"TO DETERMINE INCIDENCE OF GESTATIONAL DIABETES MELLITUS USING A SINGLE STEP DIAGNOSTIC TEST - A ONE YEAR HOSPITAL BASED PROSPECTIVE STUDY"

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Under the Guidance of

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I hereby declare that this dissertation entitled **"TO DETERMINE INCIDENCE OF GESTATIONAL DIABETES MELLITUS USING A SINGLE STEP DIAGNOSTIC TEST - A ONE YEAR HOSPITAL BASED PROSPECTIVE STUDY"** is a bonafide and genuine research work carried out by me under the guidance of **Dr. J. C. SHRAVAGE** **MD** Professor, Department of Obstetrics and Gynaecology, Jawaharlal Nehru Medical College, Nehru Nagar, Belgaum - 590 010.

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LIST OF ABBREVIATIONS USED

ACOG	-	American Congress of Obstetricians and Gynaecologists
ADA	-	American Diabetes Association
BMI	-	Body mass index
C&C	-	Carpenter and Coustan
CDA	-	Canadian Diabetes Association
CI	-	Confidence interval
CTG	-	Cardiotocograph
DF	-	Degree of freedom
DIPAP	-	Diabetes in Pregnancy Awareness and Prevention
DIPSI	-	Diabetes in Pregnancy Study Group India
dL	-	Decilitre
DM	-	Diabetes mellitus
FPG	-	Fasting plasma glucose
GCT	-	Glucose challenge test
GDM	-	Gestational diabetes mellitus
GNS	-	Glucose normal saline
HAPO	-	Hyperglycemia and Adverse Pregnancy Outcome
HbA1C	-	Glycosylated haemoglobin
HELLP	-	Hemolysis elevated liver enzyme low platelet count
IADPSG	-	International Assosication of Diabetes and Pregnancy Study groups
IDM	-	Infants of diabetic mothers
IGT	-	Impaired glucose tolerance
IOM	-	Institute of Medicine

IV	-	Intravenous
KPCO	-	Kaiser Permanente of Colorado
LGA	-	Large for gestational age
Mg	-	Milligram
MNT	-	Medical nutritional therapy
NDDG	-	National Diabetes Data Group
NGT	-	Normal glucose tolerance
NS	-	Normal saline
OGTT	-	Oral glucose tolerance test
OR	-	Odds ratio
p value	-	Probability value
PCOS	-	Polycystic ovarian syndrome
PG	-	Plasma glucose
PCOD	-	Polycystic ovarian disease
PPG	-	Post prandial glucose
RDS	-	Respiratory distress syndrome
SD	-	Standard deviation
T2DM	-	Type 2 Diabetes Mellitus
UK	-	United Kingdom
US FDA	-	United State Food and Drug Administration
WHO	-	World Health Organization
x^2	-	Chi-square

ABSTRACT

Background and Objectives

Women with GDM are at increased risk of future diabetes predominantly type 2 diabetes mellitus and is also associated with increased risk of fetal morbidity and mortality. The present study was undertaken with a single step test to detect GDM in pregnancy which has been validated and furthermore the findings of this study will also help to determine the incidence of GDM with respect to different period of gestation.

Methods

The present one year prospective study was conducted in the Department of Obstetrics and Gynaecology, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum between the period of September 2010 to August 2011 on 120 pregnant women attending the antenatal clinic. Participating patients underwent Oral glucose tolerance test with 75 gm of glucose in their first trimester. If test results negative patients underwent repeat testing at 24 to 28 weeks and if found negative, repeated test at 32 to 34 weeks.

Results

More than half (55.83%) women had age between 20 to 24 years. Overall the mean age was 23.04 ± 3.36 years and 67.50% women had BMI in the range of 19.8 to 26.0 Kg/m^2. Overall the mean BMI was 20.7 ± 3.07 Kg/m^2 and 50.83% pregnant women were multrigravida. During the first trimester 9.17% had GDM whereas 0.83% had overt diabetes. During the second and third trimester 7.45% and 12.05% patients were newly diagnosed with GDM respectively. Of the 120

patients subjected to the study, overall incidence of GDM was 23.33% and 0.83% was diagnosed with overt diabetes. During the first trimester, 83.33% patients were multigravida and this association of gravidity with GDM was statistically significant (p=0.018).

Conclusion and interpretation

This evidence is enough to evaluate the efficacy of subjecting all the pregnant women to test for diagnosing GDM in each trimester and this test should become the part of routine antenatal investigations.

Keywords

Fasting blood sugar ; Gestational Diabetes Mellitus; Oral glucose tolerance test; Type 2 Diabetes Mellitus.

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INTRODUCTION

Gestational diabetes mellitus (GDM) is defined as carbohydrate intolerance with onset or recognition during pregnancy.[1] Women with GDM are at increased risk of future diabetes predominantly type 2 diabetes mellitus (DM) and is also associated with increased risk of fetal morbidity and mortality. The prevalence of GDM in India varies from 3.8 to 21% in different parts of the country, depending on geographical locations and diagnostic methods used.[2-4]

American Diabetes Association (ADA) recommends selective screening with two step procedures. But major drawback of this criterion is that, the glycaemic cut off was validated against the future risk of these women developing diabetes and not on the fetal outcome. And method is cumbersome as it involves screening and then diagnostic test.[5,6]

World Health Organization (WHO) recommends universal screening with a two hour 75 gm oral glucose tolerance test (OGTT) with a threshold plasma glucose concentration of greater than or equal to 140 mg/dL at two hours. Shortcoming with this method is that, the criteria suggested for diagnosis of GDM was also not based on maternal and fetal outcome but probably the criteria was recommended for its easy adaptability in clinical practice.[7]

There was no significant difference between prevalence of GDM using ADA and WHO criteria. Both short term and long term morbidity in the offspring occurs at the inflection point of maternal two hour plasma glucose of more than or equal to 140 mg/dL and as such, this level assumes clinical significance.[8]

Insulin is detectable in fetal pancreas as early as nine weeks after conception.[9] An increase in beta cell mass and insulin secretion in the fetus occurs by the 16th week of gestation, in response to maternal hyperglycemia.[10] The priming of the fetal beta cells may account for the persistence of fetal hyperinsulinaemia throughout pregnancy and risk of accelerated fetal growth,[11] even when the mother enjoys good metabolic control in later pregnancy.[12] This necessitates performing the test procedures to diagnose GDM in the first trimester itself. Further, early detection and care results in a better fetal outcome.[13]

Usually screening for GDM is done at 24 weeks, if positive followed by confirmatory test which requires four blood samples to be taken from the patient and hence, cumbersome and time consuming method.

By using a single step method in the first trimester itself we will be able to pick up the cases who have pre gestational as well as early onset gestational diabetes mellitus. And the test also is less time consuming and comfortable for the patient.

In view of the above two aspects, the present study was undertaken with a single step test to detect GDM in pregnancy which has been validated and furthermore the findings of this study will also help to determine the incidence of GDM with respect to different period of gestation.

OBJECTIVE

Objectives of the present study were;

Primary objective

To find out the incidence of GDM in the community by using a single step diagnostic test.

Secondary objective

To determine the onset of GDM with respect to period of gestation

REVIEW OF LITERATURE

Background

Abnormal maternal glucose regulation occurs in three to ten percent of pregnancies. Studies suggest that the prevalence of DM among women of childbearing age is increasing. This increase is believed to be attributable to more sedentary lifestyles, changes in diet, continued immigration from high-risk populations, and the virtual epidemic of childhood and adolescent obesity. Gestational diabetes mellitus is defined as glucose intolerance of variable degree with onset or first recognition during pregnancy. Gestational diabetes mellitus accounts for 90% of cases of diabetes mellitus in pregnancy. Type II diabetes mellitus accounts for eight percent of cases of diabetes mellitus in pregnancy, and given its increasing incidence, preexisting diabetes mellitus now affects one percent of pregnancies.[14,15]

Infants of mothers with preexisting diabetes experience double the risk of serious injury at birth, triple the likelihood of cesarean delivery, and quadruple the incidence of newborn intensive care unit admission. Studies indicate that the risk of these morbidities is directly proportional to the degree of maternal hyperglycemia. For this reason, the excessive fetal and neonatal morbidity attributable to diabetes in pregnancy should be considered preventable with early diagnosis and effective treatment therapies.[16]

History[17]

Gestational diabetes (GD) as a clinical entity officially began in 1979 when the National Diabetes Data Group (NDDG) issued an updated classification of diabetes types, including one that was present only during pregnancy. In 1979, the First International Workshop-Conference on GDM also met, essentially declared GD a disease, finding it a significant health risk that needed treatment. Instead of the more neutral "Carbohydrate Intolerance of Pregnancy", the term "Gestational Diabetes Mellitus" was used (often shortened in various resources to Gestational Diabetes, GD, or GDM). Authorities felt that if the term 'diabetes' was used, women would be more likely to take the diagnosis seriously and insurance companies would be much more likely to cover treatment for it.

However, the idea of subclinical glucose levels in pregnancy affecting mother or baby (or being an early sign of future full-blown diabetes) had been discussed previously. Hadden (1998) reports incidents in the medical literature appearing as early as 1823 where diabetic-like conditions presented during pregnancy but seemed to disappear afterwards. However, greater attention to the concept that lesser degrees of hyperglycemia might negatively affect a pregnancy began to appear in the 1940s and 1950s. In these studies, researchers found increased perinatal mortality among the babies of women who developed diabetes years later, leading to the coining of the term "prediabetes in pregnancy."

Belgian researcher JP Hoet published a study on "Carbohydrate Metabolism During Pregnancy" and first used the term, "metagestational diabetes" in 1954. His investigations sparked a series of investigations in the 50s

and 60s. Jorgen Pedersen probably was the first to use the modern term "gestational diabetes" in 1967, and this was the term promoted by Dr. Norbert Freinkel and associates, later adopted by the First International Workshop-Conference on GDM.

The first major prospective study was established in Boston in 1954, and the one hour 50 gm glucose screening test was first used there. However, the emphasis was on criteria that established risk for future diabetes, not on risk to the fetus. The results from this Boston study were presented by O'Sullivan and Mahan in 1964, and showed that higher blood glucose values in pregnancy correlated with the development of diabetes later in life.

In October 1979, Dr. Norbert Freinkel (representing the American Diabetes Association) and Dr. John Josimovich (representing the American College of Obstetricians and Gynecologists) met in Chicago at the First International Workshop Conference on Gestational Diabetes Mellitus. They gathered together experts from around the world to share their clinical experience, research, and opinions about GDM. Between this conference and the re-classifications from the National Diabetes Data Group, Gestational Diabetes as an official clinical entity was born.

Definition

It is now defined as*"Carbohydrate intolerance of variable severity with onset or first recognition during the present pregnancy. The definition applies whether insulin is used for treatment or the condition persists after pregnancy but*

does not exclude the possibility that the glucose intolerance may have antedated the pregnancy."[1]

According to WHO, GDM is defined as plasma glucose concentration of greater than 140 mg/dL at two hours after an 75 gm of oral glucose tolerance test similar to that of impaired glucose tolerance test in a non pregnant state.[18]

Epidemiology

Prevalence

Worldwide

GDM is the most common metabolic disease of pregnancy. GDM affects an estimated 1,70,000 (1-14%) pregnancies each year in the United States, depending on the diagnostic criteria used and characteristics of the population.[19] 30-50% of women with GDM will have recurrent GDM in a future pregnancy.[20] Of particular concern, 20-50% of women with GDM will develop type 2 diabetes mellitus (T2DM) in the 5-10 years after delivery.[19] Recent meta-analysis reports that GDM corresponds to a 7.4 fold increased risk for developing T2DM.[20]

The National Diabetes Education Progress estimated National prevalence of GDM in United States during 2009 was approximately seven percent in women of child bearing age group 15 to 44 years.

Scenario in India

The scenario in India today is that there are over 43 million diabetics in the country. This makes India the diabetes capital of the world, with half the

diabetic population being women. There are 14 million women in India, in the age group of 20 to 39 years who are considered in the child bearing age. These women are at a high risk, given that the prevalence of Gestational Diabetes (diabetes during pregnancy) is about eight to seventeen percent in India. This is a dismal figure and is one of the highest in the world. Prevention and management of gestational diabetes is imperative since it is associated with a significant increase in still births and other complications. In Indian context the prevalence of GDM is steadily increasing from two percent in 1982 to 12% in 1991 and it has almost doubled to 16.55% in 2002.

In India, a community based study Diabetes in Pregnancy Awareness and Prevention (DIPAP), was performed to ascertain the prevalence of GDM in a cohort of 12,056 pregnant women living in urban, semi - urban, and rural areas by using WHO criteria. Among them, the overall prevalence of GDM was 13.9%.[21] Further, to ascertain the consistency of WHO criteria in diagnosing GDM, after determining the desired sample size with the required statistical power, a total of 1246 pregnant women underwent 75gm OGTT. Among them 13.2% were detected to have GDM with a two hour PG $\geq$ 140 mg/dL. This finding substantiates and validates the previous prevalence data as well as the WHO criteria. Thus 2 hour plasma glucose $\geq$ 140 mg with 75 gm oral glucose load has been accepted by the Diabetes in pregnancy Study group India (DIPSI) for diagnosing GDM.[21]

The prevalence of GDM in India varied from 3.8 to 21.0% in different parts of the country, depending on the geographical locations and diagnostic methods used.[3-7] Gestational diabetes mellitus has been found to be more

prevalent in urban areas than in rural areas. For a given population and ethnicity, the prevalence of GDM corresponds to the prevalence of impaired glucose tolerance (IGT), in non pregnant adult within that given population.

Trends in prevalence[22]

Various studies[7,22] have assessed the annual prevalence. All studies reported an increase in GDM prevalence. However, increases varied widely across studies: from 16%[22] in Montana to 127%[7] in the study in a large maternity hospital in Melbourne. These variations may depend on differences in clinical surveillance for diabetes before pregnancy, length of the time of observation, the time period the study was conducted, the racial/ethnic composition of the study population, whether GDM prevalence was controlled for changes in maternal age (usually more advanced in the latest years), whether trends were analyzed only among women who were screened for GDM, and whether laboratory glucose results were available and GDM therefore was accurately defined by the same plasma glucose thresholds over time.

The Northern California Kaiser Permanente study[23] was the only study that accurately assessed variation in penetration of screening over time. Among screened pregnancies, the age and race/ethnicity-adjusted yearly prevalence of GDM defined by hyperglycemia increased by 68%: from 3.7% in 1991 to 6.6% in 1997, and leveled off through 2000 (6.2%). The prevalence of GDM defined by hyperglycemia, a hospital discharge diagnosis, or both increased from 5.1% in 1991 to 7.4% in 1997 and then leveled off through 2000 (6.9%). Similar increases in the prevalence of GDM were observed in all ethnic groups. The prevalence of

GDM (defined by American Diabetes Association criteria or physician diagnosis) was higher among Asians and Hispanics, intermediate among African-Americans, and lower among non-Hispanic whites. The prevalence of GDM increased in all age-groups with the highest proportional increase in the youngest group, where the prevalence almost doubled from 1991 (1.4%) to 2000 (2.7%).

The South Australia study[24] examined the prevalence of GDM between 1988 and 1999. An increase of 72% in GDM prevalence among non-Aboriginal women was observed, whereas a smaller increase of 12% was observed among Aboriginal women.

The Colorado Kaiser Permanente study[23] observed an increase in GDM prevalence of ~95% between 1994 and 2002.

A recent report from Montana showed that the prevalence of GDM, as reported in the birth certificate records, increased by ~10% among white women and by ~21% among American Indian women between 2000 and 2003.

An early report from Melbourne[7] compared the prevalence of GDM in one large maternity hospital in 1979 to 1983 and 1984 to 1988. The authors demonstrated a doubling in the GDM prevalence that appeared to apply similarly to mothers who were born in many different countries and currently living in Australia.

A recent study[25] examined GDM prevalence as reported in the New York City birth certificate records in 1990 and again in 2001. The prevalence of diagnosed GDM increased by ~46%, and increments were observed in all

race/ethnicity groups. Also in this study, the prevalence of GDM was higher among Asian women.

Screening and diagnosis

Screening tests[26]

The different screening tests used are

Fasting blood glucose

An easier screening procedure with cut-off of 95 mg/dL but it is insufficient as sole marker of GDM as most cases have fasting blood glucose below putative threshold. False positive rates are as high as 30 to 57%. Fasting blood glucose level of > 125 mg/dL is diagnostic of overt diabetes during pregnancy.[27,28]

Random blood glucose

Random blood sugar value greater than 200 mg/dL is diagnostic of diabetes during pregnancy and precludes the need for any glucose challenge test. The diagnosis must be confirmed on a subsequent day in the absence of unequivocal hyperglycemia.[29]

Glucose challenge test (GCT)

This test is performed as routine out-patient procedure without regard to last meal time. Capillary blood glucose estimation is done 1 hour after giving 50 gm of glucose to the pregnant women between 24 to 28 weeks of gestation. Cut off value of 130 mg/dL has 90% detection rate for GDM whereas cut off value of

140 mg/dL has 80% detection rate. GCT has test sensitivity of 79% and specificity of 87%. American College of Obstetricians and Gynaecologists (ACOG) and ADA state the usage of either threshold. This test needs confirmation by a diagnostic and confirmatory oral glucose tolerance test and forms a part of two step technique for GDM screening.[30,31]

Oral glucose tolerance test with 75/100 gm glucose (one step technique)

This test is both screening and diagnostic test and forms an effective part of one step procedure to screen for GDM. This approach may be cost-effective in high risk populations. It should be done in the morning after an overnight fast of more than 8 hours and after at least 3 days of unrestricted diet, consuming more than or equal to 150 gm of carbohydrate per day. Patients should not smoke before the test and should remain seated during the test. A fasting blood glucose sample is drawn. The pregnant woman is given 75/100 gm of glucose in juice and the samples drawn at 1, 2 and 3 hours respectively.[32]

Diagnosis of GDM is made if two or more values are abnormal on 75/100 g oral glucose tolerance test during pregnancy. All values mentioned in Table 1 depict plasma blood sugar levels except O'Sullivan and Mahan which mentions venous whole blood. Measurement of blood glucose level in capillary blood by glucometer has made screening test easy and simple as it can be done in office setting and does not require elaborate laboratory facilities. It is important to know that capillary blood glucose levels are comparable to venous blood glucose levels during fasting state but are higher after meals.[33] In the 4th International workshop conference on GDM in 1997 a consensus was reached on replacing NDDG

criteria by Carpenter and Couston (C&C) criteria which has lower threshold values for the diagnosis of GDM so as to diagnose more cases of GDM.[34] This one stage procedure is preferred over one step approach as there are less follow-up losses, earlier detection and treatment.[35]

Glycosylated haemoglobin (A1c) and serum fructosamine

These tests are time consuming, and are expensive with low sensitivity. International expert committee and ADA now recommends the estimation of HbA1C (>6.5%) in the diagnosis of diabetes mellitus in general population but for the screening of GDM, studies are underway. Serum fructosamine levels indicate glycemic control over a shorter period, but are not indicated for diagnosis of GDM.[29,36]

Glycosuria

This test is affected by numerous physiological factors and has only 30% sensitivity.[37]

Comparison of methods of screening[40]

Of the various screening tests, OGTT is the most acceptable screening as well as diagnostic test. A number of screening procedures and diagnostic criteria (ADA, WHO, Canadian Diabetes Association [CDA], NDDG and Australasian criteria) are being followed in the same as well as in different countries. American Diabetes association recommends screening for selective (high risk) population. But compared to selective screening, universal screening for GDM detects more cases and improves maternal and neonatal prognosis. Hence universal screening

for GDM is essential, as it is generally accepted that women of Asian origin and especially ethnic Indians, are at a higher risk of developing GDM and subsequent type 2 diabetes.

ADA procedure

ADA recommends selective screening with two step procedures.

Step 1: A 50 gm glucose challenge test (GCT) is used for screening without regard to the time of last meal or time of the day.

Step 2: If one hour GCT value is more than 140 mg/dL, 100 gm oral glucose tolerance test is recommended and plasma glucose is estimated at 0, 1, 2 and 3 hours. Gestational Diabetes Mellitus is diagnosed if any two values meet or exceed FPG > 95 mg/dL, one hr PG > 180 mg/dL, two hr PG > 155 mg/dL and three hr PG > 140 mg/dL. But major drawback of this criteria is that, the glycaemic cut off was validated against the future risk of these women developing diabetes and not on the fetal outcome. And method is cumbersome as it involves screening and then diagnostic test.

World Health Organization procedure

World Health Organization recommends universal screening with a two hour 75 gm OGTT with a threshold plasma glucose concentration of greater than or equal to 140 mg/dL at two hours similar to that of IGT, outside pregnancy. Carpenter himself now recommends a two hour OGTT with 75 gm glucose. The reason for this is that "when a glucose tolerance test is administered to non-pregnant individuals, it is standard to use the 75 gm, two hour OGTT. Using a

different glucose challenge in pregnant versus non-pregnant patients leads to confusion in the laboratory and may result in errors in applying the proper diagnostic criteria. Further, the 75gm, two hour OGTT is in use during pregnancy in many countries around the world, typically using the same thresholds as in non-pregnant individuals". Shortcoming with this method is that, the criteria suggested for diagnosis of GDM was also not based on maternal and fetal outcome but probably the criteria was recommended for its easy adaptability in clinical practice.

International Association of Diabetes and Pregnancy Study Groups (IADPSG)[38] based on the Hyperglycemia and Adverse Pregnancy Outcome (HAPO) study[12] outcome recommends any one or more values of fasting plasma glucose (FPG) ≥ 92 mg/dL, 1 hr plasma glucose (PG) ≥ 180 mg/dL and two hr PG ≥ 153 mg/dL for the diagnosis of GDM. The IADPSG recommendation would result in variation in the prevalence of GDM from one centre to another depending on the choice of cut-off value used, either fasting one hr, two hr, or any two values for diagnosis. This flexibility will compromise the uniformity and likely to pose difficulty in comparing outcome data.

The HAPO study[12] was performed in response to the need for internationally agreed upon diagnostic criteria for gestational diabetes, based upon their predictive value for adverse pregnancy outcome. Increases in each of the 3 values on the 75 gm, 2-hour oral glucose tolerance test are associated with graded increases in the likelihood of pregnancy outcomes such as large for gestational age, cesarean section, fetal insulin levels, and neonatal fat content. Based upon an interative process of decision making, a task force of the International Association

of Diabetes and Pregnancy Study Groups recommends that the diagnosis of gestational diabetes be made when any of the following 75 gm, 2-hour oral glucose tolerance test thresholds are met or exceeded: fasting 92 mg/dL, 1-hour 180 mg/dL, or 2 hours 153 mg/dL. Various authoritative bodies around the world are expected to deliberate the adoption of these criteria.

Table 1. ADA and WHO criteria for the diagnosis of GDM[39]

	ADA 100 gm OGTT	**ADA 75 gm OGTT**	**WHO 75 gm OGTT**
Fasting (mg/dL)	95	95	126
1 Hr (mg/dL)	180	180	-
2 Hr (mg/dL)	155	155	140
3 Hr (mg/dL)	140	-	-

For the ADA criteria, two or more of the values form either the 100 or 75 gm OGTT must be met or exceeded to make the diagnosis of GDM. For the WHO criteria, one of the two values from the 75 gm OGTT must be met or exceeded to make the diagnosis of GDM.

Reconciliation factors between ADA and WHO[39]

Both short term and long term morbidity in the offspring occurs at the inflection point of maternal two hour plasma glucose of more than or equal to 140 mg/dl and as such, this level assumes clinical significance.

DIPSI guidelines: A single test procedure to diagnose gestational diabetes mellitus in the community[39]

Seldom, a pregnant woman visiting the ante-natal clinic for the first time comes in the fasting state. If she is asked to come on another day in the fasting state she may not return.[40,41] Hence it is important to have a test that detects the

glucose intolerance without the woman necessarily undergoing a test in the fasting state and it is preferable to perform the diagnostic test at the first visit itself.

In the antenatal clinic, a pregnant woman after undergoing preliminary clinical examination, has to be given a 75 gm oral glucose load, without regard to the time of the last meal. A venous blood sample is collected at 2 hours for estimating plasma glucose. GDM is diagnosed if 2 hr plasma glucose is $\geq$ 140 mg/dl.

Performing this test procedure in the non-fasting state is rational, as glucose concentrations are affected little by the time since the last meal in a normal glucose tolerant woman, whereas it will, in a woman with gestational diabetes.[42] After a meal, a normal glucose tolerant woman would be able to maintain euglycemia despite glucose challenge due to brisk and adequate insulin response, whereas, a woman with GDM who has impaired insulin secretion,[43] her glycemic level increases with a meal and with glucose challenge, the glycemic excursion exaggerates further.[44] Therefore, this procedure assumes clinical relevance as WHO criteria based on glucose concentration two hour after 75 gm glucose load was able to correctly identify subjects with GDM.[45] Yet another reason for recommending the single step procedure is that, the specificity of ADA screening with 50 gm 1-hr GCT without regard to time of the last meal is low.[50] Hence, instead of performing screening test using 50 gm-1 hr test and then 100 gm OGTT, this single step procedure serves both as screening and diagnostic test for GDM, is simple, economical and feasible.[46]

Advantages

- The pregnant women need not be fasting.[13,47]
- Causes least disturbance in a pregnant woman's routine activities.
- Serves as both screening and diagnostic procedure.

Timing of screening for GDM

Insulin is detectable in fetal pancreas as early as 9 weeks after conception.[48] An increase in beta cell mass and insulin secretion in the fetus occurs by the 16th week of gestation, in response to maternal hyperglycemia.[49,50] The priming of the fetal beta cells may account for the persistence of fetal hyperinsulinaemia throughout pregnancy and risk of accelerated fetal growth,[51] even when the mother enjoys good metabolic control in later pregnancy.[52] This necessitates performing the test procedures to diagnose GDM in the first trimester itself. Further, early detection and care results in a better fetal outcome.[53]

By following the usual recommendation for screening between 24 and 28 weeks of gestation, the chance of detecting unrecognised type 2 diabetes before pregnancy (pre GDM) is likely to be missed. If the two hour PG> 200 mg/dL in the early weeks of pregnancy, she may be a pre- GDM and A1c > 6 is confirmatory (normal A1c levels during pregnancy is 5.3-6). A pregnant woman found to have normal glucose tolerance (NGT) in the first trimester, should be tested for GDM around 24th- 28th weeks and again around 32nd- 34th weeks and also later weeks if necessary, particularly when rapid maternal weight gain occurs or fetal macrosomia is suspected.

Risk Factors[54]

Risk factors for gestational diabetes vary from study to study, but some remain consistent. These are listed as 'strong' associations solely due to their consistency of appearance in each study, and are put near the top. Others whose associations are less clear are listed towards the bottom. Remember that research varies and is sometimes contradictory. Some of these could be disproved at a later time.

- Family history of diabetes
- Parity (number of kids, especially 3-4 or more)
- Previous pregnancy with GDM
- Obesity
- Previous child over 4000 g (almost 9 lbs)
- Women whose own birth weights were over 9 lbs.
- Unexplained multiple miscarriages, stillbirths, or birth defects
- Weight gain in early adulthood
- Central fat distribution
- PCOS (PolysCystic Ovarian Syndrome)
- Cigarette smoking
- Multiple Pregnancies
- History of Skin/Urinary Tract/Genital Infections
- Hypertension
- Chronic Steroid Use
- Non-white ethnicity

The risk in *Asians* is less clear. Southeast Asians had increased rates, while Korean women had very low rates. Chinese women clearly had increased rates, especially if they were immigrants, but those in China also had slightly higher rates too. Japanese-Americans also have increased rates.

Women from India had very high rates in some areas, second only to those of Native Americans. This seemed true in both populations in India and in Indian populations abroad in the United Kingdom and in Fiji. However, not all areas of India showed such high rates. *Arabic* women also had slightly increased rates of GDM.

Pathophysiology

Maternal-fetal metabolism in normal pregnancy[55]

With each feeding, the pregnant woman undergoes a complex series of maternal hormonal actions (a rise in blood glucose; the secondary secretion of pancreatic insulin, glucagon, somatomedins, and adrenal catecholamines). These adjustments ensure that an ample, but not excessive, supply of glucose is available to the mother and fetus. The key features of this complex interaction include compared to nonpregnant subjects, pregnant women tend to develop hypoglycemia (plasma glucose mean = 65 to 75 mg/dL) between meals and during sleep. This occurs because the fetus continues to draw glucose across the placenta from the maternal bloodstream, even during periods of fasting. Interprandial hypoglycemia becomes increasingly marked as pregnancy progresses and the glucose demand of the fetus increases.

Levels of placental steroid and peptide hormones (eg, estrogens, progesterone, and chorionic somatomammotropin) rise linearly throughout the second and third trimesters. Because these hormones confer increasing tissue insulin resistance as their levels rise, the demand for increased insulin secretion with feeding escalates progressively during pregnancy. Twenty-four–hour mean insulin levels are 50% higher in the third trimester compared to the nonpregnant state.

If the maternal pancreatic insulin response is inadequate, maternal and, then, fetal hyperglycemia results. This typically manifests as recurrent postprandial hyperglycemic episodes. These postprandial episodes are most significantly accountable for the accelerated growth exhibited by the fetus.

Surging maternal and fetal glucose levels are accompanied by episodic fetal hyperinsulinemia. Fetal hyperinsulinemia promotes excess nutrient storage, resulting in macrosomia. The energy expenditure associated with the conversion of excess glucose into fat causes depletion in fetal oxygen levels.

These episodes of fetal hypoxia are accompanied by surges in adrenal catecholamines, which, in turn, cause hypertension, cardiac remodelling and hypertrophy, stimulation of erythropoietin, red cell hyperplasia, and increased hematocrit. Polycythemia (hematocrit >65%) occurs in 5-10% of newborns of diabetic mothers. This finding appears to be related to the level of glycemic control and is mediated by decreased fetal oxygen tension. High hematocrit values in the neonate lead to vascular sludging, poor circulation, and postnatal hyperbilirubinemia.

During a healthy pregnancy, mean fasting blood sugar levels decline progressively to a remarkably low value of 74 ± 2.7 (standard deviation [SD]) mg/dL. On the other hand, peak postprandial blood sugar values rarely exceed 120 mg/dL. Meticulous replication of the normal glycemic profile during pregnancy has been demonstrated to reduce the macrosomia rate. Specifically, when two postprandial glucose levels are maintained less than 120 mg/dL, approximately 20% of fetuses demonstrate macrosomia. Conversely, if postprandial levels range up to 160 mg/dL, macrosomia rates rise to 35%.

Effects of diabetes on fetus

Miscarriages

In all women with preexisting diabetes mellitus, there is a 9-14% rate of miscarriage. Current data suggest a strong association between degree of glycemic control prior to pregnancy and miscarriage rate. Suboptimal glycemic control has been shown to double the miscarriage rate in women with diabetes. A correlation also exists between more advanced diabetes and miscarriage rates. Patients with long-standing (>10 y) and poorly controlled (glycohemoglobin exceeding 11%) diabetes have been shown to have a miscarriage rate of up to 44%. Conversely, reports demonstrate a normalization of miscarriage rate with excellent glycemic control.[56]

Birth defects

Among the general population, major birth defects occur in one to two percent of the population. In women with overt diabetes and suboptimal glycemic

control prior to conception, the likelihood of a structural anomaly is increased four to eight fold. Although initial reports demonstrated anomaly rates as high as 18% in women with preexisting diabetes mellitus,[57] more recent reports with more aggressive preconception and first trimester management report anomaly rates between 5.1 and 9.8%.[58,59] Two-thirds of anomalies involve the cardiovascular and central nervous systems.

Neural tube defects occur 13 to 20 times more frequently in diabetic pregnancy. Genitourinary, gastrointestinal, and skeletal anomalies are also more common. The fact that no increase in birth defects occurs among the offspring of fathers who are diabetic and women who develop gestational diabetes after the first trimester is notable. This suggests that periconceptional glycemic control is the main determinant of abnormal fetal development in diabetic women.

When the frequency of congenital anomalies in patients with normal or high first-trimester maternal glycohemoglobin values was compared to the frequency in healthy patients, the rate of anomalies was only 3.4% with HbA1C of less than 8.5%, whereas patients with poorer glycemic control in the periconceptional period (HbA1C >8.5%) had a 22.4% rate of malformations. An overall malformation rate of 13.3% was reported in 105 patients with diabetes, but the risk of delivering a malformed infant was comparable to a normal population when the HbA1c was less than seven percent.[60] More recently, in a review of seven cohort studies, researchers found that patients with a normal glycohemoglobin (0 SD above normal), the absolute risk of an anomaly was two percent. At two SD above normal, this risk was 3%, with an odds ratio of 1.2 (1.1

to 1.4). As the glycohemoglobin increased so did the risk for malformation in a direct relationship.[61]

Because birth defects occur during the critical three to six weeks after conception, nutritional and metabolic intervention must be initiated well before pregnancy begins. Clinical trials of intensive metabolic care have demonstrated that malformation rates similar to those in the nondiabetic population can be achieved with meticulous preconceptional glycemic control.[59] Subsequent trials comparing a preconceptional intensive metabolic program to standard treatment over 15 years duration have demonstrated lowered perinatal mortality (0% vs 7%) and reduced congenital anomaly rate (14% to 2%). In addition, when the preconceptional counseling program was discontinued, the congenital anomaly rate increased by over 50%.[62]

Growth restriction

Although most fetuses of diabetic mothers exhibit growth acceleration, growth restriction occurs with significant frequency in pregnancies in women with preexisting type 1 diabetes. The most important predictor of fetal growth restriction is underlying maternal vascular disease. Specifically, pregnant patients with diabetes-associated retinal or renal vasculopathies and/or chronic hypertension are most at risk for growth restriction.

Growth acceleration

Excessive body fat stores, stimulated by excessive glucose delivery during diabetic pregnancy, often extends into childhood and adult life.[63]

Approximately 30% of fetuses of women with diabetes mellitus in pregnancy are large for gestational age (LGA). In preexisting diabetes mellitus this incidence appears slightly higher, 38%. Maternal obesity, common in type 2 diabetes, appears to significantly accelerate the risk of infants being LGA.[63]

A study of the effects of weight gain in women with gestational diabetes found that women with the condition whose gestational weight gain was greater than that in the Institute of Medicine's (IOM's) weight-gain guidelines had an increased risk of preterm delivery, of having a newborn who was LGA, and of requiring a cesarean delivery.[64] The chance that a newborn would be small for gestational age was greater among women with gestational diabetes whose weight gain was below the IOM guidelines.

Fetal obesity

Macrosomia is typically defined as a birth weight above the 90th percentile for gestational age or greater than 4000 grams. In pregnant diabetic women, macrosomia occurs in 15 to 45% of cases, a three fold increase from normoglycemic controls.[65]

Newborns with macrosomia experience excessive rates of neonatal morbidity, as illustrated by a study by Hunter et al in 1993, which compared the neonatal morbidity among infants of 230 women with insulin-dependent diabetes and infants of 460 women without diabetes. The infants of diabetic mothers (IDMs) had five fold higher rates of severe hypoglycemia, a four fold increase in macrosomia, and a doubled increase in neonatal jaundice.[66]

Birth injury, including shoulder dystocia and brachial plexus trauma, are more common among infants of diabetic mothers, and macrosomic fetuses are at the highest risk.

The macrosomic fetus in diabetic pregnancy develops a unique pattern of overgrowth, involving central deposition of subcutaneous fat in the abdominal and interscapular areas.[67] Skeletal growth is largely unaffected. Neonates of diabetic mothers have a larger shoulder and extremity circumference, a decreased head-to-shoulder ratio, significantly higher body fat, and thicker upper extremity skin folds compared to nondiabetic control infants of similar weights. Since fetal head size is not increased during poorly controlled diabetic pregnancy but shoulder and abdominal girth can be markedly augmented, the risk of injury to the fetus after delivery of the head (eg Erb palsy) is significantly increased.

When serial ultrasonographic examination findings from diabetic fetuses are plotted, the growth velocity of the abdominal circumference is often well above the growth centiles seen in nondiabetic fetuses and is higher than the fetal head and femur centiles. The accelerated growth of the abdominal circumference begins to rise significantly above normal after 24 weeks.

Metabolic syndrome

The adverse downstream effects of abnormal maternal metabolism on the offspring have been documented well into puberty. Glucose intolerance and higher serum insulin levels are more frequent in children of diabetic mothers as compared to normal controls. By age 10 to 16 years, offspring of diabetic pregnancy have a 19.3% rate of impaired glucose tolerance.[68]

The childhood metabolic syndrome includes childhood obesity, hypertension, dyslipidemia, and glucose intolerance. A growing body of literature supports a relationship between intrauterine exposure to maternal diabetes and risk of a metabolic syndrome later in life.[68,69] Fetuses of diabetic women that are born large for gestational age appear to be at the greatest risk.[70]

Perinatal morbidity and birth injury

Perinatal mortality[71]

In diabetic pregnancy, perinatal mortality has decreased 30-fold since the discovery of insulin in 1922 and intensive obstetrical and infant care in the 1970s. Nevertheless, the current perinatal mortality rates among women who are diabetic remain approximately twice those observed in the nondiabetic population.

Congenital malformations, respiratory distress syndrome (RDS), and extreme prematurity account for most perinatal deaths in contemporary diabetic pregnancies.

Birth injury[56]

Injuries of birth, including shoulder dystocia and brachial plexus trauma, are more common among infants of diabetic mothers, and macrosomic fetuses are at the highest risk.

Most of the birth injuries occurring to infants of diabetic mothers are associated with difficult vaginal delivery and shoulder dystocia. While shoulder dystocia occurs in 0.3-0.5% of vaginal deliveries among healthy pregnant women,

the incidence is two to four fold higher in women with diabetes. With strict glycemic control, the birth injury rate has been shown to be only slightly higher than controls (3.2 vs 2.5%).

Currently, clinical ability to predict shoulder dystocia is poor. Warning signs during labor (labor protraction, suspected fetal macrosomia, need for operative vaginal delivery) successfully predict only 30% of these events. Common birth injuries associated with diabetes are brachial plexus, facial nerve injury, and cephalohematoma.

Polycythemia[56]

A central venous hemoglobin concentration greater than 20 gm/dL or a hematocrit value greater than 65% (polycythemia) is not uncommon in infants of diabetic mothers and is related to glycemic control. Hyperglycemia is a powerful stimulus to fetal erythropoietin production mediated by decreased fetal oxygen tension. Untreated neonatal polycythemia may promote vascular sludging, ischemia, and infarction of vital tissues, including the kidneys and central nervous system.

Hypoglycemia

Approximately 15-25% of neonates delivered from women with diabetes during gestation develop hypoglycemia during the immediate newborn period.[72] Neonatal hypoglycemia is less frequent when tight glycemic control is maintained during pregnancy[73] and in labor. Unrecognized postnatal hypoglycemia may lead to neonatal seizures, coma, and brain damage.

Neonatal hypocalcemia[56]

Up to 50% of infants of diabetic mothers have low levels of serum calcium (<7 mg/100 mL). With improved management of diabetes in pregnancy, this occurrence has been reduced to 5% or less. These changes in calcium appear to be attributable to a functional hypoparathyroidism, though the exact pathophysiology is not well understood.

Postnatal hyperbilirubinemia[56]

Hyperbilirubinemia occurs in approximately 25% of infants of diabetic mothers, a rate approximately double that in a healthy population. The causes of hyperbilirubinemia in infants of diabetic mothers are multiple, but prematurity and polycythemia are the primary contributing factors. Increased destruction of red blood cells contributes to the risk of jaundice and kernicterus. Treatment of this complication is usually by phototherapy, but exchange transfusions may be necessary if bilirubin levels are markedly elevated.

Respiratory problems

Until recently, neonatal RDS was the most common and serious morbidity in infants of diabetic mothers. In the 1970s, improved prenatal maternal management for diabetes and new techniques in obstetrics for timing and mode of delivery resulted in a dramatic decline in its incidence from 31% to 3%.[74] Nevertheless, respiratory distress syndrome continues to be a relatively preventable complication.

The majority of the literature indicates a significant biochemical and physiological delay in infants of diabetic mothers. Tyden[75] and Landon[76] and colleagues reported that fetal lung maturity occurred later in pregnancies with poor glycemic control regardless of class of diabetes when infants were stratified by maternal plasma glucose levels.

The nondiabetic fetus achieves pulmonary maturity at a mean gestational age of 34-35 weeks. By 37 weeks' gestation, more than 99% of healthy newborn infants have mature lung profiles as assessed by phospholipid assays. However, in a diabetic pregnancy, presuming that the risk of respiratory distress has passed is unwise until after 38.5 gestational weeks have been completed.

Prior to contemplating any delivery before 38.5 weeks for other than the most urgent fetal and maternal indications, perform an amniocentesis to document pulmonary maturity.

Effects of diabetes on mother

Diabetic retinopathy[56]

This is the leading cause of blindness in women aged 24-64 years. Some form of retinopathy is present in virtually 100% of women who have had type 1 diabetes for 25 years or more; of these women, approximately 1 in 5 is legally blind. A prospective study showed that while half the patients with preexisting retinopathy experienced deterioration during pregnancy, all the patients had partial regression following delivery and returned to their prepregnant state by 6 months postpartum.

Other studies have suggested that rapid induction of glycemic control in early pregnancy stimulates retinal vascular proliferation.[77] However, when the total effect of pregnancy on ophthalmologic status was considered, women with pregnancies had a slower progression of retinopathy than nonpregnant women, probably because the modest deterioration in retinal status during rapid improvement in control is offset by the excellent control during the remainder of the pregnancy.

Current management recommendations include baseline ophthalmology referral for pregnant patients with diabetes, with follow-up according to degree of retinopathy.

Renal function[56]

In general, patients with underlying nephropathy can expect varying degrees of deterioration of renal function during a pregnancy. As renal blood flow and glomerular filtration rate increase 30-50% during pregnancy, the degree of proteinuria will also increase.

The most recent studies indicate that pregnancy does not measurably alter the time course of diabetic renal disease, nor does it increase the likelihood of progression to end stage renal disease. The progression to renal disease in diabetic patients appears to be related to duration of diabetes and degree of glycemic control.

Patients using the subcutaneous insulin pump have lower mean glucose levels than those using intermittent injections. The effect on progression of

nephropathy of 2 years of strict metabolic control showed that none of the patients managed on the insulin pump progressed to clinical nephropathy, while 5 patients with conventional treatment did.

Perinatal complications are greatly increased in patients with diabetic nephropathy. Preterm birth, intrauterine growth restriction, and preeclampsia are all significantly more common in women with diabetic nephropathy during pregnancy.

Chronic hypertension

This complicates approximately 1 in 10 diabetic pregnancies overall. Patients with underlying renal or retinal vascular disease are at a substantially higher risk, with 40% having chronic hypertension.[78] Patients with chronic hypertension and diabetes are at increased risk of intrauterine growth restriction, superimposed preeclampsia, abruptio placentae, and maternal stroke.

Baseline renal function determination is recommended in all patients with preexisting diabetes. Renal function assessments in each trimester should be performed in those with overt vascular disease or who have had diabetes for more than 10 years.

Preeclampsia

Consists of abrupt elevation in blood pressure, significant proteinuria, plasma uric acid levels greater than 6 mg/dL or evidence of hemolysis, elevated liver enzymes, and low platelet count (HELLP) syndrome. Preeclampsia is more frequent among women with diabetes, occurring in approximately 12% as

compared to 8% of the nondiabetic population. The risk of preeclampsia is also related to maternal age and the duration of preexisting diabetes. In patients who have chronic hypertension coexisting with diabetes, preeclampsia may be difficult to distinguish from near-term blood pressure elevations.

The rate of preeclampsia has been found to be related to the level of glycemic control, with FPG less than 105 mg/dL, the rate of preeclampsia was 7.8%, if FPG was greater than 105 mg/dL, the rate of preeclampsia was 13.8%.[78] In this same study, pregravida body mass index (BMI) was also significantly related to the development of preeclampsia.

Management

A team approach is ideal for managing women with GDM. The team would usually comprise an obstetrician, diabetes physician, a diabetes educator, dietitian, midwife and pediatrician. In practice, however, the team approach is not always possible due to limited resources.[3]

Patient Education[3]

The importance of educating women with GDM (and their partners) about the condition and its management cannot be overemphasized. The compliance with the treatment plan depends on the patient's understanding of:

- The implications of GDM for her baby and herself
- The dietary and exercise recommendations.
- Self monitoring of blood glucose
- Self administration of insulin and adjustment of insulin doses

- Identification and treatment of hypoglycemia (patient and family members).
- Incorporate safe physical activity (walking at usual pace/ arm exercise)
- Development of techniques to reduce stress and cope with the denial.

Medical Nutrition Therapy (MNT)[3]

All women with GDM should receive nutritional counselling. The meal pattern should provide adequate calories and nutrients to meet the needs of pregnancy. The expected weight gain during pregnancy is 300 to 400 gm/week and total weight gain is 10 to 12 kg by term. Hence the meal plan aims to provide sufficient calories to sustain adequate nutrition for the mother and fetus and to avoid excess weight gain and post prandial hyperglycemia.

Exercise[3]

The role of exercise in women with GDM has been controversial in the past because maternal exercise on a bicycle ergometer has been associated with fetal bradycardia. Subsequent small studies have shown small transient increases in fetal heart rate after maternal exercise. The bicycle ergometer, treadmill, and rowing ergometer led to uterine activity in 50, 40, and 10% of exercise sessions, respectively. Based on the potential benefits of exercise in women with GDM, the ADA recommends starting or continuing a program of moderate exercise in women without medical or obstetrical contraindications.

Insulin Therapy[2,3]

Insulin is essential if MNT fails to achieve euglycemia. Various criteria have been proposed for the initiation of insulin therapy. If MNT fails to achieve control that is, FPG >90 mg/dL and postmeal glucose >120 mg/dL, insulin may be initiated.

a) Preferable to start with premix insulin 30/70 of any brand

- Starting dose: 4 units before breakfast.
- Every 4th day increase two units till 10 units.
- If FPG remains> 90 mg/dL, advise 6 units before breakfast and 4 units before dinner.
- Review with blood sugar test and adjust dose further.
- Total insulin dose per day can be divided as two thirds in the morning and one third in the evening.
- Initially if post breakfast plasma glucose is high, start premix 50/50.

b) If GDM is diagnosed in the third trimester, MNT is advised for a week. Insulin is initiated if MNT fails.

c) If two hour PG> 200 mg/dL at diagnosis, a starting dose of 8 units of premixed insulin could be administered straightway before breakfast and the dose has to be titrated on follow- up. Along with insulin therapy, MNT is also advised.

Insulin analogue

If postprandial glucose is still not under control- consider using rapid acting insulin analogue. Rapid acting insulin analogues, (Aspart-Novorapid/Lispro-Humalog) have been found to be safe and effective in achieving the targeted postprandial glucose value during pregnancy.[79] Lispro analogue is approved by United States Food and Drug Adminsitration (US FDA) and Aspart has been approved for use in pregnancy both by US FDA and European Union. Novomix has been found to be safe and effective in the management of GDM.[80] Pen injectors are very useful and the patient's acceptance is excellent.

Oral Antidiabetic Drugs

Recently reports have shown good fetal outcome in GDM women who were on glyburide (micronised form of Glibenclamide). A randomized unblinded clinical trial compared the use of insulin and glyburide in women with GDM who were not able to meet glycemic goals on meal plan. Treatment with either agent resulted in similar perinatal outcomes. All these patients were beyond the first trimester of pregnancy at the initiation of therapy.[81] More studies are required before routinely recommending glibenclamide during pregnancy especially during the first trimester itself.

Metformin has been found to be useful in women with polycystic ovarian disease (PCOD) who failed to conceive.[82,83] Continuing this drug after conception is still a controversy. But there are a few studies favouring continuation of metformin throughout pregnancy. Currently, oral agents are not routinely

recommended during pregnancy though emerging data on glibenclamide and metformin is interesting.

Monitoring glycemic control

The success of the treatment for a woman with GDM depends on the glycemic control maintained with meal plan or pharmacological intervention. To know the effectiveness of treatment, monitoring of glycemic control is essential.[84-91] Once diagnosis is made, MNT is advised initially for two weeks. If MNT fails to achieve control i.e., FPG = 90 mg/dL and/or 1 ½ hr post prandial glucose (PPG) = 120mg/dL, insulin may be initiated. Once target blood glucose is achieved, woman with GDM till the 28th week of gestation require lab monitoring of both fasting and 1½ hr post breakfast once a month and at other time of the day as the clinician decides.[3]

After the 28th week of gestation, the laboratory monitoring should be more frequent atleast once in two weeks, if need be more frequently. After 32 weeks of gestation, lab monitoring should be done once a week till delivery. In high risk pregnancies, frequency of monitoring may be intensified with self monitoring of blood glucose (SMBG). Continuous glucose monitoring devices are available but these equipments need special training and are expensive. These devices may be useful in high risk pregnancies to know the glycemic fluctuations and to plan proper insulin dosage.[92]

Measuring Other Parameters

Maternal

If the glucose intolerance is detected in the early pregnancy, A1c level will be helpful to differentiate between a pre gestational diabetic and GDM. If the A1c level is more than 6%, she is likely to be a pre GDM. A1c is useful in monitoring the glucose control during pregnancy, but not for the day to day management. A1c level may serve as a prognostic value.[93]

The blood pressure has to be monitored during every visit. If blood pressure is found to be more than 130/80, advise alpha-methyldopa 125 mg and dose to be adjusted on follow-up. Examination of the fundus and estimation of microalbuminuria, every trimester is recommended particularly in women with pregestational diabetes.[93]

Fetal

Fetal surveillance

Ultrasound Fetal Measurement: Ultrasound monitoring is recommended every trimester. A fetal echo is a must at 24 week, especially in prediabetics to rule out cardiac defects. In addition, documenting foetal biophysical profile in the late trimester is advisable. Doppler umbilical blood flow measurement or cardiotocograph (CTG) may be performed around 36 weeks of gestation in GDM with other pregnancy complications such as pre-eclampsia, hypertension, antepartum hemorrhage and intrauterine growth retardation.[93]

Timing of Delivery

There is a possibility that the diagnosis of GDM may lead to increased obstetric intervention, including induction of labour and caesarean section. Delivery before full term is not indicated unless there is evidence of macrosomia, ployhydramnios, poor metabolic control or other obstetric indications (eg pre-elampsia or intrauterine growth retardation).[93]

Delivery

During labour, it is essential to maintain good glycemic control while avoiding hypoglycemia. Lower insulin requirements are common during labour (often no insulin is necessary). Maternal blood glucose level should be monitored after delivery, 24 hours post partum and if found to be high, checked again on follow-up. A neonatologist's presence at the time of delivery is ideal, more so if significant neonatal morbidity is suspected.[93]

Table 2. Plasma glucose and insulin IV fluid

Plasma glucose (At time of onset of labour)	Insulin / IV fluids
< 70 mg/dL	5% GNS – 100 ml/hr
90 to 120 mg/dL	NS – 100 ml/hr
120 – 140 mg/dL	NS – 100 ml/hr plus
140 – 180 mg/dL	4 units of Reg. insulin added with IV fluid NS -100 ml/hr plus
> 180 mg/dL	8 units of Reg. insulin added with IV fluid

Neonatal Management

The neonates of mothers with GDM are also at risk of all complications similar to the infants born to mothers with overt diabetes, particularly those infants born macrosomic.[94] In the Indian population, the normal birth weight of new born babies is between 2.5 – 3.5 kg.[95] Neonates should be monitored closely after delivery for respiratory distress. Capillary blood glucose (cut-off of 44mg/dl that is, 2.6 mmol) should be monitored at one, two and four hours after birth and then again before feeding. Early breast feeding is actively encouraged.[96]

Follow up

GDM may be viewed as:

1. An unidentified preexisting disease, or
2. The unmasking of a compensated metabolic abnormality by the added stress of pregnancy, or
3. A direct consequence of the altered maternal metabolism stemming from the changing hormonal milieu.

Gestational diabetic women require follow up. Glucose tolerance test with 75 gm oral glucose is performed after 6 weeks of delivery and if necessary repeated after 6 months and every year to determine whether the glucose tolerance has returned to normal or progressed. A small proportion of gestational diabetic women may continue to have glucose intolerance.[97]

Prevention of adverse maternal and perinatal outcomes in GDM are based in achieving maternal blood glucose as close to normal as possible. Precise

glycemic thresholds remain undetermined. Prepregnancy BMI, duration and severity of maternal hyperglycemia during pregnancy, are most important predictors of the progression to abnormal glucose tolerance/ diabetes in the follow up.[98]

GDM recurs approximately in 50% of subsequent pregnancies. The future risk of developing diabetes for a gestational diabetic is two fold, if she becomes overweight. But maintaining ideal weight approximately halves the risk. The requirement of insulin in addition to diet to maintain euglycemia during the index pregnancy is also predictive of future diabetes. The maternal health and fetal outcome depends upon the care by the committed team of diabetologists, obstetricians and neonatologists. A short term intensive care gives a long term pay off in the primary prevention of obesity, IGT and diabetes in the offspring, as the preventive medicine starts before birth.[98]

METHODOLOGY

The present study was conducted in the department of Obstetrics and Gynaecology, KLES Dr Prabhakar Kore Hospital and Medical Research Centre, Belgaum on 120 pregnant patients attending the antenatal clinic during the period of September 2010 to August 2011.

Study Design

The study design was one year prospective study.

Study period and duration

The present one year study was conducted during the period of September 2010 to August 2011.

Place

Antenatal Clinic, Department of Obstetrics and Gynaecology, KLES Dr Prabhakar Kore Hospital and Medical Research Centre, Belgaum attached to Jawaharlal Nehru Medical College, Belgaum.

Source of data

Pregnant women in first trimester registered at Antenatal Clinic, Department of Obstetrics and Gynaecology, KLES Dr Prabhakar Kore Hospital and Medical Research Centre, Belgaum.

Sample size

A total of 120 pregnant women in first trimester registered at Antenatal Clinic were studied.

Sampling procedure

The sample size was calculated based on the formula as mentioned below;

$n = 4 \times p \times q / d^2$

Where, p = prevalence that is, 17

q = 100 – p

d = Absolute error that is, 7.5

With drop out rate of 20 %

Therefore, $= 4 \times 17 \times 83/(7.5)^2$

n = 120

Selection criteria

Inclusion

- All pregnant women in their first trimester.

Exclusion

- Known diabetic patients

Procedure

The study was approved by the Institutional Ethics Committee of Jawaharlal Nehru Medical College, Belgaum. Patients attending to Department of

Obstetrics and Gynaecology at KLES Dr Prabhakar Kore Hospital and Medical Research Centre, Belgaum were evaluated based on selection criteria. Detailed obstetric history was taken and physical examination was done. The selected patients were briefed about the nature of the study, details of the test and a written informed consent was obtained (Annexure-I).

Demographic data like age, obstetric history along with relevant history were recorded on predesigned and pretested proforma (Annexure–II). A thorough clinical examination was conducted and the findings were also recorded. Body mass index was calculated based on formula;

Body Mass Index = Weight (Kg) / Height (m^2)

Body mass index in the range of less than 19.8 kg/m^2 were considered as underweight, 19.8 to 26 kg/m^2 were considered normal, 26 to 29 kg/m^2 were considered as overweight and more than 29 kg/m^2 were considered as obese.

Participating patients underwent Oral glucose tolerance test with 75 gm of glucose. If test results negative patients underwent repeat testing at 24 to 28 weeks and if found negative, repeated test at 32 to 34 weeks.

Table 3. Glycaemic criteria for categorising abnormal glucose tolerance in pregnancy

2 hours plasma glucose(mg/dL)	In pregnancy
>200	Diabetes mellitus
140-199	Gestational diabetes mellitus
120-139	Gestational glucose intolerance
<120	Normal

Statistical analysis

The data obtained was tabulated on Microsoft excel spread sheet and expressed as rates, ratios, percentages and mean ± standard deviation (SD). The comparison was done using chi-square test. A 'p' value of less than 0.05 was considered as statistically significant.

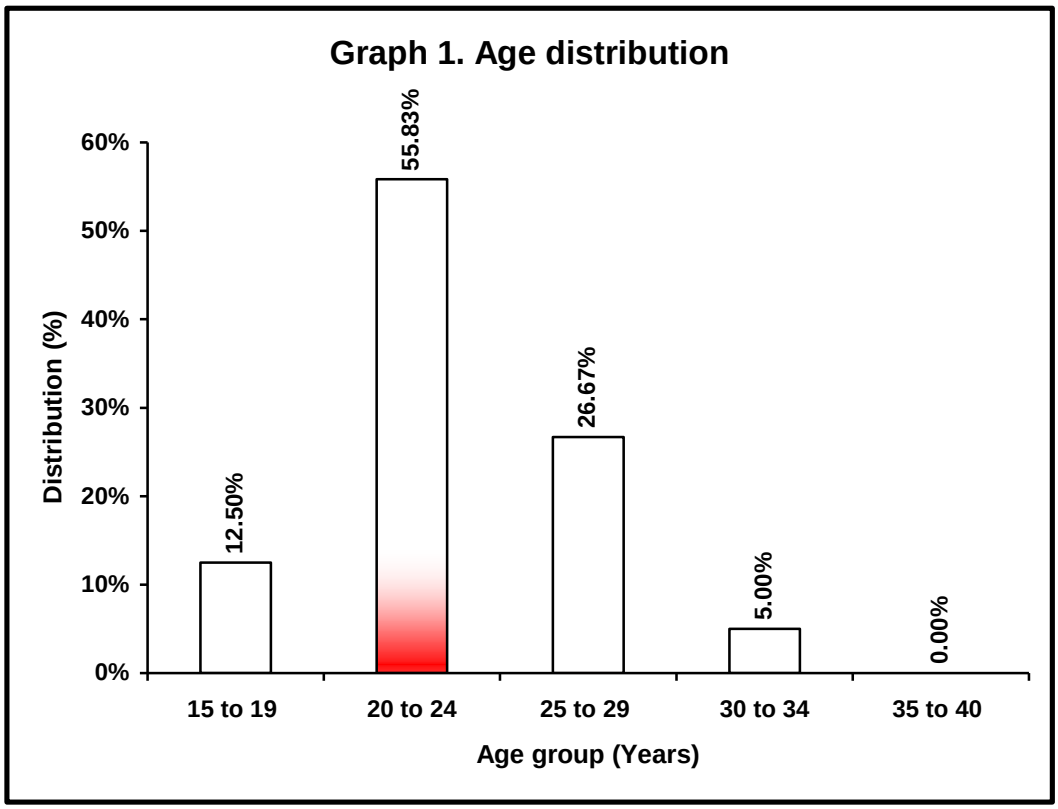
RESULTS

The present study was conducted in the Department of Obstetrics and Gynaecology, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum between the period of September 2010 to August 2011 on 120 pregnant women attending the antenatal clinic.

The data obtained was tabulated on Microsoft excel spread sheet and expressed as rates, ratios, percentages and mean ± standard deviation (SD). The comparison was done using chi-square test. The data was analysed as below.

Table 4. Age distribution

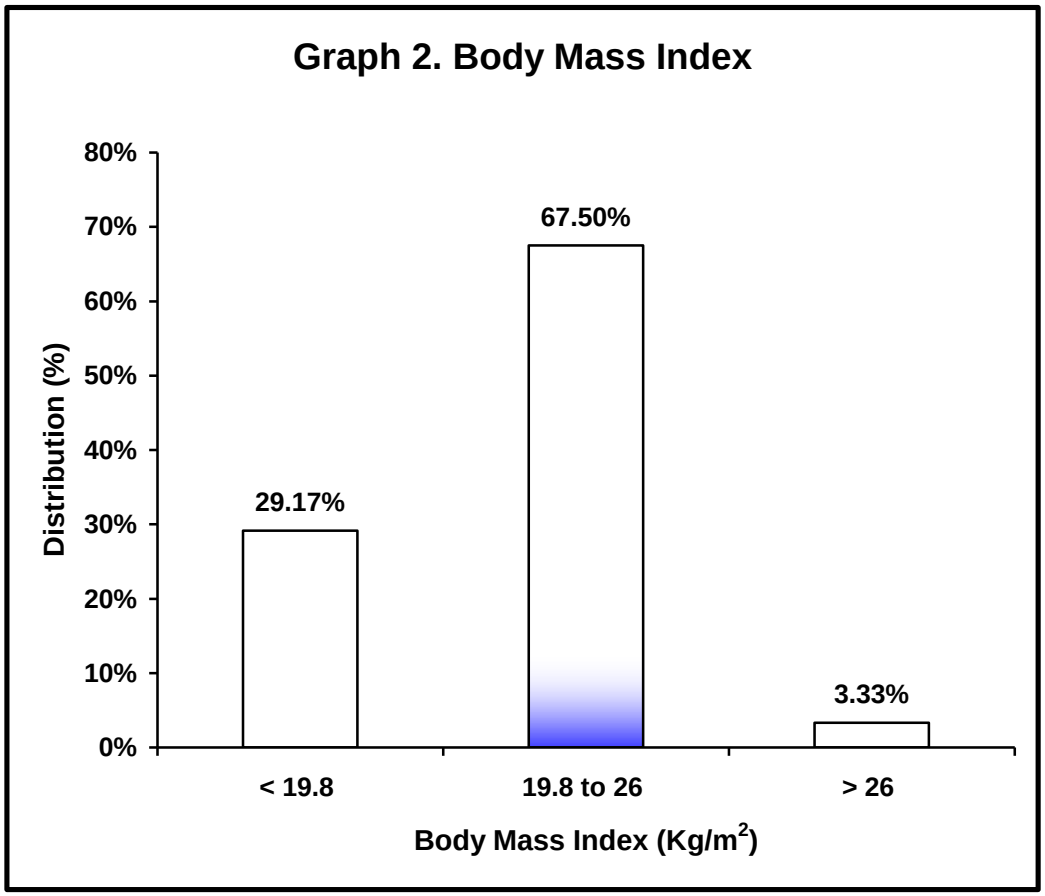
Age group (Years)	Distribution (n=120)	
	Number	**Percentage**
15 to 19	15	12.50
20 to 24	67	55.83
25 to 29	32	26.67
30 to 34	6	5.00
35 to 40	0	0.00
Total	**120**	**100.00**



In the present study, majority (55.83%) had age between 20 to 24 years followed by 25 to 29 years (26.67%), 15 to 19 years (12.50%), 30 to 34 years and none of patient had age above 35 years. Overall the mean age was 23.04 ± 3.36 years with range being 33 to 18 years.

Table 5. Body mass index

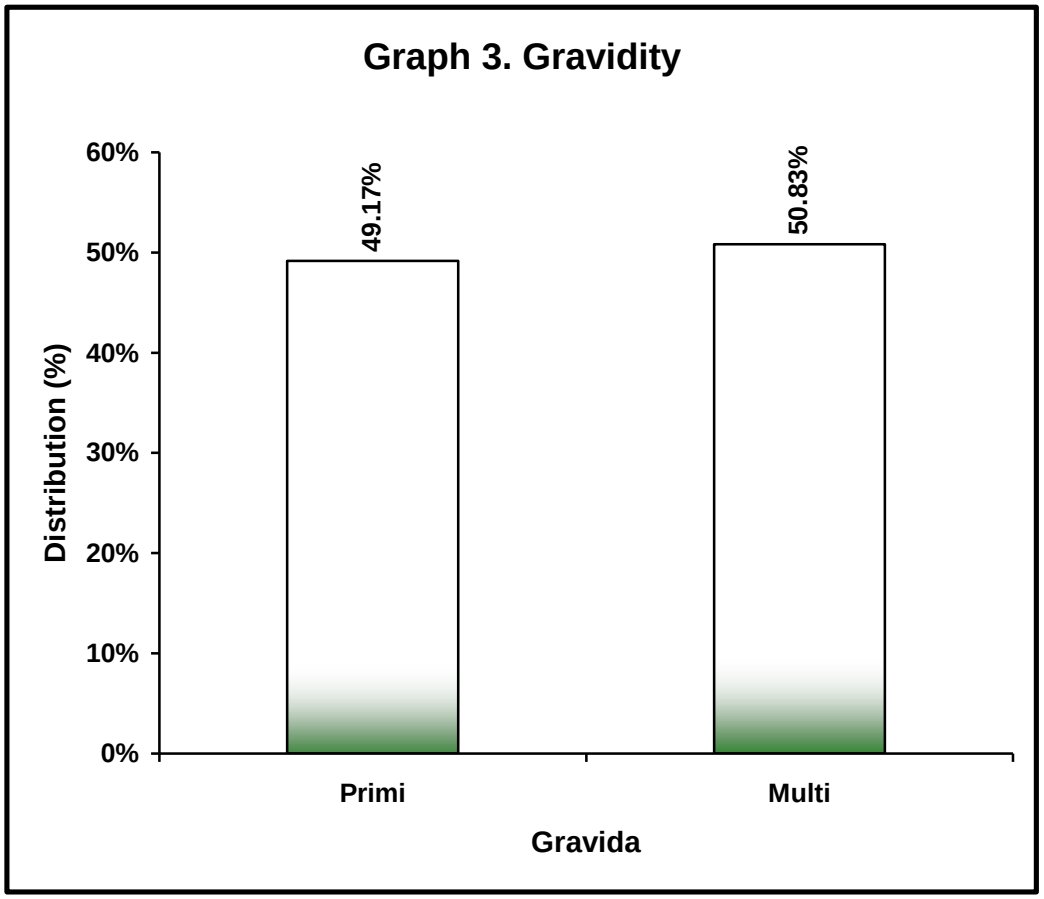
Body mass index (Kg/m^2)	Distribution (n=120)	
	Number	**Percentage**
< 19.8	35	29.17
19.8 to 26	81	67.50
> 26	4	3.33
Total	**120**	**100.00**



In this study, 81 (67.50%) women had BMI in the range of 19.8 to 26 Kg/m^2, followed by < 19.8 Kg/m^2 (29.17%) and > 26 Kg/m^2 (3.33%). Overall the mean BMI was 20.7 ± 3.07 Kg/m^2 with range being 14.33 to 30.81 Kg/m^2

Table 6. Gravidity

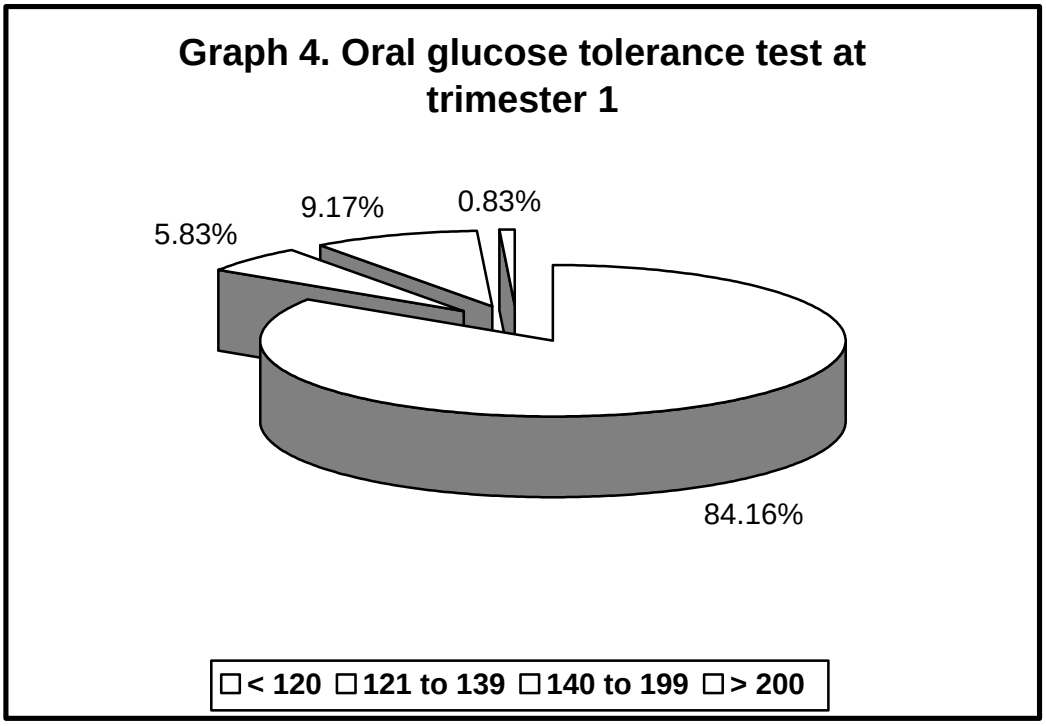
Gravida	Distribution (n=120)	
	Number	**Percentage**
Primi	59	49.17
Multi	61	50.83
Total	**120**	**100.00**



In this study, 61 (50.83%) pregnant women were multrigravida and 59 (49.17%) were primigravida.

Table 7. Oral glucose tolerance test at trimester 1.

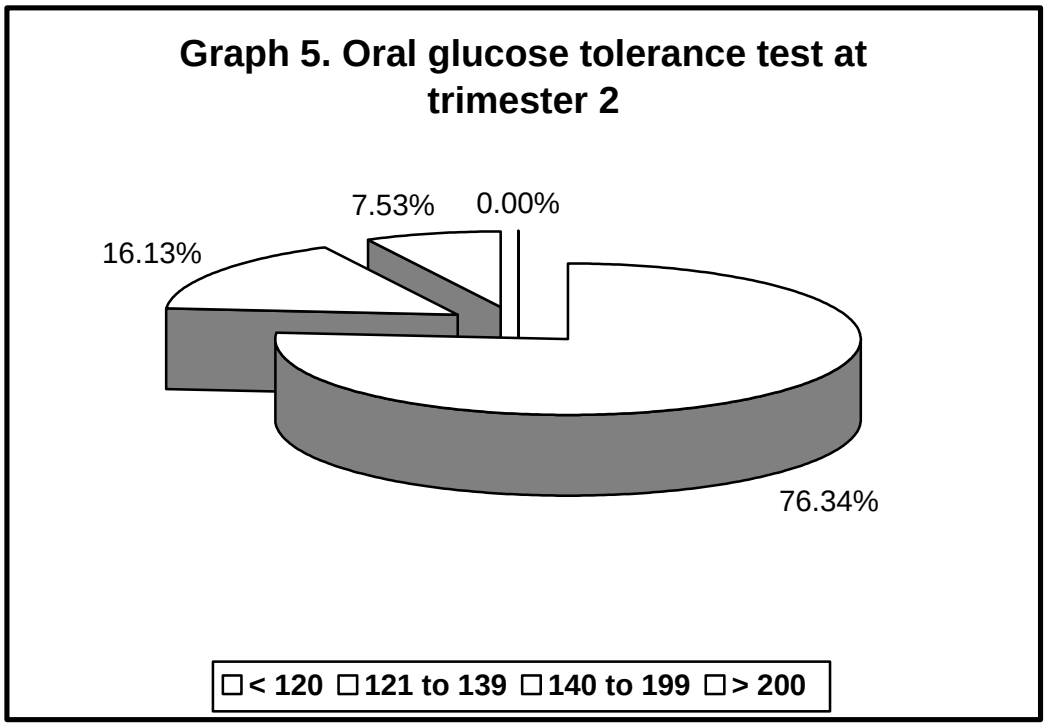
OGTT (mg/dL)	Distribution (n=120)	
	Number	**Percentage**
< 120	101	84.16
121 to 139	7	5.83
140 to 199	11	9.17
> 200	1	0.83
Total	**120**	**100.00**



In the present study during the first trimester 84.16% women had normal OGTT whereas seven (5.83%) had gestational glucose intolerance and 11 (9.17%) had GDM whereas one (0.83%) had overt diabetes.

Table 8. Oral glucose tolerance test at trimester 2.

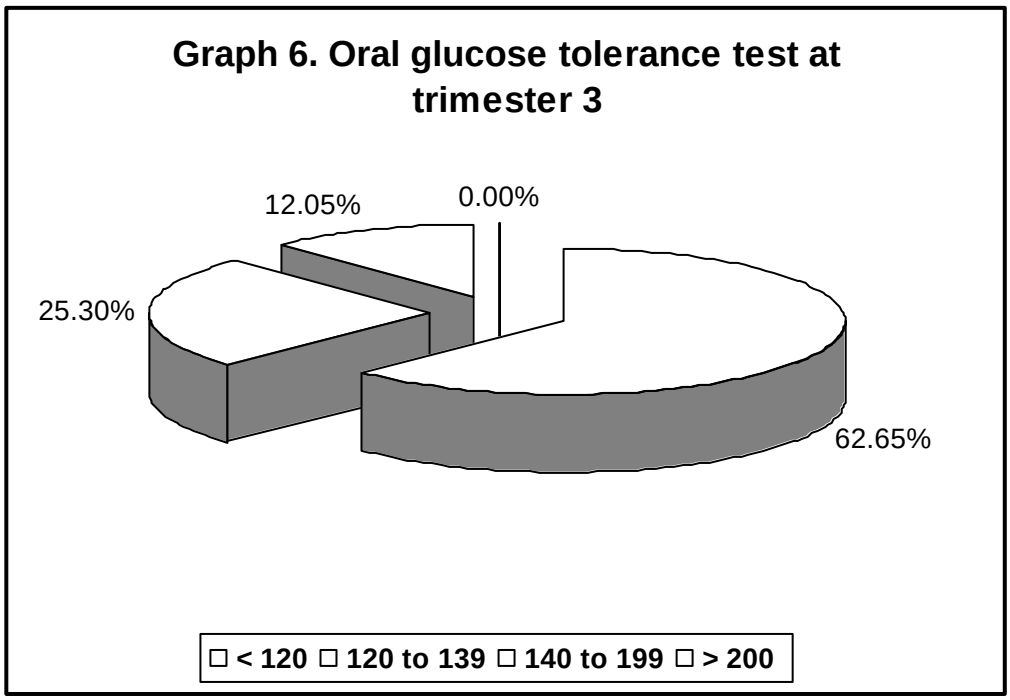
OGTT (mg/dL)	Distribution (n=93)	
	Number	**Percentage**
< 120	71	76.34
121 to 139	15	16.13
140 to 199	7	7.53
> 200	0	0.00
Total	**93**	**100.00**



In this study, during the second trimester 15 patients lost to follow up and 12 patients had GDM during first trimester. Of the remaining 93, seven (7.45%) patients were newly diagnosed with GDM and 15 (16.13%) had gestational glucose intolerance.

Table 9. Oral glucose tolerance test at trimester 3.

OGTT (mg/dL)	Distribution (n=83)	
	Number	**Percentage**
< 120	52	62.65
121 to 139	21	25.30
140 to 199	10	12.05
> 200	0	0.0
Total	**83**	**100.00**



During the third trimester, 3 more patients lost to follow up. 12 patients were diagnosed with GDM in first trimester and 7 patients were diagnosed with GDM during second trimester. Of the remaining 83 patients, 10 (12.05%) patients were newly diagnosed with GDM.

Of the 120 patients subjected to the study, overall incidence of GDM was 23.33% and 0.83% was diagnosed with overt diabetes.

Table 10. Association of age with gestational diabetes mellitus at trimester 1.

Age group (Years)	Mother with GDM (n=12)	
	Number	**Percentage**
15 to 19	2	16.67
20 to 24	3	25.00
25 to 29	6	50.00
30 to 34	1	8.33
35 to 40	0	0.00
Total	**12**	**100.00**

x^2=5.410 DF=2 p=0.066

In this study, in the first trimester, 11 patients were diagnosed with GDM and 1 patient was diagnosed with overt diabetes. Majority of the patients had age between 25 to 29 years. However the association between the age group showed no statistically significant difference between the groups (p=0.066)

Table 11. Association of age with gestational diabetes mellitus at trimester 2.

Age group (Years)	Mother with GDM (n=7)	
	Number	**Percentage**
15 to 19	1	14.29
20 to 24	3	42.86
25 to 29	1	14.29
30 to 34	2	28.57
35 to 40	0	0.00
Total	**7**	**100.00**

x^2=0.452 DF=2 p=0.797

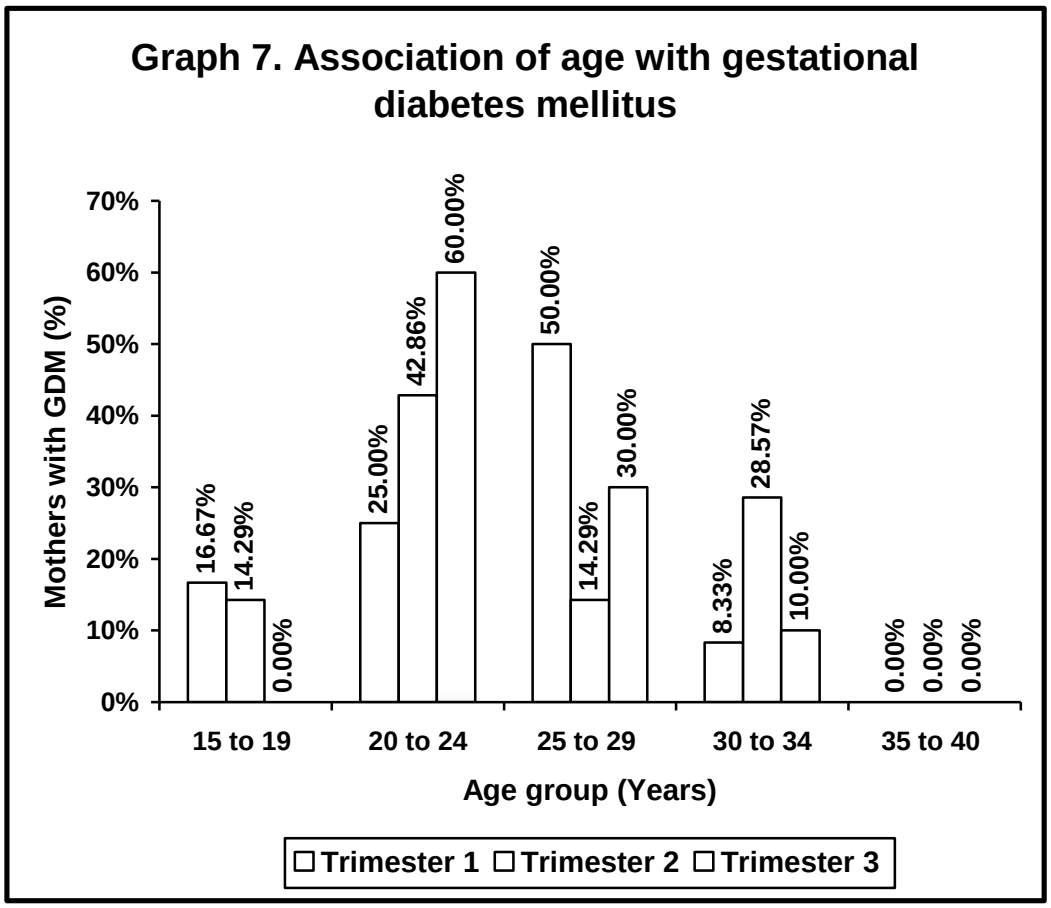
In this study, in second trimester seven patients were diagnosed with GDM. Most of the patients (42.86%) had age between 20 to 24 years. However the association of GDM with the age groups showed no statistically significant difference (p=0.797).

Table 12. Association of age with gestational diabetes mellitus at trimester 3.

Age group (Years)	Mother with GDM (n=10)	
	Number	**Percentage**
15 to 19	0	0.00
20 to 24	6	60.00
25 to 29	3	30.00
30 to 34	1	10.00
35 to 40	0	0.00
Total	**10**	**100.00**

x^2=0.246 DF=1 p=0.620

During the third trimester, 10 patients were diagnosed with GDM. Most of the patients six (60%) had age between 20 to 24 years. However the association of GDM with the age groups showed no statistically significant difference (p=0.620).



Graph 7 shows association of age with GDM at trimester one, two and three. Most of the patients six (50%) had age between 25 to 29 years during first trimester whereas during second and third trimesters three (42.86%) and six (60%) of patients were seen between the age of 20 to 24 years. The distribution of other patients is as shown in the Graph 7.

Table 13. Association of body mass index with gestational diabetes mellitus at trimester 1.

Body mass index (Kg/m^2)	Mother with GDM (n=12)	
	Number	**Percentage**
< 19.8	4	33.33
19.8 to 26	7	58.33
> 26	1	8.33
Total	**12**	**100.00**

x^2=0.086 DF=1 p=0.769

In this study during the first trimester most of the patients (58.33%) had BMI between 19.8 to 26 Kg/m^2. However association between GDM and body mass index showed no statistically significant difference (p=0.769).

Table 14. Association of body mass index with gestational diabetes mellitus at trimester 2.

Body mass index (Kg/m^2)	Mother with GDM (n=7)	
	Number	**Percentage**
< 19.8	1	14.29
19.8 to 26	4	57.14
> 26	2	28.57
Total	**7**	**100.00**

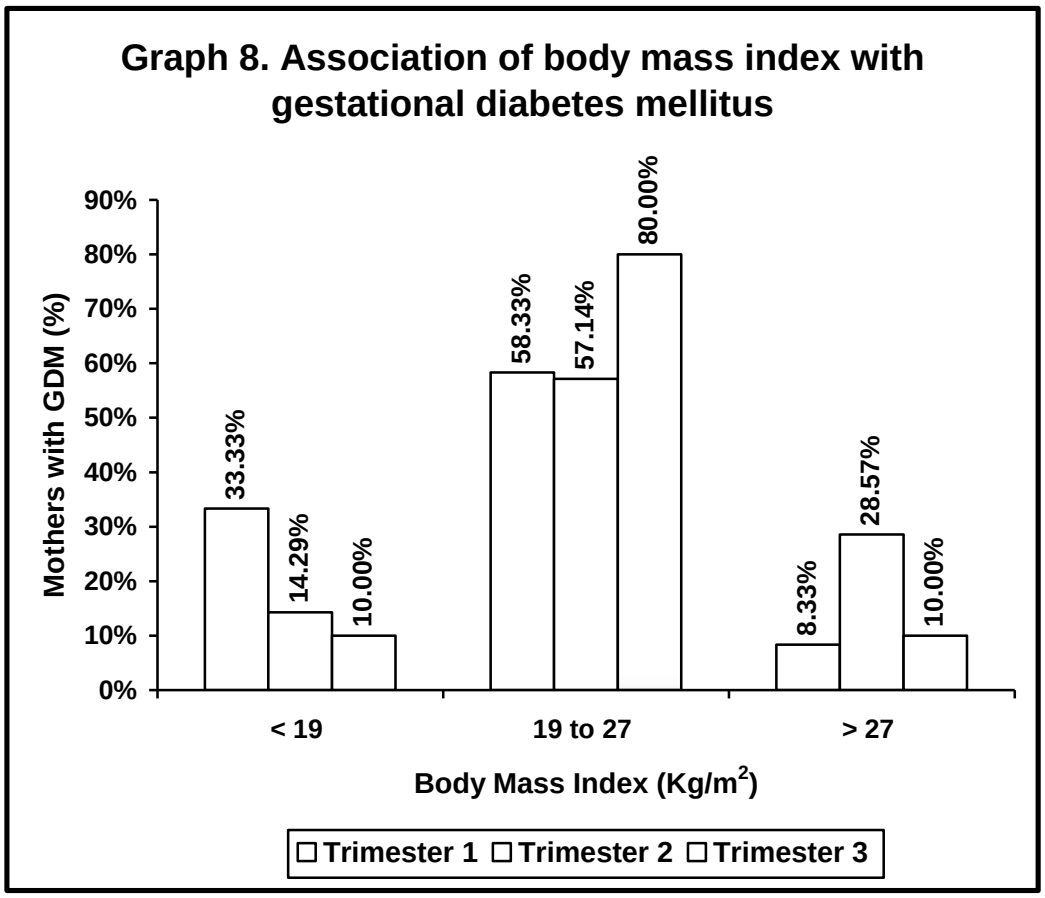
x^2=0.690 DF=1 p=0.406

In the second trimester most of the patients (57.14%) had BMI between 19.8 to 26 Kg/m^2. The association between GDM and body mass index showed no statistically significant difference (p=0.406).

Table 15. Association of body mass index with gestational diabetes mellitus at trimester 3.

Body mass index (Kg/m^2)	**Mother with GDM (n=10)**	
	Number	**Percentage**
< 19.8	1	10.00
19.8 to 26	8	80.00
> 26	1	10.00
Total	**10**	**100.00**
x^2=1.629	DF=1	p=0.202

In the present study during the third trimester though 80% of the women had BMI between 19.8 to 26.0 Kg/m^2 but, there was no statistically significant association found between GDM and body mass index (p=0.202).



Graph 8 shows association of BMI with GDM at trimester one, two and three. Most of the patients (58.33% in trimester one, 57.14% in trimester two and 80% in trimester three) had BMI between 19.8 to 26 Kg/m^2. The BMI distribution of other patients is as shown in Graph 8.

Table 16. Association of gravidity with gestational diabetes mellitus at trimester 1.

Gravida	Mother with GDM (n=12)	
	Number	**Percentage**
Primi	2	16.67
Multi	10	83.33
Total	**12**	**100.00**
x^2=5.635	DF=1	p=0.018

In the present study, during the first trimester, 10 (83.33%) patients were multigravida and this association of gravidity with GDM was statistically significant (p=0.018).

Table 17. Association of gravidity with gestational diabetes mellitus at trimester 2.

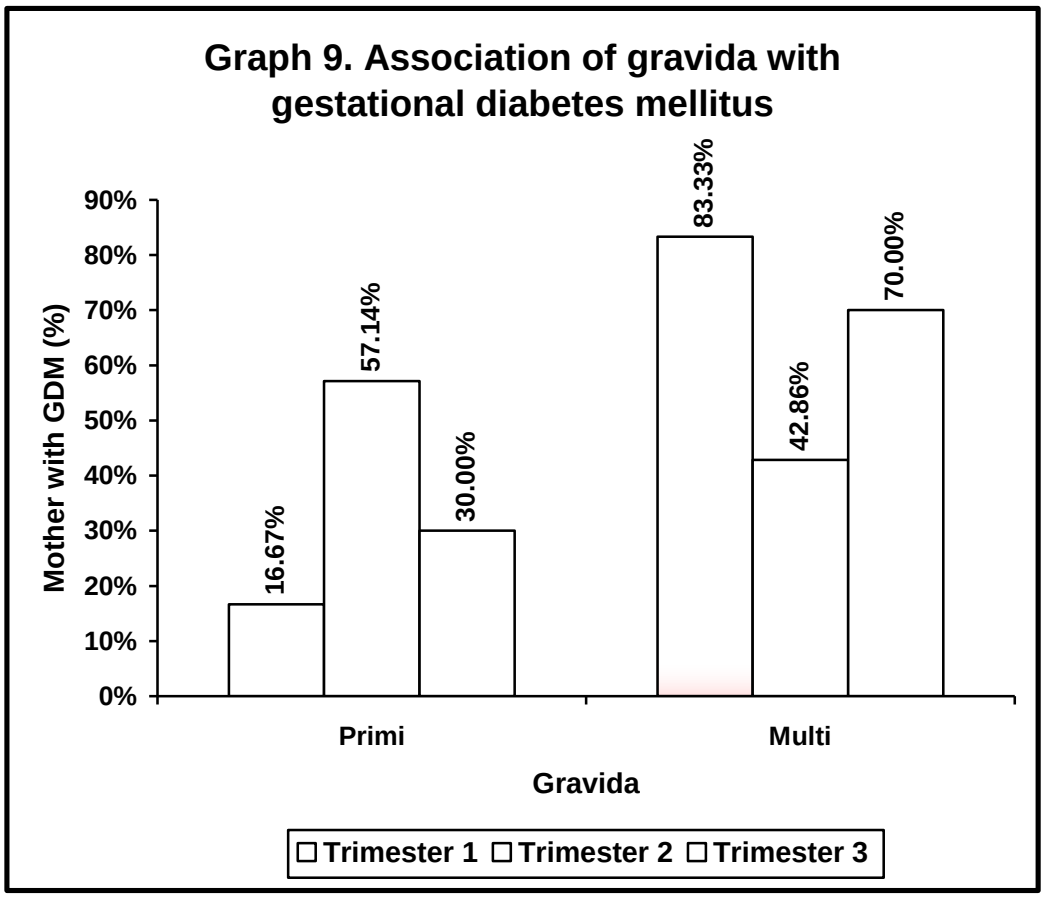
Gravida	Mother with GDM (n=7)	
	Number	**Percentage**
Primi	4	57.14
Multi	3	42.86
Total	**7**	**100.00**
x^2=0.303	DF=1	p=0.582

During the second trimester, 4 (57.14%) patients were primigravida and this association of gravidity with GDM was statistically not significant (p=0.582).

Table 18. Association of gravidity with gestational diabetes mellitus at trimester 3.

Gravida	Mother with GDM (n=10)	
	Number	**Percentage**
Primi	3	30.00
Multi	7	70.00
Total	**10**	**100.00**
x^2=1.442	DF=1	p=0.230

During the third trimester, 7 (70%) patients were multigravida and this association of gravidity with GDM was statistically not significant (p=0.230).



Graph 9 shows association of gravidity with GDM at trimester one, two and three. Most of the patients (57.14%) in second trimester were primigravida whereas in trimester one and three 83.33% and 70% were multigravida respectively. The gravidity of other patients is as shown in Graph 8.

DISCUSSION

Gestational diabetes mellitus occurs in up to 14% of all pregnancies, resulting in approximately 200,000 cases annually in the United States.[99] It can have a much higher incidence in certain minority populations with a greater predisposition to diabetes. The disorder is characterized by carbohydrate intolerance that begins or is first recognized during pregnancy. The prevalence of GDM varies in direct proportion to the prevalence of type 2 diabetes for a given ethnic group or population.[100]

When and how to screen for GDM has been debated in the literature for decades. Several studies have suggested grouping patients by low, moderate, and high risk for developing GDM. Currently, and after extensive deliberation, universal screening of all pregnant women is recommended by some groups;[100] however, the ADA recommends screening of only moderate- and high-risk pregnancies.[101]

Recognizing and treating GDM results in lowering of maternal and fetal complications. Patients with GDM are at higher risk for excessive weight gain, preeclampsia, and cesarean sections. Infants born to mothers with GDM are at higher risk for macrosomia, birth trauma, and shoulder dystocia. After delivery, these infants have a higher risk of developing hypoglycemia, hypocalcemia, hyperbilirubinemia, respiratory distress syndrome, polycythemia, and subsequent obesity and type 2 diabetes. In addition, having a history of GDM puts the mother at risk for development of type 2 diabetes or recurrent GDM in the future. Some recent data suggest an increased risk of cardiovascular disease, as well.

Fifty years ago, screening for GDM was done by taking patients' history alone. In 1973, a study[102] proposed using the 1-hour 50 gm OGCT for screening.

Several studies have suggested placing patients into risk categories based on history. Risk factors for GDM include being over-weight before pregnancy (BMI > 25 kg/m^2), having a first-degree relative with diabetes, previous glucose intolerance, previous macrosomia or large-for gestational-age baby, polycystic ovarian syndrome, age > 25 years, and being a member of an ethnic group with high prevalence of GDM.[103] Multiparous women have a very high prevalence of GDM (≤13%).[104]

The present study was an attempt to establish the incidence of GDM and to determine the onset of GDM with respect to period of gestation. This one year hospital based prospective study was conducted in the Department of Obstetrics and Gynaecology, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum between the period of September 2010 to August 2011 on 120 pregnant women diagnosed to have gestational diabetes.

In the present study, more than half (55.83%) women had age between 20 to 24 years. Overall the mean age was 23.04 ± 3.36 years with range being 33 to 18 years. Of the 120 women, 81 (67.50%) women had BMI in the range of 19.8 to 26.0 Kg/m^2, Overall the mean BMI was 20.7 ± 3.07 Kg/m^2 with range being 14.33 to 30.81 Kg/m^2 and 61 (50.83%) pregnant women were multrigravida and 59 (49.17%) were primigravida.

In the present study during the first trimester 84.16% women had normal OGTT whereas 5.83% had gestational glucose intolerance and 11 (9.17%) had GDM whereas one (0.83%) had overt diabetes.

In this study, during the second trimester 15 patients lost to follow up and 12 patients had GDM during first trimester. Of the remaining 93, seven (7.45%) patients were newly diagnosed with GDM and 16.13% had gestational glucose intolerance.

During the third trimester, 18 patients lost to follow up and 12 and 7 patients had GDM during first and second trimester respectively. Of the remaining 83, 10 (12.05%) patients were newly diagnosed with GDM.

At patients' first antenatal visit, providers should assess which category patient fits best. For normal-risk patients, it is widely recommended to screen with a nonfasting, 1-hour, 50 gm OGCT at 24-28 weeks' gestation.[105] An observational study,[106] comparing universal screening versus selective screening for GDM, found that the universally screened group had more favorable outcomes. Previous study[107] of 25,118 deliveries to determine whether following the ADA recommendations not to screen women who are < 25 years of age, have normal body weight, are not members of a high-risk racial or ethnic group, and have no family history of diabetes would result in missed GDM diagnosis found that, ≤ 10-11% of women who delivered would never have been screened for GDM, and they were missing 4% of women with GDM.[107]

For higher-risk patients, screening is warranted earlier in pregnancy. Patients with symptoms of overt severe hyperglycemia, such as polyuria and

polydypsia, may be diagnosed with a random blood glucose test result ≥ 200 mg/dl. An earlier diagnosis should trigger suspicion of preexisting type 1 or type 2 diabetes and should be investigated and managed appropriately. Screening for glycosuria has been used in the past, but given the poor sensitivity and specificity, the recent U.K. National Institute of Clinical Excellence guidelines did not recommend continuation of screening for glycosuria.[108]

Screening with a fasting blood glucose test has been shown to have a sensitivity of 70-90% and a specificity of 50-75%[109] and is therefore not considered an adequate screening method. In fact, one study[10] found that, a single fasting glucose screen failed to identify 60% of women with abnormal 2-hour blood glucose levels. Another study[110] found that, a one hour 50 gm OGCT value ≥ 140 mg/dl would have an 80% sensitivity and a proportion of women with a positive test of 14-18%. Using a cutoff value of ≥ 130 mg/dl increases sensitivity to 90%. A positive test requires further diagnostic testing.

A study[23] reported that, GDM develops in 1 to 3% of all pregnancies. Kaiser Permanente of Colorado (KPCO) study described a strong cohort effect on the prevalence of GDM. Regardless of age and ethnicity, women born more recently were at increased risk for GDM diagnosis compared with women born earlier. This finding probably reflects an increased exposure to risk factor(s) operating before childbearing age. One of the strongest risk factors for GDM[19] is obesity, the prevalence of which has been dramatically increasing over the last several decades.[111] Although Colorado has the lowest estimated prevalence of obesity in the nation, obesity among Colorado women more than doubled between 1990 and 2001. Coincidently, the prevalence of self-reported

(nongestational) diabetes increased markedly among Colorado adults, from 3.4% in 1994 to 5.1% in 2000, an increase observed in both sexes and all age and racial/ethnic groups.[112] The results on increasing GDM prevalence over the same time period were consistent with the reported trends in obesity and type 2 diabetes in Colorado. The fact that GDM prevalence was similar for the two most recently born cohorts in study would have several possible explanations like, not all the women belonging to the 1976–1990 cohort reached the childbearing age as of the date of this analysis, so the prevalence of GDM in the young age-groups with data available for comparison may be artificially low, the effect of increasing obesity on GDM prevalence is not apparent at very young ages and the increase in GDM in the younger population might have reached a plateau.[23]

Another study[45] done in Raja Sir Ramaswamy Mudhaliar lying hospital attached to the Government Stanley Medical College and Hospital, Chennai, concluded the increased prevalence of GDM in Indian population.

In this study, in the first trimester, 11 patients were diagnosed with GDM and one diagnosed with acute diabetes. Majority of the patients had age between 25 to 29 years. In second and third trimester seven and ten patients were diagnosed with GDM and most of the patients (42.86% and 60% respectively) had age between 20 to 24 years. However the association of GDM with the age groups showed no statistically significant difference at all the three trimesters ($p>0.050$).

Maternal age is an established risk factor for GDM, but there is no consensus on the age above which there is significantly increased risk of GDM.

In the literature, the lowest cutoff is ≥25 years, as recommended by the ADA, but there are little data to support this recommendation.

A study[113] to determine the age threshold for increased risk of GDM, reviewed the prevalence of GDM, diagnosed by the WHO criteria, in the singleton pregnancies from 1998 to 2001. The pregnancies were categorized according to maternal age, that is, ≤20 years, 20–24 years, 25–29 years, 30–34 years, 35–39 years, and ≥40 years. Of the 16,383 women managed in this period, 15,827 (96.6%) women continued their pregnancies beyond the first trimester, and the number (% of total) from the youngest to the oldest cohort were 318 (2.0%), 1,713 (10.8%), 4,446 (28.1%), 5,457 (34.5%), 3,279 (20.7%), and 614 (3.9%), respectively. There was a significant difference and positive correlation in the prevalence of GDM, increasing from 1.3, 2.5, 6.2, 10.3, 21.7, and 31.9%, respectively, from the youngest to the oldest cohort ($p< 0.001$). The study[113] indicated that, risk of GDM becomes significantly and progressively increased from 25 years onwards. This supports the ADA recommendation on the use of age ≥25 years as the cutoff for screening and the observation that maternal age ≥25 years is the factor most predictive of GDM. In clinical practice, maternal age of ≥25 years should be adopted instead of ≥35 years or 40 years as a risk factor for the development of GDM.

Another study[114] was performed to examine the relationship between maternal age and serum glucose levels during pregnancy, and to determine if glucose screening could be eliminated in very young women without significantly compromising the detection rate of GDM. All women between the 24th and 28th wk of gestation who were followed in a university-affiliated

prenatal clinic had a screening glucose level drawn 1 h after ingesting 50 gm glucose. Those who had a 1-h serum glucose of > 150 mg/dl subsequently underwent a 3-h glucose tolerance test. There was a progressive increase in screening serum glucose levels and a significantly higher incidence of diabetes with increasing maternal age. Only 4% of women < 20 yr had a positive screen and 8% of these had gestational diabetes. If screening had not been done in those < 20 yr, only 5% (2/36) of women with gestational diabetes would not have been detected.

In this study during all the three trimesters most of women (58.33% in first trimester, 57.14% in second trimester and 80% in third trimester) had BMI between 19.8 to 26.0 Kg/m^2. However association between GDM and BMI showed no statistically significant difference ($p>0.050$).

Pregnancy complications in overweight women were studied as early as 1945. Since then, a number of studies have reported a clear association between maternal overweight and adverse obstetric and perinatal outcomes. Data from North America have been supported by results from Danish and Swedish studies. In the UK, Sebire studied the effects of maternal obesity on pregnancy outcomes in a London cohort of 287,213 women. Since then, similar reports have been published from Wales and Scotland.[115]

Risk factors for GDM, which occurs in 2%–14% of pregnant women, include a high BMI (a measure of body fat), excessive weight gain or low physical activity during pregnancy, high dietary intake of polyunsaturated fats, glucose intolerance (an indicator of diabetes) or the birth of a large baby in a

previous pregnancy, and a family history of diabetes. High intake of saturated fat, low intake of polyunsaturated fat, and excessive gestational weight gain may increase the risk of GDM. Physical activity is also associated with decreased risk of GDM.[116]

A systematic review[117] of observational studies published in the last 30 years to assess and quantify the risk for GDM according to prepregnancy maternal BMI, it was elected as the only measure of obesity, and all diagnostic criteria for GDM were accepted. Compared with women with a normal BMI, the unadjusted pooled odds ratio (OR) of an underweight woman developing GDM was 0.75 (95% confidence interval [CI] 0.69 to 0.82). The OR for overweight, moderately obese and morbidly obese women were 1.97 (95% CI 1.77 to 2.19), 3.01 (95% CI 2.34 to 3.87) and 5.55 (95% CI 4.27 to 7.21) respectively. For every 1 kg m^{-2} increase in BMI, the prevalence of GDM increased by 0.92% (95% CI 0.73 to 1.10). The risk of GDM is positively associated with prepregnancy BMI. The study recommended that, this information is important when counselling women planning a pregnancy.

Another study[45] done in, Chennai, reported that, prevalence proportion of GDM increased with increasing BMI. However the effect of BMI did not quite reach statistical significance, but was approaching statistical significance.

In the present study, during the first trimester, 83.33% mothers were multigravida and this association of gravidity with GDM was statistically significant (p=0.018). During the second trimester, 57.14% mothers were primigravida and third trimester, 70% mothers were multigravida. However, this

association of gravidity with GDM at second and third trimester was statistically not significant ($p>0.050$).

A study[45] done in Chennai, reported that, the prevalence proportion of GDM increased with gravida, from 18.1% (confidence limits: 14.38% - 22.29%) in the primigravida to 25.8% (confidence limits: 11.86% - 44.61%) for the gravidas ≥ 4.

Overall the study indicates universal screening for glucose intolerance during pregnancy is essential as Indian women have high prevalence of diabetes and their relative risk of developing GDM is 11.3 times compared to white women.[45] Asian women are ethnically more prone to develop glucose intolerance compared to other ethnic groups.[45] GDM based on 2hr 75gm OGTT defined by WHO predicts adverse pregnancy outcome and warrants treatment.[45]

FOGSI TAG (Technical Assistant Group)[118] recommends WHO procedure of diagnosing GDM by 2-hr PG $\geq$ 140 mg/dL with 75 gm glucose load can be continued and/or IADPSG diagnostic criteria can be followed where financial and technical supports are available.

A 2 hr 75 gm post plasma glucose $\geq$ 140mg/dl serves both as screening and diagnostic criteria besides being a simple and economical one step procedure. As the routine screening for glucose intolerance during pregnancy is not done, probably the undiagnosed glucose intolerance that has been occurring in the past has resulted in the increased prevalence of diabetes in India.

CONCLUSION

The incidence of Gestational diabetes mellitus was significantly very high in the patients involved in the study.

The test used in the study for diagnosis of GDM proved to be simple, less cumbersome, cost effective and easily acceptable to the patients.

Subjecting the pregnant women to this test from the first trimester itself proved to be highly beneficial in terms of diagnosing overt diabetes and GDM in the first trimester itself so that appropriate measures can be instituted on time and will prevent future complications of neonatal morbidity and mortality.

The present study also showed association of increasing gravidity with increasing incidence of GDM, although it did not show positive correlation of either increasing BMI or increasing age with the incidence of GDM.

This evidence is enough to evaluate the efficacy of subjecting all the pregnant patients to test for diagnosing GDM in each trimester and this test should become the part of routine antenantal investigations.

SUMMARY

Women with GDM are at increased risk of future diabetes predominantly T2DM and is also associated with increased risk of fetal morbidity and mortality. The present study was undertaken with a single step test to detect GDM in pregnancy which has been validated and furthermore the findings of this study will also help to determine the incidence of GDM with respect to different period of gestation.

The present study was conducted in the Department of Obstetrics and Gynaecology, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum between the period of September 2010 to August 2011 on 120 pregnant women attending the antenatal clinic.

More than half (55.83%) women had age between 20 to 24 years. Overall the mean age was 23.04 ± 3.36 years with range being 33 to 18 years. Of the 120 women, 81 (67.50%) women had BMI in the range of 19.8 to 26.0 Kg/m^2. Overall the mean BMI was 20.7 ± 3.07 Kg/m^2 with range being 14.33 to 30.81 Kg/m^2 and 61 (50.83%) pregnant women were multrigravida and 59 (49.17%) were primigravida.

In the present study during the first trimester 84.16% women had normal OGTT whereas 5.83% had gestational glucose intolerance and 11 (9.17%) had GDM whereas one (0.83%) had overt diabetes. During the second trimester 7.45% patients were newly diagnosed with GDM and in third trimester 12.05% patients were newly diagnosed with GDM. Of the 120 patients subjected to the

study, overall incidence of GDM was 23.33% and 0.83% was diagnosed with overt diabetes.

The present study also showed association of increasing gravidity with increasing incidence of GDM, although it did not show positive correlation of either increasing BMI or increasing age with the incidence of GDM.

This evidence is enough to evaluate the efficacy of subjecting all the pregnant patients to test for diagnosing GDM in each trimester and this test should become the part of routine antenatal investigations.

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ANNEXURE I – CONSENT FORM

STUDY: TO DETERMINE INCIDENCE OF GESTATIONAL DIABETES MELLITUS USING A SINGLE STEP DIAGNOSTIC TEST – A ONE YEAR HOSPITAL BASED PROSPECTIVE STUDY.

Principal Investigator: Dr. Parul Mahajan; Postgraduate Student

Guide **:** Dr. J. C. Shravage, Professor

We request you to be a participant in above said research to be conducted at KLE'S Hospital from September 2010 to August 2011 conducted by DR PARUL MAHAJAN, Postgraduate student in the Department of Obstetrics and Gynecology at Jawaharlal Nehru Medical College, Belgaum. Ph No 9742352498.

Your participation in this study is your voluntary decision whether or not to participate will not affect your current or future relationship with the KLE'S Dr. Prabhakar Kore Hospital and Medical Research Centre.

Procedure Involved

If you agree in this research we would subject you to oral glucose tolerance test with 75 g of glucose and blood sample will be taken after 2 hours and results will be noted . If positive, then further treatment will be given. If negative, then you will be subjected again to test at 24-28 weeks and again if negative, last test will be repeated at 32-34 weeks.

Risk and benefits

There are no additional risks involved in this procedure. If any complications arise during the procedure then the patients will be treated with best of our knowledge. There will be no compensation or payment for such medical treatment.

If you attain any complication during the procedure you may contact Dr. J. C. Shravage professor and head of unit Phone No. 9448305362 and Dr. Parul Mahajan postgraduate in the dept of obstetrics and gynecology.

During the course of study you will be informed of any significant new findings such as changes in risks and benefits resulting from participation in the research.

Privacy and Confidentiality

The only people who will know that you are a research participant are members of the research team. No information about you or provided by you, during the research will be disclosed to others without your written consent. When the results of the research are published or discussed the conferences, no information will be disclosed that would reveal your identity. Any information obtained in connections with this study and that can be identified with you remain confidential and will be disclosed only with your permission.

Voluntary participation

Your participation in this study will help us identify a single step diagnostic test which is time saving and comfortable. You are free to discontinue the participation in the study at any time for any reasons and you will not be paid any reimbursement for participation in the research.If you have any questions about your rights or research as research participant you may contact Dr. V.D. Patil, Principal JNMC, Belgaum. Phone No 08312473777. You will be given a copy of this form for your information and to keep for your records.

Statement of Consent

To voluntarily agree to take part in this study I must sign on the line below: If you chose to take part in this study I may withdraw at any time I am not giving up any of my legal rights, by signing this form. My signature below indicates that I have read or have read to me this entire consent form including the risks and benefits and had all questions answered, I will be given a copy of this consent form.

Signature of the Subject:
Name: Date:
Signature of the authorized representative:
Name: Date:
Relation to the Subject:
Signature of the witness:
Name: Date:
Signature of the investigator:
Name: Date:

ANNEXURE II – PROFOMA

STUDY: TO DETERMINE INCIDENCE OF GESTATIONAL DIABETES MELLITUS USING A SINGLE STEP DIAGNOSTIC TEST- A 1 YEAR HOSPITAL BASED PROSPECTIVE STUDY

IDENTIFICATION

Sr No: _____ Date:_____

Name:_____ OP. No:_____

Age:_____ Wt:_____

Address:_____

_____

INFORMED CONSENT

Was the consent given Y N

INCLUSION CRITERIA

Is she overt diabetic? Y N

ELIGIBILITY

Is the woman eligible? Y N

OBSTETRIC HISTORY

Gravida para abortion living

MENSTRUAL HISTORY

LMP: / / EDD: / /

POG:

On General Physical Examination-

Pallor- BMI-

Vitals: PR-

BP-

CVS-

RS-

P/A-

Investigations

First trimester

Blood group:

Haemoglobin:

Urine R/M:

HIV:

Hbs Ag:

OGTT with 75 grams glucose:

Second Trimester-(24-28 weeks)

OGTT with 75 grams glucose:

Third Trimester-(32-34 weeks)

OGTT with 75 grams glucose:

RESULT:

ANNEXURE III - KEY TO MASTER CHART

EDD	-	Expected date of delivery
gm	-	Gram
Hb	-	Haemoglobin
HBsAg	-	Hepatitis surface antigen
HIV	-	Human immunodeficiency virus
IUD	-	Intrauterine death
Kg	-	Kilogram
LMP	-	Last menstrual period
m	-	Metre
NND	-	Neonatal death
NR	-	Non reactive
OGTT	-	Oral glucose tolerance test
P	-	Primi

ANNEXURE III - MASTER CHART

Serial Number	Out Patient Numbe	Age (Years)	BMI (Kg/m^2)	Obstetric History					LMP	EDD	Investigations					
														OGTT		
				Gravida	Para	Living	Abortion	Other			Hb (gm%)	HIV	HBsAg	1st trimester	2nd trimester	3rd trimester
1	1E+06	21	20.88	P	-	-	-	-	8/26/2010	6/4/2011	12.5	NR	NR	98	102	111
2	1E+06	19	17.54	P	-	-	-	-	8/15/2010	5/21/2011	10.5	NR	NR	78	156	-
3	1E+06	22	22.26	P	-	-	-	-	8/20/2010	5/27/2011	11.0	NR	NR	116	139	126
4	1E+06	21	26.74	P	-	-	-	-	8/11/2010	5/18/2011	11.0	NR	NR	92	89	101
5	1E+06	20	20.80	2	1	-	-	IUD	8/30/2010	6/6/2011	11.5	NR	NR	112	100	122
6	1E+06	24	23.30	P	-	-	-	-	8/25/2010	6/1/2011	10.5	NR	NR	68	72	82
7	1E+06	25	22.30	3	2	1	-	-	9/9/2010	6/16/2011	10.0	NR	NR	115	112	101
8	1E+06	18	18.25	P	-	-	-	-	8/1/2010	5/8/2011	9.5	NR	NR	86	92	101
9	1E+06	29	21.60	3	2	2	-	-	9/1/2010	6/8/2011	12.0	NR	NR	73	89	142
10	1E+06	24	21.09	2	1	1	-	-	9/22/2010	6/29/2011	11.0	NR	NR	81	92	132
11	1E+06	24	17.85	2	1	1	-	-	8/14/2010	5/21/2011	11.0	NR	NR	155	-	-
12	1E+06	22	25.00	2	1	1	-	-	9/13/2010	6/20/2011	11.0	NR	NR	67	72	122
13	1E+06	30	22.52	P	-	-	-	-	9/12/2010	6/19/2011	10.0	NR	NR	78	80	88
14	1E+06	21	18.08	P	-	-	-	-	9/6/2010	6/13/2011	8.5	NR	NR	70	80	94
15	1E+06	20	24.16	2	1	1	-	-	9/29/2010	7/4/2011	11.6	NR	NR	76	94	90
16	1E+06	22	18.04	3	2	1	-	IUD	11/8/2010	8/15/2011	8.5	NR	NR	168	-	-
17	1E+06	21	21.64	P	-	-	-	-	9/24/2010	7/1/2011	11.3	NR	NR	104	95	105
18	925887	25	18.36	3	2	2	-	-	9/15/2010	6/22/2011	10.0	NR	NR	87	94	78
19	1E+06	33	20.88	2	1	1	-	-	8/20/2010	5/27/2011	12.0	NR	NR	163	-	-
20	912843	21	22.22	2	1	1	-	-	8/26/2010	6/2/2011	12.3	NR	NR	107	101	72
21	939893	22	14.33	2	1	1	-	-	9/13/2010	6/20/2011	10.0	NR	NR	78	84	92
22	1E+06	20	19.19	P	-	-	-	-	10/18/2010	7/25/2011	11.0	NR	NR	96	124	126
23	1E+06	28	20.80	P	-	-	-	-	11/11/2010	8/18/2011	11.0	NR	NR	78	108	111
24	1E+06	20	18.07	2	1	-	-	IUD	9/14/2010	6/21/2011	10.0	NR	NR	96	101	102
25	1E+06	22	20.73	2	-	-	1	-	8/13/2010	5/20/2011	10.0	NR	NR	81	132	120
26	1E+06	27	22.18	P	-	-	-	-	11/14/2010	8/21/2011	11.0	NR	NR	97	-	-
27	1E+06	23	19.81	2	1	-	-	IUD	8/29/2010	6/6/2011	10.0	NR	NR	97	-	-
28	800909	23	17.06	2	1	2	-	-	7/17/2010	4/23/2011	11.0	NR	NR	68	78	90
29	1E+06	22	24.30	P	-	-	-	-	8/28/2010	6/5/2011	11.5	NR	NR	74	88	90
30	1E+06	26	26.20	3	1	1	1	-	9/5/2010	6/16/2011	11.1	NR	NR	142	-	-
31	1E+06	26	23.80	2	1	-	1	-	8/30/2010	6/6/2011	12.5	NR	NR	143	-	-
32	1E+06	20	23.53	4	3	1	-	-	7/15/2010	4/22/2011	9.0	NR	NR	129	132	142
33	1E+06	26	15.30	P	-	-	-	-	10/18/2010	7/25/2011	10.0	NR	NR	107	117	102
34	1E+06	25	16.02	2	1	1	-	-	6/26/2010	3/30/2010	9.8	NR	NR	140	-	-
35	1E+06	20	18.26	P	-	-	-	-	11/15/2010	8/22/2011	9.5	NR	NR	96	-	-
36	1E+06	20	19.80	2	1	-	-	IUD	7/17/2010	4/24/2011	11.0	NR	NR	92	74	70
37	1E+06	21	18.40	P	-	-	-	-	9/5/2010	6/12/2011	11.6	NR	NR	60	136	142
38	1E+06	25	20.30	3	2	2	-	-	10/9/2010	7/16/2011	8.0	NR	NR	83	136	100
39	1E+06	22	18.80	2	1	1	-	-	7/17/2010	4/24/2011	10.3	NR	NR	113	114	124
40	1E+06	22	19.47	P	-	-	-	-	7/29/2010	5/6/2011	12.0	NR	NR	104	120	128
41	1E+06	24	17.33	P	-	-	-	-	10/17/2010	7/24/2011	11.5	NR	NR	85	92	90
42	1E+06	22	27.33	2	1	1	-	-	13/09/2010	6/20/2011	10.0	NR	NR	67	142	-
43	770361	20	21.42	2	1	1	-	-	12/9/2010	9/16/2011	9.0	NR	NR	70	-	-
44	696736	23	19.62	3	2	2	-	-	11/5/2010	8/12/2011	10.0	NR	NR	80	94	90
45	1E+06	21	19.50	2	1	-	-	NND	9/17/2010	6/24/2011	10.0	NR	NR	80	4	90
46	1E+06	20	20.54	P	-	-	-	-	8/19/2010	5/26/2011	10.0	NR	NR	70	132	148
47	1E+06	29	29.16	3	2	2	-	-	9/9/2010	6/16/2011	8.0	NR	NR	179	-	-
48	1E+06	19	21.33	P	-	-	-	-	8/28/2010	6/5/2011	11.2	NR	NR	140	-	-
49	1E+06	25	20.80	2	1	1	-	-	8/30/2010	6/7/2011	11.0	NR	NR	96	101	128
50	1E+06	19	20.23	P	-	-	-	-	9/25/2010	7/2/2011	9.0	NR	NR	175	-	-
51	1E+06	29	19.81	2	1	1	-	-	8/21/2010	5/28/2011	10.0	NR	NR	204	-	-
52	2E+06	26	19.00	4	1	1	1	-	10/26/2010	8/2/2011	11.5	NR	NR	106	110	92

ANNEXURE III - MASTER CHART

Serial Number	Out Patient Numbe	Age (Years)	BMI (Kg/m^2)	Obstetric History					LMP	EDD	Investigations					
														OGTT		
				Gravida	Para	Living	Abortion	Other			Hb (gm%)	HIV	HBsAg	1st trimester	2nd trimester	3rd trimester
53	2E+06	24	16.40	P	-	-	-	-	11/22/2010	8/29/2011	11.0	NR	NR	88	-	-
54	1E+06	22	18.75	P	-	-	-	-	10/17/2010	7/24/2011	8.0	NR	NR	75	84	79
55	739620	25	16.66	2	1	1	-	-	11/23/2010	8/30/2011	7.5	NR	NR	99	101	123
56	1E+06	21	20.81	3	2	2	-	-	9/9/2010	6/16/2011	11.2	NR	NR	119	120	132
57	2E+06	27	17.85	2	1	1	-	-	11/24/2010	8/31/2011	9.8	NR	NR	90	94	98
58	2E+06	28	28.60	2	1	1	-	-	11/23/2010	8/30/2011	11.5	NR	NR	121	124	149
59	1E+06	23	17.11	2	1	1	-	-	10/15/2010	7/22/2011	10.0	NR	NR	80	65	88
60	1E+06	22	19.90	P	-	-	-	-	10/16/2010	7/23/2011	10.0	NR	NR	102	112	-
61	1E+06	24	15.95	2	1	1	-	-	8/23/2010	5/30/2011	11.0	NR	NR	80	128	138
62	1E+06	24	23.43	P	-	-	-	-	9/28/2010	7/5/2011	11.8	NR	NR	85	97	117
63	1E+06	24	19.20	2	1	1	-	-	9/7/2010	6/14/2011	11.2	NR	NR	74	120	142
64	893039	31	19.73	2	1	1	-	-	9/19/2010	6/26/2011	10.8	NR	NR	81	148	-
65	1E+06	21	21.90	2	1	1	-	-	9/24/2010	7/1/2011	12.0	NR	NR	56	120	120
66	1E+06	23	17.80	2	1	1	-	-	9/29/2010	7/6/2011	11.7	NR	NR	137	122	128
67	1E+06	20	21.22	P	-	-	-	-	11/12/2010	8/19/2011	12.0	NR	NR	118	120	138
68	2E+06	18	16.88	P	-	-	-	-	12/6/2010	9/12/2011	16.9	NR	NR	78	-	-
69	1E+06	30	21.40	3	1	1	1	-	11/8/2010	8/15/2011	12.6	NR	NR	93	98	156
70	2E+06	21	23.78	P	-	-	-	-	11/16/2010	8/23/2011	8.9	NR	NR	135	142	-
71	1E+06	26	19.63	P	-	-	-	-	10/16/2010	7/23/2011	11.5	NR	NR	118	101	110
72	1E+06	19	20.02	P	-	-	-	-	9/7/2010	6/14/2011	9.6	NR	NR	91	90	139
73	1E+06	18	21.60	P	-	-	-	-	9/8/2010	6/15/2011	11.0	NR	NR	71	61	80
74	1E+06	19	19.53	P	-	-	-	-	9/23/2010	6/30/2011	11.0	NR	NR	73	80	95
75	1E+06	26	20.70	P	-	-	-	-	7/3/2010	4/10/2011	10.8	NR	NR	106	97	98
76	1E+06	21	19.14	2	-	-	1	-	10/6/2010	8/13/2011	9.0	NR	NR	84	92	-
77	1E+06	20	16.66	P	-	-	-	-	9/3/2010	6/10/2011	11.0	NR	NR	102	112	132
78	1E+06	27	23.33	3	-	1	1	-	9/30/2010	7/7/2011	11.4	NR	NR	89	90	98
79	1E+06	20	26.27	3	1	1	1	-	9/16/2010	6/23/2011	10.1	NR	NR	73	88	98
80	2E+06	22	26.00	2	1	1	-	-	8/2/2010	5/9/2011	11.4	NR	NR	78	72	142
81	1E+06	24	22.22	P	-	-	-	-	8/10/2010	5/17/2011	11.0	NR	NR	74	130	111
82	1E+06	18	21.60	P	-	-	-	-	7/23/2010	4/30/2011	11.3	NR	NR	75	84	94
83	2E+06	26	16.70	P	-	-	-	-	11/10/2010	8/17/2011	10.5	NR	NR	98	111	126
84	1E+06	25	18.55	2	1	1	-	-	8/17/2010	5/24/2011	11.0	NR	NR	93	101	122
85	1E+06	20	25.10	P	-	-	-	-	7/18/2010	4/25/2011	10.0	NR	NR	101	99	90
86	1E+06	25	18.79	5	2	2	2	-	7/15/2011	4/22/2011	11.0	NR	NR	176	-	-
87	1E+06	19	22.80	P	-	-	-	-	7/7/2010	4/4/2011	11.0	NR	NR	117	118	101
88	1E+06	32	27.00	P	-	-	-	-	7/18/2010	4/25/2011	12.3	NR	NR	86	148	-
89	1E+06	26	18.90	2	2	2	-	-	7/5/2010	4/12/2011	11.0	NR	NR	92	110	102
90	1E+06	21	20.40	P	-	-	-	-	8/12/2010	5/19/2011	12.0	NR	NR	98	101	126
91	1E+06	21	22.22	P	-	-	-	-	6/15/2010	3/22/2011	10.0	NR	NR	120	119	118
92	1E+06	22	19.30	P	-	-	-	-	7/18/2010	4/25/2011	12.6	NR	NR	109	152	-
93	1E+06	28	20.54	P	-	-	-	-	8/25/2010	6/2/2011	13.0	NR	NR	79	88	92
94	2E+06	22	17.77	P	-	-	-	-	12/8/2010	9/15/2011	10.5	NR	NR	95	-	-
95	1E+06	26	30.81	3	1	1	1	-	7/12/2010	4/9/2011	13.4	NR	NR	100	172	-
96	1E+06	26	19.79	2	1	1	-	-	6/18/2010	3/27/2011	9.3	NR	NR	113	120	118
97	961191	30	20.40	3	1	1	1	-	9/2/2010	6/9/2011	11.2	NR	NR	122	101	112
98	1E+06	21	22.67	P	-	-	-	-	7/27/2010	5/4/2011	11.0	NR	NR	71	-	-
99	1E+06	21	22.30	P	-	-	-	-	6/30/2010	4/7/2011	10.2	NR	NR	78	87	145
100	1E+06	19	18.40	P	-	-	-	-	6/14/2010	3/21/2011	9.0	NR	NR	98	123	122
101	1E+06	23	19.40	2	1	1	-	-	7/25/2010	5/2/2011	8.0	NR	NR	91	92	98
102	1E+06	23	19.55	P	-	-	-	-	7/19/2010	4/26/2011	10.0	NR	NR	127	-	-
103	1E+06	27	17.74	3	2	2	-	-	9/12/2010	3/19/2011	12.0	NR	NR	112	120	132
104	1E+06	25	17.70	6	1	1	4	-	10/7/2010	7/14/2011	11.0	NR	NR	75	122	-

ANNEXURE III - MASTER CHART

Serial Number	Out Patient Numbe	Age (Years)	BMI (Kg/m^2)	Obstetric History					LMP	EDD	Investigations					
														OGTT		
				Gravida	Para	Living	Abortion	Other			Hb (gm%)	HIV	HBsAg	1st trimester	2nd trimester	3rd trimester
105	1E+06	20	26.60	P	-	-	-	-	6/25/2010	3/2/2011	11.0	NR	NR	88	101	142
106	1E+06	19	22.21	P	-	-	-	-	10/25/2010	8/1/2011	10.0	NR	NR	84	98	101
107	2E+06	21	22.05	P	-	-	-	-	-	9/25/2011	11.7	NR	NR	97	101	120
108	1E+06	20	19.89	P	-	-	-	-	7/6/2010	4/13/2011	10.5	NR	NR	72	88	101
109	1E+06	18	15.50	P	-	-	-	-	10/4/2010	7/11/2011	9.0	NR	NR	131	99	132
110	1E+06	19	19.55	P	-	-	-	-	7/23/2010	4/30/2011	11.0	NR	NR	85	86	88
111	1E+06	28	15.50	4	3	1	-	-	10/22/2010	7/29/2011	9.9	NR	NR	74	-	-
112	2E+06	23	24.30	2	1	1	-	-	12/29/2010	10/5/2011	8.0	NR	NR	89	-	-
113	1E+06	28	18.29	P	-	-	-	-	11/6/2010	8/13/2011	9.5	NR	NR	80	-	-
114	1E+06	19	20.44	P	-	-	-	-	11/6/2010	8/13/2011	10.5	NR	NR	96	-	-
115	2E+06	23	20.66	2	1	1	-	-	12/17/2010	9/24/2011	12.1	NR	NR	77	-	-
116	1E+06	22	22.22	2	1	1	-	-	10/22/2010	7/29/2011	10.0	NR	NR	102	130	112
117	1E+06	21	21.36	P	-	-	-	-	10/10/2010	7/17/2011	11.0	NR	NR	72	90	111
118	1E+06	20	21.11	3	1	1	1	-	11/12/2010	8/19/2011	9.0	NR	NR	107	124	121
119	1E+06	24	25.80	2	1	1	-	-	10/2/2010	7/9/2011	8.0	NR	NR	147	-	-
120	1E+06	25	21.20	P	-	-	-	-	9/16/2010	6/23/2011	8.9	NR	NR	76	-	-