl et al., 2014). Another population based study found 25% higher risk of CVDs in women with GDM compared to those without GDM (Goueslard et al., 2016). According to Shah and others women with GDM were at 70% higher risk of

developing coronary and cardiovascular events than women without GDM (Shah et al., 2008).

1.3.4.3 Metabolic Syndrome

Some evidence suggests positive association of GDM with metabolic syndrome (constellation of insulin resistance, hypertension and dyslipidemia). For instance, a meta-analysis of seventeen studies conducted in 2014 demonstrated 3.96 (95% CI: 2.99 - 5.26) higher odds of metabolic syndrome in women with GDM as compared to those not having GDM (Xu et al., 2014). In a follow up study of pregnant women, the risk of developing metabolic syndrome as per Adult Treatment Panel III criteria (presence of ≥ 3 risk factors) was 2.3 times higher in women with GDM than those without GDM (Gunderson et al., 2009).

1.3.4.4 Macrosomia in Offspring

Women with GDM are more likely to give birth to macrosomic babies, which increases risk for shoulder dystocia, bone fractures and nerve palsies (Buchanan et al., 2012). A cohort study conducted in Qatar reported that 10% of women with GDM gave birth to macrosomic babies versus 6% in non-GDM women ($p = 0.01$) (Bener et al., 2011).

1.3.4.5 Type 2 Diabetes in Offspring

Literature shows that offspring of women with GDM are at increased risk of glucose intolerance and type 2 Diabetes. According to a systematic review, nearly half (47%) of the cases of diabetes in youth can be attributed to GDM (Veeraswamy

et al., 2012), while another study showed that hyperglycemia in utero in Pima Indian women led to diabetes in 40% of their children (5 - 19 years) (Reece et al., 2009).

1.3.4.6 Obesity in Offspring

GDM is shown to increase the likelihood of obesity in children, adolescents and adults. In Pima Indian population, higher average body mass index (BMI) was observed in offspring aged 6 - 24 years who were born to women with GDM as compared to the offspring of women without GDM ($p = 0.003$) (Dabelea et al., 2005). Similarly, compared to 409 children of non-diabetic and non-GDM mothers, average BMI was significantly higher in 95 children (10 - 13 years) who were born to mothers with GDM and type 2 Diabetes (Crume et al., 2011).

1.3.5 Risk Factors of Gestational Diabetes Mellitus

1.3.5.1 Maternal Age

High maternal age is a significant risk factor of GDM. According to Reece et al. the risk of developing GDM was 7 - 10 times higher in pregnant women who were older than 24 years than those younger than 24 years (Reece et al., 2009). A retrospective cohort study of 656 women reported higher incidence of GDM in women aged 35 years and above versus younger women (18.6% vs 11.1%, $p = 0.01$) (Cozzolino et al., 2017). Similarly, another study showed a significant positive association of advancing maternal age, pre-pregnancy body mass index, family history of diabetes with GDM in Chinese women (Leng et al., 2015).

1.3.5.2 Race and Ethnicity

Studies have found that some ethnic groups are at a higher risk of developing GDM. Asian women are considered among the high-risk group of developing GDM. For instance, a longitudinal study conducted in the USA found that women who were from India, Middle East and Latin America were at a higher risk of developing GDM than other nationalities (Dode & Dos Santos, 2009). Similarly, according to another study from the USA, the age adjusted prevalence of GDM was the highest in Asian Indian (11%), Filipinos (9.6%) and South East Asian (8.8%) women and the lowest in White (4.2%) and Black (4.4%) women (Hedderson et al., 2010). Another study conducted in New York concluded that burden of GDM was higher in South Asian women than other nationalities that include South East Asian and East Asian women (Savitz et al., 2008).

1.3.5.3 Obesity

Obesity is considered as a strong risk factor for GDM. Moreover, a large body of evidence claims that GDM is increasing worldwide largely due to parallel rise in the burden of obesity. Studies have shown that obese women (BMI ≥ 30 kg/m^2) are at 3 times ($p < 0.001$) higher risk for developing GDM as compared to non-obese women (Reece et al., 2009; Hunt & Schuller et al., 2007). According to the results of a systematic review and a meta-analysis of eight studies, women with excessive weight gain were 40% ($p < 0.001$) more likely to develop GDM as compared to those without excessive weight gain (Rajab et al., 2012).

1.3.5.4 Family History of Type 2 Diabetes

Positive family history of type 2 Diabetes is an important risk factor of GDM. As reported by Cypryk and colleagues, 40% of women with GDM had a first degree relative with diabetes ($p < 0.05$) (Cypryk et al., 2008). While another study ascertained that positive family history of diabetes increased the risk of GDM by 115% (Yang et al., 2009). This relationship is further supported by the positive findings of a meta-analysis (Moosazadeh et al., 2017).

1.4 Overview of Vitamin D

Vitamin D is a fat-soluble hormone that exists in two major forms. Vitamin D_2 or Ergocalciferol is synthesized by yeasts and fungi and is naturally present in foods like fish, egg yolk, mushroom and dairy products. Vitamin D3 or Cholecalciferol is synthesized in the skin of mammals from 7-dehydrocholesterol by the exposure to ultraviolet B (UVB) irradiation. Vitamin D is biologically inert and requires hydroxylation for the activation. In the first step, vitamin D is converted to 25-hydroxyvitamin D 25(OH)D in the liver, also known as calcidiol. In the second step 1,25-dihydroxyvitamin D ($1,25(OH)_2D$) or calcitriol is produced in kidneys. These active forms of vitamin D are used as indicators of vitamin D status in the body (Dalgård, Petersen, Weihe, & Grandjean, 2011a). Vitamin D obtained from the food fulfills 10% of body's requirement of vitamin D while 90% of its requirement are met by the sunlight (Wagner et al., 2012).

1.4.1 Functions of Vitamin D

Vitamin D plays an essential role in maintaining various functions of the body. It helps in mineralization of bones by increasing the absorption of calcium and blocking the release of parathyroid hormone. It also regulates immune function, cell proliferation and cellular differentiation (Lips et al., 2010). In addition, it maintains normal insulin sensitivity by stimulating the secretion of insulin from the pancreas (Al-Shoumer & Al-Essa, 2015).

1.4.2 Recommended Intake of Vitamin D in Pregnant Women

There is a controversy over the ideal daily intake of vitamin D in pregnancy. In 2011, the Institute of Medicine Committee (IOM) recommended dietary intake of 600 IU of vitamin D per day in pregnancy (Institute of Medicine (US) Committee to Review Dietary Reference Intakes for Vitamin D and Calcium, 2011). As per recommendations of the Food and Nutrition Board, both pregnant and non-pregnant women aged less than 50 years are advised to take 200 IU of vitamin D per day (Mulligan et al., 2010). According to another study, 5000 IU/day are necessary to maintain normal vitamin D status in the body (Barrett & McElduff, 2010). In Scandinavia, pregnant women are advised to take 400 IU of vitamin D daily to maintain its adequate status of 25 nmol/l. In the USA and Canada, the daily recommended intake of vitamin D is 600 IU (Mulligan et al., 2010).

In the UAE and other gulf countries, guidelines for vitamin D supplementation have been developed recently. According to these guidelines, pregnant and breast feeding women are advised to take 1500 - 2000 IU of vitamin D daily (Haq et al., 2016). Besides setting up these guidelines, other initiatives such as fortification of

cooking oil, milk and milk products with vitamin D have been launched by the country to improve vitamin D levels in the population (Wimalawansa et al., 2013). However, various issues have been reported with these initiatives, which might be hampering their effectiveness. For instance, a study conducted in Al Ain in 2011 reported that the level of vitamin D fortification was not mentioned on the labels of oils. The study also found that 87% of milk products were fortified with vitamin D; however, only 39% of these fortified samples had the adequate levels (0.8-1.2 µg/100 ml) of vitamin D, 31% were under fortified and 30% were over fortified (Laleye et al., 2011). Although, this study has pointed out important issues in the fortification of food products, more research is required to support these claims.

1.4.3 Diagnosis of Vitamin D Deficiency and Insufficiency

Various guidelines exist to diagnose vitamin D deficiency and insufficiency. These guidelines vary with respect to cut-off points that are used to diagnose vitamin D deficiency and insufficiency (Kennel et al., 2010). The existence of multiple guidelines presents a major challenge in estimating and comparing the burden of vitamin D deficiency within and across populations. Also, it considerably affects the clinical management of vitamin D deficiency.

Two widely used guidelines for diagnosing vitamin D deficiency are those developed by (IOM) and the Endocrine Society Clinical Practice (Holick et al., 2011; Ross et al., 2011). The cut-off points for vitamin D concentration 25(OH)D recommended by these guidelines are elaborated in Table 1.3.

Table 1.3: Serum 25-Hydroxyvitamin D [25(OH)D] concentrations and vitamin D deficiency

25(OH)D concentration		Vitamin D status
nmol/L	ng/ml	
Institute of Medicine		
<30.0	<12.0	Deficiency
30.0-50.0	12.0-20.0	Insufficiency
≥50.0	≥20.0	Adequate/Sufficiency
>125.0	>50.0	High levels
The Endocrine Society Clinical Practice		
<50.0	<20.0	Deficiency
52.5-72.5	21.0-29.0	Insufficiency
≥75.0	≥30.0	Adequate/Sufficiency

Source: (Ross et al., 2011; Holick et al., 2011)

1.4.4 Epidemiology of Vitamin D Deficiency and Insufficiency

1.4.4.1 Worldwide and European Countries

Vitamin D deficiency is a global health problem. Approximately, one billion people worldwide are estimated to have vitamin D deficiency, while 50% have vitamin D insufficiency (Nair & Maseeh, 2012). In the US and Europe more than 40% of adults are vitamin D deficient.

Compared to the general population, vitamin D deficiency is more common in pregnant women due to increased demands of vitamin D in pregnancy (Dawodu et al., 2003; Seth et al., 2009). However, its prevalence varies remarkably across countries and continents due to various factors. Studies from the US, Australia, South Asia and the Middle East have reported that 20 - 98% of women develop vitamin D deficiency during pregnancy, while 66 - 100% develop vitamin D insufficiency (Narchi et al., 2010; Dalgård et al., 2011). Similar to these studies, a review

documented that 40 - 98% of women have vitamin D levels < 50 nmol/L (Dawodu & Wagner, 2007).

1.4.4.2 Asia and Middle Eastern Countries

There is some evidence that the levels of vitamin D are generally lower in Middle Eastern and South Asian women because of decreased dietary intake of vitamin D and inadequate sunlight exposure (Saadi et al., 2010; Nair & Maseeh, 2012; Eggemoen et al., 2016). A study conducted in Saudi Arabia found that 50% of pregnant women had vitamin D deficiency (Al-Faris et al., 2016). While several studies from other Middle Eastern countries have documented that the prevalence of vitamin D deficiency ranges between 10% and 60% (Dawodu et al., 2003; Bener, et al., 2013; Al-Mohaimeed et al., 2012).

Consistent with regional estimates, vitamin D deficiency is a major problem in the UAE. According to recent estimates, vitamin D deficiency effects 37 - 65% of the Emirati population (Laleye et al., 2011). Similar to the general population, a high proportion of pregnant women are vitamin D deficient in the country. A prospective study (75 women) showed that 69% of Emirati pregnant women were vitamin D deficient (< 10 ng/ml) (Narchi et al., 2010).

1.4.4.3 Consequences of Vitamin D Deficiency and Insufficiency

Inadequate levels of vitamin D are associated with various adverse health outcomes. Vitamin D deficiency increases the risk of osteoporosis and rickets (Holick & Chen, 2008). In pregnant women vitamin D deficiency may lead to preeclampsia, miscarriage, cesarean section and pre-term birth. In utero or early life,

inadequate levels of vitamin D increase the risk of neonatal hypocalcaemia, rickets, type 1 diabetes, asthma and schizophrenia (Nair & Maseeh, 2012; Aghajafari et al., 2013).

1.4.4.4 Risk factors of Vitamin D Deficiency and Insufficiency

Age

Vitamin D deficiency influences all age groups. Nevertheless, elderly people are at higher risk of developing vitamin D deficiency because their skin loses efficiency to synthesize vitamin D, they have inadequate intake of vitamin D and spend more time indoors (Lips et al., 2010; Nair & Maseeh, 2012).

Sex

Studies have shown that females are more likely to develop vitamin D deficiency than males particularly in Middle East countries where women cover their most of the body parts and do not get frequent exposure to sunlight (Verdoia et al., 2015).

Skin Pigmentation

Synthesis of vitamin D is associated with skin pigmentation. Melanin in the skin scatters UVR-B and delays the conversion of 7-dehydrocholesterol to pre-vitamin D3. Therefore, synthesis rate of vitamin D is slower in people with dark skin as compared to light-skinned people. In light-skinned adults, full exposure to the sun till skin turns slightly pink would generate 10,000 - 20,000 IU of vitamin D within 24 hours of exposure. In contrast, people with dark skin need ten times more exposure

to generate the same amount of Vitamin D (Bonilla et al., 2014; Nair & Maseeh, 2012).

Clothing Style

Clothing could influence the synthesis of vitamin D from the skin. In the Middle East, Africa and other Muslim countries, women practice of veil limits their exposure to sunlight. Various studies have demonstrated veil as an independent factor of vitamin D status (Lips et al., 2010; Saadi et al., 2007).

Latitude and Seasonality

Vitamin D levels differ according to the latitude. People living in Northern latitudes are more vitamin D deficient than those living in southern latitudes. Climate type and seasons also affect the levels of vitamin D (Holmes et al., 2009). In winter, vitamin D deficiency is higher than the summer in northern latitudes. In the UAE, the situation differs as in the summer vitamin D deficiency is more frequent compared to the Winter season because people avoid the sun in the summer (Al Anouti et al., 2011).

Diseases and Drugs

Some diseases such as liver disease, cystic fibrosis and Crohn's disease can cause vitamin D deficiency by affecting the metabolism and absorption of vitamin D. Also, the chronic use of steroids, immune-suppressants, anticonvulsants, rifampicin, and antiretroviral drugs can also affect the metabolism and absorption of vitamin D and calcium (Nair & Maseeh, 2012).

Dietary Consumption of Vitamin D

Research has demonstrated that the foods rich in vitamin D such as fatty fish and cod liver oil are consumed more by some countries like Sri Lanka and Vietnam as compared to Pakistanis (Lips et al., 2010).

1.5 Literature Review

1.5.1 Association Between Vitamin D Deficiency and GDM

1.5.1.1 Worldwide

Research suggests that vitamin D deficiency may contribute to the development of GDM (Burris et al., 2012; Lacroix et al., 2014; McElduff et al., 2008). However, the exact mechanism of association is unclear. Some literature describes that vitamin D is essential for maintaining insulin sensitivity and glucose homeostasis by enhancing insulin sensitivity and secretion. Also, it plays an important role in stimulating insulin receptors and taking glucose in adipose cells and muscles. Furthermore, it helps in reducing the inflammatory process that decreases the functional capacity of pancreatic ß-cells. Therefore, the deficiency of vitamin D may cause dysfunction in pancreatic ß-cells and impair the function and uptake of insulin (Joergensen et al., 2014; El Lithy et al., 2014).

The epidemiological evidence regarding the association between vitamin D deficiency and risk of GDM is contradictory. Numerous studies from various parts of the world have shown a positive association between these conditions. For instance, in 2015, a meta-analysis of twenty observational studies that included 9209 participants concluded that pooled odds of GDM were 1.53 (95% CI: 1.33-1.75)

times in women with vitamin D deficiency as compared to women with no deficiency (Zhang et al., 2015). Two other meta-analysis of thirty-one and seven studies showed that pooled odds of GDM were 1.49 (95% CI: 1.18-1.89) and 1.61 (95% CI: 1.19 - 2.18, p = 0.002) respectively in women with insufficient vitamin D versus women with sufficient levels (Aghajafari et al., 2013; Poel et al., 2012). A cross-sectional study conducted in a hospital in Turkey reported a significant association of severe vitamin D deficiency with GDM (Zuhur et al., 2013). Moreover, according to a review, seven large observational studies conducted in Iran, Korea, China and Arab Countries reported a significant association between vitamin D deficiency and GDM (Joergensen et al., 2014).

In contrast, some studies have shown no association between GDM and vitamin D. A meta-analysis that included thirteen randomized control trials found similar risk (RR: 0.88, 95% CI: 0.5 - 1.52) of GDM in both vitamin D deficient and non-deficient groups (Pérez-López et al., 2015). A prospective cohort study of 310 women carried out in Madigan Army Medical Center in Washington, USA claimed that association between vitamin D deficiency and GDM was insignificant (Adjusted OR:2.60, 95% CI: 0.28-27.4) (Flood-Nichols, et al., 2015). Similar to observational studies, a double randomized control trial failed to find a significant difference in the incidence of GDM in women who received 5000 IU (10.5%) of vitamin D in pregnancy versus those who received 400 IU daily (13%) (Yap et al., 2014).

1.5.1.2 Middle East and the UAE

Like other countries, studies carried out in the Middle East have reported conflicting findings concerning the association between GDM and vitamin D

deficiency. In addition, only a few cohort studies have been carried out in the region and none in the UAE to examine the relationship between these intricate problems.

A cross-sectional study conducted in Egypt on 160 pregnant women aged 24-40 years found that average vitamin D levels were not significantly different between vitamin D deficient and non-deficient groups (47.3 ± 10.2 vs 46.6 ± 6.1) (El Lithy et al., 2014). Another case-control study conducted in Turkey including 122 pregnant women (44 with GDM and 78 non-GDM), did not find any correlation of serum vitamin D with serum fasting glucose ($p = 0.9$), insulin levels ($p = 0.2$) or HbA1c levels ($p = 0.1$) (Ates et al., 2017).

Conversely, a cross-sectional study in Iran found significant inverse associations between serum level of 25(OH)D and HbA1c at the beginning of the pregnancy ($p < 0.001$), insulin levels in the second trimester ($p = 0.004$) and blood sugar ($p = 0.045$) after consuming 75 g glucose. Likewise, another study in Iran noted a significant difference in vitamin D levels among GDM and normal groups (16.5 ± 10.4 vs 23.0 ± 18.3, $p < 0.001$) (Maghbooli et al., 2008; Jafarzadeh et al., 2015). In Qatar, a cohort study of 1,873 Arab pregnant women above 24 weeks' gestation showed that women with vitamin D deficiency 25(OH) D < 10 ng/ml) had higher odds of GDM (odds ratio: 1.4, 95% CI: 1.1 - 11.8, $p = 0.019$) as compared to those without GDM (Bener et al., 2011).

1.5.2 Association between Diet and GDM

Diet is known to have a profound effect on the development of GDM during pregnancy. Therefore, the role of diet during pregnancy and in GDM has been explored extensively by clinical and epidemiological studies worldwide.

1.5.2.1 Red Meat

Studies have found that consumption of large amount of red and processed meat is found to be positively correlated with GDM, as cholesterol and saturated fats in the meat negatively affect insulin sensitivity and ß-cell function of pancreas, which may cause GDM. In addition, nitrates which are regularly used as preservative in processed meat are linked to the development of type 2 diabetes (Bao et al., 2014; Zhang & Ning, 2011). According to a cohort study, increasing intake of red and processed meat by one serving per day, elevated the risk of GDM by 61 and 64% respectively (C. Zhang et al., 2006). Also, a systematic review of ten prospective, six cross-sectional and five case-control studies also reported a positive association between higher consumption of red and processed meat with GDM (Zhang et al., 2015).

1.5.2.2 Dietary Fiber and Vegetables

Dietary fiber, which include cereal, vegetables and fruit fiber has been found beneficial in reducing the risk of GDM because these foods have low glycemic index and therefore can achieve better glucose control by decreasing the postprandial glycaemia and slowing down the absorption rate of the carbohydrates (Schulze et al., 2004). As per findings of a study, increasing intake of total fiber by 10g per day decreased the risk of GDM by 26% (95% CI: 9% - 49%), while 5g increment in cereal or fruit fiber per day decreased the risk of GDM by 2.15 folds as compared to common diet consumption (Zhang & Ning, 2011). A few studies have also shown the positive impact of Low Glycemic Index (LGI) on maternal fasting glucose levels and reducing risk of macrosomia (Moses et al., 2009; Louie et al., 2010). A cohort study

from China reported that the consumption of vegetables decreased the risk of GDM (He et al., 2015). While the Nurse's Health Study II noticed an inverse association between prudent dietary pattern (fruits, green leafy vegetables, poultry, fish) and GDM (Zhang et al., 2006). According to the findings of another cohort study, pregnant women who adhered to Mediterranean diet during pregnancy had a lower incidence of GDM and better glucose tolerance than those who did not adhere to Mediterranean diet (Karamanos et al., 2014).

1.5.2.3 Fatty Diet

The consumption of diet rich in fat has been linked to the increased risk of GDM. A cohort study claimed that a high fat and low carbohydrate diet is associated with increased risks of glucose intolerance and GDM (Bao et al., 2014). In the cohort study from Italy, the consumption of saturated fats was found to play an independent role in the development of GDM even in the absence of classical risk factors of GDM (Bo et al., 2001). Similarly, another cohort study reported a significant association of high intake of fat and cholesterol during pregnancy with the risk GDM (Bowers et al., 2012). Additionally, a study demonstrated that replacing carbohydrate with fat (per 1% of total calories) elevated the risk of GDM by 10% (Saldana et al., 2004).

1.5.2.4 Sweets and Sugar Beverages

The consumption of sweets and sugar beverages during pregnancy is positively associated to GDM. According to the Nurse's Health Study II, women who drank more than 5 servings of sweetened cola were at 22% higher risk of developing GDM than those who drank less than 1 serving (Chen et al., 2009). A study from China

revealed that intake of sweets during pregnancy increased risk of GDM by 23% (He et al., 2015).

1.5.3 Association Between Physical Activity and GDM

Exercise improves insulin sensitivity and glycogen synthesis, which results in lower glucose concentrations in the blood. Therefore, exercise is considered as an effective intervention in reducing the risk of type 2 Diabetes (Dempsey et al., 2004; Davenport et al., 2008). However, the evidence regarding the effect of exercise on GDM is conflicting with the majority of studies demonstrating a significant effect of exercise on lowering the risk of GDM. For instance, an observational study mentioned that the risk of GDM is reduced by 20 - 55% in those women who are engaged in various forms and intensities of physical activity during and before pregnancy (Redden et al., 2011). In addition, a prospective study of 909 women showed that women who participated in any vigorous physical activity prior 12 months of their pregnancy had a 56% lower risk of developing GDM (Dempsey et al., 2004). Another study claimed that women who participated in any vigorous physical activity twelve months before pregnancy had a 44% lower risk of developing GDM as compared to inactive women during the same period (Oken et al., 2006). Similarly, two systematic reviews concluded that physical activity intervention reduced the likelihood of GDM by 28 and 33% respectively (Russo et al., 2015; da Silva et al., 2016). In contrast to these studies, a review of thirteen randomized control trials showed an insignificant difference in the risk of developing GDM (RR: 0.92, 95% CI :0.68 - 1.23) between intervention (diet and exercise) and control group (Bain et al., 2015).

Research suggests that amount of physical activity is decreased considerably during pregnancy most probably due to symptoms of nausea and fatigue in early pregnancy and perceived risk to maternal and fetal health (Perichart-Perera et al., 2009). That is why, the Canadian Diabetes Association (CDA) encourages obstetric-risk tailored physical activity during pregnancy, while the American College of Obstetricians and Gynecologists (ACOG) advises 30 minutes of moderate physical activity on most days of the week (Chasan-Taber et al., 2011).

To our knowledge, no published data on physical activity in pregnant women are available in the UAE. However, a cross-sectional study carried out in 2009 on Emiratis mentioned that only 30% of Emirati females walked for at least 30 minutes 3 times per week (Al-Kaabi et al., 2009).

Chapter 2: Methods

2.1 Aims and Objectives

2.1.1 Aims

The overall aim of this study was to improve understanding about risk factors of GDM and the relationship between vitamin D deficiency and GDM in Emirati population. The findings of this study will guide health regulatory authorities and stakeholders in designing evidence based guidelines and interventions for screening, preventing and managing GDM in the UAE. Also, these findings will help clinicians in the early identification of high risk women and better management and prevention of GDM and its complications.

2.1.2 Objectives

2.1.2.1 Primary Objectives

- To estimate the incidence of GDM in Emirati pregnant women.
- To investigate whether vitamin D deficiency in early pregnancy (≤ 15 weeks of gestation) is associated with an increased risk of developing GDM in Emirati pregnant women.

2.1.2.2 Secondary Objectives

- To examine the association of physical activity before pregnancy with the development of GDM in pregnant Emirati women.
- To explore what type of diet consumed during early pregnancy is associated with an increased risk of GDM in pregnant Emirati women.

- To identify significant risk factors of GDM in pregnant Emirati women.

2.2 Study Design

A prospective cohort study design was adopted to estimate the incidence of GDM and to investigate the effect of vitamin D deficiency, physical activity, diet and other risk factors on the incidence of GDM. This study design has many advantages over other observational designs. First, it allows estimating the incidence of disease. Second, this design is useful in investigating multiple risk factors of diseases. Third, it enables to establish the temporal relationship between an exposure and outcome. Last, a well-designed cohort study can control for confounding factors and recall bias (information bias) as we used FFQ and GPAC questionnaires and the participants were asked about their family history of diabetes. One of the most important confounding factor to this study is the body mass index, family history of Diabetes and vitamin D supplements which have adjusted during the analysis by using logistic regression (Sedgwick et al., 2013).

2.3 Study Site

The study was conducted in Ras Al Khaimah (RAK), which is one of the seven Emirates of the UAE as it was the best destination for the principle investigator who is from RAK and no studies have been carried out on this issue in RAK. In 2015, the total population of RAK was estimated to be 345,000 (RAK Center for Statistics, 2015)

A total of eighteen primary healthcare centers are located in RAK were selected to present the whole city form East to West and South to North. These

clinics belong to the RAK medical district and operate under the umbrella of Ministry of Health. The clinics are designated to provide dental treatment, general treatment, mother and child health services, comprehensive antenatal care and nursing services to both Emirati and expatriate population. In 2015, a total of 858,850 people visited these clinics among which 21981 were antenatal visits (Statistics Department, Ras Al Khaimah Medical District [Ministry of Health], 2015).

2.4 Study Population

We chose eight primary healthcare centers from various parts of the Emirate that were more frequently utilized for antenatal care. The study population comprised Emirati pregnant women who visited these primary healthcare centers for antenatal care between March 2014 and July 2015. A total of 5918 pregnant women sought antenatal care at these clinics during that period (Statistics Department, Ras Al Khaimah Medical District [Ministry of Health], 2015).

2.5 Selection of Study Participants

2.5.1 Inclusion Criteria

The following inclusion criteria were used to select study participants;

- Emirati women who were living in RAK.
- Those women who were aged between 18 and 45 years.
- Women who were ≤ 15 weeks of gestation.

2.5.2 Exclusion Criteria

The following criteria were used to exclude study participants;

- Women who were younger than 18 years and/or older than 45 years.
- Women who initiated antenatal care after 15 weeks of pregnancy.
- Women with non-singleton pregnancies.
- Women who had previous history of GDM.
- Women who had a positive history of type 1 and type 2 Diabetes mellitus.
- Women who had abnormal liver function and/or hepatitis
- Women who had Human Immunodeficiency Virus (HIV)
- Women who had impaired kidney function

The researcher determined the eligibility of participants by reviewing their medical records followed by interviews to confirm their eligibility. Out of the total (800) women who were screened at selected eight clinics between March 2014 and July 2015, 700 women met the inclusion criteria, while 622 agreed to participate in the study. For an overview of selection process, (see Figure 2.1).

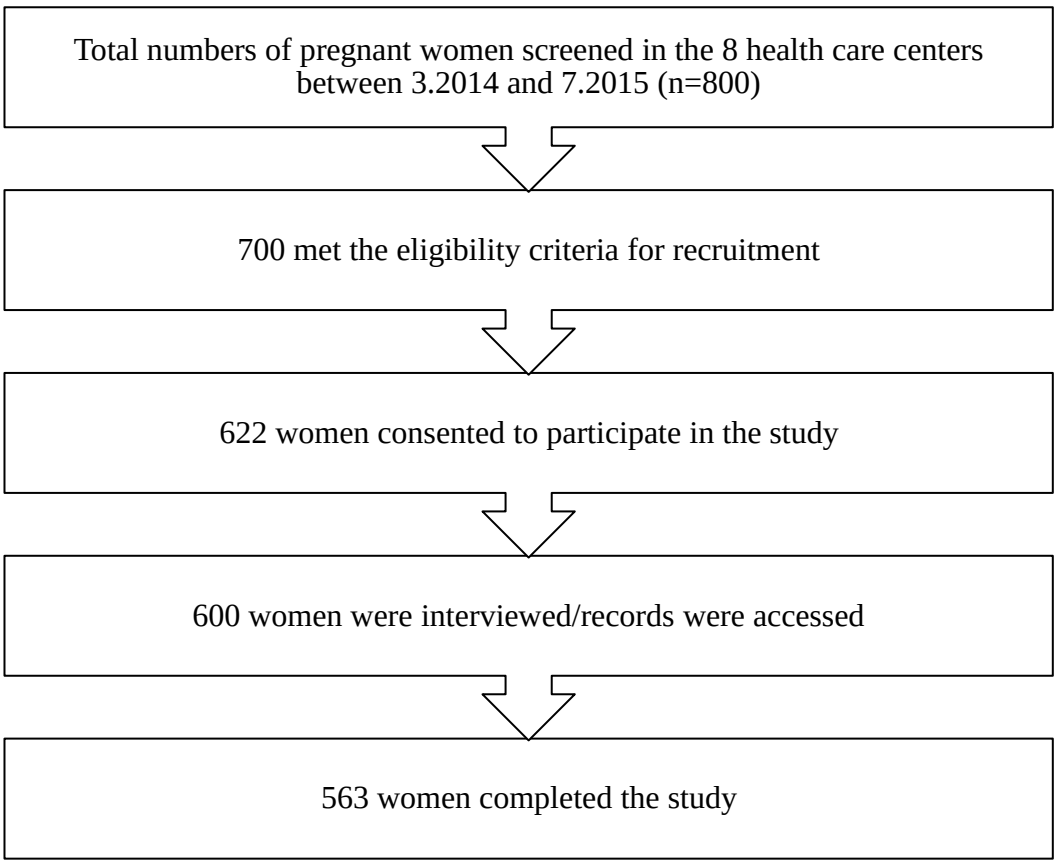

Figure 2.1: Flow chart of selection procedure of study participants

2.6 Sample Size Calculation

A sample of 507 participants (169 exposed and 338 non-exposed) was required to detect with an 80% power, a relative risk of 1.8. This minimal relevant relative risk value was based on the study by Wang and others who showed that subjects with 25(OH)D level < 25 nmol/l had a 1.8-fold higher risk of developing GDM than those with 25(OH) D level ≥ 25 nmol/l. We assumed that 10% of non-exposed women (i.e. without vitamin D deficiency) would have GDM during their follow-up. This assumption was based on the data by (Agarwal et al., 2010), who had shown that the prevalence of GDM in the UAE was 13% including both exposed (vitamin D deficient) and non-exposed women. The sample size was calculated using the function *epi.studysize* from the package *epiR* of the statistical software R version

3.0.2 (R Development Core Team et al., 2008). The probability of type 1 error (α) was set to 5% and the sample ratio of exposed to unexposed was set to 2. This choice of unexposed to exposed ratio was based on the finding by Saadi et al. (2010), that the proportion of women with a Vitamin D level in the UAE less than 25 nmol/l (i.e. exposed women) was 35.1%.

2.7 Study Measurements

2.7.1 The Outcome Variable

Gestational diabetes was the outcome variable in this study. In RAK primary healthcare centers, GDM is diagnosed in 24 - 28 weeks of gestation by using the two-step approach. In the first step, fasting blood glucose (FBG) of women is measured. Those women who are not fasting are asked to fast for at least 10 hours and come back the next day for the FBG test. In the second step, 75 g OGTT is administered to measure 2-hour postprandial blood glucose.

In this study, we obtained the data of FBG and OGTT and adopted the WHO (2013) to diagnose GDM. According to these criteria, GDM was defined as having fasting blood glucose ≥ 5.1 mmol/l or a 2-hour postprandial glucose ≥ 8.5 mmol/l in 24 - 28 weeks of gestation.

2.7.2 The Primary Exposure Variable

The primary exposure variable was vitamin D deficiency in the first trimester of pregnancy. At baseline, serum concentration of vitamin D metabolites were determined by radioimmunoassay kits from immunodiagnostic systems Cobas e-411 from Roche Company USA. As per IOM criteria, vitamin D insufficiency was

defined as serum concentration of 25(OH)D 30-50 nmol/L or 12 - 20 ng/ml and deficiency as serum concentration of 25(OH)D < 30 nmol/L or < 12 ng/ml (Ross et al., 2011) (See Table 1.3 for the cut-offs of vitamin status).

2.7.3 Other Measurements

2.7.3.1 Socio-demographic Characteristics

In socio-demographic characteristics information about age, household size, level of education, occupation, income, marital status and medical history was collected at baseline. (See Appendix 1 for details).

2.7.3.2 Anthropometric Indicators

Anthropometric indicators included height, weight and body mass index (BMI) before and during pregnancy. At baseline, height was measured in centimeters (cm) and weight in kilograms (kg) by using SACA machine. The BMI (kg/m^2) was calculated by dividing the weight in kg with height in square meters. Obesity was defined as BMI $\geq$ 30 kg/m^2 and overweight as BMI $\geq$ 25 - 29.9 kg/m^2 by using the cut-offs recommended by the World Health Organization (WHO, 2004) (See Appendix 1 for details).

2.7.3.3 Blood Pressure

Systolic and diastolic blood pressure measurements were taken at baseline by using Welch Allyn 53000 sphygmomanometers. High blood pressure was defined as systolic blood pressure $\geq$140 mmHg or diastolic blood pressure $\geq$ 90 mmHg by using

the National Institute for Health and Clinical Excellence (NICE) guidelines (NICE, 2016) (See Appendix 1 for details).

2.7.3.4 Physical Activity

The physical activity during the last seven days was measured at baseline by using The Global Physical Activity Questionnaire (GPAQ) ("Global Physical Activity Questionnaire," n.d.). The GPAQ is an internationally validated tool that is developed by the WHO. It subjectively collects information on physical activity over the past week at work; travel to and from places and recreational activities as well as sedentary behavior. It comprises 16 questions which cover vigorous and moderate activity at work, transport activity, vigorous and moderate activity during leisure time and sitting time. (See Appendix 2 for details). The intensity of physical activity is expressed in Metabolic Equivalents (METs), which is defined as the ratio of working metabolic rate relative to the resting metabolic rate. The METs were calculated by following the GPAQ guidelines and low activity level was defined as METs < 600 per week. In addition, the amount of physical activity performed during the last seven days was categorized into 'low', 'moderate' and 'high' physical activity by following the GPAQ guidelines.

2.7.3.5 Dietary Intake

The dietary intake was measured by using a validated Food Frequency Questionnaire (FFQ). It is one of the most commonly used tools in epidemiologic studies to assess long-term nutritional exposure and to study the relationship between diet and chronic diseases. A short version of FFQ abbreviated as SFFQ has been developed for the UAE and Kuwait (Dehghan et al., 2005). We modified some

questions of SFFQ to adopt it for our study. For each food item, participants indicated their average frequency of consumption over the past year of a specified serving size by checking 1 of the 9 frequency categories. We collapsed these frequency categories into 'monthly = 1 - 3 times per month ', 'weekly = 1 - 6 times per week' and 'daily = 1 - 6 times per day' consumption of food. Food items were grouped into nine broad food groups such milk and milk products, fruits, vegetables, meat and meat products, cereals and cereal products, beverages and sweets and nuts with the addition of oil and fat used for cooking and preparing the food, number of meals consumed out of the home and the vitamins and minerals supplements during the last six months (in addition to vitamin D) (See Appendix 3 for details).

2.8 Data Collection Procedure

The principal investigator received training in data collection from the Ministry of Health of the UAE. The principal investigator then trained eight nurses in data collection (one from each primary healthcare centers). Prior to data collection, the FFQ, GPAQ and socio-demographic questionnaires were translated into Arabic and pilot tested on a random sample of 25 women. After the piloting, corrections and modifications were made in questionnaires if needed.

At baseline, the principal investigator and nurses conducted face to face interviews with 600 study participants to collect the information about socio-demographic characteristics, medical history, physical activity and dietary intake in pregnancy. In addition, nurses measured blood pressure, height and weight while phlebotomists drew blood samples to measure fasting blood glucose and vitamin D.

The blood samples from each health center were transported on the same day to a tertiary care hospital laboratory for the analysis.

After collecting the baseline information, participants were informed by physicians to revisit antenatal clinics in their 24 - 28 weeks of gestation. During their follow-up visit, the blood samples were drawn to screen for GDM. The investigator assessed the medical records of participants or conducted telephonic interviews to confirm the presence of GDM during the pregnancy. The attrition rate was 11.2 %.

2.9 Ethical Considerations

2.9.1 Ethical Approval of Study

The study was approved by Al Ain Medical District Human Research Ethics Committee (AMDHREC), RAK Research Ethics Committee in RAK Medical District (RAKREC) (See Appendices 4 and 5). The AMDHREC reviews all studies that are performed on human subjects. The purpose of this committee is to ensure that human researches meet acceptable standards of scientific merits, ethics, patient safety and cultural propriety of the UAE.

2.9.2 Informed Consent

Eligible participants were given detailed information about the study and were assured of strict confidentiality (See Appendix 6). Both oral and written consent were sought from participants who agreed to participate in the study (See Appendix 7).

2.9.3 Confidentiality

A unique identification number was assigned to each participant and names were removed in the data to conceal their identity. Personal information that could identify participants was kept in a separate computer and was accessed only by the researcher. All data were stored in the password protected computer. All participants were assured that their identities will not be disclosed in any publication.

2.10 Timeline

The study was completed in a period of approximately thirty-nine months. The study was approved in March 2014 and write-up was completed in June 2017. See Table 2.1 for the detailed timeline of the study.

Table 2.1: Time line of the study

	2014			2015				2016				2017	
Items	Mar-May	Jun-Aug	Sep-Dec	Jan-Mar	Apr-Jun	July-Sep	Oct-Dec	Jan-Mar	Apr-Jun	July-Sep	Oct-Dec	Jan-Mar	Apr-Jun
Ethical approval													
Data collection													
Data analysis													
Write-up													

2.11 Data Analysis

The principal investigator entered the data in IBM Statistical Package for Social Sciences (SPSS) version 22.0. The data were inspected for inconsistencies, key-stroke errors and missing values to ensure its quality. The statistical analysis was performed in Stata SE version 14.2. In descriptive analysis, qualitative variables were summarized as frequencies and percentages, while quantitative variables were

summarized as mean ± standard deviation (± SD). The distribution of age and BMI before and during pregnancy was shown in histograms. The prevalence of obesity, high blood pressure, family history of diabetes and vitamin D insufficiency and deficiency were tabulated as well as presented in bar charts. The incidence of GDM, overall and by vitamin D status was summarized as frequencies and percentages and presented as tables and bar charts. Also, the incidence of GDM was cross-tabulated as frequencies and percentages with baseline demographic and clinical characteristics, physical activity levels and dietary intake. Chi-square and Fischer Exact tests were applied to compare differences in proportions of GDM status according to different qualitative variables. Unpaired Student t-tests and Wilcoxon Rank Sum tests were used to test average and median differences in quantitative variables by GDM status.

Simple and multiple binary logistic regression analysis were performed to ascertain the association of vitamin D deficiency, vitamin D status, vitamin D (continuous), physical activity and diet with GDM and identify other significant risk factors of GDM. In the first step, the simple logistic regression analysis was performed to estimate crude odds ratios (COR), confidence intervals (CIs) and p values of GDM for vitamin D deficiency, diet, physical activity and other risk factors. In the second step, multiple logistic regression analysis was performed to estimate adjusted odds ratios (AOR), CIs and p values of GDM for vitamin D deficiency, diet, and physical activity along with other risk factors that had p values < 0.10 in simple logistic regression. The p value < 0.05 and 95% CI were chosen to determine statistical significance. This multiple logistic regression analysis was repeated for all three types of variables of vitamin D ([vitamin D deficiency vs

normal vitamin D], [vitamin D insufficiency vs normal vitamin D, vitamin deficiency vs normal vitamin D], [vitamin D as a continuous variable]).

Chapter 3: Results

3.1 Recruitment and Follow-up

The entire data collection was completed in a period of twenty-four months approximately. More specifically, the first participant was recruited in March 2014 and the last participant in July 2015 (See Figure 3.1). The last follow-up was completed in February 2016.

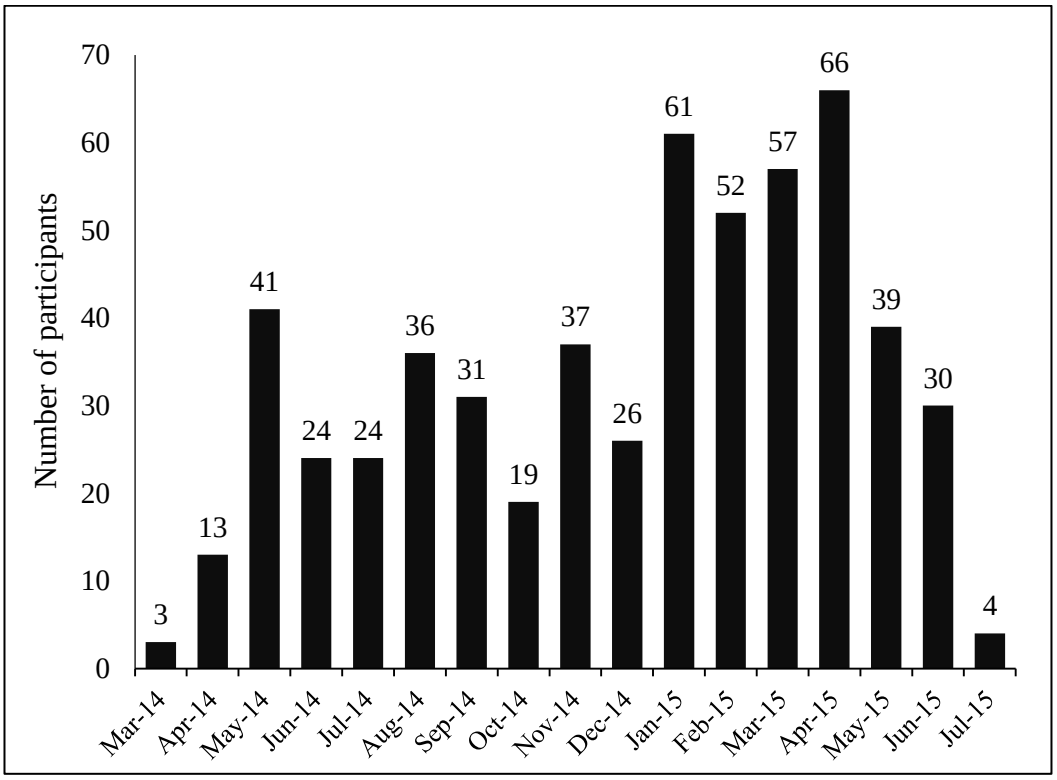

Figure 3.1: Recruitment of participants per calendar

3.2 Baseline Demographic Characteristics

A total of 563 pregnant women completed the study, while the information regarding the outcome (GDM) was available for 533 women. Sixty-seven women did not complete the study due to miscarriage before 24 weeks and loss to follow-up.

The mean age of women was 29.5 ± 5.6 years and was approximately normally distributed (see Figure 3.2). Above half of the women (52.4%) completed the high school and 36.1% had a college or university degree. The majority of women (98.9%) were married, three-fourth were housewives (75.5%) and around one fifth (18%) were working in non-government organizations. Sixty-three percent of the women had a positive family history of diabetes mellitus (Figure 3.3). (See Table 3.1 for details).

Table 3.1: Baseline demographic characteristics of women

Variables	n (%) / Mean ±SD
Age – Years, Mean ±SD	29.5 ±5.6
Number of women > 18 years, Median (iqr)	3 (2)
Education level, n (%)	
Up to primary	23 (4.1)
Up to secondary	42 (7.5)
Up to high school	295 (52.4)
≥ College/University	203 (36.1)
Marital Status, n (%)	
Married	557 (98.9)
Separated/Divorced/Widowed	6 (1.1)
Work Status, n (%)	
Government employee	93 (16.5)
Non-government employee	8 (1.4)
self employed	10 (0.2)
Student	36 (6.4)
House wife	425 (75.5)
Monthly income – AED, Median (iqr)	24000 (14000)
Family history of Diabetes Mellitus, n (%)	360 (63.9)

n: Frequency, SD: Standard Deviation, iqr: Interquartile Range, AED: Arab Emirates Dirham

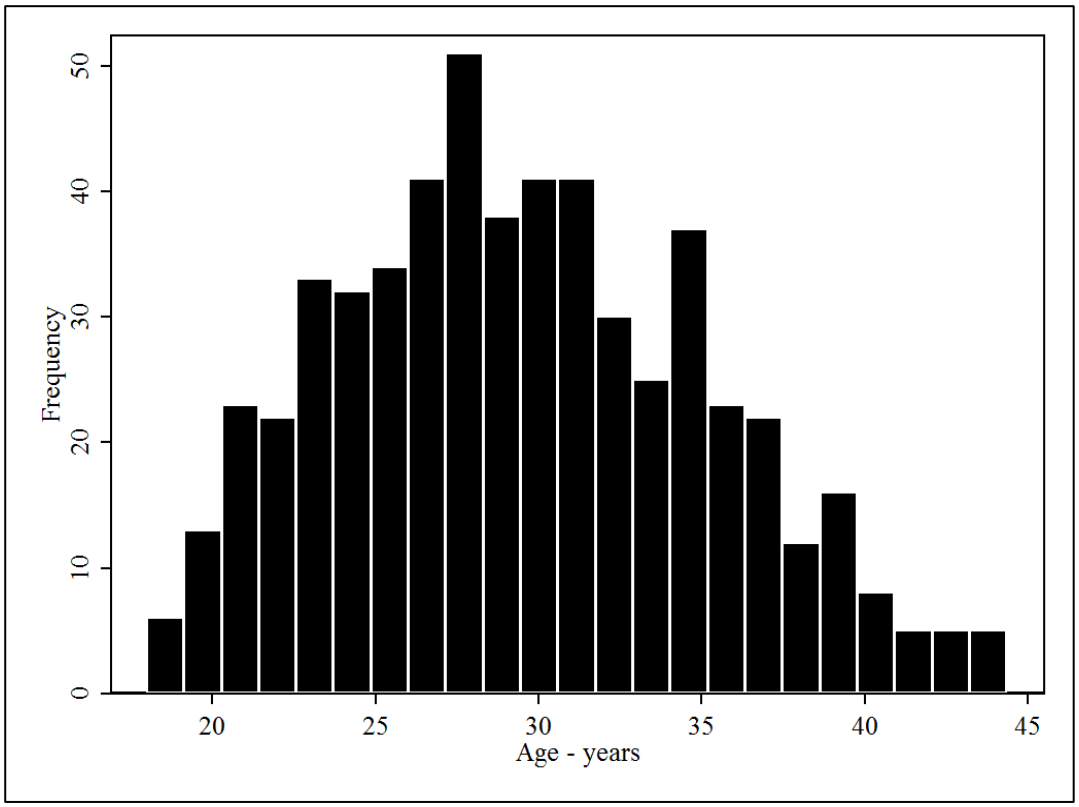

Figure 3.2: Distribution of age of women

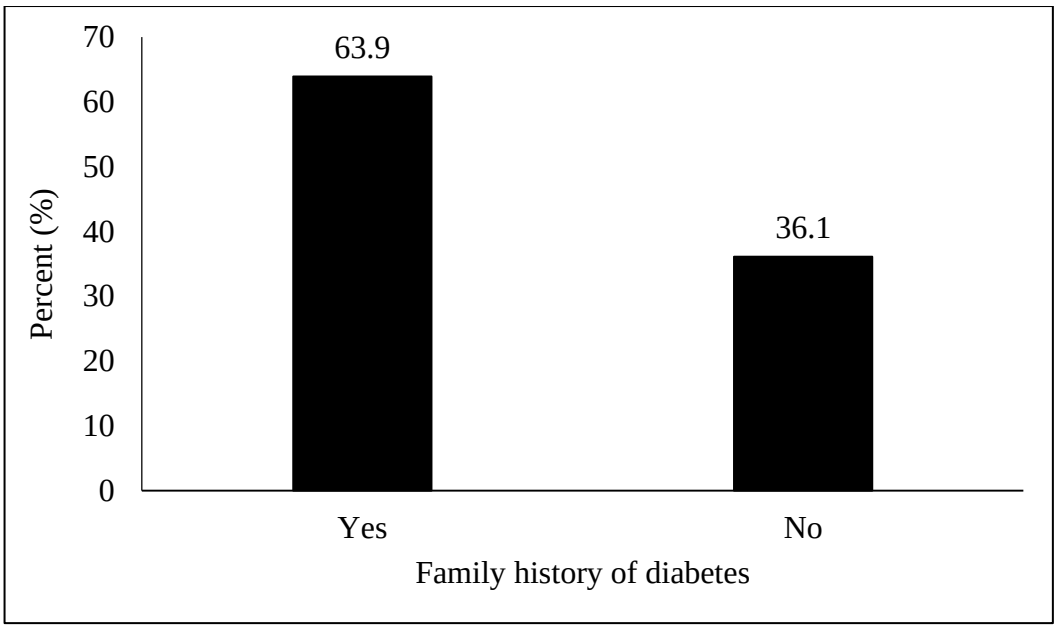

Figure 3.3: Family history of diabetes in women

3.3 Baseline Clinical Characteristics

The Table 3.2 shows that the mean body mass index (BMI) of women before pregnancy was 27.2 ± 6.8 kg/m^2 and during early pregnancy was 27.8 ± 6.8 kg/m^2. The distribution of BMI before and during pregnancy was slightly positively skewed due to high values of BMI for some women (See Figure 3.4). Approximately one fourth (26.5%) of the women were overweight and 30.5% were obese before pregnancy (see Figure 3.5). The mean systolic blood pressure was 107.1 ± 11.4 mmHg and diastolic pressure was 64.2 ± 9.5 mmHg. A small proportion (1.6%) of women had a hypertension according to NICE criteria (See Figure 3.6).

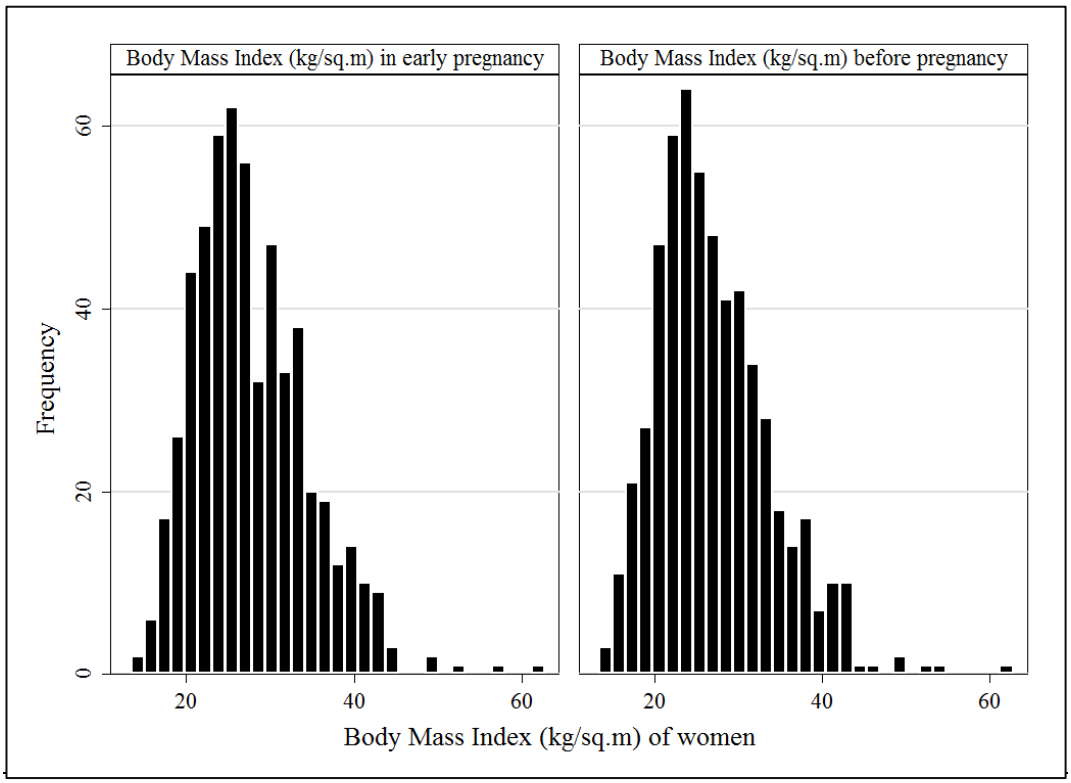

Figure 3.4: Distribution of Body Mass index of women before and during early pregnancy

Table 3.2: Baseline clinical characteristics of women

Variables	n (%) / Mean ±SD
Anthropometric indices	
Height – cm, Mean ±SD	158 ±5.3
Weight before pregnancy – kg, Mean ±SD	68.1 ±17.4
Weight during pregnancy – kg, Mean ±SD	69.7 ±17.5
Body Mass Index before pregnancy – kg/m^2, Mean ±SD	27.2 ±6.8
Body Mass Index before pregnancy categories – WHO, n (%)	
Normal (< 25.0 kg/m^2)	242 (43.0)
Overweight (25.0 - 29.9 kg/m^2)	149 (26.5)
Obese (≥ 30 kg/m^2)	172 (30.5)
Body Mass Index during early pregnancy – kg/m^2, Mean ±SD	27.8 ±6.8
Blood Pressure – mmHg	
Systolic Blood Pressure, Mean ±SD	107.1 ±11.4
Diastolic Blood Pressure, Mean ±SD	64.2 ±9.5
High blood pressure, n (%)	9 (1.6)

n: Frequency, SD: Standard Deviation, OGTT: Oral Glucose Tolerance Test, ADA: American Diabetes Association, IOM: Institute of Medicine, WHO: World Health Organization

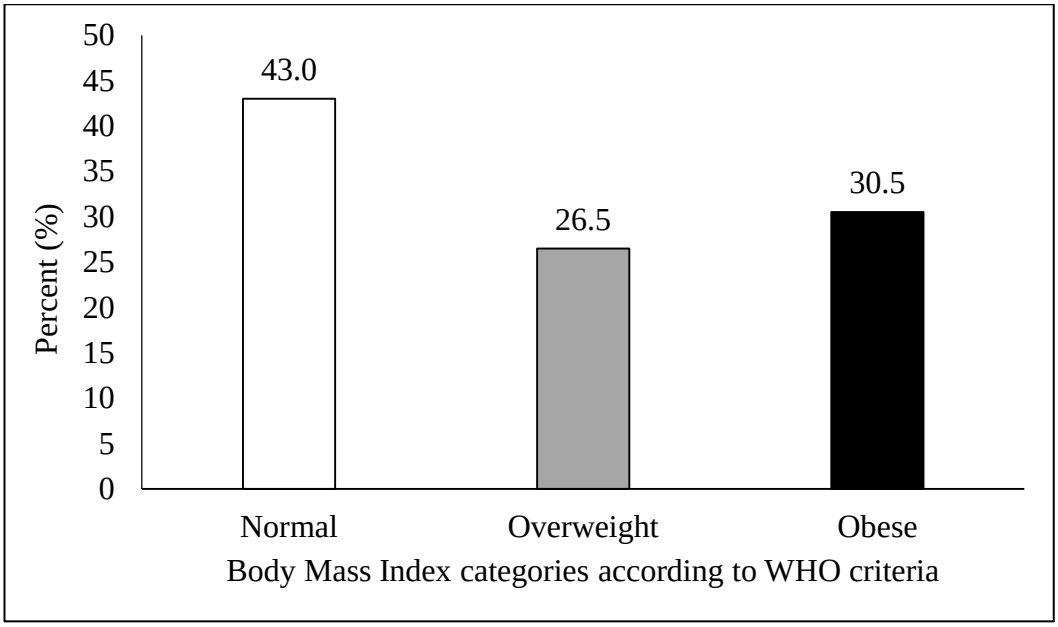

Figure 3.5: Prevalence of overweight and obesity in women

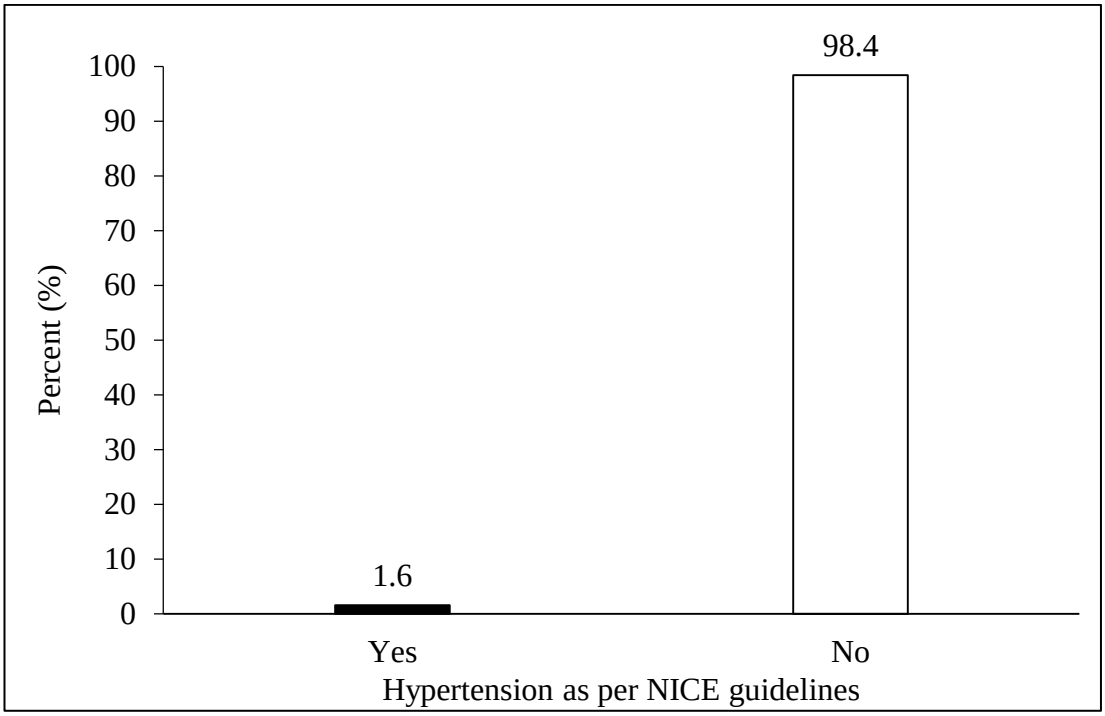

Figure 3.6: High blood pressure in women

3.4 Baseline Physical Activity Levels

Table 3.3 shows that the median (IQR) METs score per week of pregnant women was 840 (1320) minutes and sedentary time per day was 240 (280) minutes. Physical activity per day related to work was reported by 6.6% of women, travel by 51.7% and recreation by half (50.4%) of the women. According to the WHO criteria, below one tenth of the women (8.5%) reported performing high physical activity, 55.6% moderate physical activity, while 35.9% of women reported performing low physical activity (See Figure 3.7).

Table 3.3: Physical activity levels of women

Variables	n (%)
Total METs per week, Median (iqr)	840 (1320)
Low physical activity (METs <600 / week), n (%)	129 (34.4)
Physical activity levels per day, n (%)	
High	46 (8.5)
Moderate	300 (55.6)
Low	194 (35.9)
Work related moderate and vigorous physical activity per day, n (%)	37 (6.6)
Travel physical activity per day, n (%)	291 (51.7)
Recreational moderate and vigorous physical activity per day, n (%)	284 (50.4)
Sedentary time per day – minutes, Median (iqr)	240 (280)

n: frequency, iqr: Interquartile Range, METs: Metabolic Equivalents

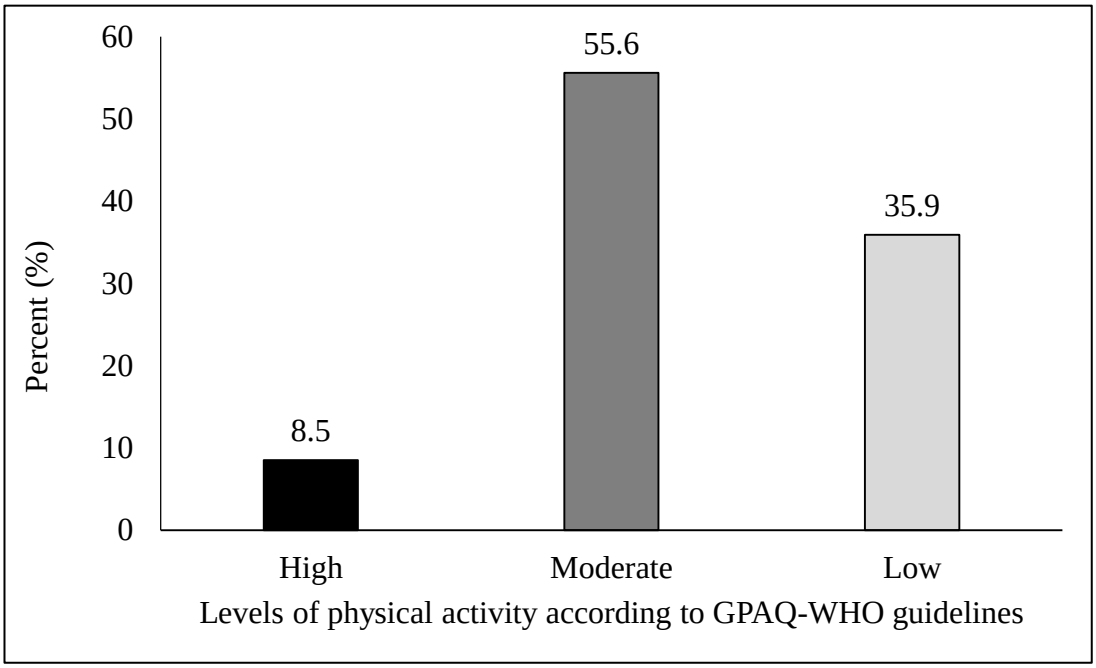

Figure 3.7: Levels of physical activity in women

3.5 Baseline Supplements and Dietary Intake

Table 3.4 shows the use of vitamin D and other supplements in women at baseline. Approximately one fifth (19.0%) of the women reported using vitamin D, multivitamins or / and mineral supplements during the last six months. Of the women who were using vitamin D supplements, the majority (98.2%) were using these supplements for a period of less than one year.

Table 3.4: Use of supplements in women

Variables	n (%)
Use of multivitamins /minerals during the last six months	107(19.0)
Duration of using multivitamins/minerals	
< 1 year	104 (18.5)
1-3 years	2 (0.4)
4-6 years	1 (0.2)
Vitamin D supplements use during the last six months	112 (19.9)
Frequency of vitamin D supplements use	
< one year	110 (98.2)
1-3 years	1 (0.9)
4-6 years	1 (0.9)

n: Frequency

Table 3.5 shows intake of milk and milk products in women. These three categories of intake (monthly, weekly and daily) correspond to the nine categories in the FFQ as we consider the daily intake 1 - 6 times per day, the weekly intake 1– 6 times per week and monthly 1 - 3 times per month. About one fourth (26.3%) of the women reported consuming milk daily, 29.8% weekly and 43.9% monthly. Nearly one fifth (19.5%) of the women were consuming yogurt daily, while the majority (61.8%) were consuming it weekly.

Table 3.5: Milk and milk products intake in women

Variables	n (%)
Milk	
Monthly	247 (43.9)
Weekly	168 (29.8)
Daily	148 (26.3)
Yogurt	
Monthly	105 (18.7)
Weekly	348 (61.8)
Daily	110 (19.5)
n: Frequency	

Table 3.6 shows the distribution of consumption of vegetables among women. A high proportion of women reported eating fresh (68.2%) and leafy (46.5%) vegetables daily. Below one fifth (19.3%) of the women reported eating cooked vegetables daily, 47% weekly and 33% monthly. The least proportion of women reported eating fried (4.2%) and boiled (1.1%) potatoes daily.

Table 3.6: Vegetables intake in women

Variables	n (%)
Fresh vegetables	
Monthly	37 (6.5)
Weekly	142 (25.2)
Daily	384 (68.2)
Cooked vegetables	
Monthly	189 (33.5)
Weekly	265 (47.0)
Daily	109 (19.3)
Leafy vegetables	
Monthly	110 (19.5)
Weekly	191 (35.0)
Daily	262 (46.5)
Boiled potato	
Monthly	441 (78.3)
Weekly	116 (20.6)
Daily	6 (1.1)
Fried potato	
Monthly	225 (39.9)
Weekly	314 (55.7)
Daily	24 (4.2)
n: Frequency	

Table 3.7 shows the distribution of fruits and nuts intake in women. Overall, the consumption of fruits per day among women was low. The most frequently consumed fruit each day by women was dates (46.0%), followed by nuts (9.2%). The least frequently consumed fruits each day by women were mango (4.4%) and grapes (4.6%).

Table 3.7: Fruits and Nuts intake in women

Variables	n (%)
Banana	
Monthly	188 (38.5)
Weekly	263 (53.9)
Daily	37 (7.6)
Grapes	
Monthly	339 (60.3)
Weekly	197 (35.1)
Daily	26 (4.6)
Mango	
Monthly	404 (71.8)
Weekly	134 (23.8)
Daily	25 (4.4)
Date	
Monthly	146 (27.9)
Weekly	158 (28.1)
Daily	259 (46.0)
Nuts	
Monthly	283 (50.3)
Weekly	228 (40.5)
Daily	52 (9.2)
n: Frequency	

Table 3.8 shows the consumption pattern of meat in women. Chicken was reported as the most frequently consumed meat by women (21.8%), followed by fish (8.2%), while processed (1.0%) and red (2.1%) meats were consumed by the lowest proportion of women.

Table 3.8: Meat intake in women

Variables	n (%)
Fresh red meat	
Monthly	189 (33.5)
Weekly	362 (64.3)
Daily	12 (2.1)
Processed meat	
Monthly	490 (87.0)
Weekly	67 (11.9)
Daily	6 (1.0)
Chicken	
Monthly	29 (5.2)
Weekly	411 (73.0)
Daily	123 (21.8)
Fish	
Monthly	83 (14.7)
Weekly	434 (77.1)
Daily	46 (8.2)
n: Frequency	

Table 3.9 presents the information on the intake of sweets and beverages in women. A significant proportion of women reported eating sweets (34.8%) daily. In beverages, the highest proportion of women reported drinking tea (62.2%) daily and 55.2% reported drinking fresh juice daily. A small proportion of women reported consuming soft drink (13.9%) daily.

Table 3.9: Sweets and beverages intake in women

Variables	n (%)
Sweets	
Monthly	91 (16.1)
Weekly	276 (49.0)
Daily	196 (34.8)
Beverages	
Soft drinks	
Monthly	345 (61.2)
Weekly	140 (24.8)
Daily	78 (13.9)
Fresh juices	
Monthly	50 (8.8)
Weekly	202 (35.8)
Daily	311 (55.2)
Tea	
Monthly	103 (18.3)
Weekly	110 (19.5)
Daily	350 (62.2)
Coffee	
Monthly	226 (40.1)
Weekly	145 (25.8)
Daily	192 (34.1)
n: Frequency	

Table 3.10 shows the frequency of intake of cereals among women. The most frequently consumed cereals each day by women were bread (88.9%) and rice (83.8%). The least frequently consumed food each day by women were pizza (0.4%) and pasta (3.2%).

Table 3.10: Cereals intake in women

Variables	n (%)
Rice	
Monthly	9 (1.6)
Weekly	82 (14.56)
Daily	472 (83.8)
Bread	
Monthly	3 (0.53)
Weekly	59 (10.4)
Daily	501 (88.9)
Pasta	
Monthly	83 (14.7)
Weekly	462 (82.1)
Daily	18 (3.2)
Pizza	
Monthly	353 (62.7)
Weekly	208 (36.9)
Daily	2 (0.4)
n: Frequency	

3.6 Baseline Distribution of Vitamin D Status

The mean serum concentration of vitamin D in pregnant women was 12.7 ± 8.1 ng/ml, below three fifth (58.3%) of the women had a vitamin D deficiency and one fourth (26.4%) had an insufficiency according to IOM criteria (See Table 3.11 and Figure 3.8).

Table 3.11: Baseline vitamin D status of women

Variables	n (%) / Mean ±SD
Vitamin D – ng/ml, Mean (±SD)	12.7 ±8.1
Vitamin D levels – IOM, n (%)	
Normal (≥ 20 ng/ml)	86 (15.3)
Insufficiency (12 - 20 ng/ml)	148 (26.4)
Deficiency (< 12 ng/ml)	327 (58.3)
Vitamin D levels – IOM, n (%)	
No deficiency (≥ 12 ng/ml)	234 (41.7)
Deficiency (< 12 ng/ml)	327 (58.3)

n: Frequency, SD: Standard Deviation, IOM: Institute of Medicine

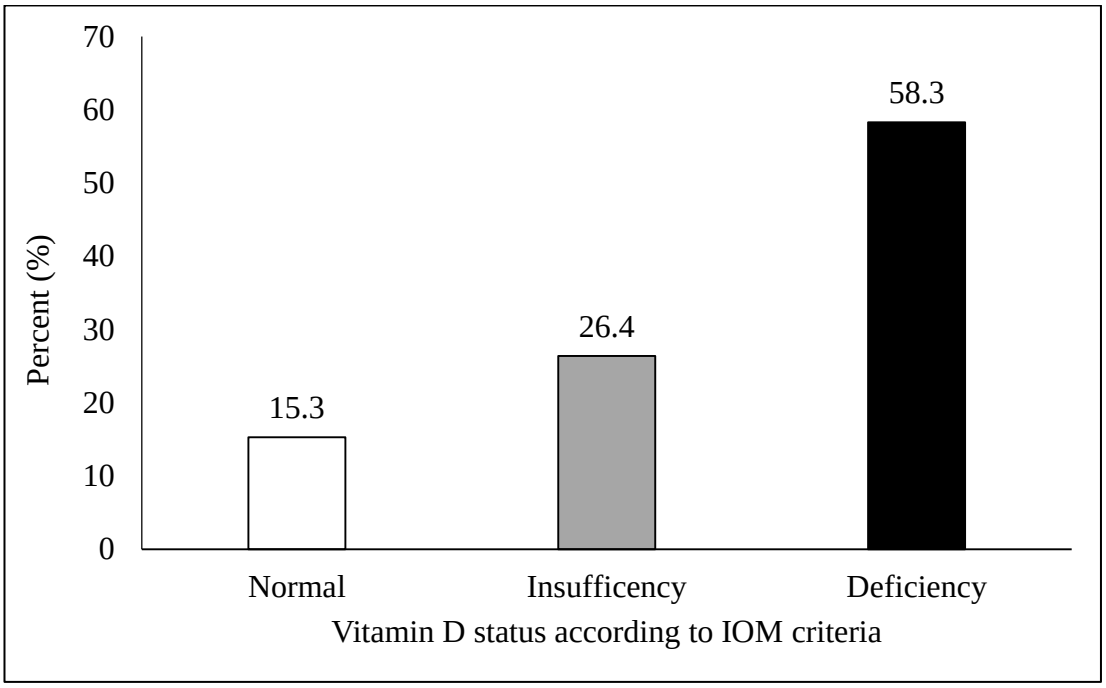

Figure 3.8: Baseline vitamin D insufficiency and deficiency in women

3.7 Incidence of Gestational Diabetes

3.7.1 Overall Incidence of Gestational Diabetes

In pregnant women, the mean fasting OGTT was 4.6 ± 0.6 Mmol/L, post-prandial OGTT was 5.8 ± 1.4 Mmol/L and fasting blood sugar was 4.7 ±0.43 Mmol/L. The overall incidence of GDM was 15.2% (95% CI: 12.4% - 18.5%) as per WHO (2013) criteria (See Figure 3.9 and Table 3.12).

Table 3.12: Gestational Diabetes status of women

Variables	n (%) / Mean ±SD
Fasting OGTT – Mmol/L, Mean (±SD)	4.6 ± 0.61
Fasting Blood Sugar – Mmol/L, Mean (±SD)	4.7 ± 0.43
Post-prandial OGTT – Mmol/L, Mean (±SD)	5.8 ± 1.4
Incidence of Gestational Diabetes – WHO, n (%)	81(15.2)

n: Frequency, SD: Standard Deviation, OGTT: Oral Glucose Tolerance Test, ADA: American Diabetes Association

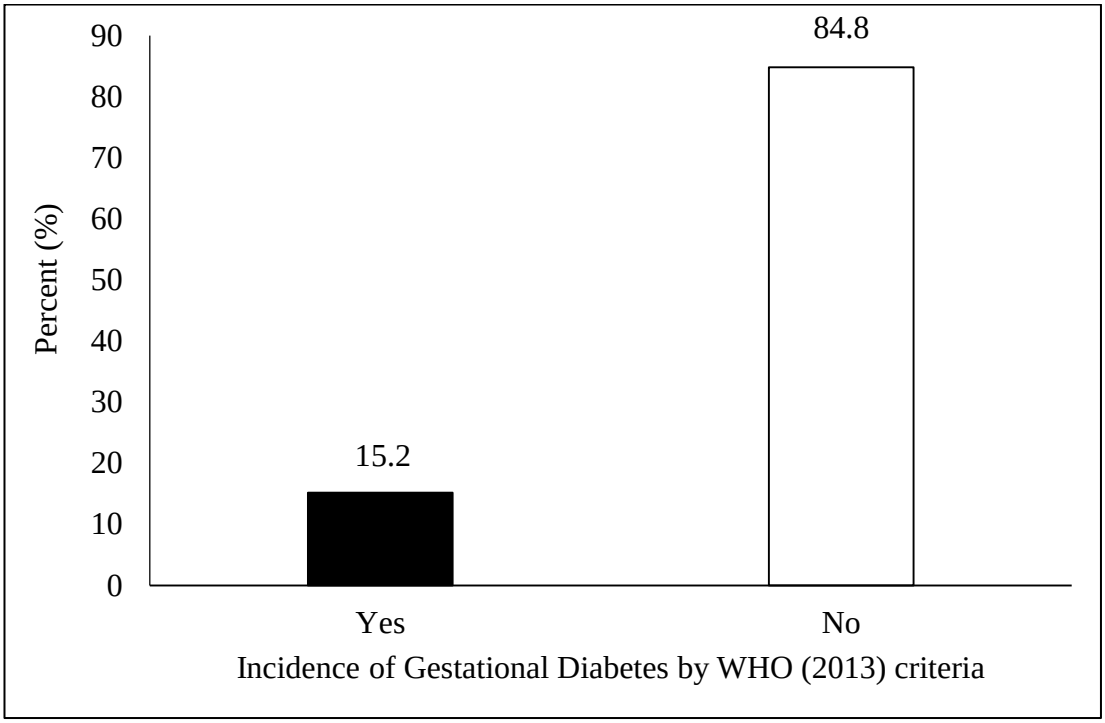

Figure 3.9: Overall incidence of Gestational Diabetes

3.7.2 Incidence of Gestational Diabetes by Baseline Demographic Characteristics

Table 3.13 shows the incidence of GDM by demographic characteristics of women. Women with GDM (31.1 ± 5.4 years) were older (p = 0.008) than those without GDM (29.3 ± 5.7 years). There were no significant differences in the incidence of GDM by education level (p = 0.941), and type of occupation (p = 0.365). The incidence of GDM was slightly higher (p = 0.089) in women with positive family history of diabetes (17.3%) as compared to women without family history of diabetes (11.5%).

Table 3.13: Incidence of GDM by baseline demographic characteristics of women

Variables	All	GDM (n=81)	No GDM (n=452)	P Value
Age – Years, Mean ±SD	533	31.1 ± 5.4	29.3 ± 5.7	0.008
Education level, n (%)				
Up to primary	22	4 (18.2)	18 (81.8)	0.941
Up to secondary	37	6 (16.2)	31 (83.8)	
Up to high school	285	41 (14.4)	244 (85.6)	
≥ College/University	189	30 (15.9)	159 (84.1)	
Work Status, n (%)				
Government employee	87	14 (16.1)	73 (83.9)	0.365
House wife	404	65 (16.1)	339 (83.9)	
Other	42	2 (4.6)	40 (95.1)	
Family history of Diabetes, n (%)				
Positive	342	59 (17.3)	283 (82.7)	0.089
Negative	191	22 (11.5)	169 (88.5)	

N: Frequency, SD: Standard Deviation
Chi-square and Fischer Exact tests were applied to compare proportions.
Unpaired t-tests were applied to compare means.

3.7.3 Incidence of Gestational Diabetes by Baseline Clinical Characteristics

Table 3.14 shows the distribution and average differences in clinical characteristics of women by GDM status. Average BMI before pregnancy (29.9 ± 8.0 vs 26.7 ± 6.3, $p < 0.001$) and fasting (5.5 ± 0.7 vs 4.5 ± 0.4, $p < 0.001$) and 2-hour postprandial (7.9 ± 1.7 vs 5.5 ± 1.0, $p < 0.001$) OGTT were significantly higher in women with GDM as compared to women without GDM. Likewise, average vitamin D levels (12.3 ± 7.9 vs 12.8 ± 8.3, $p < 0.001$ were significantly lowers in GDM women compared to those without GDM. The average systolic and diastolic blood pressures were not significantly different between women with GDM and those without GDM. The incidence of GDM was significantly ($p = 0.002$) different by BMI categories i.e. 9.6% in women with normal BMI, 15.7% in overweight women and 22.6% in obese women (See Figure 3.10).

Table 3.14: Incidence of Gestational Diabetes by baseline clinical characteristics of women

Variables	GDM (n=81)	No GDM (n=452)	P Value
Anthropometric indices			
Body Mass Index before pregnancy – kg/m^2, Mean ±SD	29.9 ±8.0	26.7 ±6.3	<0.001
Body Mass Index – Cat, n (%)			
Normal (< 25.0 kg/m^2)	22 (9.6)	207 (90.4)	0.002
Overweight (25.0-29.9 kg/m^2)	22 (15.7)	118 (84.3)	
Obese (≥30 kg/m^2)	37 (22.6)	127 (77.4)	
Body Mass Index during pregnancy – kg/m^2, Mean ±SD	30.4 ±7.8	27.4 ±6.4	<0.001
Blood Pressure – mmHg			
Systolic Blood Pressure, Mean ±SD	108.9 ±11.5	107.5 ±11.8	0.989
Diastolic Blood Pressure, Mean ±SD	67.7 ±9.2	65.3 ±18.5	0.854
High blood pressure, n (%)	79 (97.5)	445 (98.5)	0.632
Biochemical parameters			
Fasting OGTT – Mmol/L, Mean ±SD	5.5 ±0.7	4.5 ±0.4	<0.001
Post-prandial OGTT – Mmol/L, Mean ±SD	7.9 ±1.7	5.5 ±1.0	<0.001
Fasting Blood Sugar – Mmol/L, Mean ±SD	4.9 ±0.4	4.7 ±0.4	<0.001
Vitamin D – ng/ml, Mean ±SD	12.3±7.9	12.8 ±8.3	<0.001

n: Frequency, SD: Standard Deviation, OGTT: Oral Glucose Tolerance Test
Chi-square tests were applied to compare proportions. Unpaired tests were applied to compare means.

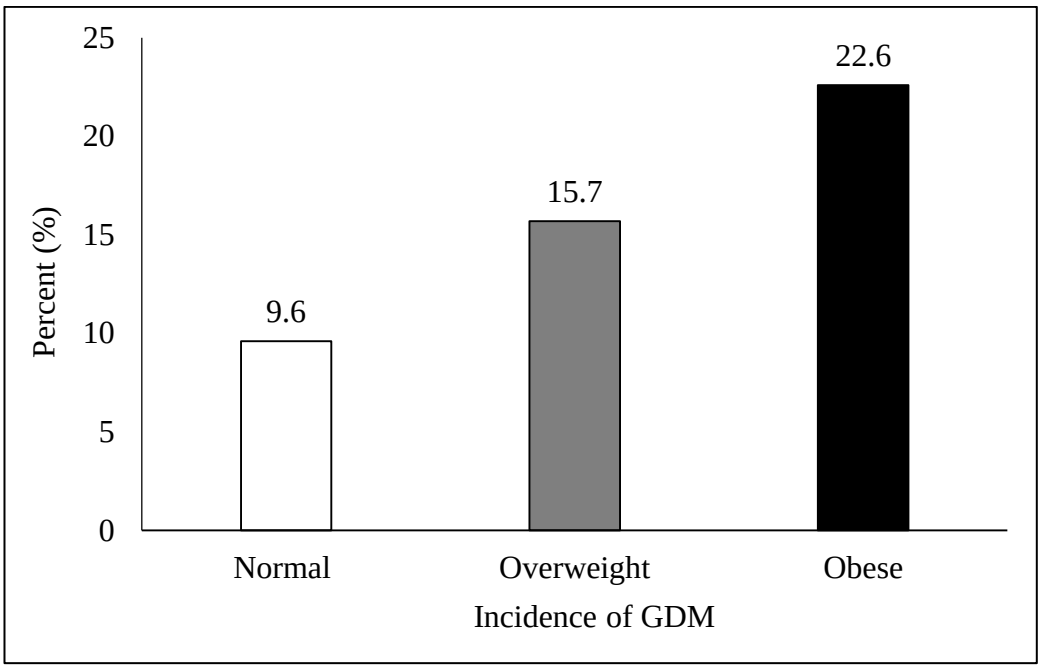

Figure 3.10: Incidence of GDM by baseline Body Mass Index categories

3.7.4 Incidence of Gestational Diabetes by Baseline Physical Activity Levels

Table 3.15 shows the comparison of physical activity levels in women with and without GDM. The three categories of the physical activity correspond to the GPAQ questionnaire as we used the GPAQ Analysis Guide (For further information: www.who.int/chp/steps).

The median (iqr) METs per week (870 [1280] vs 840 [1320], p = 0.447) and sitting time per day (300 [180] vs 240 [180], p = 0.628) were not significantly different in women with GDM versus those with no GDM. The incidence of GDM was not significantly (p = 0.329) different between women with low (11.4%) versus adequate (15.1%) METs weekly. Likewise, the incidence of GDM was similar (p = 0.821) among women who performed high (16.7%), moderate (14.2%) and low (16.0%) physical activity in early pregnancy (See Figure 3.11). Similarly, the incidence of GDM was insignificantly lower in pregnant women who performed

travel (12.7% vs 17.8%, p = 0.101) and recreational (13.5% vs 17.1%, p = 0.247) moderate and physical activities per day than those women who did not perform these activities.

Table 3.15: Incidence of Gestational Diabetes by baseline physical activity levels of women

Variables	All	GDM (n=81)	No GDM (n=452)	P Value
		n (%)	n (%)	
Total METs per week, Median (iqr)	533	870 (1280)	840 (1320)	0.447
METs, n (%)				0.329
<600 per week (Low)	123	14 (11.4)	109 (88.6)	
≥600 per week (Adequate)	238	36 (15.1)	202 (84.9)	
Physical activity levels – WHO criteria, n (%)				0.821
High	42	7 (16.7)	35 (83.3)	
Moderate	282	40 (14.2)	242 (85.8)	
Low	147	30 (16.0)	157 (84.0)	
Work related moderate and vigorous physical activity per day, n (%)				0.740
Yes	35	6 (17.1)	29 (82.9)	
No	498	75 (15.1)	423 (84.9)	
Travel related physical activity per day, n (%)				0.101
Yes	275	35 (12.7)	240 (87.3)	
No	258	46 (17.8)	212 (12.2)	
Recreational moderate and vigorous physical activity per day, n (%)				0.247
Yes	275	37 (13.5)	238 (86.5)	
No	258	44 (17.1)	214 (82.9)	
Sedentary time per day – minutes, Median (iqr)	526	300 (180)	240 (180)	0.628

n: Frequency, METs: Metabolic Equivalent, iqr: Interquartile Range
Chi-square tests were applied to compare proportions. Wilcoxon Rank Sum tests were applied to compare medians.

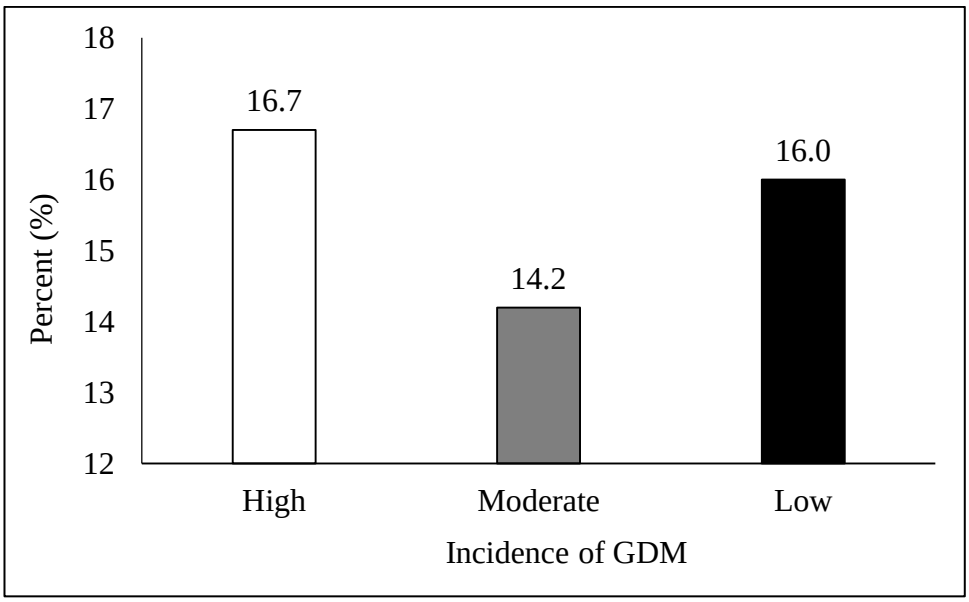

Figure 3.11: Incidence of GDM by baseline levels of physical activity of women

3.7.5 Incidence of Gestational Diabetes by Supplements and Dietary Intake

The incidence of GDM was similar in women who used multivitamin (15.1% vs 15.2%, p = 0.620) and vitamin D supplements (12.3% vs 15.9%, p = 0.347) versus those who did not use these supplements (See Table 3.16 for details).

Table 3.16: Incidence of Gestational Diabetes by supplements intake in women during the last six months

Variables	All	GDM (n=81)	No GDM (n=452)	P Value
		n (%)	n (%)	
Multivitamins /minerals supplements use during the last six months				0.620
Yes	99	15 (15.1)	84 (84.9)	
No	434	66 (15.2)	368 (84.3)	
Vitamin D supplements use during the last six months				0.347
Yes	106	13 (12.3)	93 (87.7)	
No	427	68 (15.9)	359 (84.1)	

n: Frequency
Chi-square and Fischer Exact tests were applied to compare proportions.

Table 3.17 shows the incidence of GDM by the consumption of milk and milk products. No differences in the incidence of GDM were observed by the frequency of consumption of milk (p = 0.759) and yogurt (p = 0.348).

Table 3.17: Incidence of Gestational Diabetes by milk and milk products intake in women

Variables	All	GDM (n=81)	No GDM (n=452)	P Value
		n (%)	n (%)	
Milk				0.759
Monthly	241	34 (14.1)	207 (85.9)	
Weekly	148	25 (16.9)	123 (83.1)	
Daily	144	22 (15.3)	122 (84.7)	
Yogurt				0.348
Monthly	102	20 (19.6)	82 (80.4)	
Weekly	329	48 (14.6)	281 (85.4)	
Daily	102	13 (12.7)	89 (87.3)	

n: Frequency
Chi-square and Fischer Exact tests were applied to compare proportions

Table 3.18 shows the incidence of GDM by the consumption of vegetable among pregnant women. The incidence of GDM was different (p = 0.056) among women who ate cooked vegetables daily (20.0%), weekly (16.8%) and monthly (10.3%). No significant differences were observed in the incidence of GDM by the frequency of intake of fresh vegetables (p = 0.493), leafy vegetables (p = 0.320), fried potato (p = 0.698) and boiled potato (p = 0.923).

Table 3.18: Incidence of Gestational Diabetes by vegetable intake in women

Variables	All	GDM (n=81)	No GDM (n=452)	P Value
		n (%)	n (%)	
Fresh vegetables				0.493
Monthly	36	3 (8.3)	33 (91.7)	
Weekly	135	21 (15.6)	114 (84.4)	
Daily	362	57 (15.7)	305 (84.3)	
Cooked vegetables				0.056
Monthly	184	19 (10.3)	165 (89.7)	
Weekly	244	41 (16.8)	203 (83.2)	
Daily	105	21 (20.0)	84 (80.0)	
Leafy vegetables				0.320
Monthly	105	13 (12.4)	92 (87.6)	
Weekly	179	24 (13.4)	155 (86.6)	
Daily	249	44 (17.7)	205 (82.3)	
Boiled potato				0.923
Monthly	417	62 (14.9)	355 (85.1)	
Weekly	110	18 (16.4)	92 (83.6)	
Daily	6	1 (16.7)	5 (83.3)	
Fried potato				0.698
Monthly	213	32 (15.1)	181 (85.0)	
Weekly	298	47 (15.0)	251 (84.2)	
Daily	22	2 (9.1)	20 (90.9)	

n: Frequency
Chi-square and Fischer Exact tests were applied to compare proportions

Table 3.19 shows the incidence of GDM by the consumption of fruits and nuts among pregnant women. The incidence of GDM significantly different by frequency of intake of dates in early pregnancy among women (p = 0.035). As such, it was the highest among women who ate dates daily (18.2%), followed by those who ate dates weekly (16.4%), while it was the lowest at 8.6% among those who ate dates monthly. No significant differences were observed in the incidence of GDM by the frequency of intake of banana (p = 0.642), grapes (p = 0.619), mango (p = 0.471) and nuts (p = 0.158).

Table 3.19: Incidence of Gestational Diabetes by fruits and Nuts intake in women

Variables	All	GDM (n=81)	No GDM (n=452)	P Value
		n (%)	n (%)	
Banana				
Monthly	179	28 (15.6)	151 (84.4)	0.642
Weekly	246	34 (13.8)	212 (86.2)	
Daily	36	7 (19.4)	29 (80.6)	
Grapes				
Monthly	320	45 (14.1)	275 (85.9)	0.619
Weekly	186	31 (16.7)	155 (83.3)	
Daily	26	5 (19.2)	21 (80.8)	
Mango				
Monthly	385	63 (16.4)	322 (83.6)	0.471
Weekly	126	15 (11.9)	111 (88.1)	
Daily	22	3 (13.6)	19 (86.4)	
Dates				
Monthly	140	12 (8.6)	128 (91.4)	0.035
Weekly	277	24 (16.4)	122 (84.6)	
Daily	77	45 (18.2)	202 (81.8)	
Nuts				
Monthly	272	35 (12.9)	237 (87.1)	0.158
Weekly	212	40 (18.9)	172 (83.1)	
Daily	49	6 (12.2)	43 (87.8)	

n: Frequency
Chi-square and Fischer Exact tests were applied to compare proportions

Table 3.20 shows the incidence of GDM by the consumption of meat among pregnant women. No significant differences were observed in the incidence of GDM by the frequency of intake of red meat ($p = 0.053$), processed meat ($p = 0.788$), chicken ($p = 0.108$) and fish ($p = 0.188$).

Table 3.20: Incidence of Gestational Diabetes by meat intake in women

Variables	All	GDM (n=81)	No GDM (n=452)	P Value
		n (%)	n (%)	
Fresh red meat				0.053
Monthly	179	20 (11.2)	159 (88.8)	
Weekly	342	57 (17.2)	285 (82.8)	
Daily	12	4 (33.3)	8 (67.7)	
Processed meat				0.788
Monthly	469	72 (15.3)	397 (84.7)	
Weekly/Daily	64	9 (14.1)	55 (85.9)	
Chicken				0.108
Monthly	28	3 (10.7)	25 (89.3)	
Weekly	390	67 (17.2)	323 (82.8)	
Daily	115	11 (9.6)	104 (90.4)	
Fish				0.188
Monthly	81	7 (8.6)	74 (91.4)	
Weekly	410	68 (16.6)	342 (83.4)	
Daily	42	6 (14.3)	36 (85.7)	

n: Frequency
Chi-square and Fischer Exact tests were applied to compare proportions

Table 3.21 shows the incidence of GDM by the intake of sweets and beverages. No differences in the incidence of GDM were noted with the consumption pattern of sweets ($p = 0.410$), soft drinks ($p = 0.456$), fresh juices ($p = 0.690$), tea ($p = 0.567$) and coffee ($p = 0.530$).

Table 3.21: Incidence of Gestational Diabetes by sweets and beverages intake in women

Variables	All	GDM (n=81)	No GDM (n=452)	P Value
		n (%)	n (%)	
Sweets				
Sweets				
Monthly	86	17 (19.8)	69 (80.2)	0.410
Weekly	260	36 (13.9)	224 (86.1)	
Daily	187	28 (15.0)	159 (85.0)	
Beverages				
Soft drinks				
Monthly	329	55 (16.7)	274 (83.3)	0.456
Weekly	130	17 (13.1)	113 (86.9)	
Daily	74	9 (12.2)	65 (87.8)	
Fresh juices				
Monthly	48	9 (18.7)	39 (81.3)	0.690
Weekly	194	27 (13.9)	167 (86.1)	
Daily	291	45 (15.5)	246 (84.5)	
Tea				
Monthly	94	11 (18.4)	83 (88.3)	0.567
Weekly	105	16 (19.7)	89 (84.7)	
Daily	334	54 (61.9)	280 (83.8)	
Coffee				
Monthly	213	34 (16.0)	179 (84.0)	0.530
Weekly	134	23 (17.2)	111 (82.8)	
Daily	186	24 (12.9)	162 (87.1)	

n: Frequency
Chi-square and Fischer Exact tests were applied to compare proportions

Table 3.22 shows the incidence of GDM by the consumption pattern of cereals. The incidence of GDM was not significantly different in women who ate rice (p = 0.273), bread (p = 0.720), pasta (p = 0.204) and pizza (p = 0.789) daily, weekly and monthly.

Table 3.22: Incidence of Gestational Diabetes by intake of cereals in women

Variables	All	GDM (n=81)	No GDM (n=452)	P Value
		n (%)	n (%)	
Rice				0.273
Monthly/Weekly	88	10 (11.4)	78 (88.6)	
Daily	445	71 (16.0)	374 (84.0)	
Bread				0.720
Monthly/Weekly	61	8 (11.0)	53 (86.9)	
Daily	472	73 (15.5)	399 (84.5)	
Pasta				
Monthly	80	12 (15.0)	68 (85.0)	0.204
Weekly	436	69 (15.8)	367 (84.2)	
Daily	17	0 (0.0)	17 (100.0)	
Pizza				
Monthly	332	52 (15.7)	280 (85.6)	0.789
Weekly/Daily	201	29 (14.4)	172 (35.8)	

n: Frequency
Chi-square and Fischer Exact tests were applied to compare proportions

3.8 Association between Gestational Diabetes and Vitamin D

The average vitamin D concentration and distribution of vitamin D status according to GDM status are given in Table 3.23 and Figure 3.12.

Table 3.23: Incidence of Gestational Diabetes by baseline Vitamin D status in women

Variables	All	GDM (n=81)	No GDM (n=452)	P Value
Vitamin D – ng/ml, Mean ±SD	533	12.3±7.9	12.8 ±8.3	<0.001
Vitamin D levels – IOM, n (%)				
Normal (≥ 20 ng/ml)	84	9 (10.7)	75 (89.3)	0.473
Insufficiency (12 - 20 ng/ml)	137	22 (16.1)	115 (83.9)	
Deficiency (< 12 ng/ml)	312	50 (16.0)	262 (84.0)	
Vitamin D levels – IOM, n (%)				
No deficiency (≥ 12 ng/ml)	221	31 (14.0)	190 (86.0)	0.527
Deficiency (< 12 ng/ml)	312	50 (16.0)	262 (84.0)	

n: Frequency, SD: Standard Deviation
Chi-square tests were applied to compare proportions. Unpaired tests were applied to compare means.

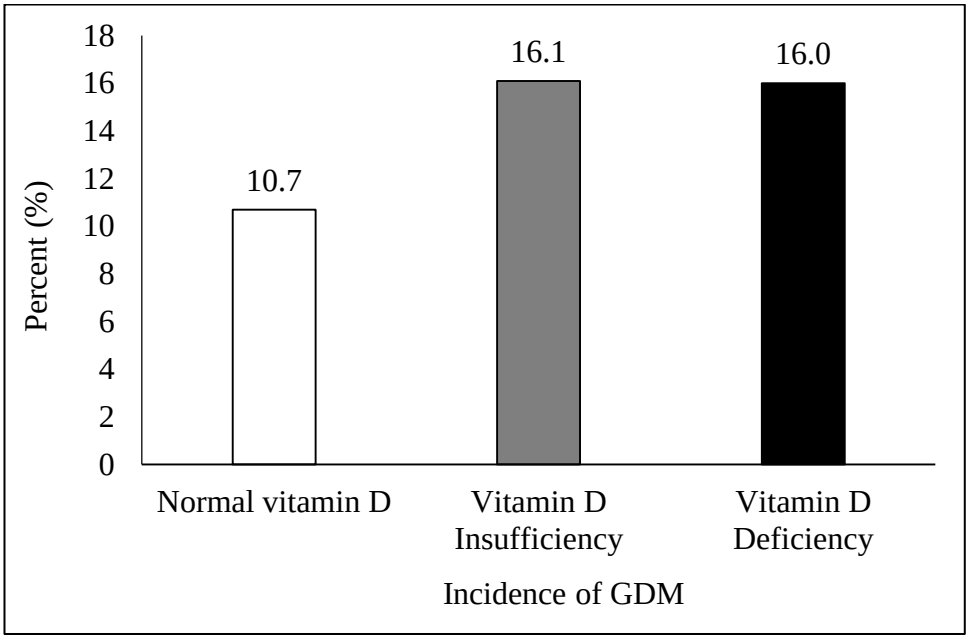

Figure 3.12: Incidence of Gestational Diabetes in women by baseline Vitamin D Status

Table 3.24 shows the results of fitting a binary logistic regression taking vitamin D status either as a continuous variable, an ordinal variable with three categories i.e.

normal, vitamin D insufficiency and vitamin D insufficiency or a binary variable with two categories i.e. vitamin D deficiency versus no deficiency. Using vitamin D as a continuous covariate, there was no statistically significant association with GDM (OR: 0.99, 95% CI: 0.96 – 1.02, p = 0.574). When vitamin D was used as an ordinal covariate, no association was found between vitamin D deficiency and GDM (OR: 1.59, 95% CI: 0.75 – 3.38, p = 0.228) and vitamin D insufficiency and GDM (OR: 1.59, 95% CI: 0.69 – 3.65, p = 0.270) as compared to women with normal vitamin D. Similarly, there was no association between vitamin D deficiency and GDM (OR: 1.17, 95%CI: 0.72 – 1.90, p = 0.527).

Table 3.24: Unadjusted logistic regression of Gestational Diabetes with Vitamin D status in women

Variables	GDM (n=81)			
	OR	SE	95% CI	P Value
Vitamin D – ng/ml – continuous	0.99	0.01	0.96 – 1.02	0.574
Vitamin D levels – IOM				
Normal	1			
Insufficiency	1.59	0.67	0.69 – 3.65	0.270
Deficiency	1.59	0.61	0.75 – 3.38	0.228
Vitamin D levels – IOM				
No deficiency	1			
Deficiency	1.17	0.29	0.72 – 1.90	0.527

OR: Odds Ratio, SE: Standard Error, CI: Confidence Interval

Table 3.25 shows multiple logistic regression analysis of GDM with vitamin D status that was adjusted for age, family history of diabetes, levels of physical activity, BMI before pregnancy, red meat intake, cooked vegetables intake and dates intake. Like unadjusted analysis, vitamin D concentration was not associated with odds of GDM (AOR: 0.99, 95% CI: 0.95 – 1.02, p = 0.450). Likewise, the odds of GDM

were not significantly different in women with vitamin D insufficiency (AOR: 2.11, 95% CI: 0.81 – 5.64, p = 0.101) and deficiency (AOR: 1.94, 95% CI: 0.88 – 5.32, p = 0.118) as compared to women with normal vitamin D status. Also, the odds of GDM were not significantly (AOR: 1.18, 95% CI: 0.70 – 1.99, p = 0.537) higher in vitamin D deficient women as compared to non-deficient women.

Table 3.25 Adjusted logistic regression of Gestational Diabetes with Vitamin D status in women

Variables	GDM (n=81)			
	AOR	SE	95% CI	P Value
Vitamin D – ng/ml – continuous	0.99	0.02	0.95 – 1.02	0.450
Vitamin D levels – IOM				
Normal	1			
Insufficiency	2.11	1.05	0.81 – 5.64	0.101
Deficiency	1.94	0.99	0.88 – 5.32	0.118
Vitamin D levels – IOM				
No deficiency	1			
Deficiency	1.18	0.62	0.70 – 1.99	0.537

AOR: Adjusted Odds Ratio, SE: Standard Error, CI: Confidence Interval
The model was adjusted for age, family history of diabetes, levels of physical activity, BMI before pregnancy, red meat intake, cooked vegetables intake and dates intake

3.9 Association between Gestational Diabetes and Physical Activity

Table 3.26 shows unadjusted logistic regression analysis of GDM with physical activity levels of pregnant women. The odds of GDM were not significantly different (OR: 0.72, 95% CI: 0.37 – 1.39, p = 0.331) between women who had adequate METs per day versus low METs per day. Similarly, compared to women who reported high levels of physical activity, the odds of GDM were not significantly different in

women who reported low (OR: 1.04, 95% CI: 0.43 – 2.58, p = 0.257) and moderate (OR: 0.87, 95% CI: 0.52 – 1.45, p = 0.582) levels of physical activity.

Table 3.26: Unadjusted logistic regression of Gestational Diabetes with physical activity in women

Variables	GDM (n=81)			
	OR	SE	95% CI	P Value
METs, n (%)				
< 600 per week	1			
≥ 600 per week	0.72	0.24	0.37 – 1.39	0.331
Physical activity levels per day				
High	1			
Moderate	0.87	0.23	0.52 – 1.45	0.582
Low	1.04	0.48	0.43 – 2.58	0.257

OR: Odds Ratio, SE: Standard Error, CI: Confidence Interval, METs: Metabolic Equivalents

Table 3.27 shows multiple logistic regression analysis of GDM with physical activity that was adjusted for vitamin D status, age, family history of diabetes, BMI before pregnancy and intake of red meat, cooked vegetables and dates. The odds of GDM were not significantly different by METs status (AOR: 0.92, 95% CI: 0.50 – 1.67, p = 0.778) and moderate (AOR: 0.78, 95% CI: 0.45 – 1.34, p = 0.372) and low (AOR: 1.09, 95% CI: 0.43 – 2.79, p = 0.850) physical activity levels.

Table 3.27: Adjusted logistic regression of Gestational Diabetes with physical activity during the last week in women

Variables	GDM (n=81)			
	OR	SE	95% CI	P Value
METs, n (%)				
< 600 per week	1			
≥ 600 per week	0.92	0.24	0.50 – 1.67	0.778
Physical activity levels per day				
High	1			
Moderate	0.78	0.23	0.45 – 1.34	0.372
Low	1.09	0.48	0.43 – 2.79	0.850

OR: Odds Ratio, SE: Standard Error, CI: Confidence Interval, METs: Metabolic Equivalents
The model was adjusted for vitamin D status, age, family history of diabetes, BMI before pregnancy and red meat, cooked vegetables and dates intake

3.10 Association between Gestational Diabetes and Diet

Table 3.28 shows simple logistic regression analysis of GDM with use of supplements. The consumption of multivitamins / minerals (OR: 1.00, 95% CI: 0.54 – 1.83, p = 0.989) and vitamin D supplements (OR: 0.74, 95% CI: 0.39 – 1.39, p = 0.349) was not significantly associated with GDM.

Table 3.28: Simple logistic regression of Gestational Diabetes with use of supplements during the last six months in women

Variable	GDM (n=81)			
	OR	SE	95% CI	P value
Multivitamins /minerals supplements use during the last six months				
No	1			
Yes	1.00	0.31	0.54 – 1.83	0.989
Vitamin D supplements use during the last six months				
No	1			
Yes	0.74	0.24	0.39 – 1.39	0.349

OR: Odds Ratio, SE: Standard Error, CI: Confidence Interval

Table 3.29 shows simple logistic regression analysis of GDM with intake of milk and yogurt in women. The odds of GDM were not significantly different with respect to frequency of consumption of milk and yogurt.

Table 3.29: Simple logistic regression of Gestational Diabetes with intake of milk and milk products in women

Variable	GDM (n=81)			
	OR	SE	95% CI	P value
Milk				
Monthly	1			
Weekly	1.24	0.35	0.71 – 2.17	0.458
Daily	1.09	0.33	0.61 – 1.96	0.753
Yogurt				
Monthly	1			
Weekly	0.70	0.21	0.39 – 1.25	0.226
Daily	0.60	0.23	0.28 – 1.28	0.186

OR: Odds Ratio, SE: Standard Error, CI: Confidence Interval

Table 3.30 shows logistic regression analysis of GDM with intake of vegetables in pregnant women. The odds of GDM were significantly higher in women who ate cooked vegetables weekly (OR: 1.75, 95% CI: 0.98 – 3.13, p = 0.058) and daily (OR: 2.17, 95% CI: 1.11 – 4.26, p = 0.024) as compared to those women who ate cooked vegetables monthly. The consumption pattern of fresh vegetables, leafy vegetables, boiled potato and fried potato were not associated with GDM.

Table 3.30: Simple logistic regression of Gestational Diabetes with intake of vegetables in women

Variable	GDM (n=81)			
	OR	SE	95% CI	P value
Fresh vegetables				
Monthly	1			
Weekly	2.02	1.31	0.57 – 7.21	0.276
Daily	2.06	1.27	0.61 – 6.93	0.245
Cooked vegetables				
Monthly	1			
Weekly	1.75	0.52	0.98 – 3.13	0.058
Daily	2.17	0.75	1.11 – 4.26	0.024
Leafy vegetables				
Monthly	1			
Weekly	1.10	0.40	0.53 – 2.26	0.804
Daily	1.52	0.51	0.78 – 2.95	0.218
Boiled potato				
Monthly	1			
Weekly	1.12	0.33	0.63 – 1.99	0.698
Daily	1.14	1.26	0.13 – 9.96	0.902
Fried potato				
Monthly	1			
Weekly	1.06	0.26	0.65 – 1.72	0.818
Daily	0.57	0.43	0.13 – 2.54	0.457

OR: Odds Ratio, SE: Standard Error, CI: Confidence Interval

Table 3.31 shows simple logistic regression analysis of GDM with intake of fruits and nuts in women. Compared to women who ate dates monthly, those women who ate dates weekly (OR: 2.10, 95% CI: 1.06 – 4.38, p = 0.048) and daily (OR: 2.38, 95% CI: 1.21 – 4.66, p = 0.012) were significantly more likely to develop GDM, while GDM was not significantly associated with intake pattern of banana, grapes, mango and nuts.

Table 3.31: Simple logistic regression of Gestational Diabetes with intake of fruits and nuts in women

Variable	GDM (n=81)			
	OR	SE	95% CI	P value
Banana				
Monthly	1			
Weekly	0.86	0.24	0.50 – 1.49	0.600
Daily	1.37	0.61	0.52 – 3.26	0.574
Grapes				
Monthly	1			
Weekly	1.22	0.31	0.74 – 2.01	0.430
Daily	1.45	0.76	0.52 – 4.05	0.473
Mango				
Monthly	1			
Weekly	0.69	0.21	37.8 – 1.26	0.229
Daily	0.81	0.51	21.2 – 2.81	0.736
Dates				
Monthly	1			
Weekly	2.10	0.76	1.06 – 4.38	0.048
Daily	2.38	1.00	1.21 – 4.66	0.012
Nuts				
Monthly	1			
Weekly	1.57	0.39	0.96 – 2.58	0.072
Daily	0.94	0.44	0.37 – 2.38	0.904

OR: Odds Ratio, SE: Standard Error, CI: Confidence Interval

Table 3.32 shows simple logistic regression analysis of GDM with intake of meat. Daily consumption red meat (OR: 3.97, 95% CI: 1.10 – 14.40, p = 0.036) was positively associated with GDM. The consumption of processed meat, chicken and fish was not associated with GDM.

Table 3.32: Simple logistic regression of Gestational Diabetes with intake of meat in women.

Variable	GDM (n=81)			
	OR	SE	95% CI	P value
Fresh red meat				
Monthly	1			
Weekly	1.59	0.44	0.92 – 2.74	0.098
Daily	3.97	2.61	1.10 – 14.40	0.036
Processed meat				
Monthly	1			
Weekly	0.88	0.35	0.40 – 1.94	0.755
Daily	1.10	1.21	0.13 – 9.58	0.929
Chicken				
Monthly	1			
Weekly	1.73	1.08	0.51 – 5.89	0.382
Daily	0.88	0.61	0.23 – 3.39	0.855
Fish				
Monthly	1			
Weekly	2.10	0.86	0.93 – 4.76	0.075
Daily	1.76	1.04	0.55 – 5.62	0.339

OR: Odds Ratio, SE: Standard Error, CI: Confidence Interval

Table 3.33 shows simple logistic regression analysis of GDM with intake of sweets and beverages. Gestational diabetes was not associated with consumption of sweets, soft drinks, fresh juices, tea and coffee.

Table 3.33: Simple logistic regression of Gestational Diabetes with intake of sweets and beverages

Variable	GDM (n=81)			
	OR	SE	95% CI	P value
Sweets				
Sweets				
Monthly	1			
Weekly	0.65	0.21	0.34 – 1.23	0.189
Daily	0.71	0.24	0.37 – 1.39	0.323
Beverages				
Soft drinks				
Monthly	1			
Weekly	0.75	0.22	0.42 – 1.35	0.335
Daily	0.69	0.26	0.32 – 1.45	0.335
Fresh juices				
Monthly	1			
Weekly	0.70	0.30	0.31 – 1.61	0.401
Daily	0.79	0.32	0.36 – 1.75	0.565
Tea				
Monthly	1			
Weekly	1.35	0.57	0.59 – 3.09	0.468
Daily	1.45	0.51	0.73 – 2.91	2.91
Coffee				
Monthly	1			
Weekly	1.09	0.32	0.61 – 1.95	0.769
Daily	0.78	0.22	0.44 – 1.37	0.388

OR: Odds Ratio, SE: Standard Error, CI: Confidence Interval

Table 3.34 shows simple logistic regression analysis of GDM with intake of cereals. Gestational diabetes was not associated with consumption of rice, bread, pasta and pizza.

Table 3.34: Simple logistic regression of Gestational Diabetes with supplements and diet intake

Variable	GDM (n=81)			
	OR	SE	95% CI	P value
Rice				
Monthly	1			
Weekly	0.39	0.35	0.07 – 2.23	0.293
Daily	0.66	0.54	0.13 – 3.26	0.615
Bread				
Monthly/Weekly	1			
Daily	1.21	0.48	0.55 – 2.65	0.631
Pasta				
Monthly	1			
Weekly	1.06	0.36	0.55 – 2.07	0.852
Pizza				
Monthly	1			
Weekly	0.92	0.23	0.56 – 1.50	0.735

OR: Odds Ratio, SE: Standard Error, CI: Confidence Interval

Table 3.35 shows multiple logistic regression analysis of GDM with diet intake that was adjusted for vitamin D status, age, family history of diabetes and BMI before pregnancy. Daily consumption of dates (AOR: 1.86, 95% CI: 1.03 – 6.49, p = 0.043) and red meat (AOR: 6.16, 95% CI: 1.31 – 28.92, p = 0.021) remained significantly associated with the development of GDM. However, weekly (AOR: 1.83, 95% CI: 0.91 – 3.69, p = 0.087) and daily (AOR: 2.15, 95% CI: 0.93 – 4.95, p = 0.072) consumption of cooked vegetables was not significantly associated with the development of GDM.

Table 3.35: Multiple logistic regression analysis of Gestational Diabetes with diet intake in women

Variables	GDM (n=81)			
	AOR	SE	95% CI	P Value
Dates				
Monthly	1			
Weekly	1.64	0.60	0.69 – 3.35	0.224
Daily	1.86	1.21	1.03 – 6.49	0.043
Red meat				
Monthly	1			
Weekly	1.29	0.42	0.68 – 2.43	0.433
Daily	6.16	4.18	1.31 – 28.92	0.021
Cooked vegetables				
Monthly	1			
Weekly	1.83	0.65	0.91 – 3.69	0.087
Daily	2.15	0.91	0.93 – 4.95	0.072

AOR: Adjusted Odds Ratio, SE: Standard Error, CI: Confidence Interval
The model was adjusted for vitamin D status, age, family history of diabetes and BMI before pregnancy

3.11 Association of Gestational Diabetes with Other Risk Factors

Table 3.36 shows simple logistic regression analysis of GDM with demographic characteristics of women. Average increase in age by one year elevated the odds of GDM by 6.0% (95% CI: 1.01 – 1.11, p = 0.008). Women with positive family history of diabetes (OR: 1.60, 95% CI: 0.95 – 2.71, p = 0.079) were insignificantly more likely to develop GDM as compared to women without family history of diabetes. No association was observed between education level, type of occupation and GDM.

Table 3.36: Simple logistic regression analysis of gestational diabetes with demographic characteristics

Variables	GDM			
	OR	SE	95% CI	P Value
Age – Years	1.06	0.02	1.01 – 1.11	0.008
Education level				
Up to primary	1			
Up to secondary	0.87	0.62	0.22 – 3.50	0.846
Up to high school	0.76	0.44	0.24 – 2.35	0.629
≥ College/University	0.85	0.50	0.27 – 2.68	0.781
Work Status				
Government employee	1			
House wife	0.99	0.32	0.53 – 1.88	0.999
self-employed/Student/Non-government employee	0.26	0.20	0.06 – 1.20	0.085
Family history of Diabetes				
Yes	1			
No	1.60	0.43	0.95 – 2.71	0.079

OR: Odds Ratio, SE: Standard Error, CI: Confidence Interval, AED: Arab Emirates Dirham

Table 3.37 shows simple logistic regression analysis of GDM with clinical characteristics of women. Average increase in BMI by one kg/m^2 increased the odds of GDM by 7% (95% CI: 1.03 – 1.10, p < 0.001). Overweight (OR: 1.75, 95% CI: 0.93 – 3.30, p = 0.082) and obese (OR: 2.74, 95% CI: 1.55 – 4.86, p = 0.001) women with high BMI were more likely to develop GDM as compared to women with normal BMI. No association was noted between high blood pressure (OR: 1.61, 95% CI: 0.33 – 7.89, p = 0.557) and GDM.

Table 3.37: Simple logistic regression of Gestational Diabetes with Body Mass Index

Variables	GDM (n=81)			
	OR	SE	95% CI	P Value
Body Mass Index before pregnancy – kg/m^2	1.07	0.02	1.03 – 1.10	<0.001
Body Mass Index categories before pregnancy				
Normal (< 25.0 kg/m^2)	1			
Overweight (25.0 - 29.9 kg/m^2)	1.75	0.57	0.93 – 3.30	0.082
Obese (≥ 30 kg/m^2)	2.74	0.80	1.55 – 4.86	0.001

OR: Odds Ratio, SE: Standard Error, CI: Confidence Interval

Table 3.38 shows multiple logistic regression analysis of GDM with clinical characteristics that was adjusted for vitamin D status, physical activity and diet intake (dates, cooked vegetables, red meat) of women. The adjusted analysis shows that positive family history of diabetes (AOR: 1.93, 95% CI: 1.02 – 3.62, p = 0.043) and BMI before pregnancy (AOR: 1.07, 95% CI: 1.02 – 1.11, p = 0.003) were significant risk factors of GDM.

Table 3.38: Adjusted logistic regression analysis of Gestational Diabetes with risk factors

Variables	GDM (n=81)			
	AOR	SE	95% CI	P Value
Age – years	1.02	0.02	0.97 – 1.07	0.520
Family history of diabetes				
No	1			
Yes	1.93	0.62	1.02 – 3.62	0.043
Body Mass Index before pregnancy – kg/m^2	1.07	0.02	1.02 – 1.11	0.003

AOR: Adjusted Odds Ratio, SE: Standard Error, CI: Confidence Interval
The model was adjusted for vitamin D status, levels of physical activity and diet intake of women.

Chapter 4: Discussion

4.1 Summary of Results

The overall incidence of GDM was 15.2% (95% CI: 12.4% - 18.5%) according to the WHO (2013) criteria. The incidence of GDM was 16.1% in vitamin D insufficient women, 16.0% in vitamin D deficient women and 10.7% in women with normal vitamin D. The prevalence of vitamin D deficiency and insufficiency was 58.3% and 26.4% respectively as per IOM criteria. Below one-tenth (8.5%) of pregnant women reported high levels of physical activity. The median METs (iqr) per week were 840 (1320) and median sedentary time per day was 240 (280) minutes. The most frequently consumed foods were bread (88.9%), rice (83.8%), fresh vegetables (68.2%), tea (62.2%), fresh juices (55.2%), leafy vegetables (46.5%) and dates (46.0%).

This study found that vitamin D insufficiency and deficiency and physical activity were not significantly associated with GDM. The positive family history of diabetes, BMI and daily consumption of dates and red meat significantly increased the likelihood of developing GDM in Emirati women.

4.2 Prevalence of Vitamin D Deficiency

The present study demonstrated a high prevalence of vitamin D insufficiency (26.4%) and deficiency (58.3%) in pregnant Emirati women according to IOM criteria. In addition to well-known factors such as low sunlight exposure and vitamin D diet (Dawodu et al., 2003), the high prevalence of vitamin D deficiency could be due to low consumption rate of vitamin D supplements among our sample. Since the

present study did not investigate reasons for low supplement use, further research is suggested in this area.

The prevalence of vitamin D deficiency estimated by our study (58.3%) is lower than its prevalence of 69% in pregnant women reported by two studies from the UAE (Hussein et al., 2016; Narchi et al., 2010). These estimates indicate that vitamin D deficiency remains a wide-spread problem in pregnant women in the UAE despite country-wide dairy food and oil fortification and supplementation of vitamin D (Laleye et al., 2011). Therefore, more population-wide and multi-sectoral interventions are needed to address this problem in the country.

The prevalence of vitamin D deficiency in pregnant women was slightly higher than Saudi women (50%), according to a study (Al-Faris et al., 2016). Whereas, another large study found a higher prevalence (86%) of vitamin D deficiency than us (Al-Shaikh et al., 2016). In addition, studies from Qatar and Iran reported the prevalence rate of vitamin D deficiency between 48 and 70% in pregnant women respectively (Bener et al., 2013; Maghbooli et al., 2008). In addition to observational studies, a recent review have concluded that prevalence of vitamin D in pregnant women of Middle East countries ranges between 50 and 65% respectively (Karras et al., 2016). Despite similar diet and life style practices, ethnicity and abundant light in the Middle East countries, variations in the prevalence of vitamin D deficiency among these studies could be due to differences in measurement methods and diagnostic cut-offs for vitamin D deficiency. Even in the presence of these limitations, these data indicate that vitamin D deficiency is a serious problem in pregnant women in the Middle East region, which has also been demonstrated by other studies (Eggemoen et al., 2016; Al-Mohaimeed et al., 2012).

4.3 Incidence of Gestational Diabetes

Our study found that 15.2% (95% CI: 12.4% - 18.5%) of Emirati women developed GDM as per WHO (2013) criteria in late pregnancy. To date, limited data are available on the burden of GDM in the UAE. Nevertheless, two hospital based follow-up studies conducted in Al Ain showed that GDM, as per ADA criteria, was present in 12.9 and 14.2% of Emirati and South Asian women (Agarwal et al., 2010; Agarwal et al., 2007). The burden of GDM shown by earlier studies is similar to our results and shows that GDM is a common condition among Emirati women and needs to be addressed urgently.

The magnitude of burden of GDM largely depends upon its diagnostic criteria, which has been demonstrated by Agarwal and colleagues in their studies (Agarwal et al., 2005; Agarwal et al., 2007). For instance, in one of their studies, the prevalence of GDM according to ADA criteria was similar (14.2%) to our study, while it increased up to 37% by using other criteria (Agarwal et al., 2007). This necessitates the need for a unified criterion for diagnosing GDM in the UAE and elsewhere so that trends of GDM can be monitored and compared within and across countries.

The incidence of GDM estimated by our study (15.2%) is higher than its global incidence of 1 - 14% WHO (2013), indicating the seriousness of this problem in the country. However, the prevalence of GDM in our study is lower than Saudi Arabia and Qatar. For instance, the prevalence of GDM was 36.6% in Saudi women according to a population based survey (Al-Rubeaan et al., 2014), while 24% of Saudi women were classified having GDM in a recent cohort study (Serehi et al., 2015). In Qatar, GDM was present in 16.3% of pregnant women (Bener et al., 2011).

On the other hand, the incidence of GDM was lower in Bahrain (12.5%) compared to our study (Rajab et al., 2012). The difference in the burden of GDM among most gulf countries despite similar ethnicity and life style factors could be due to different measurement methods and diagnostic criteria for GDM.

Consistent with the vast body of literature that the burden of GDM is higher in Middle Eastern countries than other population, our incidence rate of GDM was higher than European and American countries. For example, studies have reported that the prevalence of GDM in Australia was 9.5%, the USA 4.8%, France 12.5% and other European Countries was 2 - 6% (Moses et al., 2011; Ferrara et al., 2007; Schneider et al., 2011).

4.4 Association between Gestational Diabetes and Vitamin D

Our study did not find a significant association between vitamin D deficiency in early pregnancy and GDM. The lack of association between vitamin D status and GDM could be due to various reasons. The vitamin D deficiency alone might be neither sufficient nor a necessary factor to cause GDM. Moreover, we measured vitamin D once in early pregnancy, which may not depict its true status during pregnancy given that studies have shown progressive decline in its levels with advancing pregnancy. Another possible reason for the lack of association could be due to the diagnostic criteria of GDM.

To the best of our knowledge, it was the first cohort study that examined the association between vitamin D and GDM in the UAE. Therefore, comparable data are not available in the country. Also, studies assessing the association between vitamin D and GDM are scarce in the Gulf and other Middle East countries. As such,

only one cohort study was conducted in Qatar (Bener et al., 2013), whereas other studies that assessed the relationship between these conditions were case-control and / or cross-sectional in nature and found mixed results. To elaborate, a small cross-sectional study from Egypt like our study found similar average vitamin D levels in GDM versus non-GDM women (El Lithy et al., 2014). Another cross-sectional study conducted in Turkey also reported similar prevalence of vitamin D in women with GDM versus those without GDM (44% vs 44.7%, p = 0.9) (Ates et al., 2017). Similarly, a case-control study from Turkey did not find any correlation of serum vitamin D with serum fasting glucose (p = 0.9), insulin levels (p = 0.2) or HbA1c levels (p = 0.1) (Parildar et al., 2013). Contrary to our findings, two cross-sectional studies from Iran found an inverse association between HbA1c, insulin resistance, GDM and vitamin D (Jafarzadeh et al., 2015; Maghbooli et al., 2008). Also, a cross-sectional study conducted in Turkey showed a significant association between severe vitamin D deficiency and GDM (Zuhur et al., 2013). Similarly, a matched case-control study from Iran showed 2.66 higher odds of vitamin D deficiency in women with GDM as compared to those without GDM (Soheilykhah et al., 2010). Given these conflicting results, this study served as a valuable addition to literature concerning the association between vitamin D and GDM in the Middle East region.

Like the Middle East region, observational studies from other countries reported inconsistent results about the relationship between vitamin D and GDM. Like our study, no association was found between vitamin D deficiency and GDM among Indian women (Farrant et al., 2009). Likewise, two case-control studies from the UK showed that vitamin D levels in early pregnancy were not significantly different by GDM status (Makgoba et al., 2011; Savvidou et al., 2011). Furthermore, a nested

case control study carried out on pregnant women in the USA reported a lack of association between first trimester vitamin D levels and GDM (Baker et al., 2012). Also, a Korean cohort study found that levels of vitamin D were similar throughout pregnancy in both GDM and non-GDM groups (Park et al., 2014). In contrast to our study, a prospective study from Australia revealed significant and inverse association between serum vitamin D concentration (29 weeks of gestation) and fasting glucose (Clifton-Bligh et al., 2008). Two nested case control studies from the USA and one study from Canada demonstrated more than two-folds higher risk of GDM with lower levels of vitamin D in early pregnancy (Arnold et al., 2015; Cuilin Zhang et al., 2008; Parlea et al., 2012). Also, a cross-sectional study in Turkey showed that only women with severe vitamin D deficiency were more likely to have GDM (Zuhur et al., 2013). Similarly, two large nested case control studies carried out in China and India claimed vitamin D deficiency in early pregnancy as an independent risk factor of GDM (Jain et al., 2015). The conflicting results documented by earlier studies might be due to methodological issues such as sample size, study design, gestational age at which GDM and vitamin D were measured and methods adopted to measure vitamin D. Other reasons include criteria for diagnosing GDM and vitamin D and ethnic and genetic characteristics of study populations.

Contrary to conflicting results of observational studies, systematic reviews and meta-analysis have unanimously shown that vitamin D deficiency is a significant risk factors of GDM. Wei and colleagues in their meta-analysis of 12 studies showed 1.38 times increase in odds of GDM (95% CI: 1.12-1.70) due to vitamin D insufficiency in early pregnancy (S.-Q. Wei et al., 2013). Similarly, another meta-analysis by Lu and colleagues comprising 20 observational studies reported 1.45 times greater risk

of GDM (95% CI: 1.15 - 1.81, p < 0.001) with vitamin D insufficiency (Lu & Zhang, 2016). Similarly, Zhang and colleagues concluded that vitamin D deficiency increased the odds of GDM by 1.53 (95% CI: 1.33-1.75), while odds of GDM were 1.61 (1.19 - 2.17; p = 0.002) times in vitamin D deficient versus non-deficient women according to Poel et al (Zhang et al., 2015; Poel et al., 2012). A meta-analysis that included 31 studies confirmed that vitamin D insufficiency (OR 1.49, 95% CI: 1.18 - 1.88) and lower vitamin D levels (Pooled average difference: -7.36 nmol/L, 95% CI: -10.16 to -4.56 nmol/L) were significantly associated with an increased risk of GDM (Aghajafari et al., 2013). Despite the consistent findings, the quality of this meta- analysis is compromised by many factors such as the observational study designs, diverse study populations, different laboratory methods and timings of measuring vitamin D and GDM and heterogeneity in diagnostic criteria and definition of GDM and vitamin D.

4.5 Association between Gestational Diabetes and Diet

To our knowledge, this was the first study that assessed the role of diet in the development of GDM among Emirati women. Our data showed that daily consumption of dates and red meat in early pregnancy significantly increased the risk of GDM while fiber, fruits, vegetables and beverages were not associated with increased risk of GDM. Our results suggest that diet plays an important role in the development of GDM and educating pregnant women about maintaining a healthy and well-balanced diet can be an effective intervention in preventing the incidence of GDM.

Plausible biological mechanisms for the association between meat consumption and GDM are not very clear. The red meat contains cholesterol and saturated fats, which negatively affect insulin sensitivity and ß-cell function of pancreas and thereby may increase the risk of GDM. According to another assumption, AGEs and iron present in the meat increase the risk of type 2 diabetes and GDM (Bao et al., 2014; Zhang & Ning, 2011).

Epidemiological evidence regarding relationship between fat and meat consumption and GDM is recent and largely favors our study findings. For instance, Bao and others found that intake of high animal protein in particular red meat increased the risk of GDM by two-folds (Bao et al., 2013). According to another cohort study, high intake of saturated fats during pregnancy significantly increased the risk of GDM (Saldana et al., 2004). Also, the Nurses' Health Study II revealed that intake of Western diet that primarily contained red and processed meat increased the risk of GDM (C. Zhang et al., 2006). Another large prospective study identified that only high intake of animal fat and cholesterol was associated with increased risk of GDM (Bowers et al., 2012). Furthermore, a study from China demonstrated that consumption of unsaturated fats significantly reduced the risk of GDM (Wang et al., 2000). Another study showed that consumption of red (OR:2.37, 95% CI: 1.49, 1.49-3.78, $p < 0.001$) and processed meat (OR:2.01, 95% CI: 1.26 - 3.21, $p = 0.003$) before pregnancy significantly increased the risk of GDM in a Mediterranean cohort (Marí-Sanchis et al., 2017). In line with cohort studies, a case-control study found that the consumption of saturated fats doubled the odds of GDM, while of unsaturated fats decreased the odds of GDM by 15% (Bo et al., 2001). On the other

hand, a cohort study carried out by Radesky reported no association between red meat consumption and risk of GDM (Radesky et al., 2008).

Dates are among the most consumed fruits in the UAE and have high glycemic index and medium glycemic load (Harvard Medical School, 2015). Although, relationship of GDM has not been done directly with dates; a wealth of research comprising mainly clinical trials has explored the role of low and high glycemic diet in the development of GDM. A large cohort study documented 2.15 increased risk of GDM among those women who ate high glycemic and low fiber diet (Zhang et al., 2006). A small clinical trial demonstrated a significant control in postprandial glucose due to low glycemic index diet in women (Grant et al., 2011). Another clinical trial showed that number needed to use insulin was reduced by half in those who received low glycemic index diet in women with GDM (Moses et al., 2009). In contrast, Redesky and others reported no association of high carbohydrate diet and any dietary pattern with risk of GDM respectively (Radesky et al., 2008).

In addition to observational studies and clinical trials, current systematic reviews and meta-analysis have backed our results and concluded that low glycemic diet significantly improved glucose and insulin control in women with GDM and healthy diet reduced the incidence of GDM. However, the most of these reviews have emphasized that existing observational studies and clinical trials that were included in analysis had small sample size and lacked quality to draw any conclusions and recommendations about modifying current dietary recommendations in pregnancy (Wei et al., 2016; Viana et al., 2014; Louie et al., 2013; Louie et al., 2010). Therefore, more research in this area is needed to better understand the contribution of dietary factors in the development of GDM.

4.6 Association between Gestational Diabetes and Physical Activity

Adequate exercise has various beneficial effects on the course of pregnancy, labor and health of both mother and fetus (Dempsey et al., 2004). However, research has shown that amount of physical activity is decreased significantly particularly in early pregnancy due to nausea and fatigue and perceived risk to maternal and fetal health (Perichart-Perera et al., 2009). This issue might be one of reasons for low physical activity levels of pregnant women in our study. Other reasons might be associated with life style practices and extreme weather conditions. However, we could not find any study on barriers of physical activity among Emirati pregnant women, therefore comparisons cannot be made.

In this study, moderate and high physical activity in early pregnancy did not lower the risk of GDM among Emirati women. We did not find any study related to this research area in the UAE and neighboring countries. However, our results are against the bulk of studies conducted in different countries. For instance, an observational study mentioned that the risk of GDM was decreased by 20 - 55% in those women who are perform various types and intensities of recreational physical activity during and before pregnancy (Redden et al., 2011). Moreover, according to a prospective study, women who performed vigorous physical activity 12 months before their pregnancy had a 56% lower risk of developing GDM (Dempsey et al., 2004). Another study showed that women who performed recreational physical activity during first twenty weeks of pregnancy were at 44% lower risk of developing GDM than inactive women (Oken et al., 2006). Also, two systematic reviews found that likelihood of GDM was reduced by 25 and 18% respectively in physical activity intervention groups versus control groups (Russo et al., 2015; Da Silva et al., 2016).

In contrast, some evidence has reported lack of association between physical activity and the risk of GDM, which is in line with our results. For instance, a review of thirteen randomized control trials revealed that risk of GDM was insignificant between intervention (diet and exercise) and control group (Bain et al., 2015). Ploeg did not find any association between sedentary time, physical activity and development of GDM in proceeding three years (Ploeg et al., 2011).

The lack of association between low physical activity and GDM in our study could be due to the utilization of a self-reported physical activity measurement tool, which might have diluted the magnitude of association between these variables. In addition, physical activity during the first trimester of pregnancy might not be as significant risk factor as physical activity before pregnancy or later trimester. Therefore, we recommend using objective tools for measuring physical activity for more reliable findings and exploring the possible role of time of physical activity in the development of GDM.

4.7 Association between Gestational Diabetes and Body Mass Index

The present study found that increase in pre-pregnancy BMI by one unit increased the likelihood of GDM by 7% after controlling for physical activity, diet, vitamin D and age. The association between obesity and GDM is explained by various mechanisms in the literature. Obesity brings various metabolic changes in pregnancy including insulin resistance, which can lead to the development of GDM. Obesity is also known to be associated with defects in insulin receptors. Moreover, in obesity abundant adipocytes are released, which may produce excess inflammatory

markers and eventually leads to the development of GDM (Kaaja & Rönnemaa, 2008).

Our findings are consistent with previous epidemiological data that have consistently demonstrated obesity to be a strong predictor of GDM. According to some studies, BMI above 30 kg/m^2 increases 2 - 4 fold risk of GDM (Mohammadzadeh et al., 2015; Lin et al., 2016; Radesky et al., 2008). Systematic reviews and meta-analysis have also confirmed this association and have demonstrated an increase in strength of association of GDM with severity of obesity. According to Chu and others the risk of GDM was two, four and eight times higher among overweight, obese and very obese women respectively as compared to normal weight women (Chu et al., 2007). Another meta-analysis reported that overweight, moderately obese and morbidly obese women were two, three and four times likely to have GDM respectively (Torloni et al., 2009).

Although, an extensive body of evidence has confirmed association between increasing BMI and GDM, the magnitude of association varies significantly across studies. The possible reasons could include genetic predisposition to GDM in obese different populations, differences in measurement and diagnostic guidelines of GDM and obesity and presence of interaction and confounding factors which were not handled in individual studies. Regardless of these limitations, it is obvious from our study and previous data that obesity is a strong risk factor of GDM in Emirati women and elsewhere and should be tackled at global scale.

4.8 Association between Gestational Diabetes and Family History of Diabetes

Research has extensively shown that family history of diabetes is an established risk factor of GDM. For instance, Salomon et al. reported that family history of diabetes increased the risk of GDM by 68% (Solomon et al., 1997). Lin and colleagues observed seven-folds higher risk of GDM in women with positive family history than those without family history of diabetes (Lin et al., 2016). Cianni found two times higher prevalence of GDM in pregnant women with positive family history of diabetes (14.5 vs. 7.3%) compared with women with negative family history of GDM (Di Cianni et al., 2003). Likewise, Yang and Erem found that two-fold and 4.5 fold higher risk of GDM respectively in women with positive family history of diabetes than those with negative family history of diabetes (Yang et al., 2009; Erem et al., 2015).

Coinciding with global estimates, studies from the Middle East and gulf countries have considered the family history of diabetes as a strong risk factor of GDM. A cohort study from Iran and cross-sectional studies from Turkey and Yemen found that the incidence and prevalence of GDM was significantly higher in women with positive family history of diabetes (Shirazian et al., 2009; Duman et al., 2015; Ali et al., 2016). To add further, a systematic review concluded that women with positive family history of diabetes were 3.46 times more likely to have GDM than those without any history of type 2 diabetes (Moosazadeh et al., 2017).

Our results are in accordance with earlier studies from gulf countries and elsewhere as we found 93% higher odds of GDM in women having positive family history of diabetes versus those with negative family history of diabetes. The

consistency of findings confirms that family history of diabetes is a crucial risk factor of GDM. Therefore, pregnant women must be screened for the presence of family history of diabetes along with other major risk factors while screening for GDM.

4.9 Strengths of the Study

This was the first cohort study in the UAE that estimated the incidence of GDM in the UAE and prospectively assessed the association of vitamin D deficiency and other factors with the development of GDM. In addition, the measurement of vitamin D, physical activity and diet in early pregnancy enabled the researcher to establish the temporal relationship between maternal vitamin D deficiency and subsequent risk of GDM in second and third trimester of pregnancy.

Although, more than 80% of the participants had vitamin D deficiency or insufficiency, the sample size of 563 pregnant women was adequate to compare exposed and non-exposed groups. Also, this sample size achieved the power of 80% to detect the true difference in risk of GDM in vitamin D deficient women versus non-deficient women.

Cohort studies are subjected to high rate of loss to follow-up. The high follow-up rate reduced attrition bias (the attrition rate was 11.2 %) and did not undermine the power of study.

It was a well-designed study that used strict inclusion criteria. The strict criteria allowed the researcher to minimize selection bias and excluded potential confounding factors of GDM such as multi-parity, chronic diseases and previous history of GDM.

This study used internationally validated tools and diagnostic criteria to measure exposures and the outcome. The two-step method was employed to diagnose GDM and IOM criteria to determine vitamin D deficiency. Secondary exposures such as physical activity and diet intake were measured using GPAQ and FFQ. This approach allowed the researcher to accurately measure and compares our results with most of other studies. Moreover, this study measured all known confounding factors and included these in statistical analysis to determine the association between vitamin D and GDM.

Although, the study was conducted in one Emirate of the UAE; its findings can be generalized to all Emirati women because of similar living and socio-cultural characteristics of women across all Emirates.

4.10 Limitations of the Study

This study prospectively assessed the temporal association of vitamin D deficiency, physical activity (during the last week) and diet (during the last year) with the subsequent development of GDM. However, observational nature of this study could not establish causal relationship between vitamin D deficiency and GDM and underscores the need of well-designed experimental studies.

Although, it was a well-designed study that measured and adjusted for all known confounders of vitamin D and GDM, there is every possibility that some unknown confounding factors were not measured by the researcher. Therefore, residual confounding may exist in the relationship between vitamin D and GDM. Considering this limitation, randomized control trials would be an ideal choice for studying the relationship between these conditions.

The information regarding physical activity was collected by using the GPAQ, which is a widely used and internationally validated tool. However, it collects self-reported data on physical activity in the past one week. This limitation might have led to over- or under-reporting of physical activity and recall bias. These two limitations may partly explain the lack of significant association between physical activity and the development of GDM. In the view of this limitation, objective methods of measuring physical activity are suggested to accurately assess the relationship between physical activity and GDM.

Studies have consistently shown that vitamin D levels vary throughout the pregnancy. However, in this study, vitamin D levels were measured only once in the first trimester of pregnancy. Therefore, a single measurement of vitamin D does not reflect the status of vitamin D in pregnancy and might have affected its degree of association with GDM.

Frequencies of food intake were used as a proxy for a quantitative indicator in the present study, the misclassification of food intake might have occurred. Such bias could have resulted in insignificant results with many of food groups. Second, we assessed food intake 'in the past Year'. The information during this period might not be representative of dietary habits throughout early pregnancy as it represents the dietary intake before pregnancy. However, previous studies have suggested that overall dietary patterns remain stable during pregnancy. Therefore, objective and accurate tools are needed to determine the exact association between dietary pattern and GDM.

4.11 Conclusion

This study found that vitamin D deficiency and low physical activity were not significant risk factors of GDM, while daily consumption of dates and red meat, positive family history of diabetes and increasing BMI were identified as significant risk factors of GDM among Emirati women. In addition, the incidence rate of GDM and prevalence rate of vitamin D deficiency was high in Emirati population.

4.12 Recommendation

Prevention of GDM by lifestyle changes including diet and physical activity may ensure a healthier future for both child and mother. These findings suggest that dietary modification and weight management interventions are required in pregnancy to reduce the risk of GDM and prevent its short and long-term maternal and neonatal complications. All women should receive diet therapy and nutritional advices from an appropriately skilled dietitian, to promote facilitate weight control and improve insulin sensitivity.

As the prevalence of vitamin D deficiency and insufficiency was high, we recommend that the main food items in like breakfast cereals, rice, flour, cooking oil, dairy products, fruit juice, eggs and bread should be fortified with enough amount of vitamin D and the women should be advised to be exposed to the sun at least 20 – 30 minutes for 3 - 4 days weekly.

More experimental studies are required to measure physical activity and dietary intake and unified methods and diagnostic criteria for GDM and vitamin D are recommended to accurately investigate the risk factors of GDM.

4.13 Output of the study

The abstract of the study has been presented in two conferences

1. Poster presentation (22 - 23 March, 2017) in "Vitamin D deficiency, diet, physical activity and development of Gestational Diabetes in Emirati women in Ras Al Khaimah - UAE" at 16th Global Diabetes Conference and Medicare Expo, Holiday Inn, Rome, Italy
2. Poster presentation (9 - 10 March, 2017) in "Diet, Physical activity in early pregnancy and development of GDM in Emirati women in Ras Al Khaimah - UAE" at 6th International Conference Vitamin D Deficiency, Nutrition and Human Health (MENA conference), Intercontinental Hotels & Resorts, Abu Dhabi, U.A.E.

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Appendix 1: Socio-demographic Characteristics Questionnaire

Socio-demographic Characteristics Questionnaire

Gestational diabetes mellitus and vitamin D deficiency in RAK (2014-2016) **United Arab Emirates University - Medicine and Health Sciences - Public Health Department**		
Code	**Response**	
1	File/ Card number:	
2	Participant's name:	
3	Contact number 1: Contact number 2:	
4	Health care center's name:	
5	Date of your last menstrual period:	
6	Date of birth/ age:	
7	Date of drawing first blood sample:	
8	Date of first visit:	
9	In total, how many years have you spent at school or in full-time study (excluding pre-school)?	Years _____
10	What is the **highest level of education** you have completed?	No formal schooling 1 Less than primary school 2 Primary school completed 3 Secondary school completed 4 High school completed 5 College/University completed 6 Post graduate degree 7 Refused 8
11	What is your **marital status**?	Currently married 1 Separated2 Divorced 3 Widowed 4 Refused 5
12	Which of the following best describes your **main work status** over the past 12	Government employee 1 Non-government employee 2 Student 3

	months?	Homemaker 4 Retired 5 Unemployed (able to work) 6 Unemployed (unable to work)7 Self-employed 8 Refused 9
13	How many people older than 18 years, including yourself, live in your household?	Number of people _____
14	Taking **the past year**, can you tell me what the average earnings of the household have been? *(RECORD ONLY ONE, NOT ALL2)*	per month _____ **OR** per year _____ Refused 0
Medical History		
15	Do you have a family history of Diabetes?	Yes 1 No 2 I Don't know 3
16	Do you have diabetes mellitus?	Yes 1 No 2 I Don't know 3
17	Have you had gestational diabetes before?	Yes 1 No 2 I Don't know 3
18	Do you have Hepatitis or liver diseases?	Yes 1 No 2 I Don't know 3
19	Do you have Aids?	Yes 1 No 2 I Don't know 3
20	Do you have kidney diseases?	Yes 1 No 2 I Don't know 3
21	Are you vitamin D deficient?	Yes 1 No 2 I Don't know 3
This part should be filled by the principal investigator or the research assistant		
22	Height	in Centimeters (cm):
23	Weight in pregnancy:	in Kilograms (kg):
24	Body Mass Index (BMI) in pregnancy :	
25	Weight before pregnancy:	in Kilograms (kg):
26	Body mass index (BMI) before pregnancy:	_____
27	Blood Pressure:	mm Hg
28	Place of doing blood analysis:	

29	Fasting blood glucose at baseline	mmol/l:
30	Vitamin D level	ng/ml:
31	OGTT (24-28) weeks - fasting OGTT (24-28) weeks - 2hr (75 gm)	mmol/l: mmol/l:
32	Do you have diabetes after (24-28) weeks of pregnancy or after the delivery:	Yes ( ) No ( )

Name of Health Care Center: _____

Interviewer name: _____

Signature: _____

Date: _____

Appendix 2: Global Physical Activity Questionnaire

Global Physical Activity Questionnaire

Gestational diabetes mellitus and vitamin D deficiency in RAK (2014-2016)
United Arab Emirates University - Medicine and Health Sciences - Public Health Department

CORE: Physical Activity

Next I am going to ask you about the time you spend doing different types of physical activity in a typical week. Please answer these questions even if you do not consider yourself to be a physically active person.
Think first about the time you spend doing work. Think of work as the things that you have to do such as paid or unpaid work, study/training, household chores, harvesting food/crops, fishing or hunting for food, seeking employment. *[Insert other examples if needed]*. In answering the following questions 'vigorous-intensity activities' are activities that require hard physical effort and cause large increases in breathing or heart rate, 'moderate-intensity activities' are activities that require moderate physical effort and cause small increases in breathing or heart rate.

	Question	Response	Code
Working and job related physical activity			
1	Does your work involve vigorous-intensity activity that causes large increases in breathing or heart rate like *[carrying or liftingheavy loads, digging or construction work, running]* for at least 10 minutes?	Yes 1 No 2 *If No, go to P 4*	**P1**
2	In a typical week, on how many days do you do vigorous-intensity activities as part of your work?	# of days	**P2**
3	How much time do you spend doing vigorous-intensity activities at work on a typical day?	Hour Minute	**P3 (a-b)**
4	Does your work involve moderate-intensity activity, which causes small increases in breathing or heart rate such as brisk walking *[or carrying light loads]* for at least 10 minutes continuously?	Yes 1 No 2 *If No, go to P 7*	**P4**
5	In a typical week, on how many days do you do moderate-intensity activities as part of your work?	# of days:	**P5**
6	How much time do you spend doing moderate-intensity activities at work on a typical day?	Hour Minute	**P6 (a-b)**
Travel and transportation related physical activity			
The next questions exclude the physical activities at work that you have already mentioned. Now I would like to ask you about the usual way you travel to and from places. For example, to work, for shopping, to market, to place of worship. *[Insert other examples if needed]*			
7	Do you walk for at least 10 minutes continuously to get to and from places?	Yes 1 No 2 *If No, go*	**P7**

		to P 10	
8	In a typical week, on how many days do you walk for at least 10 minutes continuously to get to and from places?	# of days:	**P8**
9	How much time do you spend walking for travel on a typical day?	Hour Minute	**P9 (a-b)**
Question		**Response**	**Code**
Recreational and leisure time activities			
The next questions exclude the work and transport activities that you have already mentioned. Now I would like to ask you about sports, fitness and recreational activities (leisure)			
10	Do you do any vigorous-intensity sports, fitness or recreational *(leisure)* activities that cause large increases in breathing or heart rate like *[running or football]* for at least 10 minutes continuously? *[INSERT EXAMPLES] (USE SHOWCARD)*	Yes 1 No 2 *If No, go to P 13*	**P10**
11	In a typical week, on how many days do you do vigorous-intensity sports, fitness or recreational *(leisure)* activities?	# of days:	**P11**
12	How much time do you spend doing vigorous-intensity sports, fitness or recreational activities on a typical day?	Hour Minute	**P12 (a-b)**
13	Do you do any moderate-intensity sports, fitness or recreational *(leisure)* activities that cause a small increase in breathing or heart rate such as brisk walking, *[cycling, swimming, and volleyball]* for at least 10 minutes continuously? *[INSERT EXAMPLES] (USE SHOWCARD)*	Yes 1 No 2 *If No, go to P16*	**P13**
14	In a typical week, on how many days do you do moderate-intensity sports, fitness or recreational *(leisure)* activities?	# of days:	**P14**
15	How much time do you spend doing moderate-intensity sports, fitness or recreational *(leisure)* activities on a typical day?	Hour Minute	**P15 (a-b)**
Sedentary behavior (sitting)			
The following question is about sitting or reclining at work, at home, getting to and from places, or with friends including time spent sitting at a desk, sitting with friends, traveling in car, bus, train, reading, or watching television, but do not include time spent sleeping.			
16	How much time do you usually spend sitting or reclining on a typical day?	Hour Minute	**P16 (a-b)**

Appendix 3: Adult Semi-Quantitative Food Frequency Questionnaire

Adult Semi-Quantitative Food Frequency Questionnaire

During the past year, on average, how often have you consumed the following food?

(Please check the appropriate box)

Dairy products								
1. Milk: Serving = 1 cup =200 ml								
>6/day ☐	4-5/day ☐	2-3/day ☐	1/day ☐	5-6/wk ☐	2-4/wk ☐	1/wk ☐	1-3/mo ☐	< 1/ mo ☐
2. Yogurt: Serving = 1 cup =200 ml								
>6/day ☐	4-5/day ☐	2-3/day ☐	1/day ☐	5-6/wk ☐	2-4/wk ☐	1/wk ☐	1-3/mo ☐	< 1/ mo ☐
Fruits								
3. Fruits: **Banana**: Serving = 1 medium								
>6/day ☐	4-5/day ☐	2-3/day ☐	1/day ☐	5-6/wk ☐	2-4/wk ☐	1/wk ☐	1-3/mo ☐	< 1/ mo ☐
4. Dates: Serving = 3 medium								
>6/day ☐	4-5/day ☐	2-3/day ☐	1/day ☐	5-6/wk ☐	2-4/wk ☐	1/wk ☐	1-3/mo ☐	< 1/ mo ☐
5. Grapes: Serving = 10 peces								
>6/day ☐	4-5/day ☐	2-3/day ☐	1/day ☐	5-6/wk ☐	2-4/wk ☐	1/wk ☐	1-3/mo ☐	< 1/ mo ☐
6. Mango: Serving = 1 medium								
>6/day ☐	4-5/day ☐	2-3/day ☐	1/day ☐	5-6/wk ☐	2-4/wk ☐	1/wk ☐	1-3/mo ☐	< 1/ mo ☐
Vegetables								
7. Fresh vegetables : Serving = 1 cup								
>6/day ☐	4-5/day ☐	2-3/day ☐	1/day ☐	5-6/wk ☐	2-4/wk ☐	1/wk ☐	1-3/mo ☐	< 1/ mo ☐
8. Cooked Vegetables: Serving = ½ cup								
>6/day ☐	4-5/day ☐	2-3/day ☐	1/day ☐	5-6/wk ☐	2-4/wk ☐	1/wk ☐	1-3/mo ☐	< 1/ mo ☐
9 . **Green leafy vegetables** (spinach, mint, lettuce): Serving = 1 cup								
>6/day ☐	4-5/day ☐	2-3/day ☐	1/day ☐	5-6/wk ☐	2-4/wk ☐	1/wk ☐	1-3/mo ☐	< 1/ mo ☐
Meat								
10. Fresh red meat (lamb or beef etc): serving = 90-120 g								

>6/day ☐	4-5/day ☐	2-3/day ☐	1/day ☐	5-6/wk ☐	2-4/wk ☐	1/wk ☐	1-3/mo ☐	< 1/ mo ☐
11. Processed meat (lamb or beef or chiken etc): Serving = 90-120 g								
>6/day ☐	4-5/day ☐	2-3/day ☐	1/day ☐	5-6/wk ☐	2-4/wk ☐	1/wk ☐	1-3/mo ☐	< 1/ mo ☐
12. Fresh white meat (chiken or poultary): Serving = 90-120 g								
>6/day ☐	4-5/day ☐	2-3/day ☐	1/day ☐	5-6/wk ☐	2-4/wk ☐	1/wk ☐	1-3/mo ☐	< 1/ mo ☐
13. Fish: Serving is medium size fish ~200 g								
>6/day ☐	4-5/day ☐	2-3/day ☐	1/day ☐	5-6/wk ☐	2-4/wk ☐	1/wk ☐	1-3/mo ☐	< 1/ mo ☐
Breads, cereals and starches								
14. White rice: Serving = 1/2 cup (cooked) ~ 100 g								
>6/day ☐	4-5/day ☐	2-3/day ☐	1/day ☐	5-6/wk ☐	2-4/wk ☐	1/wk ☐	1-3/mo ☐	< 1/ mo ☐
15. Bread: serving = 1 medium								
>6/day ☐	4-5/day ☐	2-3/day ☐	1/day ☐	5-6/wk ☐	2-4/wk ☐	1/wk ☐	1-3/mo ☐	< 1/ mo ☐
16. Pasta and spaghetti: Serving = ½ cup (cooked) ~ 100 g								
>6/day ☐	4-5/day ☐	2-3/day ☐	1/day ☐	5-6/wk ☐	2-4/wk ☐	1/wk ☐	1-3/mo ☐	< 1/ mo ☐
Drinks								
17. Tea: Serving: 1 cup = 200 ml								
>6/day ☐	4-5/day ☐	2-3/day ☐	1/day ☐	5-6/wk ☐	2-4/wk ☐	1/wk ☐	1-3/mo ☐	< 1/ mo ☐
18. Coffee or Nescafe: Serving: 1 cup = 200 ml								
>6/day ☐	4-5/day ☐	2-3/day ☐	1/day ☐	5-6/wk ☐	2-4/wk ☐	1/wk ☐	1-3/mo ☐	< 1/ mo ☐
19. Fresh or caned juice: Serving = 1 cup ~ 200 ml								
>6/day ☐	4-5/day ☐	2-3/day ☐	1/day ☐	5-6/wk ☐	2-4/wk ☐	1/wk ☐	1-3/mo ☐	< 1/ mo ☐
20. Coke, Pepsi or any kind of soft drink: Serving = 1 cup ~ 200 ml								
>6/day ☐	4-5/day ☐	2-3/day ☐	1/day ☐	5-6/wk ☐	2-4/wk ☐	1/wk ☐	1-3/mo ☐	< 1/ mo ☐
Sweets								
21. Sweets (baklava, konafa, cookies, chocolate, mahlabiyyeh.. etc)**:** Serving: 100 g (1/2 cup)								
>6/day ☐	4-5/day ☐	2-3/day ☐	1/day ☐	5-6/wk ☐	2-4/wk ☐	1/wk ☐	1-3/mo ☐	< 1/ mo ☐

Seeds and nuts								
22. Seeds and nuts (almond, cashew, peanut, pistachio, walnut etc): Serving = 10								
>6/day ☐	4-5/day ☐	2-3/day ☐	1/day ☐	5-6/wk ☐	2-4/wk ☐	1/wk ☐	1-3/mo ☐	< 1/ mo ☐
Miscellaneous								
23. Pizza: Serving: 1 medium slice								
>6/day ☐	4-5/day ☐	2-3/day ☐	1/day ☐	5-6/wk ☐	2-4/wk ☐	1/wk ☐	1-3/mo ☐	< 1/ mo ☐
24. Boiled potato: Serving = 200 g (1 cup)								
>6/day ☐	4-5/day ☐	2-3/day ☐	1/day ☐	5-6/wk ☐	2-4/wk ☐	1/wk ☐	1-3/mo ☐	< 1/ mo ☐
25. French fries: Serving = 100 g (½ cup)								
>6/day ☐	4-5/day ☐	2-3/day ☐	1/day ☐	5-6/wk ☐	2-4/wk ☐	1/wk ☐	1-3/mo ☐	< 1/ mo ☐
26. What kind of oil usually used for cooking at home?								
Corn ☐	Sunflower ☐	Canola ☐	Olive ☐	> 1 type ☐	I do not know ☐			
27. What is the frequency of using oil in cooking at home? Serving = ½ cup								
>6/day ☐	4-5/day ☐	2-3/day ☐	1/day ☐	5-6/wk ☐	2-4/wk ☐	1/wk ☐	1-3/mo ☐	< 1/ mo ☐
28. What kind of cooking fat usually used in cooking at home?								
Butter ☐	Ghee ☐	Palm ☐	> 1 type ☐	I Do not know ☐	I do not use ☐			
29. What is the frequency of using fat in cooking at home? Serving = ½ cup								
>6/day ☐	4-5/day ☐	2-3/day ☐	1/day ☐	5-6/wk ☐	2-4/wk ☐	1/wk ☐	1-3/mo ☐	< 1/ mo ☐
30. How often do you eat meals at a fast food/non-fast food restaurant and at work?								
>6/day ☐	4-5/day ☐	2-3/day ☐	1/day ☐	5-6/wk ☐	2-4/wk ☐	1/wk ☐	1-3/mo ☐	< 1/ mo ☐
Vitamins and Minerals								
31. Do you regularly take vitamins or minerals during the past six months?								
Yes ☐	No ☐	Do not know ☐						
32. If yes, how often you take vitamins or minerals?								
< one year ☐	1-3 years ☐	4-6 years ☐	>6 years ☐					
33. Do you regularly take vitamin D pills during the past six months?								
Yes ☐	No ☐	Do not know ☐						
34. If yes, how often you take vitamin D pills?								

< one year ☐	1-3 years ☐	4-6 years ☐	>6 years ☐

Appendix 4: Al Ain Medical District Human Research Ethics Committee Approval

UAEU College of Medicine and Health Sciences

جامعة الإمارات العربية المتحدة
United Arab Emirates University

13th May 2014

Dr. Abderrahim Oulhaj
Institute of Public Health
College of Medicine and Health Sciences, UAE University
Al Ain, UAE.

Dear Dr. Abderrahim,

Re: Al Ain Medical District Human Research Ethics Committee - Protocol No. 14/21 - The relationship between vitamin D deficiency, diet, physical activity and the incidence of Gestational Diabetes Mellitus (GDM) in Ras Al Khaima (RAK) population in United Arab Emirates.

Thank you very much for submitting your application to the Ethics Committee.

Your submitted documents were reviewed by the committee and I am pleased to provide you ethical approval of your project.

May I reiterate, should there be any ethical concern arising from the study in due course the Committee should be informed.

Annual reports plus a terminal report are necessary and the Committee would appreciate receiving copies of abstracts and publications should they arise.

I wish to take this opportunity to wish you success with this important study.

This Ethics Committee is an approved organization of Federal Wide Assurance (FWA) and compliant with ICH/GCP standards.

With kind regards,

Yours sincerely,

U.A.E. UNIVERSITY FACULTY OF MEDICINE & HEALTH SCIENCES

Dr. Fawaz Torab

Chair, Al Ain Medical District Human Research Ethics Committee

Appendix 5: RAK Medical District Research Ethics Committee Approval

Ras Al Khaimah Medical District
Ras Al Khaimah – United Arab Emirates

Date: 5/03/2014
Sharifa Ali Abdulrahman Hashem
The relationship between vitamin D deficiency, diet and physical activity and the prevalence of Gestational Diabetes Mellitus in Ras Al Khaima in United Arab Emirates.

Address: Community medicine 00971506477247

Dear Dr. Sharifa Ali Abdulrahman Hashem
RAKREC Reference :0011/2013 :Please quote this number on all correspondence

The Research Ethics Committee has reviewed the above application at its meeting held on 30/01/2014.

Ethical Opinion
A favorable ethical opinion was given for the above research on the basis described in theApplication form, protocol and supporting documentation subject to the conditions:

1. The understanding that the research team complies with ICH-GCP guideline and all applicable regulations governing the conduct of clinical studies
2. The favourable opinion applies only to the following research site (S): RAK
3. Management permission or approval must be obtained from each site prior to the start of the study at the site concerned.
4. Annual progress reports from the date of approving the study must be submitted to the RAKREC.
5. Safety reporting:
6. Study Termination:

a. Any fatal SAEs and any SUSARs originating from any of the study sites approved must be reported to the REC within 7 calendar Days for fatal/life threatening events and 15 calendar days for other events.
b. Periodic safety reports (Safety information from the Annual Progress Reports, Development Safety Update Reports (DSURs) or findings and recommendations from Data Monitoring Committees) must be submitted whenever available.
a. In case of premature termination of the study, the REC should be notified within 15 days of termination.
b. In case of a planned termination/end of study, the REC should be notified within 90 days of its conclusion.

7. Study should commence within 6 months of the approval date.

8.The end of Study Report/Summary of study outcome should be submitted within 6 months of end of study.

9. The RAKREC should be notified of serious breaches of the protocol or of the conditions or principles of Good Clinical Practice (GCP) within 15 days.

10- The approval of your study expires on 4/03/2015. Should you wish to continue the study after this date, please submit an application for renewal together with the Annual Study

Appendix 6: Informed Consent (Facts about the Study)

جامعة الإمارات العربية المتحدة
كلية الطب والعلوم الصحية
قسم طب المجتمع

Facts about the Study	**حقائق عن الدراسة**
Purpose: We are doing this study in eight primary health care centers (Ras Alkhaimah, Al-Digdaga, Al-Dhait, Julfar, Al-rams, Al-mamoura, Al-Jazirah Al-Hamra, Shamal and Al-Nakheel health care centers), in RAK city in the UAE. To find out the risk factors for Gestational Diabetes Mellitus and the relationship between vitamin D deficiency and developing this disease. The results which will be obtained from this study will help us find out the risk factors of Gestational Diabetes Mellitus in Emirati citizens in RAK city in UAE. **Researchers:** A multidisciplinary team consisting of researchers from the Department of Community Medicine, (UAEU). The principal investigator Mrs. Sharifa Ali (PhD student), and the advisor Dr. Abdureehim Oulhaj. **Selection criteria:** 514 of Emirati pregnant women aged (18-45) in the eight primary health care centers in RAK city in the UAE will be asked to participate in this study. **When?** Scheduled to begin the process of selection and data collection in May 2014 and will continue to the beginning of February 2016. Benefits to participants: You will help to contribute valuable information about diet and physical activity patterns among pregnant women in the UAE. This information will help researchers to identify the risk factors that are related to the development of gestational diabetes in Emirati pregnant women. To manage and reduces GDM and type 2 diabetes.	**الغرض :** تشمل هذه الدراسة النساء الحوامل اللواتي يترددن على في ثمانية مراكز للرعاية الصحية الأولية عيادة الحوامل (مركز النخيل، مركز رأس الخيمة، مركز المعمورة، مركز جلفار مركز شمل، مركز الدقداقة، مركز الظيت، ومركزالجزيرة الحمراء الصحي) في إمارة رأس الخيمة بدولة الإمارات العربية المتحدة وذلك للتعرف أسباب إنتشار سكري الحمل في الدولة، كما تتيح هذه الدراسة التعرف على العلاقة بين سكري الحمل ونقص فيتامين د، حيث أثبتت بعض الدراسات أن هناك علاقة بين نقص فيتامنين د والإصابة بسكري الحمل بالإضافة إلى دراسة نمط الحياة من ممارسة الرياضة والغذاء لدى الحوامل المواطنات في الإمارة . **الباحثون:** يقوم بهذه الدراسة باحثون من قسم الصحة العامة بجامعة الإمارات العربية المتحدة لنيل درجة الدكتوراة للقائم الرئيسي للبحث وهي الطالبة شريفة علي عبدالرحمن بالإضافة إلى المشرف العام على البحث وهو د.عبدالرحيم الحاج. **معايير الاختيار:** سيطلب من (514) إمرأة إماراتية حامل تتراوح أعمارهم ما بين 18- 45 سنة في المراكز الصحية الثمانية في إمارة رأس الخيمة بدولة الإمارات العربية المتحدة المشاركة في هذه الدراسة. **متى؟** من المقرر أن تبدأ عملية الاختيار وجمع البيانات في مارس 2014 وستستمر إلى فبراير 2016 **فوائد للمشاركين:** تتيح هذه الدراسة التعرف على العلاقة بين سكري الحمل ونقص فيتامين د، حيث أثبتت بعض الدراسات أن هناك علاقة بين نقص فيتامنين د والإصابة بسكري الحمل بالإضافة إلى دراسة نمط الحياة من ممارسة الرياضة والغذاء لدى الحوامل المواطنات في الإمارة. تساعد هذه المعلومات الباحثين في تحديد عوامل الخطورة المرتبطة بسكري الحمل عند المواطنات الإماراتييات وبالتالي التقليل من حالات سكري الحمل وكذلك النوع الثاني من السكري حيث أثبتت الدراسات أن 10-60% من سكري الحمل ممكن أن تتحول إلى النوع الثاني من السكري خلال 5-10 سنوات بعد الولادة إذا لم يتبع النظام الغذائي الصحي المتوازن .
What participant will ask to do?	**ماذا سيفعل المشاركون:**

1) A study staff will do an interview with you which will last 30-45 minutes. 2) We will ask you to complete three questionnaires (Food Frequency Questionnaire, Physical Activity Questionnaire and demographic information questionnaire). 3) Blood will be drawn from each participant as a part of the routine care in the health care center to measure vitamin D level, fasting blood sugar in the first visit and OGTT (oral glucose tolerance test) will be done at (24-28) gestation's weeks. ***Questions?*** *Please call* : Sharifa Ali, *Phone: 00971506477247* Email: sharifa_ali_hashem@hotmail.com	1. سيقوم الباحث بإجراء مقابلة مع كل حامل تستغرق 30-45 دقيقة يتم من خلالها استكمال ثلاث استمارات تتناول المعلومات الديموغرافية، التغذية وأنماط ممارسة النشاط البدني. 2. القياسات الحيوية (الوزن والطول ، وضغط الدم). 3.سيتم سحب عينة من الدم من كل مشاركة في البحث كجزء من العمل الروتني والعلاج المقدم في المركز الصحي مع الإحتفاظ ب 3 مل من الدم لقياس مستوى فيتامني د فيما بعد. كما سيتم عمل تحليل احتمال السكر في الأسبوع (24-28) حيث سيتم إعطاء الحامل شراب الجلوكوز 75 جم ومن بعدها إجراء تحليل السكر بعد ساعتين كجزء من العمل الروتيني للمركز. **للاستفسارات:** **يرجى** الاتصال على الباحثة : شريفة علي عبدالرحمن هاتف رقم:0506477247 بريد الكتروني: sharifa_ali_hashem@hotmail.com

Appendix 7: Consent to Participate in a Research Study

Consent to Participate In a Research Study

TITLE OF STUDY: The relationship between vitamin D deficiency, diet, physical activity and the development of Gestational Diabetes Mellitus in Ras Al Khaima in the UAE.

UAEU Principal Investigator: Sharifa Ali Hashem Abdulrahman Albelooshi

Phone number: 00971504475985

Department: Community Medicine

Co-Investigator: Dr. Abderrahim Oulhaj

Department: Community Medicine

Phone number: 00971506477247

Study Contact phone number: 00971506477247

We are asking you to participate in an epidemiologic study that is a cohort study from the United Arab Emirates University (UAEU).

You will be one of 714 of pregnant Emirati women who are counseling the primary health care centers (Al Nakheel, Al Mamoura, Al Dhait, Aldigdaga, Alrams, Julfar, Shamal and RAK Health care centers) in RAK city in the UAE. We describe details of this study below. We want you to understand this information so that you can decide whether or not you want to be in this study. Please ask questions if there is anything that you do not understand. We will give you a copy of this form to keep after signing.

What is the purpose of the study?

We are doing this study in RAK city in the UAE to find out the relationship vitamin D deficiency, diet, and physical activity and development of Gestational Diabetes. The results which we will obtain from this study will help us to find out the risk factors for Gestational Diabetes Mellitus in Emirati citizens in RAK city in UAE, which could provide national guidelines to control the disease.

How long will you be in this study?

There will be one meeting which will last approximately 30-45 minutes.

What will you are asked to do during the study?

4) A study staff will do an interview with you which will last 30-45 minutes.
5) We will ask you to complete three questionnaires (Food Frequency Questionnaire, Physical Activity Questionnaire and demographic information questionnaire).
6) Blood will be drawn from each participant as a normal routine care in the health care center to measure Fasting Blood sugar in the first visit and OGTT (75 g 2hr postprandial) will be done at 24-28 gestation's weeks, and 3ml (about a teaspoon) blood will be stored for vitamin D analysis .
7) You will be called after delivery by the principal investigator to conform the development of gestational diabetes, if it has not been mentioned in your medical record.

What are the possible risks and discomforts of being in the study?

This study poses no risk to you. However, this study might involve the following discomforts to you.

The in-person interviews include some personal questions about your behaviors (diet and physical activity) and demographic information which may make you uncomfortable.

Weight, height and blood pressure will be measured.

Blood will be drawn as a part of the routine care in the lab of the health care center or Saqer hospital or Obaidallah hospital to measure Fasting Blood Sugar in the first visit, and 3ml of the blood will be stored for vitamin D analysis. OGTT will be done as a part of the routine care on (24-28) weeks of gestation.

What are the benefits of me being in the study?

You will help contribute valuable information about diet and physical activity patterns for the pregnant women in RAK city in the UAE. This information will help researchers identify risk factors that are related to developing gestational diabetes in Emirati women in UAE and to explore the relationship between gestational diabetes and vitamin D deficiency, future generations are likely to benefit as this results could lower the prevalence of type 2 diabetes which is very common in UAE.

Are there any costs?

It will not cost you any money to be in this study.

Protection of privacy:

Your will be assigned a study number. All information you give will be stored only with your study number, not with your name. Personal information that can identify you and link you to your study number will be kept separate, and all information you provide in this study will be kept completely confidential. These will be stored on password protected computer files and only study staff will have access to that information. We will make every effort to protect the identity of all participants in this study.

Right to refuse or to drop out of the study:

Your being in this study is your choice and your participation is voluntary. You can decide not to be in this study at any time. You may refuse to answer questions and still be part of this study. You may also choose to be in some parts of the study and not in others. If you wish to drop out of the study or if you have any questions, please call the study staff at 00971506477247 or email sharifa_ali_hashem@hotmail.com.

Offer to answer questions:

Today you can ask all questions you may have about this study. If you have more questions you can call us at 00971506477247 or send email to sharifa_ali_hashem@hotmail.com

Institutional Review Board approval:

The Ethics Committee in RAK Medical District and the Institutional Review Board (IRB) in UAE both reviewed this study. These groups make sure that researchers take care of study subjects.

If you have questions about your rights as a subject, you can call Institutional Review Board (IRB) in UAEU at: **+97137137463**

And the Ethics Committee in RAK Medical District:

Dr. Abdullah Alabaasi – Saqer Hospital at: 0097172223666

Participant's Agreement:

I, the undersigned, have had the nature and purpose of the above named study explained to me. I freely give my consent to be in this study. I understand that participation is voluntary and that I may withdraw from the study at any stage. I understand that not participating or withdrawing from the study will not have any adverse effect on my employment or medical care. I have been given a subject information sheet and the contact details of the Principal Investigators should I have any questions at a later stage. I understand that any information I give will be treated in the strictest confidence and will not be given to anyone outside the investigating team without my express permission. After signing, I understand I will get a copy of this consent form.

_____ _____

Signature of Research Subject Date

_____

Printed Name of Research Subject

_____ _____

Signature of Person Obtaining Consent Date

_____

Printed Name of Person Obtaining Consent

_____ _____

Signature of Field Investigator Date

_____

Printed Name of Field Investigator