DISSERTATION ON

SERUM URIC ACID IN EARLY PREGNANCY
A MARKER FOR GESTATIONAL DIABETES MELLITUS

Dissertation submitted to

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M.S. OBSTETRICS AND GYNAECOLOGY

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CERTIFICATE

This is to certify that this dissertation entitled "**SERUM URIC ACID IN EARLY PREGNANCY A MARKER FOR GESTATIONAL DIABETES MELLITUS**" is a bonafide original work of **Dr. NITHYA D** in partial fulfillment of the requirements for M.S Branch -VI (Obstetrics & Gynaecology) Examination of the Tamilnadu Dr.M.G.R. Medical University to be held in APRIL - 2017. The period of study was from Sept 2015 to August - 2016.

Prof.Dr.M.VANITHAMANI, M.S., MCh.,
THE DEAN,
THANJAVUR MEDICAL COLLEGE
THANJAVUR - 613004

Prof. DR. S.PRADEEBA M.D., OG
HEAD OF THE DEPARTMENT
DEPT. OF OBSTETRICS AND GYNAECOLOGY
THANJAVUR MEDICAL COLLEGE
THANJAVUR - 613004

DECLARATION

I, **Dr. NITHYA D**, solemnly declare that dissertation titled "**SERUM URIC ACID IN EARLY PREGNANCY A MARKER FOR GESTATIONAL DIABETES MELLITUS"** is a bonafide work done by me at Thanjavur Medical College, Thanjavur during September 2015 to August 2016 under the guidance and supervision of **Prof.Dr.S.PRADEEBA, M.D.,OG.,** Head of the department, Department of Obstetrics and Gynaecology, Thanjavur Medical College, Thanjavur.

This dissertation is submitted to Tamilnadu Dr. M.G.R Medical University towards partial fulfillment of requirement for the award of **M.S Degree (Branch -VI) in Obstetrics and Gynaecology**.

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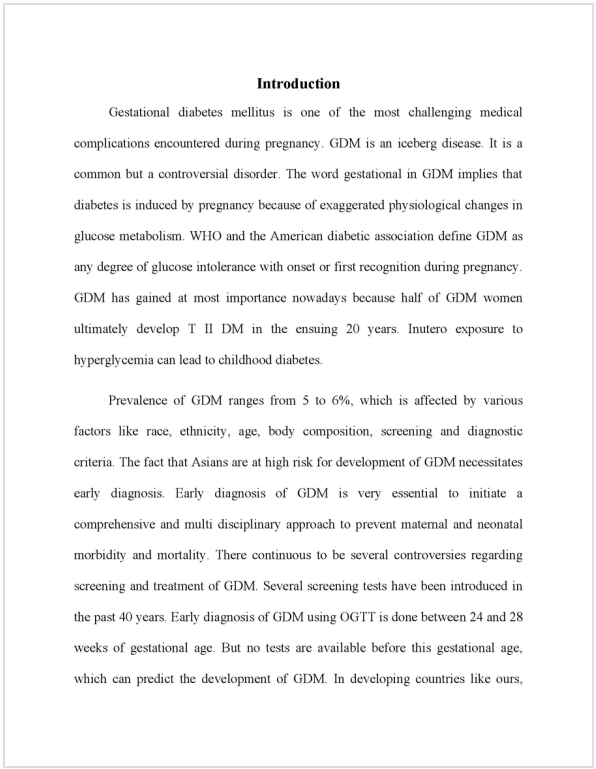

Introduction

Gestational diabetes mellitus is one of the most challenging medical complications encountered during pregnancy. GDM is an iceberg disease. It is a common but a controversial disorder. The word gestational in GDM implies that diabetes is induced by pregnancy because of exaggerated physiological changes in glucose metabolism. WHO and the American diabetic association define GDM as any degree of glucose intolerance with onset or first recognition during pregnancy. GDM has gained at most importance nowadays because half of GDM women ultimately develop T II DM in the ensuing 20 years. Inutero exposure to hyperglycemia can lead to childhood diabetes.

Prevalence of GDM ranges from 5 to 6%, which is affected by various factors like race, ethnicity, age, body composition, screening and diagnostic criteria. The fact that Asians are at high risk for development of GDM necessitates early diagnosis. Early diagnosis of GDM is very essential to initiate a comprehensive and multi disciplinary approach to prevent maternal and neonatal morbidity and mortality. There continuous to be several controversies regarding screening and treatment of GDM. Several screening tests have been introduced in the past 40 years. Early diagnosis of GDM using OGTT is done between 24 and 28 weeks of gestational age. But no tests are available before this gestational age, which can predict the development of GDM. In developing countries like ours,


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INTRODUCTION

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be more cost effective. Serum uric acid is associated with insulin resistance. Two mechanisms have been hypothesized by which uric acid can cause insulin resistance. Uric acid causes endothelial dysfunction and decreases nitric oxide production by endothelial cells. In animals insulin action on glucose uptake into cells in the skeletal muscles and adipose tissue is dependent on nitric oxide. Thus decrease in nitric oxide lead to decreased glucose uptake and the development of insulin resistance. Another mechanism is that uric acid may induce insulin resistance and causes inflammation and oxidative stress in adipocytes, which is a contributor to the development of metabolic syndrome. It has been proven that higher levels of uric acid are noted at 24 to 28 weeks of gestation in women with GDM when compared with women without GDM. Normally during pregnancy, the serum uric acid level decreases significantly between 8 and 24 weeks of gestation due to increased glomerular filtration rate and reduced re-absorption of uric acid from renal tubules. In first trimester, it likely approximates preconception uric acid level, and elevated levels may identify women who are predisposed to metabolic syndrome with an increased risk of developing gestational diabetes mellitus. This concept would be useful in predicting GDM at an earlier gestational age, there by aiding in initiating timely and appropriate management to prevent maternal and fetal morbidity and mortality.

AIM OF THE STUDY

To correlate between first trimester uric acid level and its association with subsequent development of gestational diabetes mellitus

REVIEW OF LITERATURE

Gestational diabetes mellitus is defined as carbohydrate intolerance of variable severity with onset or first recognized during pregnancy (ACOG,2013)[1].

Short history of gestational diabetes mellitus

The recorded history of diabetes in pregnancy over the past 200 years is essentially the story of recognition of the adverse effects of hyperglycemia on both mother and fetus. Much effort has been spent on the problem of categorizing the degree of hyperglycemia which would justify treatment and how to identify the mother at risk.

The first documented evidence of the effect of hyperglycemia in pregnancy in the modern era was in 1824, when Bennetwitz et al recorded a case of severe fetal macrosomia and stillbirth in 22 year old multi gravid women in Berlin[2].

However until the discovery of insulin in 1923 there was no effective treatment for this condition, and the outcome of pregnancy for both mother and the fetus was usually disastrous. Belgium researcher J.P.Hoet(1954) was the first to use the term “meta gestational diabetes” and published his study on “carbohydrate metabolism during pregnancy”[3].

In 1967 Jorgen Pederson et al probably were the first to use the modern term "Gestational diabetes mellitus"[4] and this was promoted by Frienkel.N et al in 1980 in Chicago who published a paper of "Pregnancy and progeny", incorporating several important insights on to the pathophysiology of glucose metabolism in both mother and the fetus[5].

The first international workshop conference on gestational diabetes mellitus in 1979[6], essentially declared, GDM as a disease with significant health risk that needed treatment. Thus instead of more neutral "carbohydrate intolerance of pregnancy" the term "Gestational Diabetes Mellitus" evolved.

The first major prospective study was established in 1954 in Boston and the one hour 50 gm glucose screening test was used there. The result from this study presented by O Sullivan and Mahan et al in 1964 showed that hyperglycemia in pregnancy correlated with development of diabetes latter in life[7].

Prevalence of gestational diabetes mellitus

Globally, the prevalence ranges between 1 and 14% of all pregnancies (Person B et al)[8]. But studies conducted in different parts of country averages the incidence of GDM in Indian population to be 16.55% (Seshiah V et al 2004).[9]

The Australian carbohydrate intolerant study (ACHOIS) undertaken in 14 centers in Australia and four centers in UK reported GDM affected 2 to 9 % of pregnancy (Crowther CA et al 2005)[10].

Tuffnell, Whilst et al 2003 in their systematic review of treatment for GDM and impaired glucose tolerance (IGT), for seven cochrane data based study state that 3 to 6% pregnancies are affected by GDM[11].

Classification during pregnancy :(Williams Obstetrics book 24th edition)[50]

1. Etiological classification of diabetes mellitus: [50]

Type 1:

β- cell destruction, usually absolute insulin deficiency

Immune- mediated

Idiopathic

Type 2:

Ranges from predominantly insulin resistance to predominantly an insulin secretary defect with insulin resistance

Other types:

- ✓ Genetic mutations of beta cell function- MODY1-6,others
- ✓ Genetic defects in insulin action

- ✓ Genetic syndromes-Down,Klinefelter,Turner
- ✓ Diseases of the exocrine pancrease-pancreatitis,cystic fibrosis
- ✓ Endocrinopathies-Cushing syndrome,pheocromocytoma,others
- ✓ Drug or chemical induced-glucocorticoids,thiazides,β-adrenergic agonists,others
- ✓ Infections-congenital rubella,cytomegalovirus,coxsackie virus
- ✓ Gestational diabetes

White classification in pregnancy (American journal of med 1949)[79]

A: Abnormal glucose tolerance test at any age or of any duration treated only by diet therapy

B: Onset at age 20 years or older and duration of less than 10 years

C: Onset at age 10 to 19 years or duration of 10 to 19 years

D: Onset before 10 years of age, duration over 20 years, benign retinopathy, or hypertension (not preeclampsia)

– D1: Onset before age 10 years

– D2: Duration over 20 years

– D3: Calcification of vessels of the leg (macrovascular disease)

– D4: Benign retinopathy (microvascular disease)

– D4: Hypertension (not preeclampsia)

R: Proliferative retinopathy or vitreous hemorrhage

F: Renal nephropathy with over 500 mg/d proteinuria

RF: Criteria for both classes R and F

G: Many pregnancy failures

H: Evidence of arteriosclerotic heart disease

T: Prior renal transplant

Gestational diabetes

– A1: Controlled by diet and exercise

– A2: Requires insulin

Classification scheme recommended by ACOG (1986)[50]

Class	Onset	Plasma Glucose Level		Therapy
		Fasting	2-Hour Postprandial	
A_1	Gestational	< 105 mg/dL	< 120 mg/dL	Diet
A_2	Gestational	> 105 mg/dL	> 120 mg/dL	Insulin
Class	**Age of Onset (yr)**	**Duration (yr)**	**Vascular Disease**	**Therapy**
B	Over 20	< 10	None	Insulin
C	10 to 19	10 to 19	None	Insulin
D	Before 10	> 20	Benign retinopathy	Insulin
F	Any	Any	Nephropathy[a]	Insulin
R	Any	Any	Proliferative retinopathy	Insulin
H	Any	Any	Heart	Insulin

[a]When diagnosed during pregnancy: proteinuria ≥ 500 mg/24 hr before 20 weeks' gestation.

Now the ACOG (2012, 2013), no longer recommended the white classification.

Classification proposed by American Diabetes Association (2012)[50]

Gestational diabetes: diabetes diagnosed during pregnancy that is not clearly **overt** (type 1or type 2) diabetes

Type I Diabetes

Diabetes resulting from β cell destruction leading to absolute insulin deficiency

a. without vascular complications
b. with vascular complications

Type II Diabetes

Diabetes from inadequate insulin secretion in the face of increased insulin resistance

a. with vascular complications
b. without vascular complications

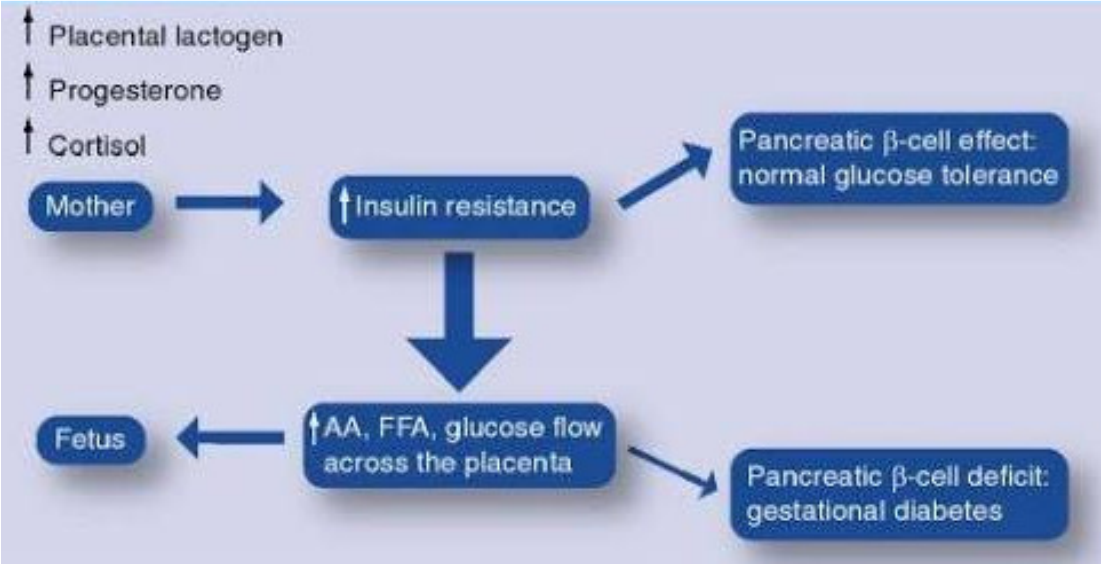
Other types of Diabetes

a. Genetic in origin
b. Associated with pancreatic disease
c. Drug induced
d. Chemically induced

Pathogenesis

Pregnancy is a condition of

1. Accelerated starvation
2. Facilitated anabolism
3. Hyperinsulinism
4. Insulin resistance



Increased placental lactogen, progesterone,and cortisol during pregnancy results in increased insulin resistance and development of GDM.

Pregnancy confers a state of insulin resistance and hyperglycemia that predisposes women to develop diabetes. GDM occurs when women pancreatic function is not sufficient to overcome the diabetogenic environment of

pregnancy. Basal glucose and insulin level remains unchanged in early trimester and glucose is normal (Butte NF et al 2000)[12].

As pregnancy progresses, basal as well as postprandial insulin secretion increases to reach twice the non-pregnant value by the 3rd trimester(Lesser KB et al 1994)[13].

Insulin sensitivity in late normal pregnancy is 45 to 70% lower than that of non-pregnant women (Freemark et al 2006)[14].

Mechanism responsible for insulin resistance

Plasma levels of placental lactogen increases with gestation. Higher levels may increases lipolysis and liberation of free fatty acids (Frienkel, 1980)[5]

This increased free fatty acid concentration may aid increased tissue resistance to insulin.

When insulin levels and responses are expressed relative to each individual's degree of insulin resistance, a large defect in pancreatic β cell function is consistently found in women with prior GDM(Bachanan et al 2001)[15]

Defects in the binding of insulin to its receptor in skeletal muscle do not appear to be involved in insulin resistance in GDM (Damm P et al 1993)[16].

Other defects, like alteration in insulin signaling pathway, reduced expression of PPARγ and reduced insulin mediator glucose transport have been found in skeletal muscle or fat cells of women with GDM(Xiang AH et al 2005) [17].

Recently development of GDM is triggered by an antigenic load which is the fetus itself. Human leukocyte antigen – G (HLA – G) expression which functions to protect the fetus from immune attack by down regulation cytotoxic T cell responses to fetal trophoplast antigen is postulated to protect pancreas as well. The interaction between HLA- G and nuclear factor – KB (NF- KB) is the central event leading to GDM development. In future it may be possible to use recombinant HLA gene for prevention of GDM in high risk patients (Oztekin-O, 2007).[18]

Problems due to gestational diabetes mellitus

Both overt diabetes mellitus and gestational diabetes mellitus pose many risks to the mother as well as fetus.

MATERNAL:

- ✓ Increased risk of preeclampsia
- ✓ Increased risk of caesarean section
- ✓ Polyhydramnios
- ✓ Preterm labour

- ✓ Post partum haemorrhage
- ✓ Nephropathy
- ✓ Retinopathy
- ✓ Increased incidence of infection/hypo and hyperglycaemia, DKA
- ✓ Later –recurrent GDM

-TII Diabetes mellitus

FOETAL:

- ✓ Macrosomia
- ✓ Congenital malformation
- ✓ Neonatal hypoglycemia
- ✓ Hyperbilirubinemia
- ✓ Hypocalcaemia
- ✓ Birth trauma
- ✓ Early childhood obesity

Maternal effects

Gestational diabetes mellitus have increased risk of pre eclampsia. It occurs in 10 % of women with GDM. Gaggar F et al 2005 found that most common complication in GDM patients are gestational hypertension(36.4%) followed by abruption placenta(20%)[19]

Many studies have shown pre eclampsia develops in younger nulliparous , obese and in women who gains significant weight in pregnancy. Risk of super added preeclampsia is 35 to 60% in women who have micro albuminuria in early pregnancy. Pre eclampsia occurs in women with pre gestational diabetes is well documented but there are conflicting reports as to the effect of GDM on development of hypertensive disorders (Joffe GM et al 1998).[20]

There was 10 % increased risk of polyhydromnios in women with GDM. Dashe and colleagues in 2000 found that amniotic fluid index parallels the amniotic fluid glucose level among women with diabetes [21]. In 2006 Vink and associates linked poor maternal glucose control to macrosomia and hydromnios.[22] Women with elevated glycosylated hemoglobin (HbA1c) value in 3rd trimester were more likely to have hydromnios (Idris et al 2010)[23].

Risk of preterm labor chorio amnionitis and urinary tract infection also increased. Women with GDM developed twice the number of urinary tract infection than who don't have GDM due to increased glucose in urine beyond normal glycosuria in pregnancy (Ian Donald's practical obstetric problems) [24]

Certain tocolytics and antenatal steroid given in pregnancy complicated by preterm labor worsen the hypoglycemia and predispose the women to ketoacidosis. Fever and dehydration also precipitates ketoacidosis and sudden fetal loss. 4 to 15% of maternal mortality occurs due to keto-acidosis in

pregnancy. It is increasingly reported in women with type 2 or even those with gestational diabetes mellitus (Sibai, 2014).[25]

The risk of developing type 2 diabetes mellitus after pregnancy in women with gestational diabetes is 10% per year. The incidence is high in first five years after pregnancy and then decreases (Neston et al 2002).[26]

Similar to women with overt diabetes, GDM is also associated with increased frequency of caesarian section rate. Gagger et al 2005 found that 19.15% increased caesarian rate in women with gestational diabetes mellitus [19]. After delivery women with GDM have increased risk for metabolic syndrome, disturbed endothelial function and are prone to develop cardiovascular morbidity (Valpreda S et al 2007)[27]

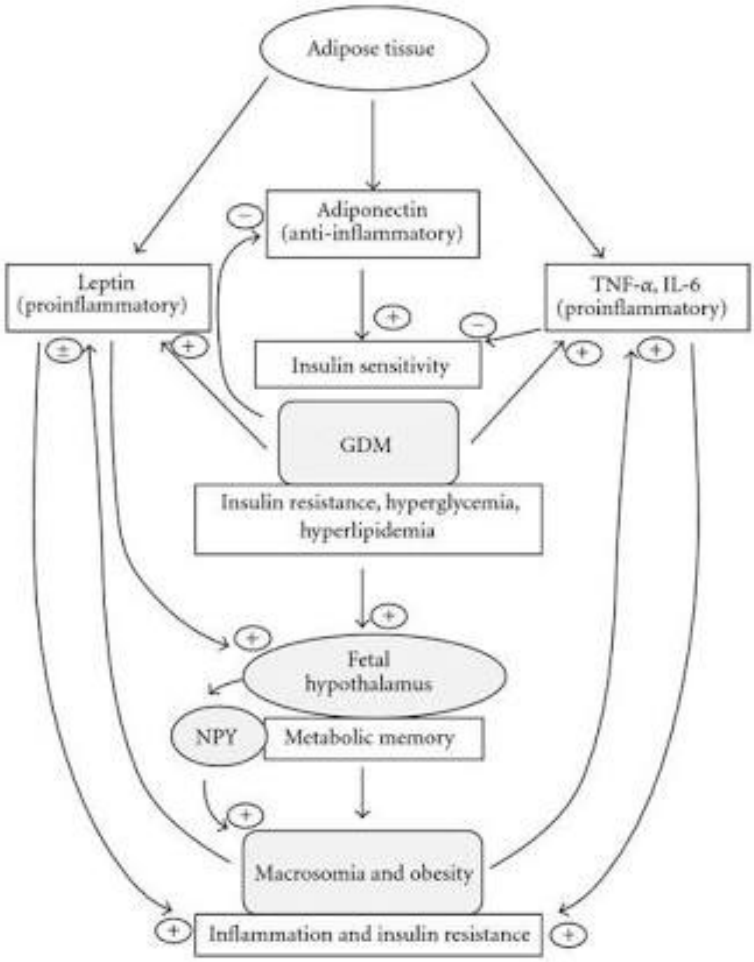
Effects of GDM on the fetus (Arias' High risk pregnancy and delivery book 4th edition) [36]

Fetal effects include

1. Abnormalities in growth – macrosomia, growth restriction and congenital malformation
2. Fetal oxygenation problem – Sudden intrauterine death, respiratory distress syndrome
3. Chemical imbalance after delivery
4. Long term sequlae

1. Abnormalities in growth

Maternal hyperglycemia leads to fetal hyperinsulinemia which is responsible for increased fat deposition and macrosomia, organomegaly, increased erythropoietin and reduced surfactant production (Pederson J et al)[4]. Some authors also suggest that maternal obesity rather than GDM may be the determining factors in development of macrosomia (Oken N et al 1997, Dang K et al 2000)[28]



Macrosomia leads to increased risk of shoulder dystocia. There was three fold increased risk of shoulder dystocia when birth weight is more than four thousand gram (Acker DB 1985;Ginsberg NA et al 2001)[29]. It also increases the risk of intra partum asphyxia, respiratory distress syndrome and polycythemia. ACOG suggest that if GDM remains undiagnosed or untreated the risk of macrosomia is high as 20 %(Chatfield J, 2001)[30]

The HAPO study 2008[31] showed a strong correlation between maternal glucose levels (even below the values diagnosis of GDM) and increased in birth weight and cord blood serum C peptide levels. Unlike overt diabetes, rates of congenital anomalies don't appears to be increased in women with GDM (Sheffield JS 2002)[32]. Maternal glycosilated hemoglobin level in first trimester helps to predict it.

2. Fetal oxygenation problems

Oxygen consumption increased by 30% in gestational diabetes. Increased erythropoietin secretion results in polycythemia and hyperviscosity which causes neonatal strokes, seizures, neonatal enterocolitis and sudden fetal demise.(IAN DONALD'S practical obstetrics book) [24]

Sudden fetal death occurs due to

1. Maternal hypoglycemia
2. Ketoacidosis
3. Chronic hypoxia
4. Placental villous edema impairs nutrient transfer

In 2003, American diabetic association concluded that fasting blood sugar more than 105mg/dl is associated with increased risk of fetal death during the final 4 to 8 weeks[33].

3. Chemical imbalance

Maternal hypoglycemia causes fetal hypoglycemia results in sudden intrauterine death. Other complications like hypocalcaemia and hypomagnesaemia within 72 hours of birth. Risk of hyperbilirubinaemia is increased due to preterm delivery and ineffective erythropoiesis. Incidence of hypoglycemia and hyperbilirubinemia increased in gestational diabetes. Iron deficiency anemia also occurs, which results in neuro developmental and behavioural abnormalities (Lozoff B et al 2000)[34]

4. Long term complications

Infants of gestational diabetes mellitus have increased risk of developing obesity, type 2 diabetes, cognitive impairment and cardiovascular diseases(Tam WH, Yang X et al 2008)[35]

Risk assessment and various screening test for gestational diabetes mellitus (ARIAS" HIGH RISK PREGNANCY AND DELIVERY 4th EDITION)[36]

Low risk (Blood sugar screening not routinely required)

1. Members of ethnic group with low prevalence of GDM
2. Age less than 25 years
3. No known diabetes in first degree relatives
4. No history of abnormal glucose metabolism
5. Normal weight before pregnancy
6. Normal weight at birth

Moderate risk (these women needs blood sugar testing at 24 to 28 weeks- 1 or 2 step procedure)

1. Members of ethnic group with high prevalence of GDM
2. Age more than 25 years
3. Diabetes in first degree relatives
4. Over weight before pregnancy
5. Weight high at birth

High risk (In these women blood sugar testing should be done as soon as possible)

1. Marked obesity
2. Strong family history of type 2 diabetes
3. Previous history of GDM, impaired glucose metabolism or glycosuria
4. High risk ethnic group(Indian, African, Hispanic and middle eastern)

Screening tests

There is a debate regarding the preferred screening protocol for gestational diabetes mellitus. First screening test for GDM was proposed in 1973.When universal screening is employed, patient with no risk factor should undergo one hour glucose test (GCT) at 24 to 28 weeks of gestation. Patient with known risk factors that indicate the possibility of glucose intolerance may be tested at the onset of prenatal care.

Two step tests:-

According to 1997 recommendations by American Diabetes Association's Fourth International Workshop on GDM [37] screening and diagnosis were undertaken as a two step approach. Initially screening is done with 50 gm of glucose challenge test. Patient receives 50 grams of glucose and one hour later, blood is drawn for testing. A glucose value above 140 mg/dl is considered as abnormal and then patients are subjected to the second test, three hour glucose tolerance test with 100 grams of glucose.

Diagnosis of GDM by 100gm 3-hr OGTT by Carpenter and Coustan (1982)[38]

To perform glucose tolerance testing (OGTT), clinician first draws a fasting glucose sample and administered100 gram of glucose. Blood for glucose value is drawn at 1 hour, 2 hour and 3 hours.

	Carpenter coustan criteria(1982)	National diabetes data group
FBS	95mg/dl	105mg/dl
1 hour	180mg/dl	190mg/dl
2 hour	155mg/dl	165mg/dl
3 hour	140mg/dl	145mg/dl

Two or more values should be abnormal for diagnosis.

ACOG 2001 practice bulletin states that universal screening is the most sensitive and more practical approach but it notes that low risk women may be excluded from screening as per the American diabetic association (ADA) recommendation. (ACOG practice bulletin September 2001)[39]

"NICE guidelines 2008[40]" recommended screening at 24 to 28 weeks using 75 gram OGTT. Diagnosis made on basis of criteria defined by WHO (FBS $\geq$ 126 mg/dl and 2 hour value of 140 mg/dl)

ACOG 2013 recommended two step tests[41].

Single step approach:-

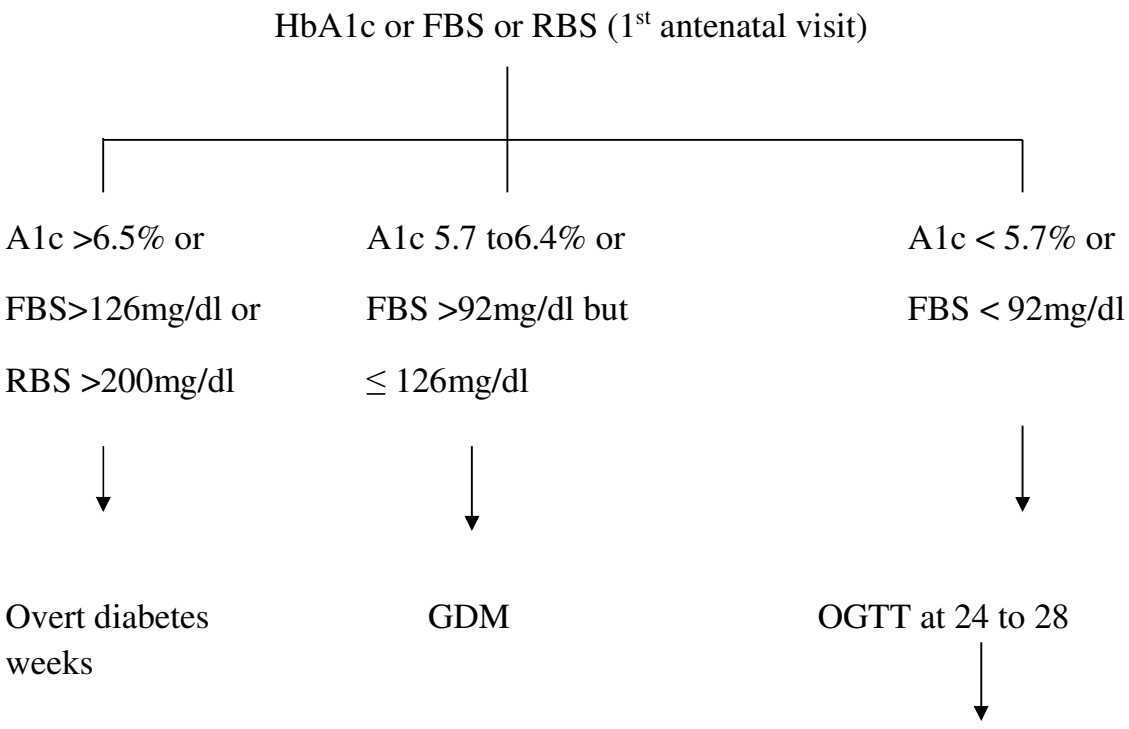
1. Diabetes in pregnancy study group (DIPSI) [42] recommended a single step diagnostic procedure for all patients (Universal screening). This has been approved by Ministry Of Health, Govt. Of India and also by WHO.

Procedure:-

Pregnant women is given 75 grams glucose orally irrespective of her fasting status or timing of last meal. GDM is diagnosed if the post prandial 2 hour value is more than 140 mg/dl.

2. HAPO trial 2008[31]

The study was conducted in 25000 Caucasians using 75 gram oral glucose tolerance test between 24 and 32 weeks gestation(Metzegerbe et al 2010).The values are analyzed with birth weight >90th percentile, neonatal hypoglycemia, primary caesarean section rate, cord –serum c-peptide level >90th percentile.



If abnormal - GDM

American diabetic association(2013) and International association of diabetes and pregnancy study(IADPSG) in 2010 recommended one step test using 75 gram 2 hour OGTT based on HAPO trial(Hyperglycemia and pregnancy outcome)

75 gram 2 hour OGTT test (IADPSG guidelines 2011)[43]

Preparation of patient:-

- Unrestricted diet in previous 3 days
- Overnight fasting 8 to 14 hours
- Test done in morning
- Should not be ambulated
- Smoking avoided

Criteria to diagnose:-

- Fasting >92 mg/dl(5.1mmol/L)
- 1 hour >180mg/dl(10.0mmol/L)
- 2 hour >153 mg/dl (8.5mmol/L)

Diagnosis is made when any one value is exceeded.

Cut off values are lower than traditional value and were considered after result of HAPO trial, suggested increased complications even below the cut offs in traditional tests.

Traditional test (Carpenter and NDDG guidelines) cut offs were based on data that was derived mathematically, but in recent guidelines (ADA and IADPSG) cut offs were derived from adverse outcomes at mean glucose level of HAPO study.

Maternal glycosylated hemoglobin levels in first trimester helps to predict the occurrence of congenital anomalies in pregestational diabetes (Kicklighter SD .2001)[44]

HBA1C <7%-No greater risk

7.8 -9.5% - 5 % Anomalies

>10 % -22 %Anomalies

So HbA1C up to 6.5 % was considered normal and acceptable for the first trimester control

Various screening test criteria's for GDM diagnosis (Management of high risk pregnancy book 2nd edition) [80]

	Method	Screen positive	Diagnostic test	Threshold level
WHO	One step	NA	75gm OGTT	Fasting>126mg/dl 2hours≥140mg/dl One annormal value needed for diagnosis
DIPSI	One step	NA	75gm OGTT(irrespective of fasting status)	2 hours≥140mg/dl
ACOG	Two step	50gm GCT glucose≥135mg/dl or≥140mg/dl is elevated.the lower threshold should be consideredin population with higher prevalence of GDM	100gm OGTT	Fasting≥95mg/dl 1hour≥180mg/dl 2hour≥155mg/dl 3hours≥140mg/dl More than 2 abnormal value needed for diagnosis
ADA	One step	NA	75gm OGTT	Fasting≥92mg/dl 1hour≥180mg/dl 2hour≥155mg/dl One abnormal value needed for diagnosis
IADPSG	One step	NA	75gm OGTT	Fasting≥92mg/dl 1hour≥180mg/dl 2hour≥153mg/dl One abnormal value needed for diagnosis
CDA	Two step(preferred) Or one step	50gm GCT(2step) glucose≥140mg/dl	75gm OGTT(1STEP)	Fasting 1hour 2hour One abnormal value needed for diagnosis

- DIPSI-Diabetes in pregnancy study group India
- WHO-World health organization
- ACOG-American college of obstetrics and gynaecology
- ADA-American diabetes association
- CDA-Canadian diabetic association
- NA-Not applicable
- IADPSG-International association of diabetes and pregnancy study group

Uric acid

Uric acid is the end product of purine degradation[45].They is derived from both from breakdown of body proteins and also from diet. The richest sources of purines includes kidney, liver, sardine, lentils, sweet bread, anchovies, mushrooms, asparagus and spinach. Uric acid is excreted thro kidneys. 2/3rd of uric acid is excreted via the kidneys and the remaining is excreted via the stool. The level of uric acid that will cause GDM is not known. It has been recognized in recent years that the normal ranges of uric acid is varying widely. Serum uric acid levels has to be tested several times over a period as it has a wide normal range as well as the uric acid level varies day to day and shows seasonal variation in the same person. Urine uric acid level also used to diagnose gout.

Serum uric acid reference value (Lippincott Williams book 9th edition 2011)[46]

- Adult male – 2.5 to 8mg/dl
- Adult female- 1.9 to 7.5mg/dl

Uric acid level fall by1/3rd in early pregnancy and reaches non-pregnant level by term.

- Children ages 10 to 18 years

  Males - 3.6 to 5.5mg/dl

  Females - 3.6 to 4.4mg/dl

- Elderly

Male – 2 to 8.5mg/dl

Female – 2 to 8 mg/dl

Normal range of urinary uric acid is 250 to 750mg/24 hours. It is important to check laboratory reference values for each setting.

Conditions associated with hyperuricemia:-(Mark D et al, 1999)[47]

1. Renal failure
2. Alcoholism
3. Gout
4. Dehydration
5. Leukemia and lymphoma
6. Starvation
7. Metabolic acidosis
8. Toxemia of pregnancy
9. Infectious mononeucleosis
10. Hyperlipidemia
11. Hemolytic anaemia
12. Chemotherapy and radiotherapy

Changes is uric acid concentrations during normal pregnancy (Lind T et al ,1984)[48]

Serum uric acid concentrations have been studied in a group of healthy women before conception, at regular intervals throughout pregnancy and 12 weeks after delivery. Serum uric acid level is decreased at 8 weeks of pregnancy when compared to the pre pregnancy levels and this decreased level was maintained upto24 weeks of pregnancy. Then there will be a raise in the uric acid concentration to reach a level above the pre-pregnancy value and remains elevated for a period of 12 weeks in the post partum period. If clinical management during the second half of pregnancy is to be based on increase in serum uric acid concentration, then such increase will have to be carefully interpreted against the raise in concentration which occurs as part of physiological response to normal pregnancy.

In the year 1989 Carter J et al[49] published that the fall in the early trimester is due to the effect of estrogen and increased plasma volume and glomerular filtration rate

Changes in normal pregnancy (Williams Obstetrics 24th Edition) [50]

	Normal values(mg/dl)
Pre-pregnancy	2.5 to 5.6
First trimester	2.0 to 4.2
Second trimester	2.4 to 4.9
Third trimester	3.1 to 6.3

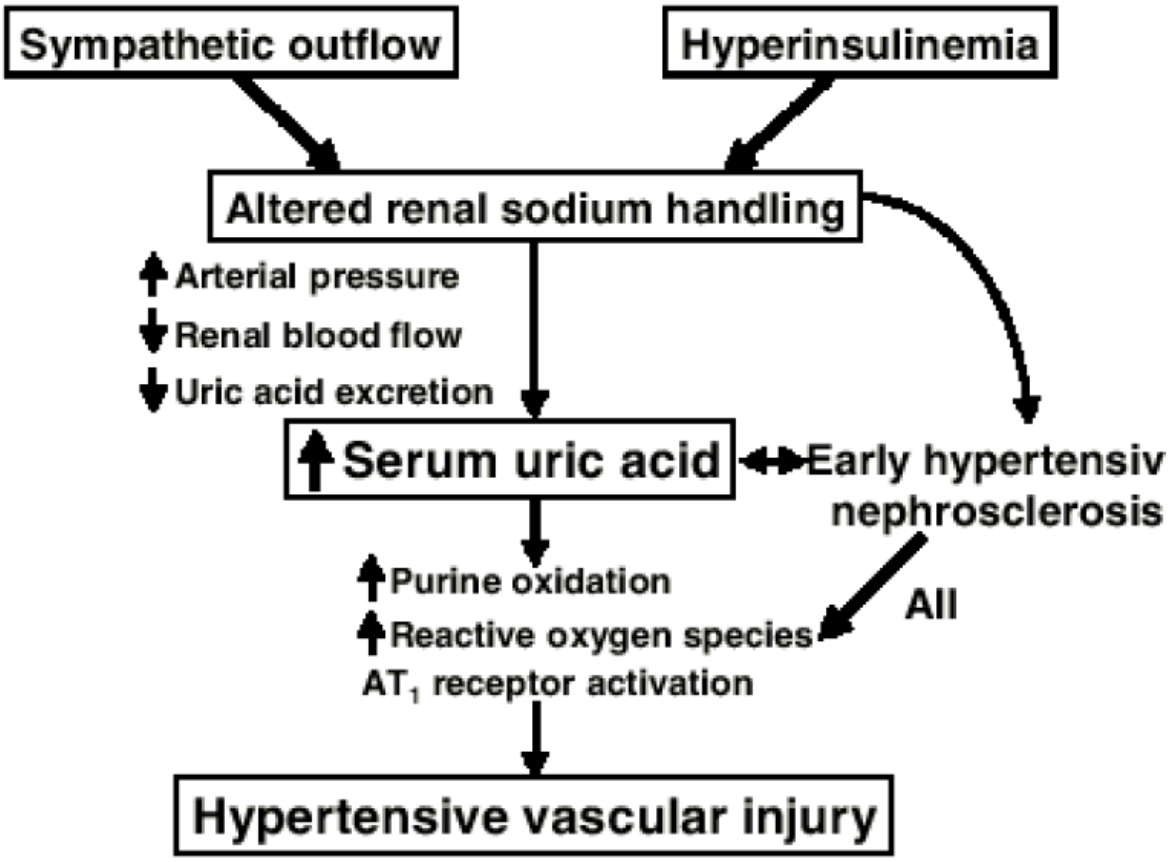
Uric acid is also associated with insulin resistance in non- pregnant individuals (Halkin H et al,(1987)[51]

Association between uric acid and GDM

The association between uric acid and insulin resistance is causal. Two mechanisms have been hypothesized by which uric acid causes insulin resistance. In the year 2003, Cook S et al studied in animals that insulin action on glucose uptake into the cells in the skeletal muscles and the adipose tissues which depends on nitric oxide and this reduced nitric oxide leads to reduced glucose uptake and development of insulin resistance[52].

Nakagawa et al,(2005) states that uric acid causes endothelial dysfunction and decreased nitric oxide production by the endothelial cells[53]. Another mechanism is that uric acid causes inflammation and oxidative stress in adipose

tissues which is associated with onset of metabolic syndrome in mice (Farukawa – S et al 2004: Sautin- YY et all 2007) [54].



Hyper uricemia during the first trimester of pregnancy is associated with high risk of developing GDM. There was 3.25 fold higher risk of developing GDM when the uric acid level in first trimester was in the 4th quartile(S Katherine Laughon et al, (2009)[55].

Even though the uric acid was strongly associated with BMI, the risk of developing GDM was increased among women with elevated uric acid level in first trimester of pregnancy which is independent of BMI[55].

In2009 Laughon et al ,(2009)[55];showed that , Serum uric acid level during the first trimester of pregnancy likely approximates pre-conception level of serum uric acid, and raised level of uric acid may identify women who are at the risk of developing metabolic syndrome with an increased risk of developing GDM, independent of obesity. Alternatively, uric acid decreases early in pregnancy, so perhaps women with elevated uric acid have a poor adaptation to pregnancy (i.e. abnormal placentation), putting them at risk for adverse pregnancy outcomes such as GDM.

Association between uric acid and GDM

Simmi kharb et al (2000)[56] studied the relationship between ascorbic acid and uric acid levels in women with gestational diabetes mellitus. He stated that significant low vitamin c levels and high serum uric acid levels were observed in women with GDM in their study.

In 2006 Gungor ES, Danishman N et al (2006)[57] conducted a study regarding association between serum uric acid, creatinine, albumin and development of GDM.

Laughon et al in 2009[55] concluded serum uric acid in the highest quartile had 3.25 fold increased risk of developing GDM. This effect was concentration dependent.

Rasika C et al in their study from 2014[58] concluded that the first trimester elevated uric acid concentration is associated with increased risk of GDM development.

Jianjun zhou, xiazhao et al(2012)[59] measured lipids and uric acid concentration at 20 weeks of gestation and showed hyperurecemia have increased risk of development of pre-eclampsia and GDM.

In 2012, wolak t et al conducted a study and concluded elevated uric acid in first 20wks of pregnancy is associated with higher risk for GDM and preeclampsia.[60]

Sindhiya anbalagan, mirunalinie et al 2012-2014[61] conducted a study and concluded rise in serum uric acid showed statistical significance in development of GDM.

In 2013 Aparna Kappaganthu ,sachan et al studied that increased uric acid in first trimester have associated with onset of GDM[62].

Shery Angel Rajkumar et al,(2014)[63] concluded that patients with abnormal uric acid level in first trimester had higher risk of developing GDM.

In the year 2015, Balinga Pundalik and Thanga suchitra et al[64], studied 175 pregnant women out of which 8 developed GDM and concluded uric acid in early pregnancy as a predictor of GDM

Possible effects of early diagnosis of GDM

1. **Reduction in perinatal mortality rate**

Increased fetal death occurs due to undiagnosed GDM. The overall decrease in perinatal mortality in recent years due to better antenatal surveillance and earlier intervention (Morb Mortal Wkly 2002)[65]

In 2004, Benerjee et al, found that early diagnosis and effective management resulted in 60% reduction in perinatal mortality[66]

2. **Reduction of rate of Macrosomia:**

Langer et al, 1994[67] showed a significantly reduced incidence of both macrosomia and shoulder dystocia using an intensified management strategy.

There are fairly consistent data showing that screening and subsequent management of GDM may reduce the incidence of macrosomia.(Naylor et al 1995)[68].

3. **Reduction in preeclampsia:**

There are conflicting reports as to the effect of GDM on development of hypertensive disorders of pregnancy (Joffe GM et al, 1998).Alwan et al., 2009 in their study concluded that effective surveillance and treatment of GDM has positive benefit on preeclampsia occurrence.[69]

4. **Reduction in caesarian section rate:**

Tuffnell; Alwan N et al.,(2009)[69] showed 54% reduction in caesarian section rate in their study due to better surveillance and early intervention.

5. **Reduction of immediate neonatal metabolic complications related to maternal hyperglycemia**

Many neonatal units have surveillance protocol for both babies of GDM mothers and macrosomic babies without a maternal history of GDM.

Curet LB et al.,in 1997 and Naeham Z et al., in (1999)showed that maternal euglycaemia , hypocalcaemia, hyperbilirubinemia ,and polycythemia[70]

6. **Prevention of long term effects of GDM on both the mother and the child:**

Wein P et al in 1993 had stated that earlier identification of GDM had some health benefits due to consequent increased surveillance and early diagnosis of TII diabetes mellitus.[71]

In 1998, vohr BR et al., had reported a significant reduction in the incidence of Diabetes and obesity in childhood of GDM mothers with early diagnosis and effective management.[72]

MATERIALS AND METHODS

This is a prospective study conducted at Govt. Raja Mirasudar Hospital attached to Thanjavur Medical College, Thanjavur. The study was conducted over a period of one year from September 2015. The sample size was ascertained after a power calculation with the help of statistician. A total of one hundred and eighty seven ante natal women less than 14 weeks of gestational age who attended the outpatient antenatal department were included in this study. Aim of study was explained and informed written consent obtained. Ethical clearance was given for this study.

Inclusion criteria:-

Antenatal women with gestational age < 14 weeks whose fasting blood sugar was <92 mg/dl were included.

Exclusion criteria:-

- Pregestational diabetes mellitus
- Gestational diabetes mellitus
- Renal disease
- Tuberculosis
- Bronchial asthma
- Liver diseases

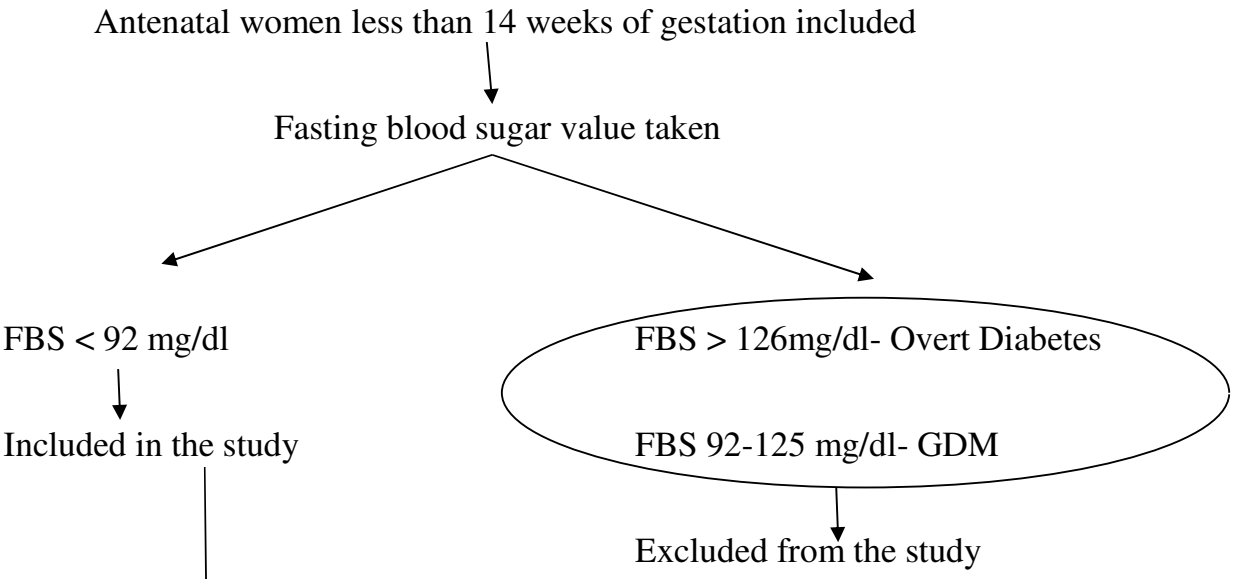
- Cardiovascular diseases
- Gout
- Connective tissue disorder
- Chronic hypertension
- Drugs causing hyperuricemia (pyrizinamide . ethambutol, levodopa and theophylline)

Detailed history was obtained from the patient. General examination and per vaginal examinations were done. Ultra sonogram was done to confirm the gestational age

The following details were also collected for the purpose of the study:

- Age
- Socioeconomic class
- Dietary habits
- Parity
- Risk factors
- Height , weight and BMI
- Fasting blood sugar
- Base line serum uric acid level

Procedure of the study:-



Measurement of serum uric acid level done

Followed up around 24 to 28 weeks – GDM

Screening done with OGTT (75 grams of glucose) , IADPSG criteria

Measurement of serum uric acid level:-

Venous sample (2ml) was withdrawn from antenatal women who are included in the study. The sample was centrifuged to separate the serum and stored at -70 degree centigrade till examination. Uric acid measured using colorimetric assay with detection limit of 10mg/dl. The coefficient was 0.9%.

Screening of gestational diabetes mellitus:

All antenatal women were followed up around 24 to 28 weeks and GDM screening done with 75 gm glucose (OGTT) as per IADPSG criteria

IADPSG criteria (2011):

OGTT is performed in the morning after overnight fast of at least 8 hours

Fasting ≥92mg/dl

1hour ≥180mg/dl

2hours ≥153mg/dl

Diagnosis of GDM is made when any one value is elevated.

Data was documented in a proforma. The collected data was analyzed using Chi-square test, ANOVAtest, student t test for statistical analysis.

A receiver operator curve analysis was done to decide on a cut off for serum uric acid levels which would serve as a marker to predict subsequent development of GDM.

RESULTS

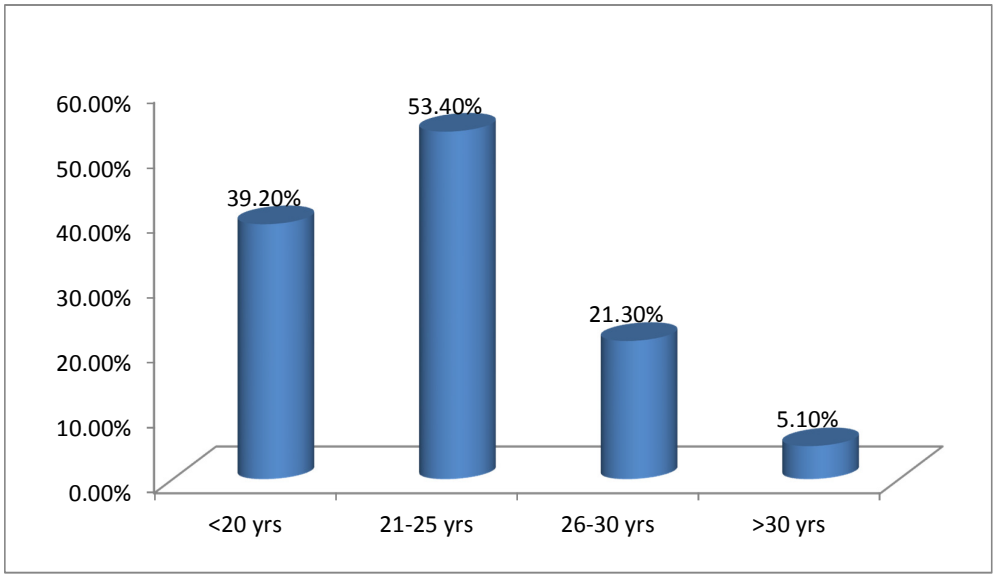
One hundred and eighty seven pregnant women were enrolled in this study. Of these nine were lost follow-up. The mean age of the sample was 23.6 years (SD=3.3). The majority was primigravida (64.6%). Base line body mass index was calculated using weight and height data. The majority (93.3%) had a BMI between 18.5and 24.9, with the mean BMI being 21.9(SD=2.09.)

Table: 1: Maternal age group distribution:

Age	Frequency N= 178	Percent
Less than 20 Years	36	20.2
21 - 25 Years	95	53.4
26 - 30 Years	38	21.3
More than 30 Years	9	5.1

Mean age of the sample was 23.6 years (SD=3.3).

Figure 1: Age distribution



In our study 53.4% were between 21- 25 years, 39.2% were less than 20 years, 21.3% were between 26 to 30 years and 5.1% were above 30 years

Table 2: Serum uric acid levels and development of GDM in different age group

Age (in years)	Uric acid concentration(mg/dl)	OGTT status		SI
	Range	Normal	Abnormal(GDM)	
≤20	1.6-4.2	30	6	X^2 = 11.409 Df = 3 P < 0.05 Significant
21-25	1.7-4.0	93	2	
26-30	1.8-4.2	33	5	
>30	1.9-4.1	7	2	

Fifteen out of one hundred and seventy eight women developed gestational diabetic mellitus on follow up. Table 2 shows that the mean serum uric acid level increases with age, and this was found to be statistically significant (P value<0.001). The results also showed that a significantly higher proportion of older women developed GDM compared to younger women (P value<0.05)

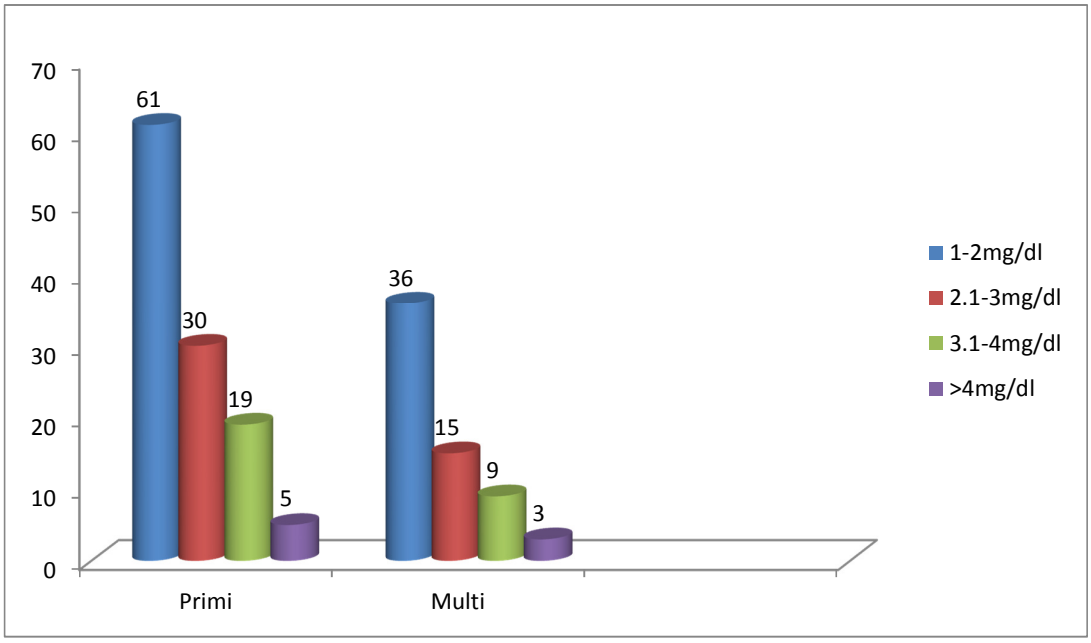
Parity and serum uric acid levels

Table 3: Distribution of serum uric acid level according to parity

Parity	Serum uric acid levels at <14 weeks				
	1-2 mg/dl	2.1-3mg/dl	3.1-4mg/dl	>4mg/dl	Total
Primi	61	30	19	5	115
Multi	36	15	9	3	63

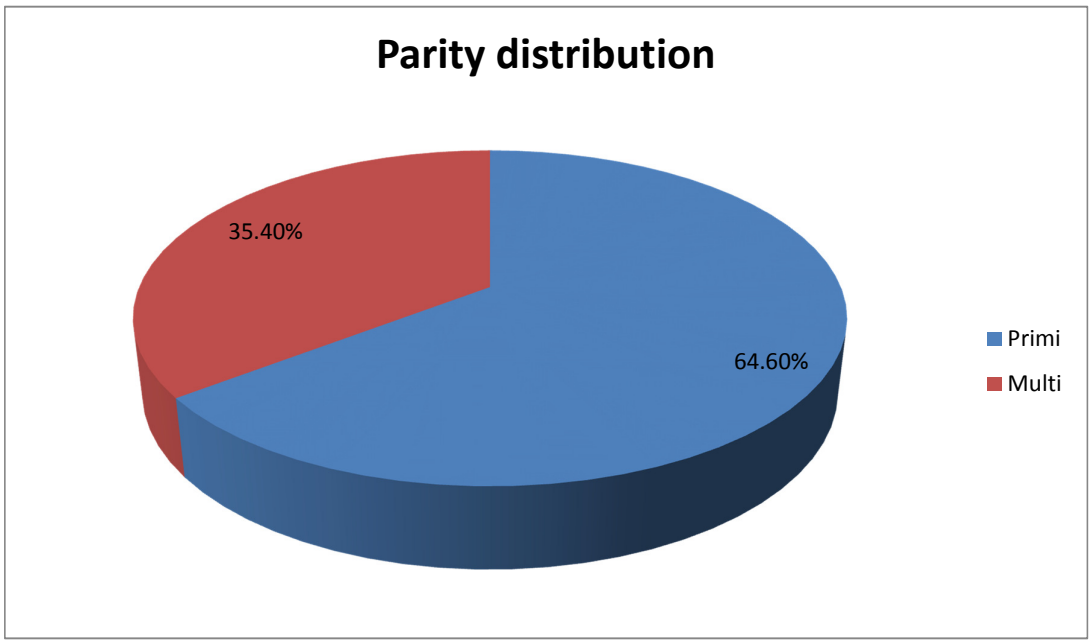
There was no association between parity and the serum uric acid level at less than 14 weeks of pregnancy (P=0.538)

Figure 2: Serum uric acid distribution according to parity



61 patients in primigravida and 36 patients in multigravida had serum uric acid between 1-2 mg/dl. 30 patients in primigravida and 15 patients in multigravida had serum uric acid levels between 2.1-3mg/dl. 19 patients in primigravida and 9 patients in multigravida had uric acid level between 3.1-4 mg/dl. 5 patients in primigravida and 3 patients in multigravida had uric acid level more than 4mg/dl.

Figure 3: Parity distribution



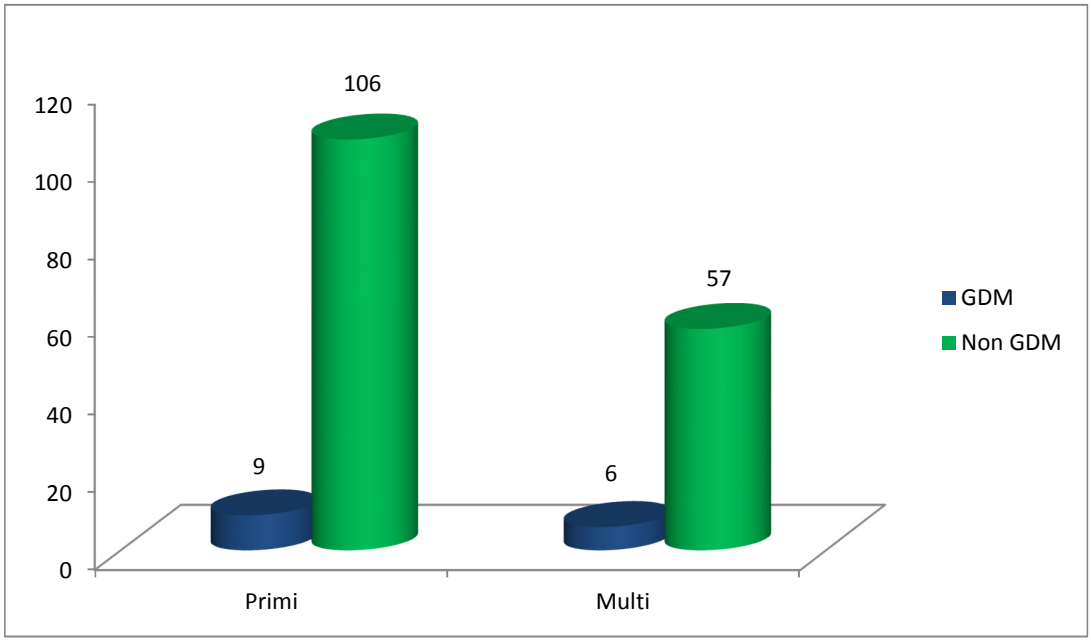
Among one hundred and seventy eight women studied most of them were primigravida (64.6%).

Table 4: Distribution of GDM according to parity

Parity	Frequency N=178	Percent	GDM	SI
Primi	115	64.6%	9(7.82%)	x2 = 2.839
Second	47	26.4%	3	DF = 3
Third	9	5.1%	2	P = 0.417
>third	7	3.9%	1	

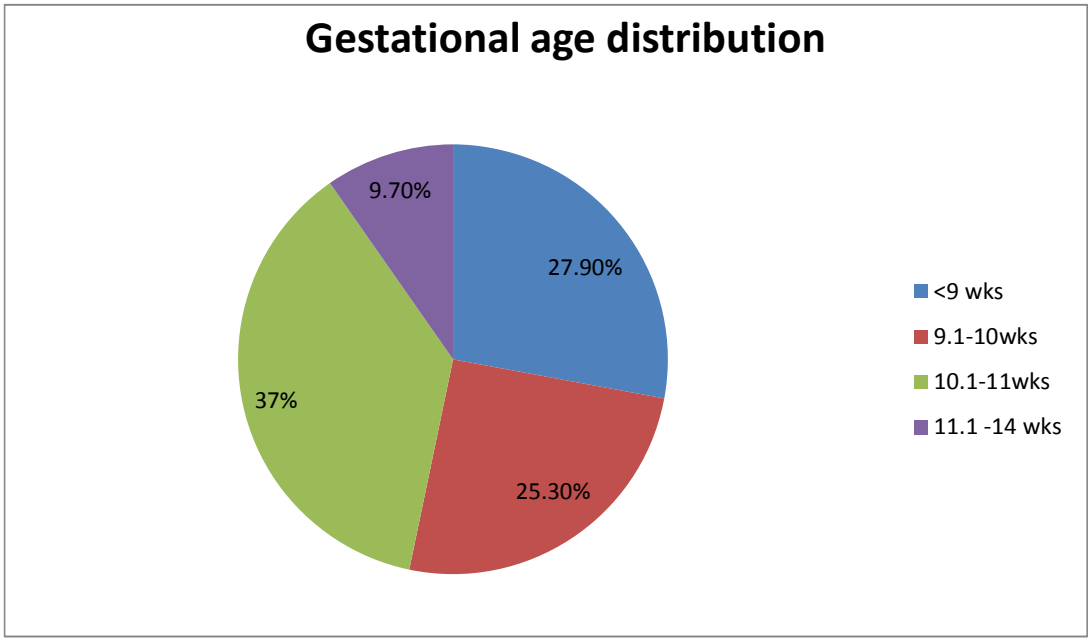
Primigravidae constituted 64.6% of the total study sample. Out of which nine (7.82%) developed GDM. But it was not statistically significant (P=0.417)

Figure 4: Development of GDM according to parity



In our study 9 out of 115 primigravidae developed GDM and 6 out of 57 multigravidae developed GDM.

Figure 5: Gestational age distribution



In our study 37% of patients were included between 10.1 and 11 weeks of gestation, 27.9% were less than 9 weeks of gestation, 25.3% were between 9.1 and 10 weeks of gestation and 9.7% were between 11.1 and 14 weeks of gestation

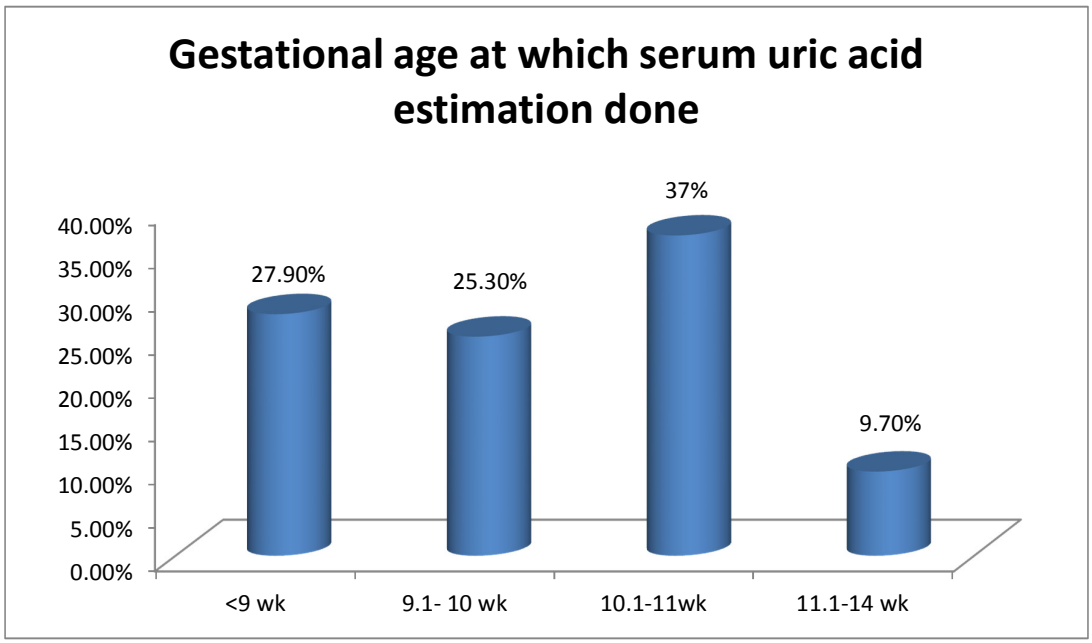
Table 5:- Mean gestational age at which serum uric acid estimation was done

GA		Number	Percent	Valid percent	Cumulative percent
Valid	Below 9 wk	50	27.9	27.9	27.9
	9.1-10 wk	45	25.3	25.3	53.2
	10.1- 11 wk	66	37	37	90.3
	11.1 14 wk	17	9.7	9.7	100
	Total	178	100	100	

In our study the highest number of serum uric acid estimation were done between 10.1 and 11 weeks of gestation

There was no significant variation in serum uric acid levels at different gestational age in our study.

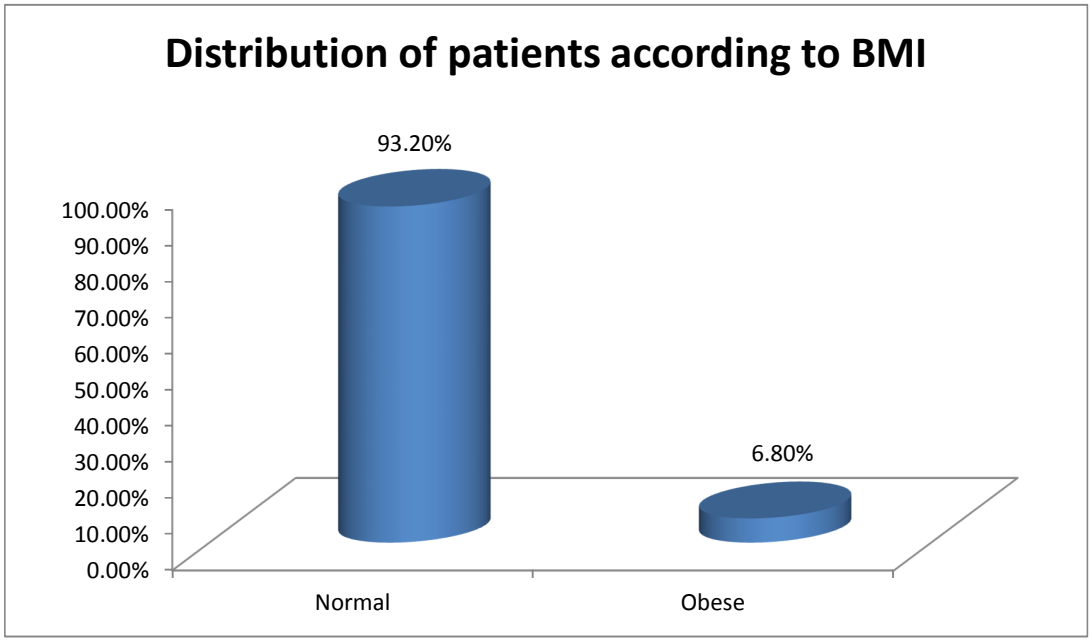
Figure 6: Gestational age at which serum uric acid estimation done



In our study 37% of serum uric acid estimation was done between 10.1 - 11 weeks of gestation. 27.9% were less than 9 weeks 25.3% were between 9.1 and 10 weeks of gestation and 9.7% were between 10.1 and 14 weeks.

BMI and Serum Uric Acid

Figure 7: Distribution of patients according to BMI



In our study most of the women studied were normal BMI (93.2%)

Table 6: Comparison of BMI according to quartile distribution of serum uric acid

BMI	Serum uric acid at < 14 weeks(mg/dl)				Total	
	1-2	2-3	3-4	>4		
Normal	30	72	55	9	166 (93.3%)	P value =0.194
Obese	2	4	2	1	12 (6.7%)	

93.3% had normal BMI. Majority of them (127) had serum uric acid levels in second and third quartile and 6.7% were obese with their serum uric acid levels in second and third quartile.

There was no significant association between BMI and serum uric acid levels in our study.

Table 7: Correlation between BMI and development of GDM

BMI	OGTT with 75 grams glucose		Total	SI
	Normal	Abnormal		
Normal	151	15	166	X^2 =1.184 Df =1 P = 0.277
Obese	12	0	12	

No correlation was observed between BMI and development of GDM in our study.

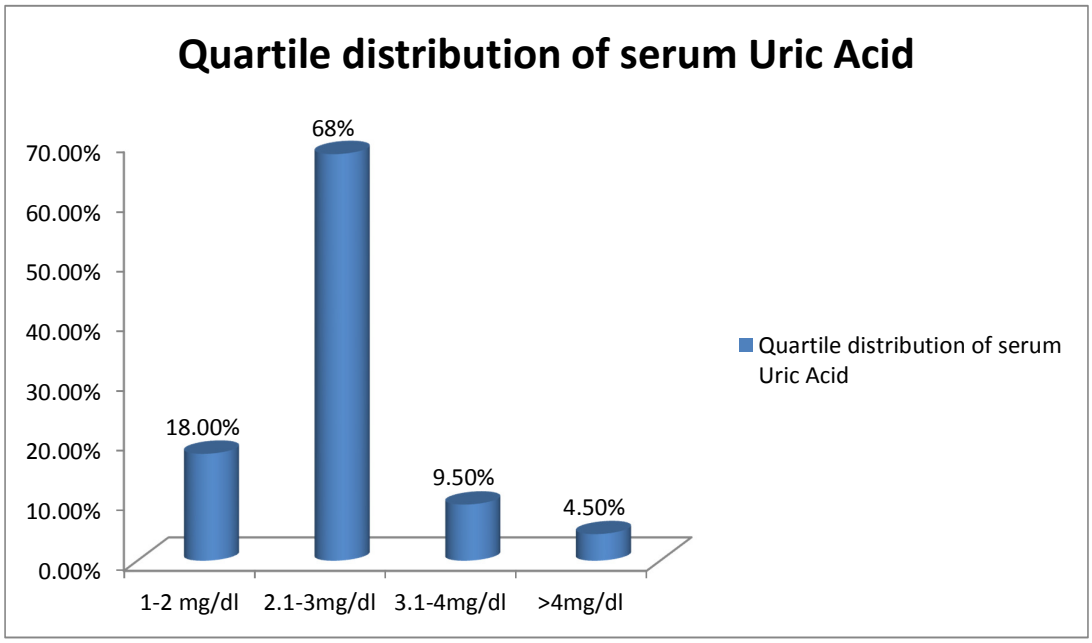
The data was analyzed to explore the association of serum uric acid levels with development of GDM (Table 8). The results shows that a significantly higher proportion of women with higher serum uric acid levels developed GDM compared to those with lower serum uric acid levels($P<0.01$)

Table 8- Correlation of serum uric acid level with OGTT status

Serum uric acid concentration (mg/dl)		OGTT Status	
	No.of subjects	Normal	Abnormal (GDM)
1.0 - 2.0	32	32	0
2.1 - 3.0	121	119	2
3.1 - 4.0	17	12	5
>4.0	8	0	8

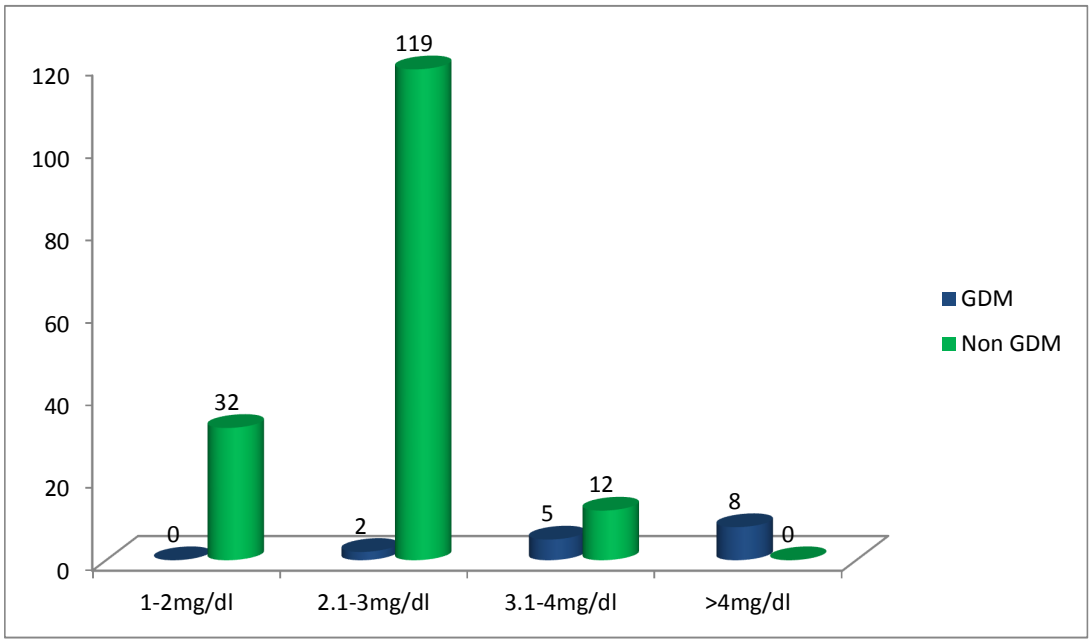
Most of GDM occurs when serum uric acid levels increases

Figure 8:



In our study 68% of pregnant women had serum uric acid level between 2.1-3 mg/dl, 18% between 1- 2 mg/dl, 9.5% between 3.1 and 4mg/dl and 4.5% had serum uric acid level above 4mg/dl.

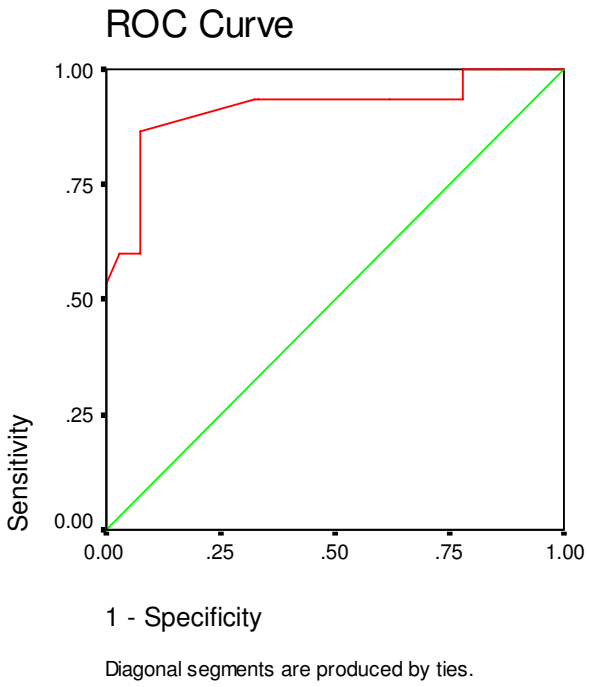
Figure 9: Relation between GDM and Quartile distribution of serum uric acid



In our study 8 patient with serum uric acid level more than 4mg/dl, 5 patients with serum uric acid between 3.1 and 4mg/dl and 2 patients with serum uric acid level between 2.1 and 3mg/dl developed GDM.

Finally, a receiver operator curve analysis was done to ascertain a suitable serum uric acid cut off so as to suggest as a marker for subsequent development of GDM

Figure 10: ROC curve for serum uric acid in relation to an out come of GDM



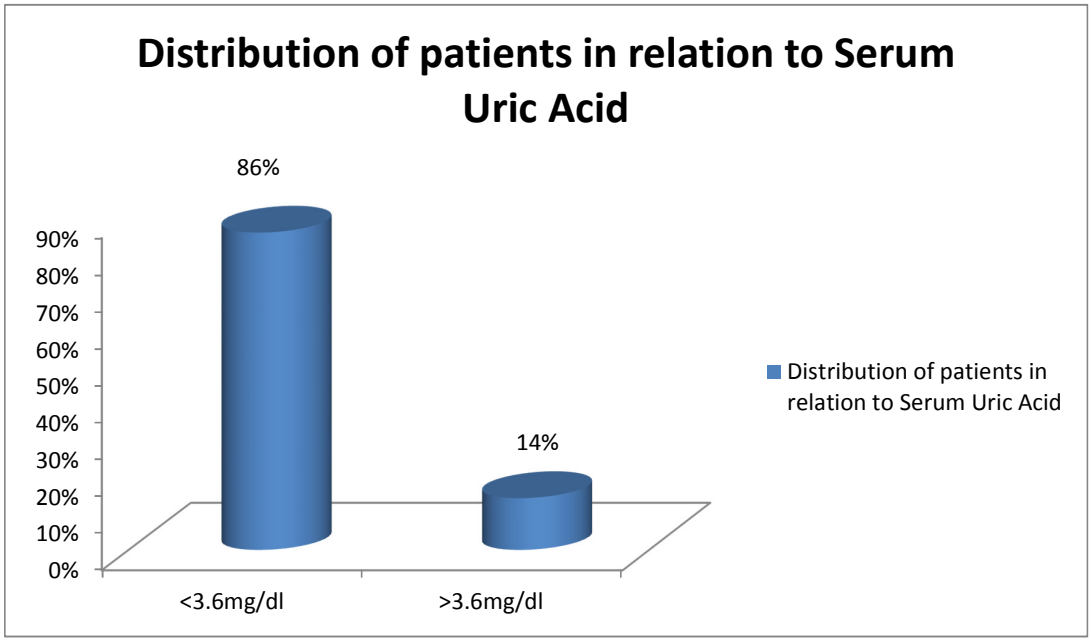
Area under the curve –0.914 standard error- 0.051.

Table 9 : Distribution of cases in relation to serum uric acid

Sr uric acid(mg/dl)	Frequency	Percent	Valid Percent	Cumulative Percent
Less than 3.6	153	86.0	86.0	86.0
More Than 3.6	25	14.0	14.0	100.0
Total	178	100.0	100.0	

In our study 86% of patients had serum uric acid <3.6mg/dl and 14% of them had serum uric acid >3.6mg/dl.

Figure 11:-



In our study 86% of them had uric acid level <3.6mg/dl and 14%had uric acid level >3.6mg/dl

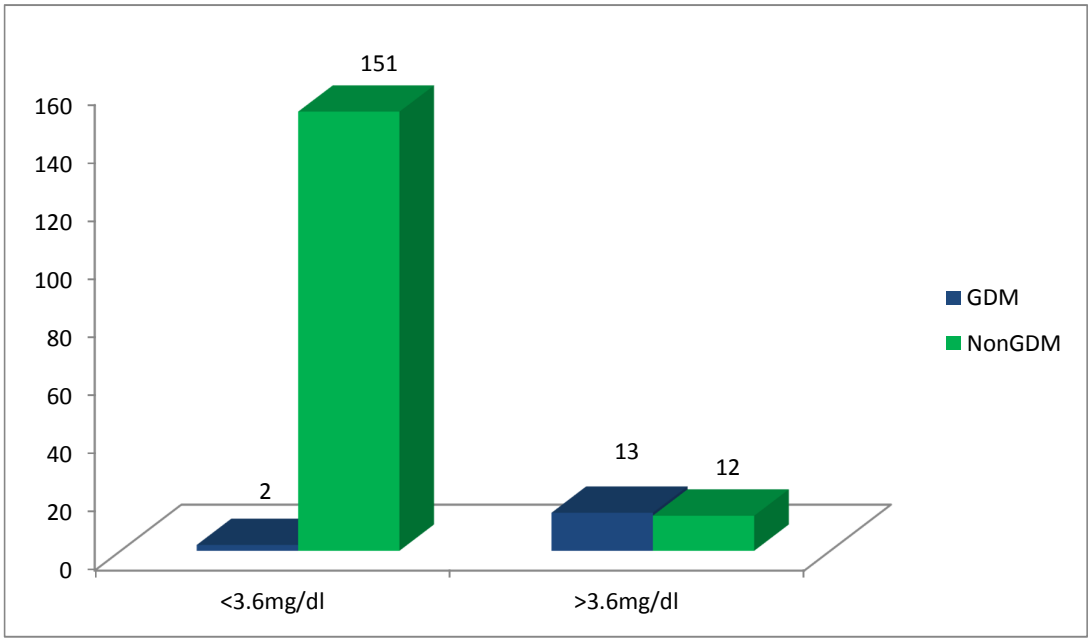
Table 10: – Distribution GDM cases using serum uric acid cut off 3.6mg/dl

Uric acid(mg/dl)	GDM	Non GDM	Total
<3.6	2	151	153
>3.6	13	12	25
Total	15	163	178

2 patients developed GDM with serum uric acid <3.6 mg/dl and 13 patients with uric acid >3.6 mg/dl. This shows development of GDM increases with increase in uric acid concentration.

A cut off serum uric acid level of 3.6mg/dl was found to have 92% sensitivity; specificity of 99%, for the development of gestational diabetes mellitus, as shown in table 10.

Figure 12: Relation between serum uric acid and GDM



In our study out of 25 patients with serum uric acid level more than3.6mg/dl, 13 patients developed GDM and out of 153 patients with serum uric acid level less than 3.6mg/dl, 2 developed GDM.

Chi square test

	Value	Df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	71.559[a]	1	.000		
Continuity Correction[b]	65.141	1	.000		
Likelihood Ratio	46.971	1	.000		
Fisher's Exact Test				.000	.000
Linear-by-Linear Association	71.157	1	.000		
N of Valid Cases	178				

a. 1cells (25.0%) have expected count less than 5. The minimum expected count is 2.11.

b. Computed only for a 2x2 table

Increased serum uric acid was associated with higher incidence of development of GDM, which is statistically highly significant (P<0.01)

Risk factors and GDM

Table 11: Risk factors stratification in the total population studied

Risk factors	No of patients	GDM
Family H/O DM	8	4
Previous H/O GDM	6	2
PCOD	3	0
BOH	7	1
Prev H/O Macrosomia	5	1

GDM developed significantly when they had previous H/O GDM and family H/O DM

Table 12:- Distribution of risk factors with development of GDM

Uric acid(mg/dl)	Number of women	Risk factors	No risk factors	GDM	
				With RF	Without RF
<3.6	153	19	134	2	0
>3.6	25	10	15	6	7

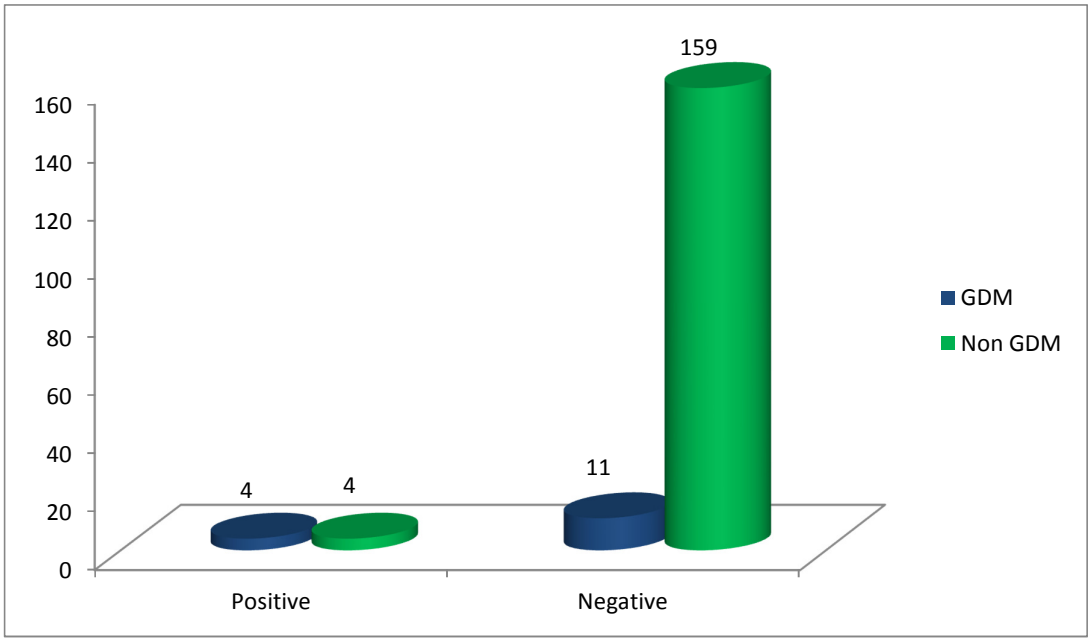
Out of 153 women with serum uric acid level <3.6mg/dl, 134 of them had no risk factors and 19 of them had risk factors. Among the 25 women with serum uric acid >3.6mg/dl, 10 of them had risk factors and 15 of them had no risk factors

Out of 153 women with serum uric acid level less than 3.6mg/dl, 19 women had risk factors of which 2 developed GDM. Out of 25 women with serum uric acid level more than 3.6mg/dl, 6 out of 10 women with risk factors and 7 out of15 with no risk factors developed GDM.

Table 13: Family history and GDM occurrence

		OGTT		Total
		Normal	Abnormal	
F/H	Negative	159	11	170
	Positive	4	4	8
Total		163	15	178

Figure 13: Relation between family history of DM and GDM



In our study 4 patients had family H/O DM and all were developed GDM

Chi-Square Tests

	Value	Df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	18.761[a]	1	.000		
Continuity Correction[b]	13.544	1	.000		
Likelihood Ratio	10.314	1	.001		
Fisher's Exact Test				.002	.002
Linear-by-Linear Association	18.655	1	.000		
N of Valid Cases	178				

a. 1 cells (25.0%) have expected count less than 5. The minimum expected count is .67.

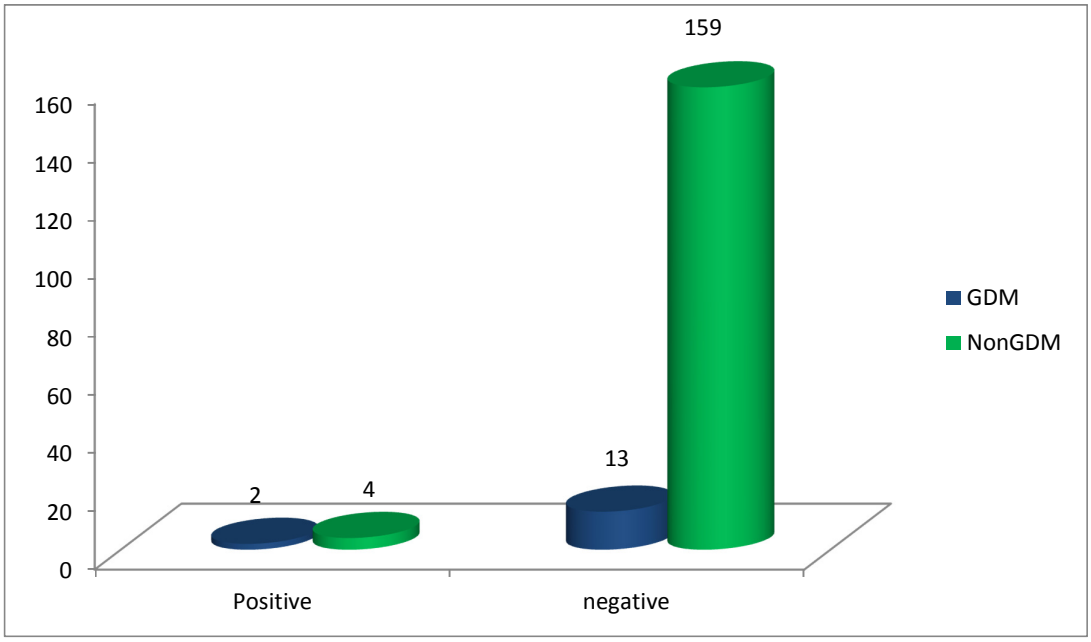
b. Computed only for a 2x2 table

Table 14: Previous history of GDM and GDM occurrence

		OGTT		Total
		Normal	abnormal	
Pre GDM	Negative	159	13	172
	Positive	4	2	6
Total		163	15	178

In our study only two women developed GDM out of 6 women with previous history of GDM

Figure 14:- Relation between previous H/O GDM and GDM occurrence



In our study 6 women had previous H/O GDM out of which 2 patients developed GDM in present pregnancy

Chi-Square Tests

	Value	Df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	4.991[a]	1	.025		
Continuity Correction[b]	2.210	1	.137		
Likelihood Ratio	3.135	1	.077		
Fisher's Exact Test				.048	.048
Linear-by-Linear Association	4.963	1	.026		
N of Valid Cases	178				

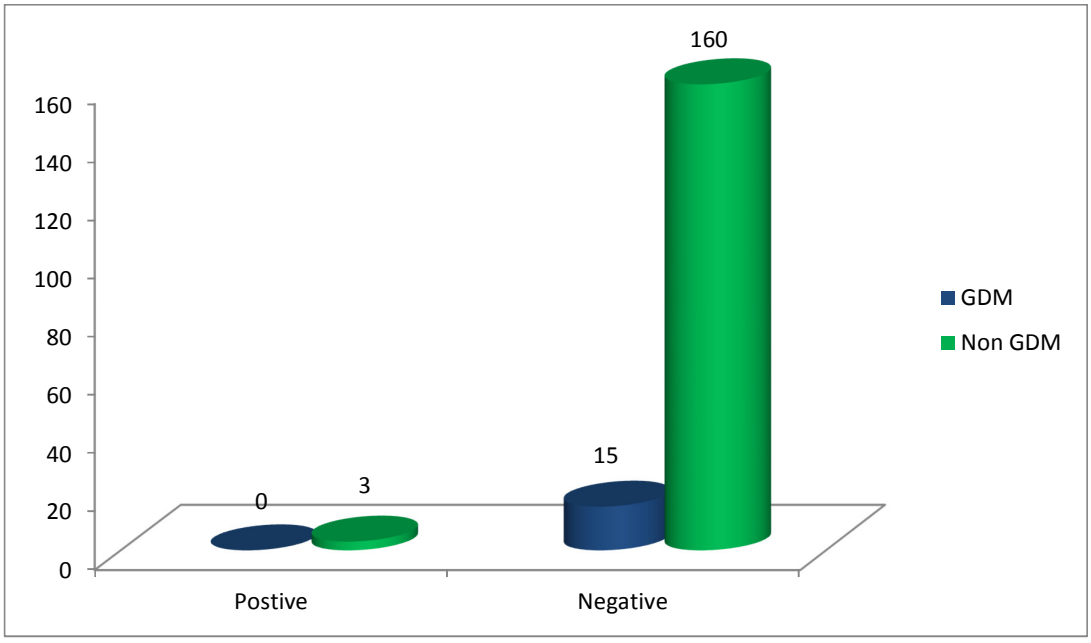
a. 1cells (25.0%) have expected count less than 5. The minimum expected count is .51.

b. Computed only for a 2x2 table

Table 15: PCOD and GDM occurrence

		OGTT		Total
		Normal	abnormal	
PCOD	Negative	160	15	175
	Positive	3	0	3
Total		163	15	178

Figure 15: Relation between PCOD and GDM



In our study 3 had PCOD but none of them developed GDM

Chi-Square Tests

	Value	Df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	.281[a]	1	.596		
Continuity Correction[b]	.000	1	1.000		
Likelihood Ratio	.533	1	.465		
Fisher's Exact Test				1.000	.767
Linear-by-Linear Association	.279	1	.597		
N of Valid Cases	178				

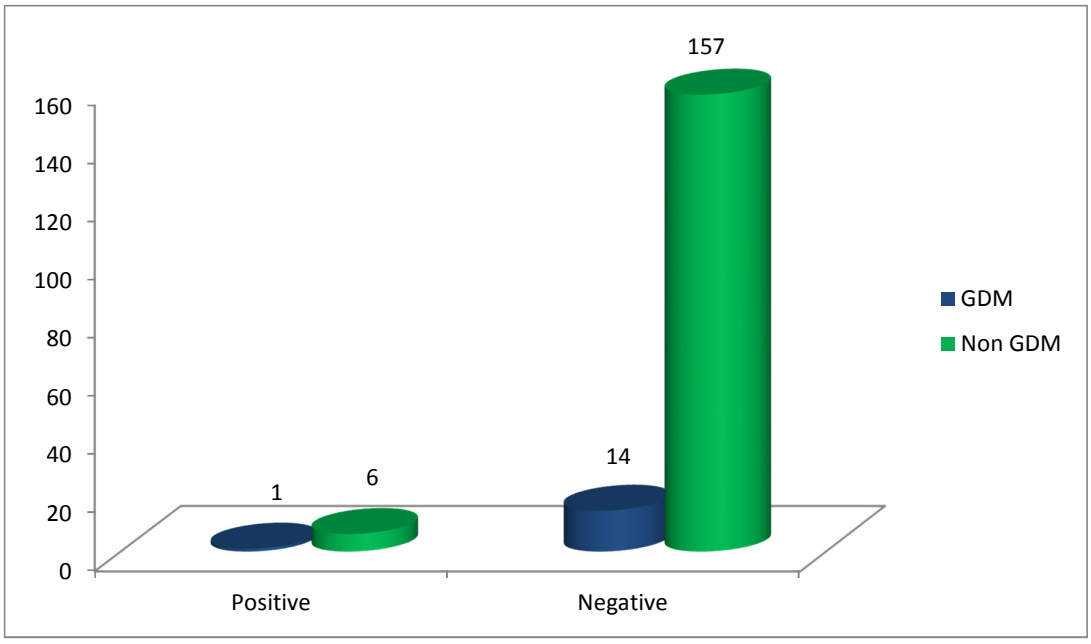
a. 2 cells (50.0%) have expected count less than 5. The minimum expected count is .25.

b. Computed only for a 2x2 table

Table 16: BOH and GDM occurrence

		OGTT		Total
		Normal	Abnormal	
BOH	Negative	157	14	171
	Positive	6	1	7
Total		163	15	178

Figure 16:- Relation between BOH and GDM



In our study 7 women had previous H/O BOH among which one developed GDM

Chi-Square Tests

	Value	Df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	.324[a]	1	.569		
Continuity Correction[b]	.000	1	1.000		
Likelihood Ratio	.275	1	.600		
Fisher's Exact Test				.466	.466
Linear-by-Linear Association	.322	1	.570		
N of Valid Cases	178				

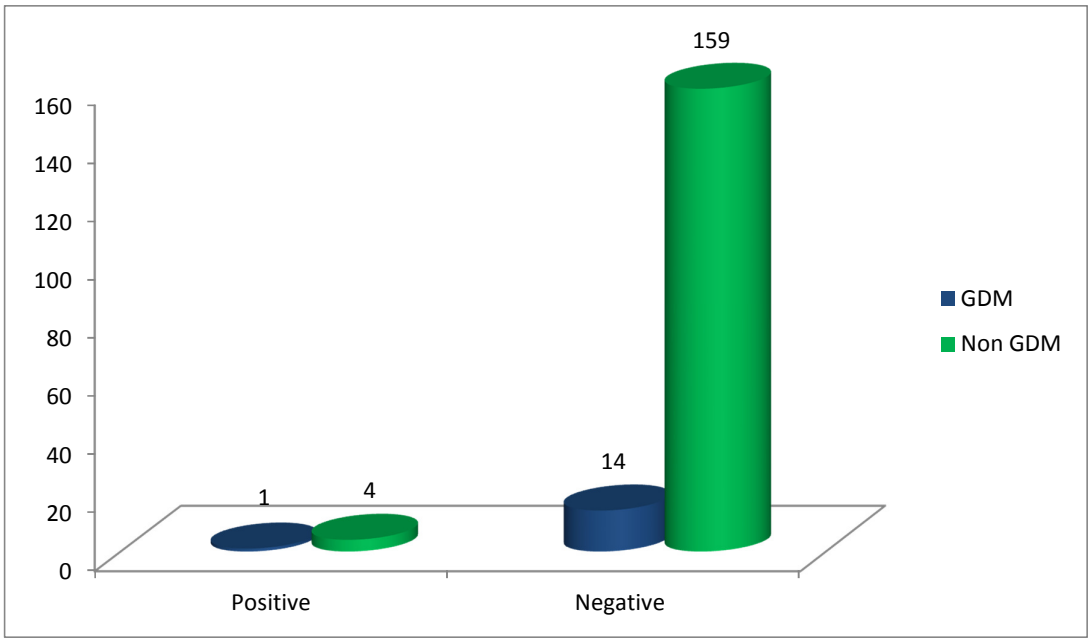
a. 1cells (25.0%) have expected count less than 5. The minimum expected count is .59.

b. Computed only for a 2x2 table

Table 17: Previous history of macrosomia and GDM occurrence

		OGTT		Total
		Normal	abnormal	
Macro	Negative	159	14	173
	Positive	4	1	2
Total		163	15	178

Figure 17:-Relation between previous H/O Macrosomia and GDM



In our study women had prev H/O macrosomia out of which one patient developed GDM

Chi-Square Tests

	Value	Df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	.893[a]	1	.345		
Continuity Correction[b]	.016	1	.898		
Likelihood Ratio	.673	1	.412		
Fisher's Exact Test				.359	.359
Linear-b y-Linear Association	.888	1	.346		
N of Valid Cases	178				

a. 2 cells (50.0%) have expected count less than 5. The minimum expected count is .42.

In our study there was a moderately significant correlation between the previous history of GDM and OGTT at 24 to 28 weeks with P value of <0.048 and a significant correlation between the family history of diabetes and OGTT at 24 to 28 weeks of pregnancy(P <0.05)

DISCUSSION

Early intervention and appropriate management in patients with gestational diabetes mellitus or at increased risk for developing gestational diabetes mellitus will helpful in preventing the adverse maternal and perinatal outcome and also protect them from long term consequences. Untreated carbohydrate intolerance during pregnancy is associated with higher incidence of maternal morbidity and mortality. The purpose of screening, treatment, and management of gestational diabetes mellitus is to prevent stillbirth, congenital anomalies, recurrent abortion, preeclamsia, intrauterine death and decrease incidence of macrosomic babies, thereby reducing maternal and perinatal morbidity and mortality. All over the world several studies have shown the association of hyperuricaemia in the first trimester with development of gestational diabetes mellitus later in life.

This prospective study was conducted in Raja Mirasudhar Hospital attached to Thanjavur Medical College, Thanjavur for a period of one year from September 2015.Study was undertaken to find out the association of elevated first trimester uric acid levels with development of GDM. The sample size of 187 patients was estimated using power calculation based on the prevalence of GDM, and was guided by the statistician.

In our study, amongst the background variables analyzed, age seemed to be significantly associated with an increase in serum uric acid level and development of GDM (P<0.05).This finding is consistent with previous studies that have reported increasing incidence of GDM and high serum uric acid levels with increasing age amongst women. (Carolan et al (2012).,Qui et al .,(2013).[73]

Out of 178 women studied, 64.6%were primigravidae and 55.4% were multigravidae. In our study, there was no significant difference in serum uric acid levels between primigravidae and multigravidae at <14 weeks of pregnancy (P=0.538).The same finding has been observed by Dunlop. W et al., in their study on effect of renal handling of uric acid in pregnancy in (1977)[74].On the contrary Aparna K et al.,(2014)[62]; has reported significantly higher mean uric acid levels in multiparous women.

In our study we found no difference in the incidence of development of GDM in relation to parity (P=0.417) which was consistent with the results of Aparna K., et al.,(2014)[62].

In 2012, Nagalakshmi C.et al.,had stated that development of GDM is increased among primigravida[75].While Al Rowally et al.,(2010); had shown in their study that multiparous women were at increased risk of developing GDM compared to nulliparous women[76] .

Analyzing the body mass index, 93.3% of pregnant women studied were normal BMI (BMI<24.9) and majority of them had their serum uric acid levels in second and third quartile.6.7% were obese (BMI>25) with their serum uric acid levels also in second quartile and third quartile. Though there was some proportional increase in serum uric acid levels with increase in BMI, it was not found statistically significant in our study.

It was also found in our study that BMI is not statistically associated with development of gestational diabetes mellitus.(P=0.217).This was in agreement with the results of Laughon .KS et al.,(2008)[55];and Aparna K et al.,(2014)[62]; who reported that the association between elevated uric acid at early trimester and risk of development of GDM was independent of body mass index .

In risk factor stratification majority of patients had no family history of diabetes though they had higher levels of blood glucose at 24 and 28 weeks of pregnancy. There was significant correlation between family history of diabetes and one step test with OGTT at second trimester (P<0.05%).

This finding of our study was consistent with that of Ratnakaran . R et al., (2007)[77] .Study conducted by Rasika C, Sunita samal et al.,2014)[58] showed that established risk factor for GDM relevant in women with family history of diabetes but not be the principal determinant of hyperglycemia in women without significant family history.

In our study there was a moderately significant correlation (p=0.048) between previous history of GDM and OGTT at 24 to 28 weeks of pregnancy. Similar finding was also observed in studies done by Sindhuja Anbalagan et al., (2012 -2014)[61].

Other risk factors like bad obstetric history, Poly cystic ovarian disease, and previous history of macrosomia were not significantly associated with development of GDM. Poly cystic ovarian disease was found to be the main risk factor for development of GDM according to Toulis et al.,(2009); but it was not observed in our study.

The results from our study suggest that increased serum uric acid in early trimester was associated with higher incidence of level of gestational diabetes mellitus. This finding is in keeping with the studies of Laughon et al., (2008)[55]; study and Aparna Kappaganthu et al., (2014)[62]; which also found a dose related increase in risk of development gestational diabetes mellitus with increase in serum uric acid levels. They also suggest that elevated serum uric acid could serve as a marker for subsequent development of GDM.

To explore this further, we conducted a receiver operator characteristic analysis to ascertain appropriate cut- off for serum uric acid level that might best predict GDM development. Borger et al., conducted a study and suggested that hyperuricemia in first trimester could be used as an effective marker for later development of metabolic syndrome and T II diabetes mellitus.

However none of our patients were actually hyperuricemic (defined as serum uric acid >6 mg/dl)This not withstanding rise in serum uric acid levels was still associated with a higher risk of development of GDM.A cut –off of 3.6mg/dl seemed to achieve a good balance of sensitivity and specificity in our study population.

Katherine et al.,(2008)[55];found that serum uric acid levels of more than 3.6 mg/dl in early gestation is associated with a threefold increased risk of development of gestational diabetes mellitus.

In 2012,Zhou .j et al[59]., in their study ,measured lipids and uric acid concentration in thousand healthy multigravidae at twenty weeks of pregnancy and showed that hyperuricemic women experienced a 1.99 fold risk for pre eclampsia and a 2.34 fold risk for GDM development. Our findings are coincides with the association of increased uric acid with increased risk of gestational diabetes mellitus in the non pregnant population (Halkin H et al,.1987)[51] and also the early pregnancy uric acid concentration in our study were similar to those reported by others.

In our study there was a highly significant correlation between serum uric acid at<14 weeks of gestation and development of GDM.(Pearson correlation).This is due to the fact that serum uric acid levels normally fall in the early trimester and mid trimester and rises to non pregnant values in late pregnancy. Elevated or high normal levels of serum uric acid in first trimester may be associated with a pre existing metabolic derangements which lead to poor maternal physiological adaptations and predisposes the pregnant women to development of pregnancy complication like gestational diabetes mellitus.

In our study we did not follow up the women after 28 weeks of pregnancy and hence feto-maternal outcomes were not analyzed and this was the potential limitation of our study.

CONCLUSION

The aim of doing a screening test for GDM in the antenatal period is to identify the asymptomatic women who will later develop complications of pregnancy and to institute effective treatment so that we can be able to reduce the morbidity and mortality. Currently, the complications of gestational diabetes mellitus in pregnancy are diagnosed only after mid-late gestation. It is important to recognize that the pathology is already established at the time of diagnosis of gestational diabetes mellitus in the week of pregnancy. By the time, the diagnosis of gestational diabetes mellitus is made the potential perinatal outcome may become irreversible.

Hence it becomes mandatory to do the diagnostic/predictive tests to diagnose the gestational diabetes mellitus at the earliest. At present estimation of serum uric acid is one of the tests available which can predicts the occurrence of GDM. Even though the risk factors like obesity, previous history of GDM, family history of Type II DM, PCOD, previous history of macrosomia, BOH, are associated with the development of GDM, our study showed that pregnant women without these risk factors also developed GDM when the serum uric acid level is more than 3.6mg/dl. Serum uric acid estimation is simple to perform, affordable to all classes and available in most places.

Though our study results suggest that serum uric acid level estimation in first trimester can be used as a marker to predict GDM in pregnant women, large scale studies are required before it can be recommended as a routine first trimester screening test for prediction of gestational diabetes mellitus. So that the dreadful complications of GDM can be avoided in future.

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PROFORMA

NAME:

AGE:

OP NUMBER:

SES:

PARITY:

BOOKED/UNBOOKED:

LMP:

EDD:

GESTATIONAL AGE AT RECRUITMENT:

DATE OF USG:

OBSTETRIC HISTORY:

PAST MEDICAL/DRUG HISTORY

PERSONAL HISTORY

FAMILY HISTORY:

GENERAL EXAMINATION:

Height - Weight - - BMI

Pulse rate - Blood pressure -

CVS EXAMINATION:

RS EXAMINATION:

PER ABDOMINAL EXAMINATION:

BLOOD INVESTIGATIONS:

Fasting blood sugar (<15 weeks of GA)

Serum uric acid level

OGTT with 75g of glucose at 24 to 28 wks

INFORMATION SHEET

We are conducting a prospective study on **SERUM URIC ACID IN EARLY PREGNANCY- A MARKER FOR GESTATIONAL DIABETES MELLITUS** in the department of Obstetrics and Gynaecology, Raja Mirasudar Hospital, Thanjavur – 613001.

- At the time of announcing the results and suggestions, name and identity of the patients will be confidential.

- Taking part in this study is voluntary. You are free to decide whether to participate in this study or to withdraw at any time; your decision will not result in any loss of benefits to which you are otherwise entitled.

- The results of the special study may be intimated to you at the end of the study period or during the study if anything is found abnormal which may aid in the management or treatment.

Signature of investigator **Signature of participant**

Date:

CONSENT FORM

I _____ hereby give consent to participate in the study conducted by **DR.NITHYA .D,** post graduate in department of OBSTETRICS & GYNAECOLOGY, RAJA MIRASUDAR HOSPITAL , THNJAVUR 613001, and to use my personal clinical data and result of investigation for the purpose of analysis and to study the nature of disease. I also give consent for further investigations

Place :

Date : Signature of Participant

MASTER CHART

Sr.no	Name	Age	Parity	BMI	GA	F/H	Pre GDM	PCOD	BOH	Macro	FBS	Sr.Uric A	GA	FBS	1HR	2HR
1	Majlin Begum	29	3	19.5	9W+1D	-	-	-	-	-	86	2.8	26W+1D	76	156	134
2	Radhika	19	1	18.5	8W+4D	-	-	-	-	-	88	1.6	24W+6D	82	162	140
3	Sudali	25	1	20	9+4	-	-	-	-	-	76	2.6	26+4	78	164	142
4	Suganya	22	2	21.5	10+0	-	-	-	-	-	72	3.6	24+6	74	158	136
5	Gokila	28	4	20.5	10+3	-	-	-	+	-	68	2.8	27+4	82	170	144
6	Jeyapriya	24	2	21.5	9+3	-	-	-	-	-	75	2.6	26+3	84	176	142
7	Yogeshwari	31	3	19.8	9+5	-	-	-	-	-	82	2.4	25+2	86	168	140
8	Sandhya	20	1	18.5	7+3	-	-	-	-	-	89	3.6	24+5	76	156	132
9	Amirthavalli	19	1	19	10+2	+	-	-	-	-	66	2.8	25+4	94	176	154
10	Jamunarani	20	1	20.5	9+4	-	-	-	-	-	90	1.2	26+1	88	172	144
11	Gowri	27	2	23	9+2	-	-	-	-	-	68	2.8	25+3	84	170	142
12	Maheswari	21	1	24	9+1	-	-	-	-	-	78	2.6	24+2	76	154	130
13	Selvakumari	19	1	22.5	8+2	-	-	-	-	-	76	2.8	25+3	78	156	144
14	Gowthami	25	2	20.5	9+5	-	-	-	-	-	74	2.8	24+1	80	174	146
15	Anjugam	19	1	22.5	9+3	-	-	-	-	-	76	2.8	27+1	84	176	150
16	Dhanalakshmi	22	2	23.5	9+0	-	-	-	-	-	78	1.6	26+4	80	168	138
17	Asha	28	2	22.5	10+2	-	-	-	-	-	72	2.6	25+2	76	174	142
18	Saranya	22	1	20.5	10+0	-	-	-	-	-	68	4.2	24+5	88	182	148
19	Shervika	23	2	20	9+5	-	-	-	-	-	84	2.4	26+0	84	176	152
20	Revathi	19	1	18.5	7+5	-	-	+	-	-	78	3.6	27+1	76	170	138
21	Sumithra	27	2	19	9+3	-	-	-	-	-	86	2.8	24+3	82	164	134
22	Malathi	24	1	19.5	10+2	-	-	-	-	-	88	3.6	25+1	74	166	140
23	Tamilselvi	20	1	22	12+5	-	-	-	-	-	78	2.4	26+2	76	168	142
24	Akila	31	2	24.5	9+2	-	-	-	-	-	72	1.3	24+2	58	162	136
25	Hemaladevi	29	3	23.5	10+3	-	-	-	+	-	82	2.8	26+5	86	176	148
26	Revathi	24	1	22	8+2	-	-	-	-	-	80	2.6	27+3	84	178	138

Sr.no	Name	Age	Parity	BMI	GA	F/H	Pre GDM	PCOD	BOH	Macro	FBS	Sr.Uric A	GA	FBS	1HR	2HR
27	Usha	25	1	19.5	11+0	-	-	-	-	-	70	2.8	28+0	82	174	140
28	Iniya	21	1	22	7+3	-	-	-	-	-	86	2.6	24+3	74	158	134
29	Vennila	19	1	23	10+5	-	-	-	-	-	80	4.2	25+2	90	186	156
30	surya	25	1	24.5	9+4	-	-	-	-	-	74	1.4	24+1	86	176	148
31	Vimala	20	1	21.5	7+5	-	-	-	-	-	82	2.8	24+6	80	172	142
32	Nathiya	32	3	22	10+3	-	-	-	-	-	86	2.8	24+5	68	166	134
33	Rupa	20	2	20.5	9+5	-	-	-	-	-	76	2.6	25+2	70	176	142
34	Meena	23	1	23	13+4	-	-	-	-	-	68	2.6	26+1	82	172	140
35	Renganayagi	24	1	24.5	10+4	+	_	-	-	-	72	4.2	27+3	86	192	154
36	Arogyaselvi	24	2	22.5	8+4	-	-	-	-	-	84	1.6	27+5	80	174	138
37	Suganya	20	1	20	9+2	-	-	-	-	-	80	2.8	26+4	84	176	138
38	Chitra	26	1	22.5	10+5	-	-	-	-	-	76	2.2	25+6	86	170	142
39	Sudha	21	1	23	9+0	-	-	-	-	-	76	2.6	26+1	88	174	150
40	Rameela	20	1	24.5	10+5	-	-	-	-	-	74	1.8	24+2	84	168	142
41	Amutha	31	2	21.5	9+5	-	+	-	-	-	82	2.6	26+5	78	158	136
42	Deivamani	20	1	22.5	8+2	-	-	-	-	-	86	2.8	24+3	76	146	132
43	Selvi	27	1	21	10+4	-	-	-	-	-	80	3.6	24+5	94	180	152
44	Kalaiarasi	22	1	19.5	12+5	-	-	-	-	-	74	2.6	25+1	86	174	138
45	Arthi	19	1	20	10+3	-	-	-	-	-	70	1.2	26+0	88	166	140
46	Rajammal	23	2	21.5	9+4	-	-	-	-	-	68	2.6	27+2	80	158	136
47	Karpagam	25	2	20	8+0	-	-	-	-	+	64	2.4	27+5	68	170	138
48	Ilavarasi	24	1	21	10+5	-	-	-	-	-	72	2.8	26+5	78	172	146
49	Nathiya	21	1	20.5	7+4	-	-	-	-	-	78	2.6	24+2	84	178	156
50	Sathyaseela	23	1	19.5	10+1	-	-	-	-	-	82	1.6	25+1	82	154	132
51	Akilandeshwari	27	4	18.5	9+3	-	-	-	+	-	76	2.4	24+4	76	158	130
52	Arokyamary	19	1	20	9+0	-	-	-	-	-	80	2.6	25+4	86	172	142
53	Nithya	23	1	22	10+2	-	-	-	-	-	86	2.4	26+1	80	174	140

Sr.no	Name	Age	Parity	BMI	GA	F/H	Pre GDM	PCOD	BOH	Macro	FBS	Sr.Uric A	GA	FBS	1HR	2HR
54	Sheelarani	24	2	23.5	13+4	-	-	-	-	-	84	1.6	24+5	76	168	138
55	Kavitha	20	1	22.5	10+3	+	-	-	-	-	82	4.2	26+1	84	178	162
56	Chellamathi	25	4	21.5	8+1	-	-	-	-	-	88	2.8	27+5	80	168	150
57	Vennila	28	3	20.5	10+4	-	-	-	-	-	72	2.6	28+0	76	164	142
58	Sathya	19	1	23	8+2	-	-	-	-	-	76	2.6	24+2	76	172	144
59	Jeevitha	21	1	24.5	11+0	-	-	-	-	-	82	1.6	24+5	70	166	138
60	Vidya	25	2	21.5	9+4	-	-	-	-	-	84	2.6	25+3	82	176	146
61	Tamilmani	22	1	22.5	8+3	-	-	-	-	-	86	2.4	26+0	68	166	138
62	Vasundradevi	25	2	25	10+3	-	-	-	-	-	88	2.6	25+5	66	172	142
63	Revathi	32	4	24	12+5	-	-	-	+	-	78	2.8	24+6	84	162	130
64	Muthulakshmi	23	1	21.5	10+3	-	-	-	-	-	74	2.6	25+5	86	178	148
65	Priya	20	1	22.5	9+5	-	-	-	-	-	70	1.2	26+1	80	176	146
66	Nandhini	23	1	23.5	8+4	-	-	-	-	-	68	2.6	27+2	78	168	136
67	Subha	28	2	22.5	10+5	-	+	-	-	-	64	4.2	26+5	96	180	148
68	Shakilabanu	19	1	21.5	10+3	-	-	-	-	-	70	1.8	25+2	76	168	146
69	Gomathi	21	1	22	7+5	-	-	-	-	-	72	2.6	24+3	78	174	140
70	Sripriya	22	1	21.5	9+6	-	-	-	-	-	76	2.4	26+2	68	170	150
71	Rajathi	19	1	22.5	10+4	+	-	-	-	-	82	4.2	27+1	90	188	146
72	Mahilarani	23	2	21.5	10+3	-	-	-	-	-	80	2.2	24+1	66	172	136
73	Chinnaponnu	20	1	20	7+1	-	-	-	-	-	88	2.4	25+3	76	174	142
74	Paulinmary	31	3	19.5	11+0	-	-	-	-	-	76	1.8	26+4	78	176	150
75	Anuvidya	24	2	18	13+4	-	-	-	-	-	72	2.6	24=5	84	174	142
76	Krithiga	19	1	19.5	8+2	-	-	-	-	-	88	2.8	27+2	86	176	138
77	Prabavathy	21	1	24	8+1	-	-	-	-	-	68	2.8	24+5	84	176	140
78	Nanci	23	1	23.5	10+1	-	-	-	-	-	76	1.6	25+2	78	164	136
79	Sudha	22	1	22.5	9+3	-	-	-	-	-	82	2.8	26+1	82	174	150
80	Nageshwari	20	1	21.5	8+3	-	-	-	-	-	84	2.6	26+4	86	170	142

Sr.no	Name	Age	Parity	BMI	GA	F/H	Pre GDM	PCOD	BOH	Macro	FBS	Sr.Uric A	GA	FBS	1HR	2HR
81	Vijayarani	24	1	24	10+3	-	-	-	-	-	86	2.4	24=3	76	166	138
82	Ezhilarasi	26	2	20.5	12+4	-	+	-	-	-	78	2.6	24+2	78	168	142
83	Mariyammal	20	1	20	10+3	-	-	-	-	-	70	2.2	25+0	84	172	140
84	Rajeshwari	25	2	19.5	11+0	-	-	-	-	-	64	2.4	25+6	80	176	138
85	Manjuladevi	27	2	18	8+4	-	-	-	-	-	80	1.4	26+1	78	168	134
86	Yazhini	20	1	19.5	8+3	-	-	-	-	-	76	3.8	27+0	88	182	152
87	Thenmozhi	21	1	22.5	8=1	-	-	-	-	-	68	1.8	27+2	84	170	142
88	Rekha	29	4	20	10+1	-	-	-	+	-	58	2.8	26+4	86	172	146
89	Abirami	21	1	21	9+5	-	-	-	-	-	62	1.6	25+3	80	174	140
90	Muthulakshmi	20	1	22.5	7+5	-	-	-	-	-	66	2.7	26+1	76	158	132
91	Nadhiya	23	1	23	9+2	-	-	+	-	-	74	2.6	24+3	84	164	148
92	Suganthii	24	1	24	10+3	-	-	-	-	-	82	2.4	24+5	80	168	150
93	Imakulate	31	2	24.5	13+1	-	-	-	-	-	70	2.4	25+4	88	176	144
94	Jeenath begam	29	2	22.5	8+4	-	-	-	-	-	82	4.2	26+1	90	178	156
95	Gayathri	25	1	21.5	10+3	-	-	-	-	-	86	2.4	25+3	86	176	134
96	Sudha	27	2	22.5	8+2	-	-	-	-	-	76	2.6	24+2	84	176	150
97	Gowri	23	1	23.5	10+3	-	-	-	-	-	82	2.8	25+3	80	178	138
98	Kavitha	21	1	22.5	9+3	-	-	-	-	-	84	2.6	24+3	76	164	142
99	Dhavamani	24	1	24	10+2	-	-	-	-	-	78	2.8	24+5	84	172	138
100	Selvanayagi	19	1	20.5	9+2	-	-	-	-	-	74	1.8	25+1	86	178	146
101	Komaladevi	26	2	18.5	10+4	+	-	-	-	-	68	2.6	26+2	80	176	140
102	Angayarkani	23	1	19	8+1	-	-	-	-	-	72	1.2	26+4	86	168	136
103	Regapreethi	28	2	18.5	13+2	-	-	-	-	+	86	2.8	27+1	78	158	132
104	Anish fathima	24	1	19.5	10+5	-	-	-	-	-	78	3.8	28+0	72	164	136
105	Indhumathi	20	1	19	7+2	-	-	-	-	-	70	1.4	26+5	78	168	146
106	Punitha	19	1	20	7+1	-	-	-	-	-	62	2.6	27+1	84	176	142
107	Gomathi	21	1	22	10+2	-	-	-	-	-	60	2.8	26+5	78	166	140

Sr.no	Name	Age	Parity	BMI	GA	F/H	Pre GDM	PCOD	BOH	Macro	FBS	Sr.Uric A	GA	FBS	1HR	2HR
108	Arogyamary	22	1	24	9+5	-	-	-	-	-	78	2.4	24+3	74	168	136
109	Kalaiselvi	20	1	21.5	8+1	-	-	-	-	-	82	1.6	25+1	78	172	138
110	Amuthaselvi	23	1	19	10+3	-	-	-	-	-	76	2.8	26+4	84	176	138
111	Poongodi	25	2	18.5	10+3	-	+	-	-	-	74	2.6	26+1	78	160	132
112	Vanitha	19	1	19.5	13+1	-	-	-	-	-	78	3.8	24+5	96	178	152
113	Arogya	21	1	20.5	8+3	-	-	-	-	-	62	1.4	26+1	68	152	130
114	Priyadharshini	27	1	19	11+0	-	-	-	-	-	68	2.8	25+3	70	160	142
115	Jeenath nilophar	21	1	18.5	9+0	-	-	-	-	-	82	2.6	24+3	72	158	132
116	Bharathi	22	1	18	10+3	-	-	-	-	-	68	2.8	25+1	76	162	134
117	Pragatha	19	1	19.5	9+3	-	-	-	-	-	78	2.4	24+2	80	170	142
118	Kalaiselvi	22	1	18.5	10+4	-	-	-	-	-	74	1.8	25+5	84	166	132
119	Thenmozhi	20	1	23.5	8+4	-	-	-	-	-	78	2.6	26+3	74	164	138
120	Deepa	24	2	25.5	9+5	-	-	-	-	-	82	2.4	27+2	78	160	136
121	Vanathi	27	2	24	10+5	-	-	-	-	-	86	3.8	27+5	90	192	152
122	Suganya	27	2	23.5	12+2	-	-	-	-	-	84	1.6	24+2	82	156	130
123	Rajamani	25	1	24	10+4	-	-	-	-	-	72	2.8	25+1	70	158	132
124	Sridevi	21	1	26	8+1	-	-	-	-	-	82	2.6	24+5	68	158	136
125	Prabavathy	27	2	22.5	9+5	+	-	-	-	-	86	2.4	25+2	72	156	130
126	Tamil ilakiya	26	2	25.5	7+5	-	+	-	-	-	76	3.8	26+2	66	152	130
127	Anushya	20	1	21.5	10+2	-	-	-	-	-	78	1.6	26+3	78	166	142
128	Tamilmani	22	1	23.5	8+5	-	-	-	-	-	76	2.8	26+1	70	158	134
129	Amuthakani	28	2	24	10+3	-	-	-	-	-	82	2.8	24+5	82	166	146
130	Mary britila	28	3	22	9+3	-	-	-	-	+	80	4.2	24+3	96	180	146
131	Sujatha	20	1	23.5	8+0	-	-	-	-	-	72	2.6	25+2	70	164	138
132	Suganyamani	22	1	21.5	10+4	-	-	-	-	-	68	2.8	26+1	76	166	138
133	SRIPRIYA	25	2	22.5	11+5	-	-	+	-	-	70	1.4	27+2	78	168	142
134	Akilandeshwari	23	1	24.5	10+5	-	-	-	-	-	68	2.8	26+5	84	170	140

Sr.no	Name	Age	Parity	BMI	GA	F/H	Pre GDM	PCOD	BOH	Macro	FBS	Sr.Uric A	GA	FBS	1HR	2HR
135	Mangayarkarasi	26	1	19.5	8+3	-	-	-	-	-	68	2.6	25+1	78	152	136
136	Rani	21	1	22.5	10+3	-	-	-	-	-	72	2.4	25+3	80	148	140
137	Mary	27	2	24	9+5	-	-	-	-	-	66	2.6	26+1	82	144	132
138	Vijayarani	22	1	25	11+0	-	-	-	-	-	58	2.4	25+2	84	156	134
139	Ponnarasi	28	2	23.5	9+6	+	-	-	-	-	76	2.6	24+4	78	162	136
140	Suriya	22	1	22.5	8+4	-	-	-	-	-	74	1.2	25+0	70	158	140
141	Krithiga	22	1	21.5	10+3	-	-	-	-	-	86	2.4	26+2	76	162	136
142	Lavanya	23	1	22	10+5	-	-	-	-	-	82	3.6	26+5	80	172	140
143	Malarpriya	22	1	24	8+1	-	-	-	-	-	80	2.8	27+2	82	176	142
144	Boomadevi	29	5	23.5	12+4	-	-	-	+	-	66	1.8	25+5	78	164	138
145	Ilakiya	22	1	24	7+5	-	-	-	-	-	58	2.6	24+3	76	166	142
146	Priya	26	2	21.5	10+5	-	-	-	-	-	72	2.8	25+1	78	164	136
147	Maheshwari	23	1	25.5	10+2	-	-	-	-	-	84	3.8	25+3	84	172	138
148	Jeyaseeli	26	2	28	1	-	-	-	-	-	70	2.4	26+2	82	168	134
149	Udayarani	23	1	22.5	9+2	-	-	-	-	-	76	1.2	27+1	80	166	138
150	Vimaladevi	21	1	21.5	10+3	-	-	-	-	-	82	2.6	24+4	78	158	130
151	Kamala	25	2	27	13+6	-	-	-	-	-	78	1.8	25+5	70	160	142
152	Rajapriya	31	4	23.5	8+5	-	-	-	+	-	86	3.8	26+3	86	182	150
153	Tamilpriya	25	1	26	10+5	-	-	-	-	-	74	2.8	27+1	82	158	132
154	Umamaheshwari	21	1	21.5	10+1	-	-	-	-	-	76	2.6	24+3	76	164	138
155	Malarvizhi	28	2	20.5	8+2	-	-	-	-	+	80	2.8	25+1	72	158	130
156	Rathi	23	1	23.5	9+1	-	-	-	-	-	82	2.4	26+2	74	164	136
`157	Sowmiya	21	1	22.5	10+5	-	-	-	-	-	86	2.6	27+1	80	172	138
158	Buvaneshwari	23	1	24	10+4	-	-	-	-	-	76	3.6	24+2	74	168	134
159	Alagi	27	2	25	8+4	-	-	-	-	-	68	2.8	24+5	78	170	142
160	Nishanthi	24	1	20.5	13+5	-	-	-	-	-	70	3.6	25+0	82	176	138
161	Valli	22	1	19.5	9+2	-	-	-	-	-	72	2.6	26+3	80	174	146

Sr.no	Name	Age	Parity	BMI	GA	F/H	Pre GDM	PCOD	BOH	Macro	FBS	Sr.Uric A	GA	FBS	1HR	2HR
162	Rasiya	23	1	20.5	10+5	-	-	-	-	-	76	2.8	25+1	78	176	136
163	Princy	29	1	22	8+0	-	-	-	-	-	72	2.4	27+2	72	156	134
164	Komalavalli	33	3	20.5	10+2	-	+	-	-	-	68	2.8	24+0	84	194	146
165	Manjuladevi	22	1	21	13+4	-	-	-	-	-	76	2.6	25+3	78	158	136
166	Tamilvidya	22	1	23	8+5	-	-	-	-	-	58	2.6	26+4	74	162	140
167	Maheshwari	21	1	22.5	9+5	-	-	-	-	-	74	2.4	27+1	78	168	136
168	Priyavathani	26	2	24.5	11+0	-	-	-	-	-	82	2.8	26+3	82	166	134
169	Suriyakala	28	3	23.5	9+4	-	-	-	-	-	70	1.2	25+4	84	168	130
170	Ragini	23	1	22.5	10+3	-	-	-	-	-	68	2.2	25+1	78	172	142
171	Thenmozhi	27	2	21.5	7+6	+	-	-	-	-	54	3.6	24+2	76	164	136
172	Sudhandradevi	24	1	24	10+4	-	-	-	-	-	64	2.6	25+6	80	148	130
173	Nirmala	23	1	21.5	9=1	-	-	-	-	-	68	2.8	26+3	76	172	148
174	Amsavalli	22	1	26.5	9+4	-	-	-	-	-	78	2.6	25+1	76	168	134
175	Vaideeshwari	28	2	20.5	9+1	-	-	-	-	+	62	3.6	26+2	82	176	142
176	Rajalakshmi	23	1	24.5	9+3	-	-	-	-	-	80	2.8	27+1	84	170	144
177	Rubadevi	23	1	28.5	12+5	-	-	-	-	-	76	2.4	26+3	86	164	136
178	Sathyapriya	25	2	24.5	9+5	-	-	-	-	-	66	2.6	25+4	80	166	132