DISSERTATION ON

UNIVERSAL SCREENING FOR GESTATIONAL DIABETES MELLITUS BY SINGLE STEP PROCEDURE

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CERTIFICATE

This is to certify that this dissertation in **"UNIVERSAL SCREENING FOR GESTATIONAL DIABETES MELLITUS BY SINGLE STEP PROCEDURE"** is a work done by **DR. D. VIJAYA MEENAKSHI,** under my guidance during the period 2005-2008. This has been submitted in partial fulfillment of the award of M.D. Degree in Obstetrics and Gynaecology (Branch – II) by the Tamilnadu Dr. M.G.R. Medical University, Chennai – 32.

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INTRODUCTION

Pregnancy induces progressive changes in maternal carbohydrate metabolism. As pregnancy advances insulin resistance and diabetogenic stress due to placental hormones necessitate compensatory increase in insulin secretion. When this compensation is inadequate GDM develops. Magnitude of complications are equal in GDM than in women with pre GDM.

Universal Screening is strongly recommended for the population ethnically proven to high prevalence of type 2DM. In much of the world, GDM is diagnosed if 2 hrs Blood glucose ≥ 140 mg/dl. GDM woman has increased incidence of caesarian section, pre eclampsia and macrosomia.

A short term intensive care not only results in the safe motherhood but also gives a long term pay off in the primary prevention of obesity, IGT, and diabetes in the off spring as the "Preventive Measures Starts in Intrauterine Life".

Metabolic adaptations that occur during pregnancy are to accommodate a rapidly growing tissue transplant, the conceptus. The conceptus brings about alterations in maternal fuel metabolism and hormones.

Fuel metabolism in normal pregnancy

In non GDM pregnancy:

- Facilitated insulin action during the first half of pregnancy
- Diabetogenic stress during the second half of pregnancy

In early weeks of pregnancy

- Increased insulin fasting concentration
- Increased glucose stimulated insulin release (Peak 18-20 wks)
- Increased estrogen and progesterone which induces Beta cell hyperplasia.

Finally ends in hyperinsulinemia, insulin being anabolic and anti catabolic hormone favours:

- Tissue glycogen storage
- Peripheral glucose utilization from liver
- Needs to reduce FBS by 10%

Later weeks of gestation

Increase in Human placental lactogen, Prolactin and Cortisol leads to diabetogenic stress. Due to this, maternal insulin sensitivity reduces by 50%, metabolic alterations under influence of insulin and placental hormones facilitates anabolism during feeding

and accelerated catabolism during fasting.

Fasting glucose is constantly low due to constant intake of glucose by the fetus. Low FBG due to deficient glucogenic amino acid alanine and glycine called “substrate deficiency syndrome”.

In second half of the pregnancy insulin resistance and diabetogenic stress due to placental hormones necessitate compensatory increase in insulin secretion, GDM occurs when this compensation is inadequate.

Etiological classification of diabetes mellitus:

Type 1A: Immune mediated β cell destruction.

Type 1B: Idiopathic β cell destruction

Type 2: May range predominantly insulin resistance to predominantly insulin secretory defect with insulin resistance.

Genetic Defect in β cell function:

Genetic syndrome - Downs, klienfelter syndrome, turner Syndrome.
Exocrine pancreas - Pancreatitis, cystic fibrosis.
Endocrinopathies - Cushing syndrome, pheochromocytoma, and others.
Drugs - β agonist, thiazides.

Infections - congenital Rubella, CMV, Cocksackie

Classification of diabetes complicating pregnancy

	Onset	**FBG**	**2 hrs PPG**	**Therapy**
A1	Gestational	< 95 mg/dl	< 120 mg/dl	Diet
A2	Gestational	> 95 mg/dl	> 120 mg/dl	Insulin
Class	**Age of onset**	**Duration**	**Vascular disease**	
B	Over 20 yrs	< 10 yrs	None	Insulin
C	10-19 yrs	10-19 yrs	None	Insulin
D	< 10 yrs	> 20 yrs	B. Retinopathy	Insulin
F	Any	Any	Nephropathy	Insulin
R	Any	Any	Pro. Retinopathy	Insulin
H	Any	Any	Heart	Insulin

Maternal Metabolic changes during pregnancy in GDM

1. Reduced fasting plasma glucose level
2. Increased fasting and post prandial plasma insulin levels
3. Increased PPBS glucose levels
4. β cell hypertrophy and hyperplasia
5. Reduced insulin sensitivity and increased lipolysis

Pathogenesis

Increased maternal age and obesity are significant contributing genetic factors. In about 20% of GDM patients sluggish early insulin secretion cannot be demonstrated, due to increased elaboration / heightened / sensitivity to one or more of the gestational counter hormones

Post receptor defect in the insulin signaling cascade appears to be a cause for the reduced insulin sensitivity in pregnant women with normal glucose tolerance and gestational diabetes.

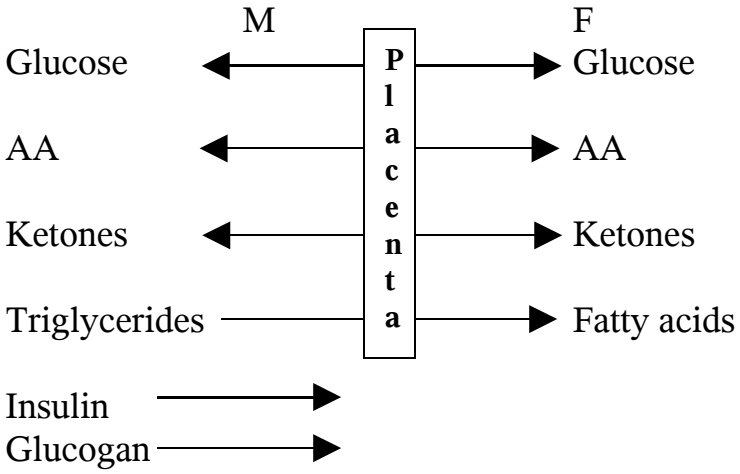
IR substrate (IRS-1) expression is reduced in all pregnant women compared to non pregnant controls, this down regulation is due to cytokine tumour necrosis

factor.Simply the pathophysiology of GDM has been related to excessive insulin antagonism by the pregnancy contrainsulin factors

When maternal insulinogenic compensation is inadequate to offset these factors, gestational diabetes will supervene. Reduced β cell function that occurs in GDM women may be the indication for the future susceptability to diabetes.

Consequences on fetus:

1) Consequences of metabolic changes revolve around maternal hyperglycemia and fetal hyperinsulinemia. Glucose traverse the placenta by facilitated diffusion and amino acid by active transport and enter the fetal circulation. Placental glucose transport is dependent on the glucose transporter (GLUT) family and GLUT- 1 is the principal transporter.



With increase in gestational age, 2-3 fold increase in expression of syntiotrophoblast glucose transportation occurs, aminoacid by active transport. All this are regulated by insulin, any disturbance in the secretion and action of insulin influence the whole nutrient composition of the fetus and fetal hyper insulinemia.

Maternal abnormal mixture of nutrients gain access to the developing fetus and modify phenotype gene expression in newly forming cells with thereby causing permanent short and long term effects in the offspring.

Fetal problems associated with Maternal hyperglycemia:

First Trimester	Second Trimester	Neonatal
Malformations Growth Retardation Fetal Wastage	Hypertrophic Cardiomyopathy Polyhydramnios Erythraemia Placental insufficiency	Hypoglycemia Hypocalcaemia Hyperbilirubinemia Respiratory Distress Macrosomia > 4 kg

	preeclampsia Fetal loss	Hypomagnesemia Low IQ

The mechanism suggestive of the teratogenic effect in early post implantation stage of the embryo, affecting the normal functioning yolk sac which regulates the nutrient transport from maternal plasma to embryo during early neural tube development.

Oxidative metabolism and generation of free oxygen radicals that may be toxic to the embryo. Glucose induces mutation in embroyonic DNA.

Hence excellent control of maternal metabolism commence before conception and must be maintained during first 8 weeks. Supplementing with folic acid, antioxidants play role in preventing malformations from 7.5 to 0.8%.

Definition: GDM is defined as carbohydrate intolerance of variable severity with onset or first recognisation during present pregnancy, includes the glucose intolerance that may have ante dated the present pregnancy.

GDM is due to sluggish first phase insulin release and also due to effect of anti insulin hormones for glucose utilization, insulin secretion in pregnancy.

Insulin Secretion in GDM and Non GDM

	GDM	Non GDM
Insulin secretion	↑	↑
Glucose stimulated Insulin Secretion	↑	↑↑
Peak Plasma insulin	Late	N
1st phase insulin	-	More
2nd phase insulin	Same	Same

Woman with normal glucose tolerance increases her insulin secretion over and above the insulin resistance, maintains glycemic level, do not develop GDM. 30% GDM women will progress to type 2 DM in 2-20 years after pregnancy.

Etiology and Pathogenesis:

1. Auto immune destruction of β cells
2. Impaired β - cell function
3. Increased insulin degradation
4. Decreased tissue sensitivity to insulin
    a. Impaired insulin – insulin receptor binding
    b. Impaired intracellular insulin signaling

Effect of maternal fuels on fetal development: The hyperglycemia – hyperinsulinism hypothesis of Pedersen has been modified to include contributions of

other maternal fuels besides glucose that are also responsive to maternal insulin. All of these can influence the growth of the fetus and the augmentation of fetal insulin secretion. Within this formulation, growth will be disproportionately greater in insulin-sensitive than in insulin – insensitive tissues on the fetus. “Indian women have 11 fold increased risk of developing GDM compared to White women.”

Indicators for screening:

	High risk		**Low risk**
1)	Age > 25 years	-	Age < 25 years
2)	IUD / anomaly	-	Low ethnic group
3)	Recurrent pregnancy loss	-	No family history of DM
4)	Family history of DM	-	BMI – normal
5)	Macrosomia	-	Good obstetric output
6)	Obese women		
7)	PIH		
8)	Polyhydramnios		

9) Twin pregnancy

Screening:

Urine glucose:

During pregnancy renal threshold for glucose is lowered. It renders glycosuria less specific for detection of GDM hence not recommended as screening test.

Blood glucose:

The usual recommendation for screening is between 24 and 28 weeks of gestation. The recent concept is that all pregnant women should undergo glucose tolerance test in the 1st trimester itself. If negative, repeat test around 24 to 28 weeks and 32 to 34 weeks.

ADA Recommendation:

1. One Step Procedure:

Diagnostic 100 gm oral glucose tolerance test without prior serum glucose screening.

2. Two Step Approach:

- Initial screening by 50 gm oral glucose and if Blood Glucose > 140 mg% patient is asked for diagnostic OGTT, this method identifies upto 80% of GDM.

3. Carpenter and Coustan diagnostic criteria:

The American Diabetes Association has adopted Carpenter and Coustan criteria.

Time	100 g OGTT	75 g OGTT (sacht's criteria)
Fasting	95 mg/dl	95 mg/dl
1 hr	180 mg/dl	180 mg/dl
2 hr	155 mg/dl	155 mg/dl
3 hr	140 mg/dl	

Two or more of the venous plasma concentrations must be met or exceeded for a positive diagnosis.

WHO Criteria

A standard OGTT should be performed after over night fasting by giving 75 g of glucose. Plasma glucose is measured at fasting and after 2 hours. Pregnant women who meet WHO criteria for IGT (2 hrs PG > 140 mg/dl) are classified as having gestational diabetes mellitus (GDM).

	FPG	**2 hrs PG**
IGT	< 126 mg/dl	140-200 mg/dl
Diabetes	> 126 mg/dl	> 200 mg/dl

If fasting plasma glucose is more than 126 mg and / or 2 hr post glucose more than 200 mg probably she has been having undetected diabetes prior to conception and can be confirmed by $HbA1_c$ estimation.

Glycosylated Hemoglobin ($HbA1_c$)

$HbA1_c$ is not suitable for screening for gestational diabetes, since it yields false positive results in 41% and false negative in 26%. $HbA1_c$ estimation is useful in pre-gestational diabetes to know the retrospective blood glucose control at the time of conception.

Serum Fructosamine:

Like $HbA1_c$ serum Fructosamine is not a useful screening test for gestational diabetes. This test is useful to assess the short-term state of maternal glucose control during the past two weeks.

Selective screening leaves 45.4 % of pregnant woman unscreened, out of which 35% has GDM. Uniform policy of adopting WHO screening and diagnostic criteria is recommended for the following reasons.

1. GDM diagnosis based on two hours 75 gm OGTT defined either WHO or ADA predicts further development of DM in mother.

2. Criteria recommended by WHO is simple and cost effective and is practiced in many centers.

3. Further assuring that effective treatment is available, WHO criteria of 2 hrs PPGS > 140 mg / dl identify large number of cases may have greater potential for prevention.

4. One step procedure is both diagnostic and screening.

Management:

The important predictor of fetal outcome either in pre gestational or Gestational

diabetes is the glycemic control attained immediately before and during pregnancy. The plasma glucose level of normal pregnant women is less than 90 and 120 mg% respectively during fasting and non-fasting states. Hence the best fetal outcome can be expected by maintaining the mean plasma glucose level around 105 mg.

Practical self management skills are essential for attaining good glycemic control in preparation for pregnancy and during pregnancy.

1. Appropriate meal plan.
2. Self monitoring of blood glucose. (SMBG)
3. Self administration of insulin and adjustment of insulin doses.
4. Treatment of hypoglycemia (family members and patient).
5. Safe physical activity.
6. Development of techniques to reduce stress.

A. Medical Nutrition Therapy (MNT)

All women with GDM should receive nutritional counseling. 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. Approximately 30 to 40 kcal/kg ideal body weight or an increment of 30 kcal/day above the basal requirement is needed. Pregnancy is not the ideal time for obesity correction.

As a part of the MNT, pregnant woman are advised to wisely distribute their calorie consumption especially the breakfast into two equal halves and consuming the portions with a two hour gap in between. MNT is suggested for 2 weeks.

B. Insulin Treatment

Insulin is essential if MNT fails to achieve euglycemia. In normal pregnancy, the FBG concentration ranges between 55 and 70 mg/dl, the 1 hr PPBS level is < 120 mg/dl.

SMBG is to be performed before breakfast and 2½ hrs after each meal. GDM women usually have high post breakfast plasma glucose level compared to post lunch and post dinner. A few GDM women do have post dinner plasma glucose also high. Insulin is started within 1 to 2 weeks, if FBS is more than 90 mg/dl even after MNT.

Peaking of plasma glucose is high with breakfast (due to dawn phenomenon). Plasma glucose value is 12% higher than whole blood value. If FPG concentration on OGTT is > 120 mg/dl the patient is started with insulin immediately with Meal plan.

In this regimen two third of the total daily dose of insulin is given in the morning and one third in the evening. For each combination one third dose should be regular

insulin and two third intermediate acting insulin. With this regimen if the patient continues to have fasting hyperglycemia, the intermediate acting insulin has to be given at bedtime instead of before dinner.

Insulin dose is individualized. Initial dose should be as low as 4 units and adjusted later. The above regimen of regular and intermediate acting insulin in the morning corrects hyperglycemia in most cases.

Inclusion of fetal growth might provide the opportunity to reduce glucose testing in low risk pregnancies. Maintenance of mean blood glucose less than 105 mg% is ideal for good fetal outcome, this would prevent the newborn from hypoglycemia.

As long as fetus is in the uterine compartment it has enough fuel to maintain its blood glucose level.

When fetus is delivered, the supercharged β cells of neonate continue to secrete insulin. But there is no fuel supply from the maternal compartment and the new born develops hypoglycemia. Neonatal hypoglycemia is due to poor control of diabetes in the mother.

Though oral Anti diabetic drugs are not recommended, reports have shown good fetal outcome in GDM women – on glyburide (micronised glibenclamide). Metformin has been found to be useful in women with polycystic ovarian disease.

Self glucose monitoring is needed once in a week, once target is achieved, once in a month FBS and PPBS up to 28 weeks, more than28 wks once in 15 days till 32 weeks, then once in a week till delivery. In high risk cases frequency intensified with SMBG. Others include fundus examination, estimation of microalbuminuria.

Obstetrical Management procedures

Procedure	**Risk Based on glycemic control, vascular disease**	
	Low Risk	**High Risk**
Dating Ultra Sound	8-12 Weeks	8-12 Weeks
Prenatal Genetic Diagnosis	As Needed	As Needed
Fetal Echo Cardiography	18-22 Weeks	18-22 Weeks
USG for fetal growth	28 and 37 Weeks	Monthly
Biophysical Profile	36 Weeks, Weekly	27 Weeks, 1-3 /Week
Amniocentesis for lung maturity	-	35 – 38 Weeks
Induction of Labor	40 Weeks	35-38 Weeks

Intra partum Diabetic Management: Metabolic studies in non GDM women, during labour revealed that glucose turn over is increased fourfold with little changes in

insulin level during active labour, insulin requirement is zero while glucose is required at 2.6 mg / kg / min. Labour should be induced in the morning, IV saline should be used as medium.GDM women does not require insulin once labour begins, no insulin is needed after expulsion of placenta.

GDM requires follow up and glucose tolerance test with 75 gm oral glucose test after 6 weeks and if necessary repeated after 6 months. GDM recurs approximately in 50% of subsequent pregnancies. Maintaining ideal body weight approximately solves 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 diabetologist, obstetricians and Neonatalogists.

REVIEW OF LITERATURE

History

Diabetes mellitus was well recognized as medical disorder more than 2000 years ago.

1500 BC, Greek Father of Medicine Hippocrates mentioned “making water too often” Aristotle referred to “Wasting of the Body”. Reference in the ancient book “disease of rich, brought about by gluttony, or over indulgence in flour and sugar.”

Dr. Elliott Joslin is rembered as the proston physician who bridged the period immediately before insulin discovery and the existing clinical demonstration of its effectiveness in the following decade.

In the pre insulin days, death of mother during and soon after pregnancy from uncontrolled DM was the major risk.

O’ Sullivan first used the term gestational diabetes mellitus in 1961. GDM is defined as the carbohydrate intolerance of varying severity with onset or first recognized during pregnancy during the 1st work shop 1980, Chicago.

The first prospective study of carbohydrate metabolism in pregnancy was established by Boston 1954, using 50 gm 1 hour screening test.

HG Bennewitz: DM – symptom of pregnancy in 1824 from University of Berlin was the first reference to diabetes in pregnancy. “disease appeared along with pregnancy at the very same time, while pregnancy lasted it lasted, it terminated soon after pregnancy”.

Norbert Frenikel and Broyd Metzger ensured that the concept of GDM is now firmly imprinted on the obstetric mind, major place as an epidemiological tool not only on immediate out come of the pregnancy but also on the long term effects on both mother and baby.

There are several identifiable predisposing risk factors for GDM in the absence of risk factors for less incidence of GDM.(1)

Study was performed on 1251 pregnant women, the mean age of these pregnant women is 23-24 years, 16.5% of them found to have GDM. Study concludes that increased prevalence of GDM in our population necessitates the universal screening for glucose intolerance in pregnancy.

Using 2 hour plasma glucose > 140 mg% is simple and economical particularly for countries ethnically more prone to high prevalence of diabetes mellitus (2).

GDM was twice as common in the daughters of diabetic mothers 11% than father 5% (p 0.002). An excess of maternal transmission of diabetes is consistent with an

epigenetic effect of hyperglycemia in pregnancy acting in addition to genetic factors to produce diabetes in the next generations (3).

Early diagnosis and treatment may result in decreased perinatal morbidity in women with early diagnosed diabetes requiring higher insulin dose than lately diagnosed GDM (4).

Comparative study of 2 routine screening strategies for gestational diabetes mellitus concludes universal screening seems to be most appropriate routine screening strategy, because it is difficult to know exactly the specific risk factors of a population to do selective screening (5).

With high prevalence of diabetes, high proportion of patient potential to develop GDM is identified with a selective screening in this study. Universal screening for GDM, the best way to identify patient and prevent adverse obstetrical and neonatal outcome (6).

GDM was significantly higher and correlated in women with positive history of diabetes, increasing age then previous pregnancies, prepregnancy overweight and short stature (7).

GDM is a transient abnormality of glucose intolerance during pregnancy. It is variously estimated that 3-5% of pregnancies are complicated by diabetes 1-6% develop

significant hyperglycemia during pregnancy to meet criteria for diagnosis of diabetes. 20-50% of women with GDM develop type 2 diabetes mellitus.

More controversial in the diagnosis of GDM. Coustan succinately summarized the issues surrounding the diagnosis of GDM by posing the four key questions,

1. What level of maternal hyperglycemia worsens the pregnancy out come?
2. Does intervention improve out come?
3. Is such intervention cost effective?
4. What is the optimum screening / diagnostic test?

Successful screening test requires that the condition should be prevalent in the target population, procedure should be cost effective and the treatment improves the prognosis. 20-30% of untreated GDM women give birth to infant >4 kg. 6-20% has increased pregnancy induced hypertension in pregnancies marked as GDM.

The principle benefit of successful screening for GDM is the ability to identify group of women at risk subsequently developing diabetes mellitus.Such woman successfully targeted to modify life style and comply regular follow up to aid early identification of diabetes mellitus.

All the recognized pregnancy complications of diabetes mellitus are exacerbated

by hyperglycemia, hence strict attention to glycemic control periconceptionally and through out pregnancy is required.

Because of heterogenous nature of pregnancy out come, the cost effectiveness of screening for GDM is low universal screening should be justified.

Overt diabetes with FBS >126 mg% according to ADA (2004) is used because data indicate the risk of retinopathy rises dramatically at this fasting level.

Women diagnosed to have GDM early in pregnancy are at high risk group (8). Murphy and colleagues studied to avoid glucometer for screening (9)

Word **'gestational'** implies that diabetes is induced by pregnancy, from exaggerated physiological changes in glucose metabolism or type 2 diabetes unmasked and discovered during pregnancy.

More than half of women with GDM ultimately develop overt diabetes in ensuring 20 years and there is mounting evidence of large complications that include obesity and diabetes in their offspring.

Despite more than 30 years research there is no consensus regarding the optimal approach to screen for gestational diabetes mellitus. For the definite diagnosis WHO 1985 recommended 75 gm - 2 hr glucose tolerance test approach is used.

ADA (1999 a) has concluded that fasting hyperglycemia > 105 mg / dl increases risk of fetal death during last 4-8 weeks of gestation.

GDM have babies with increased fat deposition in back and shoulder leading to shoulder dystocia 3% (Magee and collegues) – and 4% GDM babies require i.v. glucose therapy for hypoglycemia. Neonatal hypoglycemia is defined when the blood glucose is < 45 mg / dl (10).

Although uncomplicated GDM with less severity increases risk of fetal macrosomia, neonatal hypoglycemia, jaundice, polycyethemia, hypocalcemia may complicate GDM as well.

The true definition of hyperglycemia in pregnancy judged by the internationally acceptable 75 gm oral glucose tolerance test ‘awaits the result of large hyperglycemia and adverse pregnancy out come study (HAPO) (11).

Study conducted on 4300 pregnant women involving over 90 PHC and some private practitioners. It used one step procedure where only one blood sample have to be collected. It was found that 17% had GDM, study was conducted in all 3 trimester, early screening could go a long way in avoiding the dreaded complications of disorder.

The merit of this study is to compare the well accepted methods for diagnosis of GDM and determine the best method. One step procedure may be better tolerated

compared to 2 step procedure with respect to number of visits, amount of drink and length of testing. Diagnosis by single test may avoid unnecessary delay in initiation of therapy and still identify these patients at risk for type 2 diabetes mellitus.

AIM OF STUDY

1. To know the Incidence of GDM in our population.

2. Effectiveness of screening using single step procedure with 75 gm oral glucose.

3. To substantiate that universal screening is necessary in our population.

4. To analyse maternal and perinatal outcome in GTT positive and GTT negative patients.

MATERIALS AND METHODS

Prospective Study was done in, Kilpauk Medical College and Hospital, having deliveries of about 7500 to 8500 per annum, with daily antenatal patient attendance of 120 – 130.

Randomly selected 500 patients in gestational age 14 – 36 weeks by clinical examination height, 1st trimester weight, general examination, obstetric examination of the patient, from June 2006 to August 2007 of 14 months duration. These women were booked for delivery at KMCH.

A detailed history was taken regarding family history, past history and about current pregnancy. Selected patients for study was given dates to come in fasting state, FBS taken and 75 gm oral glucose was given in 200 ml of water. 2 hours later blood sugar was taken.

Glucose estimation done at diabetology department. Test sample was collected in glass tube with sodium fluoride for inhibiting glucose utilization and EDTA for anti coagulation.

Criteria for diagnosing GDM by WHO criteria of 2 hours blood sugar level 140 mg % and above is to be diagnosed as GDM. Patients diagnosed as GDM were closely monitored with frequent antenatal checkup. Intrapartum monitoring, mode of delivery,

details regarding neonatal complications were observed.

INCLUSION CRITERIA

- All pregnant women irrespective of age and parity.
- Gestational age between 14 and36 weeks.

EXCLUSION CRITERIA

- Known Diabetes mellitus.
- Gestational age more than 36 weeks and less than 14 weeks
- Patients on drugs steroids, Calcium Channel blockers, Thiazides

RESULTS AND ANALYSIS

Table 1: Incidence:

GDM	No. of Patients	Percentage
Yes	33	6.60
No	467	93.40
	500	100%

2 hr blood glucose ≥ 140 mg%, incidence is 6.6%

Blood glucose ≥ 130 mg%, incidences is 8%

Blood glucose ≥ 120 mg%, incidence is 10.8%

Table 2: Age Distribution :

S.No.	Age(yrs)	Non GDM	GDM	Percentage GDM
1	< 20	86	1	3.04
2	21-25	252	12	36.36
3	26-30	93	12	36.36
4	31-35	30	6	18.18
5	36-40	6	2	6.06
		467	33	100%

Mean Age 24.32 years, less than 20 years the Incidence is 3.04%, 72.72% is in between 21-30 years.

Table 3: Body Mass Index

BMI	Non GDM	GDM	Percentage
Normal < 25	332	12	36.36
Over Weight 25-30	114	16	48.48
Obesity > 30	21	5	15.16
	467	33	100%

Mean BMI is 23.52

GDM women with Obesity is 15.16% and over weight is 48.48%.

Table 4: Family History of DM

Family H/o	Non GDM	GDM	Percentage GDM
No	432	22	66.67
Yes	35	7	21.21
Pr. GDM	0	4	12.12
	467	33	100%

In GDM women , no family History of Diabetes in 66.67%, with family history in 21.21%.

Table 5: Obstetric Score

Gravida	GDM	Non GDM	Percentage GDM
Primi	4	190	12.12
G2	7	179	21.21
G3	13	59	39.39
G4	3	30	9.09
G5	4	9	12.12
G6	2	0	6.06
	33	467	100%

Abortions	GDM	Non GDM	Percentage GDM
A0	22	363	66.67
A1	8	73	24.24
A2	1	22	3.03
A3	2	8	6.06
A4	0	1	0
	33	467	100%

GDM women 12.12% were primi, 60.6% were Gravida 2 and Gravida 3, Nulli para were 48.48%, no fetal wastage in 66.67%.

Table 6: Gestational Age

S.No.	GA in weeks	Non GDM	GDM	Percentage GDM
1	14-20	96	3	9.09
2	21-24	133	9	27.27
3	25-28	142	1	3.03
4	29-32	72	7	36.36
5	33-36	24	8	24.24
		467	33	100%

In GDM patients GA less than 20 weeks 9.09%, between 29-32 weeks 36.36%, GA upto 36 weeks is 24.24%

Table 7: Fasting blood sugar

FBS	GDM	Non GDM	Percentage GDM
< 95 mg	6	415	18.18
96-125	20	51	60.61
>125	7	1	21.21
	33	467	100%

Fasting blood sugar: Mean 115 mg%. Fasting Blood Sugar up to 125 mg% is 78.79%, more than 125mg% is 21.21%.

Table 8: Post Prandial Blood Glucose - GDM

PPBS	NO	Percentage
< 160 mg	17	53.13
161-200 mg	9	28.13
> 200 mg	6	18.74
	33	100%

PPBS: Mean 178 mg% PPBS more than 200mg% is 18.74% and Blood Sugar Less than 160 mg% is 53.13%.

Table 9: Risk Factors

Risk Factors	No. of Patients	Percentage
No	22	66.67
PIH	3	9.09
Hydrammios	3	9.09
Pr. CHD	1	3.03
Pr. NTD	1	3.03
Pr. Twin	3	9.09
	33	100%

With no risk factors in 66.67% of GDM Women, previous IUD 6.06%, previous Birth Weight More than 4Kg is Nill, Previous Congenital Anomaly is 6.06%.

Table 10: Mode of Treatment

Mode of Treatment	No	Percentage
Meal Plan	28	84.85
Insulin	5	15.15
	33	100%

28 GDM women were started on meal plan, 5 patients were started on insulin. 27.27% of patients started with MNT had been supported with insulin later.

Table 11: GA at termination of Pregnancy

GA (weeks)	No	Percentage

Undelivered	9	27
32	1	3
36	2	6
37	4	11
38	11	33
39	6	20
	33	100%

33% GDM women were terminated at 38 weeks of gestational age, 20% were delivered at 39 weeks. 3 had pre-term delivery.

Table 12: Mode of Delivery

27% were delivered by labour natural, 27% by Caesarian section, 15.50% by Repeat Caesarian.

Table 13: GTT negative patients

Mode of Delivery	Number
Lab: Natural	320
Forceps	12
LSCS	80
Undelivered	15
Lost follow up	30
Total	467

Table 14: Indication for LSCS - GDM

Indication	No	Percentage
Breech	1	7
GDM with mobile head	4	28.5
CPD II^0	1	7
Fetal Distress	2	15
PPROM	1	7
Rpt. LSCS	5	35.5
	14	100

7% had been operated for CPD II°, 15% had LSCS for Fetal Distress, 35.5% had Rpt.

LSCS, emergency LSCS 28%, elective LSCS 72%.

Table 15: Birth Weight

B. Weight (Kgs.)	Non GDM	GDM	Percentage

0	55	9	27
< 2.5	147	3	9.09
2.6 – 3	167	5	15.15
3.1 – 3.5	86	8	24.24
> 3.6 – 3.9	12	8	24.24
	412	33	100%

24.24% had birth weight between 3.1 to 3.5 kg, 24.24% had weight more than 3.6 Kg. In GDM patients no macrosomia noted in this study.

Table 16: NICU Care

Neonatal complications	Non GDM	GDM
Hypoglycemia	10	3
Hypocalcemia	0	0
Hyperbilirubinemia	26	6
Macrosomia	2	0
Congenital anomaly	0	0
Respiratory distress	16	2

Three babies of GDM mother had features of hypoglycemia, 2 babies had blood sugar less than 25 mg, 1 has blood sugar less than 30 mg.

Table 17: BMI and GDM

BMI	GDM	Non GDM	Total
Non Obese	12	333	345
Obese	21	134	155
Total	33	467	500

Obese women are more prone to GDM rather than non obese women.

P: 0.000027

Table 18: Elderly mother and GDM

Age	GDM	Non GDM	Total
< 30 Yrs	23	431	454
> 30 Yrs	10	36	46
Total	33	467	500

Elderly mother greater than 30 years are more prone to GDM than women less than 30 Years. P – 0.000014.

Table 19: Birth Weight GDM and Non GDM

	Number	Mean	SD	95% of CL	
				LCL	UCL
GDM	24	3.28 kg	0.54	3.05	3.51
Non GDM	412	2.70 kg	0.48	2.66	2.75

P = 0.000. GDM babies mean 3.28 kg.

Non GDM babies mean 2.7 kg.

DISCUSSION

The prevalence of GDM varies in direct proportion to the prevalence of NIDDM in a given population or ethnic group. Prevalence of GDM in United States is 2 – 5%, less than 1% is noted in China, Srilanka, Italian Women.

Highest was found in Pima / Papago and India 14 – 22%.study conducted with 891 patients, 16.2% is the incidence in North Chennai. In South Chennai 15% is the incidence of GDM in the study conducted with 1002 patients (12).

In some population diabetes was undiagnosed prior to the study. IGT was mostly overlooked in routine clinical practice. Dooley et al demonstrated that race as well as maternal age and degree of obesity must be taken into account in comparing the prevalence of GDM in different populations. Influence of race and disease predicts prevalence and perinatal outcome (13).Incidence of GDM is 6.6% in this study.

Over the next 2-3 decades there will be 80 million reproductive age women with Diabetes in world, of this 20 millions will be in India alone, creating potential for extremely high rates of maternal and infant mortality (14).

Number of prospective and retrospective studies have substantiated that the frequency of adverse fetal out come increase with 2 hour PG $\geq$ 120 mg% and taking

care of women has resulted in better fetal outcome. Incidence of GDM is 10.8%, if the cut off value is ≥ 120 mg% in this study (15).

Xiong et al Studied that incidence of GDM is 22.4% compared to 10.3% in women more than 35 years (16). In this study 38% GDM women are more than 30 years, out of 33 women 10 were more than 30 years, $P < 0.000014$. Boet et al proved that prevalence of GDM increases from 1.5 /1000 deliveries to 4.2/1000 for women aged more than 30 years (17).

Jimenez et al 41.8 % were older than 30 years of age, 26.2% were younger than 25 of age. The positive predictive value of the screening test for a single risk factor was 22.9 (18). Age adjusted OR (95% CI) for women with Multigravida or more deliveries compared with primi (19). Among GDM women multigravida more than 3, accounts for 66% in the study.

Obesity more than 91kg is detected with 15.8% of GDM compared with 7.3% of normal groups (20). Koustal et al, women with previous GDM had higher BMI 26.4 to 23.8 and waist hip ratio 0.8 in GDM compared to normal 0.77 (21). In this study out of 33 patients 21 were obese, $P < 0.000027$.

Compared with controls GDM patients showed higher prevalence of PCOS,

greater clinical and biochemical evidence of hyperandrogenism and insulin resistance and higher prevalence of PIH. GDM developed in 20% of PCOS compared to 8.9% in controls (22). Out of 33 GDM women 6.06% had been treated for PCOS. GDM accounts 30.6 % in women whose mother has GDM versus 3.5% in controls (23). In this study 66.67% GDM positive women were with out family history of diabetes.

Recurrence of GDM is 35.6%. Multivariate models shows that infants birth weight in index pregnancy and maternal pre pregnancy weight gain before subsequent pregnancy, were predictive of recurrent GDM (24).12.12% is the recurrence rate of GDM in this study.

Higher incidence of GDM rate in triplets than the reduction group 22.3 Vs 5.8% (25). Recurrence rate of GDM 35 to 85% is influenced by parity, BMI, early diagnosis of GDM, Insulin requirements, weight gain and by the interval between the pregnancy.

High risk individual requires both initial screening and repeated testing during and after pregnancy (26). Christine C et al compared the incidence of GDM in twin with that of triplets mother with triplets, 30 was more at a risk of developing GDM $P < 0.05$. Family history and risk factors was not contributing (27). 9.09% of GDM patients had previous twin pregnancy in the study.

Pregnancy total weight gain outside the institute of medium recommendation and rates of maternal weight gain are associated with Neonatal complications–Macrosomia,

hypoglycemia and hyperbilirubinemia than those women whose weight gain was in the recommended range (28). The cummulative risk of developing type 2 DM for GDM patient was 25.8% at 15 years post diagnosis (29).

Canadian Diabetic Association study of 100 gm Vs 75gm reference study of 58000 patients completed in 2004. Study concludes that single step screening is better tolerated than other methods.

Gultonen and Terano (1993) reported that cases of PIH and pre eclampsia contributed to the incidence two times more common among GDM than controls (30). 9.09% GDM women has been associated with severe PIH in this study.

Jacobson reported incidence of polyhydramnios is 2% in GDM compared to 0.5 – 0.7% of hydramnios in control group. In this study 9.90% GDM women had hydramnios. Increase caesarian rate was significantly higher in gestational diabetes and overt diabetes than in control group (31).

O Sullivans (1982) have shown that 50% of all GDM will develop impaired GTT or NIDDM with in 10 years of their index pregnancy. Pregnancy may disclose intolerance without clinical symptoms, pre disposed women with good diabetic control however decrease the incidence of congenital malformation even in patients with vascular complications (32).

According to coustan et al 1989 universal screening is more cost effective than selective screening for gestational diabetes in ethnic group population. Diagnosis of GDM by OGTT based on initial GCT Screaning leaves 21.5% undiagnosed. Single step 75gm oral glucose serves both screening and diagnostic procedure (33). Out of 23 delivered women 15 turned up for follow up, OGTT is within normal limits after 6 weeks.

“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 measures starts in intrauterine life.”

SUMMARY

- Incidence of GDM is 6.06%.
- Mean age group is 24years.
- Elderly women > 30 years are more Prone to GDM.

  P < 0.000014.
- Obese women with BMI > 25 were prone to GDM then non obese women,

  P < 0.000027.
- 66.67% GDM diagnosed women has no family history of diabetes.
- 60.6% were multigravida, no fetal wastage in 66.67%.
- 9.09% diagnosed to have GDM in less than 20 weeks of gestational age.
- 66.67% had no associated risk factor.
- 21.21% has FBS > than 125mg% and 18.75% had PPBS more than 200mg %.
- 84.85% of GDM patients had treated with meal plan.
- 27.27% among meal plane group has been switched over to insulin after MNT.

CONCLUSION

- Incidence of GDM is 6.6% in the study conducted.

- Universal screening by single step procedure is convenient, economical and suitable alternative screening test with out sacrificing these sensitivity expected for screening test.

- Thereby early detection and effective management to maintain optimal blood glucose concentration will reduce perinatal mortality and morbidity and adverse effect for the mother in future.

- Despite years of meticulous study, paucity of information still exits regarding the optimal maternal glucose levels that should be aimed for in order to reduce the embryonic, fetal and perinatal morbidity and yet not cause any harm to intra uterine development.

- The goal is to encourage early referral of both pre gestational and gestational diabetic women so that the tight glycemic control will be instituted at the proper time in order to prevent maternal hyperglycemia complications.

- The key finding here is that the risk of overweight and obese children rises in step with higher levels of blood sugar during pregnancy. By treating Gestational Diabetes, future risk of children becoming overweight, obese, PCOS, Diabetes

drops considerably.

- To help expectant women to enjoy the arrival of their sweet ones, the Government of Tamil Nadu has planned the GDM screening project in all Government Hospitals from March 08, 2007 (GO No. 356 Health and Family welfare), on Women's Day since "Women Health is Nation's Wealth" in order to ensure the early diagnosis of GDM, to reduce infant mortality rate in the state.

BIBLIOGRAPHY

3. Ben Harouch et al, *Diabet Med* 2004, Feb 21(2): 103 -13 related articles.

4. SeshiaeV et al, *J. Association of physician of India* 2004: Sep 25: 707-11.

5. Mclean M et al, *Diabetic Med* 2006, Nov 23 (11): 1213-15. Related articles.

6. Sandoval et al, *gynecol and obstet* – 2006 Apr : 74 (4) : 199 – 204

7. Benchi Mol M et al, *obstet gynecol*, Fertile 2006 Feb: 34 (2)107 – 14.

8. Agarwal M et al, screening in high risk population, *gynecol obstet* : 2006 273 (6) 323 -30.

9. Diciannai G. el, *Diabetes Res Clinic Pract* 2003 Nov 612 (2) : 137 – 7.

10. Bartza et al, *Am. J. Obst. Gynec*. 2000:182: 346.

11. GDM, *obstet gynecol* 83: 1038 (1994).

12. JAMA, influence of diagnostic criteria for GDM and prenatal mortality, 1993:26:609.

13. HAPO Study Co operation research group, *Int. J .of obstetrics and gynecol ,* 2002 , 78,69 -77.

14. Anjalakshi et al, Balaji et al*, Journal OGGSI*, 2007, 7-11.

15. *Diabetes care,* 1991: 40: 25 – 9.

16. Raviendar Madan et al, 17th IDF congress, Mexico 2000.

17. Seshiah. V et al, DIPAP – Data presented at WDF, Diabetes summit, Hanoi, Feb 2006.

18. Xiong et al, *Int. J. Obstet and Gynecol* , 2001: 75 : 221 – 8.

19. Boet et al, *Diabetologia,* 2001; 44; 972 -8.

20. Jimenez et al Predictive value of screening for GDM, *Acta obstet and gynecol scand, 2*000: 79: 991- 8.

21. Ege land et al, GDM population based study. *Br.Med J,* 2002: 321 :

546–7

22. Wang et al, GDM prevalence and risk factors. *Int. J ob and gynecol,* 2001: 75: 221 – 8.

23. Koustal et al, prevalence of PCOS with GDM, *clincal endocrinol*, 2000: 53: 501- 7

24. Mikola et al, PCOS women with obstetric outcome, human reproduction, 2001: 16: 226 – 9.

25. Irgens et al, birth characteristics of women who developed GDM. *Br. Med J* , 2000: 321: 546- 7.

26. Mac Neil et al, recurrence of GDM. *Diabetes care,* 2001: 24: 659 – 62

27. Sivan E et al, Impact of fetal reduction on GDM. *Obstet of gynecol*, 2002: 99: 91- 4.

28. ARD Ann J et al, *Diabetes care*, 2007 Feb: 30:251

29. Christine C et al, *obst. Gynecol*, April 2006: 107:655.

30. Monigue et al, *obst. Gynecol*, 2006: 108: 1153-1161.

31. Anna et al, *Diabetes care,* 2007, 30:878-883.

32. Gultonen and Terano, Hypertension and PIH in women with GDM, 1993:72:269-272.

33. Ingrid et al, Acta obstetrica et gynecological Scandinavian, 2004,83:46-51.

34.JAMA: Body weight and subsequent DM, 249: 942- 952.

35. AMJ, *Obs & gynecol,* 1989: 161: 981.

PROFORMA

Perform – Screening for GDM

S.No	:	Date	:
A.N. No	:	Height	:
Unit	:	Weight	:
Parity	:	BMI	:
LMP	:		
EDD	:		

Name and Address : Age :

MD Since : Consanguinity :

Family history

PCOS

Menstrual H/O :

Present Pregnancy:

- Abortions
- Congenital Anomaly
- Preterm Delivery
- Unexplained still birth
- Unexplained neonatal death
- Big babies
- Polyhydramnios

Obs H / O – GA Type of Delivery Baby Wt Sex GC

Baby – Whether Admitted in NICU

O / E

INV:

Date / GA USG

Time

FBS

2 Hrs PPBS

Results

Treatment Plan:

Follow up:

- Mode of Delivery
- Associated Cpl

Foetal Outcome

Apgar

Weight

Associated Complications

Neonatal Stay

After Peurparium – 6 Weeks OGTT

ABBREVIATIONS

BMI	**-**	Body mass index
CHD	**-**	Congenital Heart disease
CMV	**-**	Cyto Megalo virus
F dis	**-**	Fetal Distress
F	**-**	Forceps
F+, M+	**-**	Father, mother diabetic
FBS/FBG	**-**	Fasting blood sugar/glucose
GA	**-**	Gestational age
GDM / DM-		Gestational diabetes mellitus / Diabetes mellitus
IGT	**-**	Impaired glucose tolerance
IR-S	**-**	Insulin Receptor Substrate
IUD	**-**	Intra uterine death
LN	**-**	Labor natural
LSCS /CS	**-**	Lower segment caesarian section / caesarian section
MNT	**-**	Medical nutrition therapy
NIDDM	**-**	Non insulin dependent diabetes mellitus
NTD	**-**	Neural tube defect
OGCT	**-**	Oral glucose challenge test
OGTT	**-**	Oral glucose tolerance test
PCOS	**-**	Polycystic ovarian syndrome
PIH	**-**	Pregnancy induced hypertension
PPBS	**-**	Post prandial blood sugar
PPROM	**-**	Preterm premature rupture of membranes
Pr / Rpt	**-**	Previous / repeat