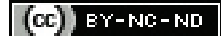


Screening and Re-screening of Gestational Diabetes Mellitus at 24-28 Weeks and 32-34 Weeks of Gestation and Evaluation of Foetal Maternal Outcome: A Longitudinal Study

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ABSTRACT

Introduction: Gestational Diabetes Mellitus (GDM) has a great impact on maternal and foetal outcome. Timely diagnosis and proper management have immense importance to prevent adverse outcomes.

Aim: To determine the incidence rate of GDM, and its risk factors and also to determine the importance of re-screening for detection of GDM at 32-34 weeks.

Materials and Methods: A hospital-based longitudinal study was conducted from April 2020 to June 2021 in the Department of Obstetrics and Gynaecology, Burdwan Medical College, Burdwan, West Bengal, India. Screening and diagnosis for GDM were performed by estimating a 2-hour blood glucose level after intake of 75 gm of glucose, irrespective of the meal at 24-28 weeks by one-step procedure i.e., Diabetes in Pregnancy Study groups in India (DIPSI). A total of 300 antenatal mothers were selected serially from antenatal OutPatient Department (OPD). All the screen-negative pregnant women were re-screened again at 32-34 weeks. Demographic variables and maternal risk factors like age, parity, Body Mass Index (BMI), family history of diabetes, previous GDM, previous history of foetal loss macrosomia and polyhydramnios were noted. Foeto-maternal complications like hypoglycaemia, Intrauterine Foetal Death (IUFD), preeclampsia and sepsis were recorded. Frequency and percentage of each parameter was calculated. The risk estimates between GDM and

without GDM were analysed by odds ratio with 95% confidence interval and p-value were calculated. The p-value <0.05 was considered significant.

Results: The screen-positive cases for GDM were 26 (8.7%) at 24-28 weeks and 8 (2.9%) at 32-34 weeks of gestation. Preeclampsia was noted in 5 (14.7%) cases and 4 (11.8%) GDM mothers suffered from Postpartum Haemorrhage (PPH) (p-value <0.0001). Rate of caesarean section was high 76.5% among GDM mothers (p-value <0.0001). Average birth weight of new born baby of mothers with and without GDM were 2.5324±0.6503 kg and 2.7297±0.2145 kg, respectively (p-value=0.0003). IUFD was noted in 2 (5.9%) cases. Preterm delivery was observed in 25 (73.5%) cases and admission to Neonatal Intensive Care Unit (NICU) was 11 (32.4%) (p-value <0.001). Out of 274 pregnant mothers who had blood sugar <140 mg/dL by DIPSI method at 24-28 weeks were designated as screen negative and they were re-screened at 32-34 weeks of gestation. Eight cases (2.92%) were found screen positive after re-evaluation (odds ratio, 3.1551, 95% CI, 1.4033-7.0938, p-value=0.00358).

Conclusion: Pregnancy in women with GDM has an increased risk of maternal and perinatal complications. Timely screening and diagnosis of GDM and appropriate treatment can reduce adverse foeto-maternal outcomes. Re-screening of initial screen negative women is very important, otherwise significant number of cases will be missed.

Keywords: Body mass index, Foeto-maternal outcome, Gestational age

INTRODUCTION

Any degree of glucose intolerance with the onset or first recognition during pregnancy is defined as GDM [1]. GDM, a substantial number of which progresses to type-2 diabetes in later life is increasing worldwide and recurrence of GDM is also seen in subsequent pregnancies [2]. The prevalence of GDM in India varies from 3.8-21% in different parts of the country depending on geographical locations and diagnostic methods used [3]. The prevalence of GDM is increasing because of the increased prevalence of obesity, in addition to the advanced maternal age of more than 25 years. Other risk factors for GDM include a strong family history of diabetes, persistent glycosuria, polycystic ovarian syndrome, macrosomia in past obstetric history [4]. The precise time for diagnosis of GDM is very crucial.

In this regard, the 2010 International Association of Diabetes and Pregnancy Study Groups (IADPSG) criteria for GDM diagnosis widely adopted internationally, recommended universal screening with a 75 gm of Oral Glucose Tolerance Test (OGTT) at 24-28 weeks gestation [5]. A universal screening which is simple feasible, acceptable, economic by a single step procedure was in need in Indian scenario as Indian women have the high frequency of GDM.

Fulfilling the abovementioned needs, DIPSI recommended a single step procedure to screen and diagnose GDM irrespective of the last meal status [6]. Mohan V et al., concluded that the DIPSI in non fasting OGTT criteria cannot be recommended for the diagnosis of GDM due to low sensitivity [7].

Identification of women with glucose intolerance is important to improve short and long-term foeto-maternal complications. Increased risks of foetal compromise come from maternal hyperglycaemia, which leads to foetal hyperglycaemia and foetal hyperinsulinaemia. This gives rise to various complications like IUFD, Respiratory Distress Syndrome (RDS), hypoglycaemia, cardiac anomalies, neonatal jaundice, impaired calcium and magnesium homeostasis, polycythaemia, and many more in neonates. Mother with GDM may develop preeclampsia, infection, polyhydramnios, PPH and diabetic ketoacidosis. In the long run the mother remains a potential candidate to develop type II diabetes mellitus [8]. Improved outcome therefore depends upon diagnosis of all potential cases and good glycaemic control [9].

Increased prevalence of GDM have negative impacts on various maternal and neonatal outcome. The risk for adverse outcomes drastically increases as a result of impaired glucose tolerance that

may appear in later months of pregnancy even in those who are euglycaemic in early gestation [10].

The primary aim of the present study was to estimate the incidence rate of GDM by screening and diagnosis by a single-step procedure by using 75 gm oral glucose at 24-28 weeks of gestation and again at late gestation (32-34 weeks) in previously screened negative mothers. The secondary aim was to study the risk factors associated with GDM and to assess the foetal and maternal outcome.

MATERIALS AND METHODS

A longitudinal hospital-based study was conducted in the Department of Obstetrics and Gynaecology, Burdwan Medical College and Hospital, Burdwan, West Bengal, India from April 2020 to June 2021 after Institutional Ethical Clearance (IEC) (BMC/Ethics/079 dated 28th Jan 2020). Informed written consent was taken from all eligible mothers.

Inclusion criteria: All mothers with singleton pregnancy were included in the study.

Exclusion criteria: Multiple pregnancies, known cases of diabetes and mothers on drugs like corticosteroid, anticancer, antipsychotic and Antiretroviral therapy (ART) cases were excluded from the study.

Sample size calculation: Sample size was calculated by the following formula:

$$n = Z^2 \times p \times (1-p) / \Delta^2$$

{n=sample size; z=z value (e.g.,:1.96 for 95% confidence level), Δ is the confidence interval i.e., 0.04 for $\pm 4\%$; p-value=percentage picking a choice i.e., 14%, expressed as a decimal to 0.14}.

The study included 300 pregnant mothers who attended antenatal OPD by serial sampling method till the desired level of sample size was achieved.

Study Procedure

Detailed history of pregnant mother was taken including age, parity, gestational age, history of recurrent pregnancy loss, macrosomia or stillbirths, family history of diabetes etc. Detailed clinical examination was performed and pulse, Blood Pressure (BP), BMI [11] were recorded. Routine blood and urine samples were examined along with obstetric ultrasound examination. All pregnant women underwent a single step procedure to screen and diagnose GDM at 24-28 weeks. Blood glucose level was estimated by glucose oxidase method two hours after taking 75 grams of glucose in 300 mL of water irrespective of last meal status. Those having two hours of blood glucose level ≥ 140 mg/dL were considered as GDM [12]. Those women who were screen negative in the initial assessment, were re-screened at 32-34 weeks of gestation.

Women having GDM were treated first by Medical Nutritional Therapy (MNT) for two weeks. If MNT fails to lower blood glucose to the target level, an oral hypoglycaemic agent (metformin) and/or insulin were used. All mothers in the study groups were followed-up till delivery and early neonatal period to assess maternal outcomes like preeclampsia, sepsis, polyhydramnios, preterm labour, mode of delivery, PPH, and foetal outcome such as foetal macrosomia, IUFD, birth weight, neonatal RDS, hypoglycaemia, hyperbilirubinaemia etc., NICU admissions were also recorded.

STATISTICAL ANALYSIS

For statistical analysis, data were collected and tabulated into Microsoft excel sheet and then analysed by Statistical Package for the Social Sciences (SPSS) (version 27.0; SPSS Inc, Chicago IL, USA) and Epi Info 7. Descriptive statistics (frequencies, percentage, mean, and standard deviation (SD) were used to describe participant's characteristics. A Chi-square test was employed to compare categorical data between women with GDM and without GDM as well as to examine the distribution of independent variables and each adverse maternal outcome. Independent sample t-test was also used for the comparison of the mean difference of continuous variables. The p-value of <0.05 was considered statistically significant.

RESULTS

During the study, 300 pregnant mothers who were screened for GDM at 24-28 weeks of gestation, 26 (8.7%) patients were diagnosed to have GDM. Re-screening of initial screen negative 274 mothers was performed at 32-34 weeks and GDM was found in 8 (2.9%) cases. Overall GDM was noted in 34 per 300 cases (11.3%) [Table/Fig-1].

Gestational age	Total cases	Screen positive (GDM) n (%)	Screening negative n (%)	Odds	Odds ratio (95% CI)	Chi-square value	p-value
24-28 weeks	300	26 (8.7)	274 (91.3)	0.09	3.1551 (1.4033-7.0938)	8.4876	0.00358
32-34 weeks	274	8 (2.9)	266 (97.1)	0.03			

[Table/Fig-1]: Screening of antenatal mothers by GTT (DIPSI method) at different gestational ages.

Over all GDM cases, 34/300=11.33%

The demographic characteristics showed that 21 cases (44.7%) of pregnant GDM mothers were in 31-35 years of age and 17 cases (50%) were multiparous (odds ratio, 0.6319; p-value=0.2062) [Table/Fig-2,3].

Age (years)	Non GDM n (%)	With GDM n (%)	Total	Chi-square value	p-value
≤ 20	36 (100)	0	36 (100)	74.5830	<0.0001
21-25	131 (100)	0	131 (100)		
26-30	73 (84.9)	13 (15.1)	86 (100)		
31-35	26 (55.3)	21 (44.7)	47 (100)		
Total (row %)	266 (88.7)	34 (11.3)	300		

[Table/Fig-2]: Association of age groups in study populations.

Parity	Non GDM	With GDM	Total	Chi-square value	Odds ratio	p-value
Multiparous	103	17	120	1.5977	0.6319 (0.3088-1.2832)	0.2062
Row %	85.8	14.2	100			
Col%	38.7	50.0	40.0			
Nulliparous	163	17	180			
Row %	90.6	9.4	100			
Col%	61.3	50.0	60.0			
Total (row %)	266 (88.7)	34 (11.3)	300			

[Table/Fig-3]: Association of parity with and without GDM.

Different variables like history of diabetes, history of pregnancy loss and stillbirths were noted in 6 (17.64%), 2 (5.88%) and 5 (14.7%) cases of GDM mothers, respectively [Table/Fig-4].

Variables	N (%)
Age (in years), n=300	
≤ 20	36 (12.0)
21-25	131 (43.7)
26-30	86 (28.7)
31-35	47 (15.6)
Parity, n=300	
Multiparous	120 (40)
Primiparous	180 (60)
Gestational age 24-28 weeks (n=300)	
GDM	26 (8.7)
Non GDM	274 (91.3)
32-34 weeks (n=274)	
GDM	8 (2.9)
Non GDM	266 (97.1)
Family H/o diabetes	
GDM (34)	6 (17.6)
Non GDM (266)	21 (7.89)

H/o Recurrent pregnancy loss	
GDM (34)	2 (5.88)
Non GDM (266)	4 (1.50)
H/o Macrosomia	
GDM (34)	2 (5.88)
Non GDM (266)	3 (1.13)
H/o stillbirths	
GDM (34)	5 (14.71)
Non GDM (266)	20 (7.52)

[Table/Fig-4]: Analysis based on different variables of interest.

The incidence of infection, preeclampsia, and preterm delivery was 5 (14.7%), 5 (14.7%) and 25 (73.5%), respectively among GDM mothers [Table/Fig-5].

Twenty-six women (76.5%) of GDM mothers were delivered by caesarean section (odds ratio, 0.0935; p-value <0.0001) [Table/Fig-6]. Thirty-one (91.2%) babies were born without any hypoglycaemia, and RDS was noted in 4 (11.8%) cases among neonates of GDM mothers [Table/Fig-7].

Maternal morbidities		Non GDM (n=266)	With GDM (n=34)	Chi-square value	p-value
Infection	No, n (%)	266 (100)	29 (85.3)	39.7807	<0.0001
	Yes, n (%)	0	5 (14.7)		
Preeclampsia	No, n (%)	266 (100)	29 (85.3)	39.7807	<0.0001
	Yes, n (%)	0	5 (14.7)		
IUFD ^s	No, n (%)	266 (100)	32 (94.1)	15.7521	<0.0001
	Yes, n (%)	0	2 (5.9)		
Postpartum Haemorrhage (PPH)	No, n (%)	266 (100)	30 (88.2)	31.7170	<0.0001
	Yes, n (%)	0	4 (11.8)		
Polyhydramnios	No, n (%)	266 (100)	32 (94.1)	15.7521	<0.0001
	Yes, n(%)	0	2 (5.9)		
Preterm	No, n (%)	256 (96.2)	9 (26.5)	142.3985	<0.0001
	Yes, n (%)	10 (3.8)	25 (73.5)		

[Table/Fig-5]: Association of different maternal morbidities in study groups.

^sIUFD: Intrauterine foetal death

MOD	Non GDM	With GDM	Chi-square value	Odds ratio	p-value
LSCS	62 (23.3)	26 (76.5)	41.1028	0.0935 (0.0403-0.2170)	<0.0001
VD	204 (76.7)	8 (23.5)			
Total	266	34			

[Table/Fig-6]: Mode of delivery with GDM and normal pregnancies.

n (col%), MOD: Mode of delivery; LSCS: Lower segment caesarean section; VD: Vaginal delivery

Foetal complications		Non GDM (n=266) (%)	With GDM (n=34) (%)	Chi-square value	p-value
Hypoglycaemia	No	266 (100)	31 (91.2)	23.707	<0.0001
	Yes	0	3 (8.8)		
RDS [†]	No	266 (100)	30 (88.2)	31.7170	<0.0001
	Yes	0	4 (11.8)		
Congenital anomaly (anencephaly)	No	266 (100)	33 (97.1)	7.8497	0.0050
	Yes	0	1 (2.9)		
Foetal macrosomia	No	266 (100)	32 (94.1)	15.7521	<0.0001
	Yes	0	2 (5.9)		
Hyperbilirubinaemia	No	265 (99.6)	31 (91.2)	16.3529	<0.0001
	Yes	1 (0.4)	3 (8.9)		
NICU admission	No	261 (98.1)	23 (67.6)	55.4474	<0.0001
	Yes	5 (1.9)	11 (32.4)		

[Table/Fig-7]: Foetal complications in non GDM and GDM groups.

[†]RDS: Respiratory distress syndrome

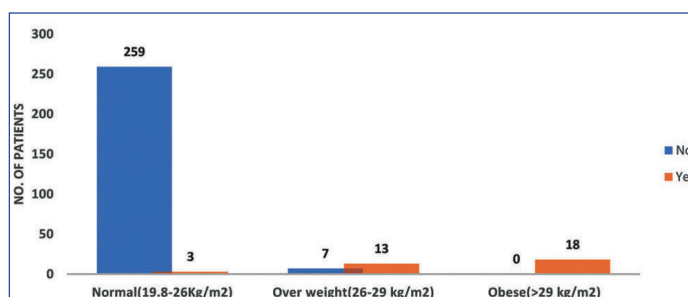
The newborns delivered in GDM mothers had mean birth weight of 2.5324±0.6503 kg, and mean Appearance, Pulse, Grimace, Activity, and Respiration (APGAR) score at 1 and 5 minutes were 8.0882±2.2879 and 8.4706±2.2460, respectively [Table/Fig-8].

[Table/Fig-9] represents the association of BMI with GDM and without GDM. In GDM groups 18 (52.9%) patients were obese and 13 (38.2%) cases were overweight (p-value <0.0001).

Parameters		Number	Mean±SD	Median	Min	Max	p-value*
Birth weight (kg)	Non GDM	266	2.7297±0.2145	2.7000	1.8000	3.4000	0.0003
	GDM	34	2.5324±0.6503	2,5000	1.8000	4.3000	
APGAR score at 1 min (<7)	Non GDM	266	9.1842±0.5562	9.000	7.0000	10.0000	<0.0001
	GDM	34	8.0882±2.2879	9.000	0.0000	10.0000	
APGAR at 5 min (<7)	Non GDM	266	9.2030±0.4557	9.0000	8.0000	10.0000	<0.0001
	GDM	34	8.4706±2.2460	9.0000	0.0000	10.0000	

[Table/Fig-8]: Distribution of foetal weight and APGAR: Appearance, pulse, grimace, activity, and respiration score at 1 and 5 minutes.

*p-value is calculated by independent sample t-test



[Table/Fig-9]: Association of BMI with GDM and without GDM in pregnancy.

Twenty-three (67.65%) neonates in the study population of GDM had normal birth weights between 2.6-3.9 kg and 4 (11.76%) had birth weights more than 4 kg. Anencephaly was noted in one case. Among seven babies having birth weight of <2.5 kg, two babies were Foetal Growth Restriction (FGR) due to preeclampsia, two had IUFD and rest were preterm.

DISCUSSION

In the present study, gestational diabetes was noted in 34 cases (11.3%) whereas Swain S et al., and Wong T et al., noted GDM in (5% and 86.1%) cases, respectively [10,13]. The overall incidence of GDM was also lower (5.7%) as noted by Sulochana M et al., [14]. The difference in different geographical areas was due to socio-demographic profiles and criteria used for screening and diagnosis of GDM. Asian population have a higher risk of GDM (11.9%) compared to the rest of the groups [15].

In the present study, pregnant women over the age of 30 years were significantly less (15.7%) as fewer women opt for pregnancy during the later year of life although, the majority of them develop (21/34, 61.8%) GDM. Age and obesity influence the likelihood of GDM. In the present study, 40% of pregnant women were multigravida and 60% were nulliparous which correlates well with the study of Swain S et al., [10]. The incidence of GDM in multiparous women was 50% and the association of nulliparity and multiparity with diagnosed GDM in present study was not statistically significant (odds ratio, 0.6319; p-value=0.2062). Few studies have shown that high parity is to be associated with a high prevalence of GDM [16,17]. The higher rate of GDM among multigravida may be due to the confounding effect of maternal age. The incidence of GDM in obese person in present study was 18 (52.9%), whereas Sulochana M et al., noted significant correlation between obesity and the incidence of GDM [14].

In present study, women having complications like polyhydramnios, in the GDM group was 2 (5.9%), whereas in the non GDM women, it was 0. The corresponding findings of polyhydramnios in GDM and non GDM groups in the study of Sulochana M et al., were 3 (14.2%) and 10 (2.6%), respectively [14].

With respect to the mode of delivery, caesarean section was significantly higher among GDM patients (odds ratio 0.0935; p-value <0.0001) in present study. Similarly, Shingala KD et al., also noted a high caesarean section rate (60%) in their study [18]. Several studies showed a positive correlation between GDM and preeclampsia. This significantly increases maternal and perinatal morbidity and mortality [19,20]. The present study was associated with neonatal hypoglycaemia (8.8%) and RDS (11.8%) in the newborn babies of GDM mothers which were like to the findings of Swain S et al., [10]. IUFD was noted in 2 (5.9%) cases among GDM mothers in present study which was comparable to 6% in the study by Saxena P et al., [21].

Twenty-three (67.65%) neonates in the present study population of GDM had normal birth weights between 2.6-3.9 kg and 4 (11.76%) had birth weights of more than 4 kg. Anencephaly was noted in one case. Among seven babies having a birth weight of <2.5 kg, two babies were FGR due to preeclampsia, two had IUFD and the rest were preterm. A study by Shingala KD et al., showed 65% of babies had birth weight between 2.6-3.9 kg and (13.75% had weight above ≥ 4 kg indicating good glycaemic control [18]. In present study, NICU admission for various reasons was required in 32.4% of newborn babies of GDM mothers. Association of NICU admission among GDM patients was statistically significant (Odds ratio=24.9652; p-value <0.0001) when compared with non GDM mothers. About 76% of infants of GDM mothers required NICU admission in the study of Reddy KM et al., [19].

So, universal screening and re-screening for GDM, better antenatal care, supervision of delivery and expert paediatric care of newborn babies will be more practical to overcome the burden of complications. If the GDM is not well-controlled primarily, the metabolic abnormalities of glucose metabolism may affect the mother and foetus in later life.

Limitation(s)

The study was done in a single centre only. The study was carried out only in a tertiary care hospital, so hospital bias cannot be ruled out. The ongoing Coronavirus Disease-2019 (COVID-19) pandemic and lockdown hampered the study process further.

CONCLUSION(S)

The GDM is a frequently encountered complication of pregnancy. Multiparity, advanced maternal age, higher BMI are the risk factors for GDM. Women with GDM have an increased risk of maternal and perinatal complications. Universal screening of GDM in all antenatal clinics should be employed at 24-28 weeks by a single step screening and diagnostic procedure as it is safe, fast, cheap, easy to perform, and patient friendly. There is a clear need to repeat the screening procedure

at 32-34 weeks of gestation among those who are screened negative in earlier weeks, otherwise, a significant number of GDM cases will be missed. This implies good maternal care and intervention strategies.

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