GESTATIONAL DIABETES MELLITUS- PREVALENCE AND OBSTETRIC OUTCOME

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ABSTRACT

BACKGROUND

We wanted to identify the prevalence and foetomaternal outcome of gestational diabetes mellitus in antenatal patients attending IMCH, Government Medical College, Kozhikode.

METHODS

This is a retrospective cohort study of singleton pregnancies, irrespective of age and parity, who delivered in our institution in 2017. Cohort was identified from the parturition register and data was collected from the case records. The variables studied are age, obstetric score, BMI, HbA1c level, diagnosis, management, mode of delivery and neonatal outcome.

RESULTS

In total, 400 pregnant women were studied. Prevalence was found to be 16%. Multigravidae showed twice and grand-multigravidae had 5 times increased risk of developing gestational diabetes. Obese group had a significantly high prevalence of GDM. Patients with positive family history and a past history of gestational diabetes had 11 times and 6 times more risk of gestational diabetes in the index pregnancy. As per the study, a 2-h 75-g OGTT value of $\geq$ 140 mg/dl has 6 times more risk. An increased rate of induction of labour (63%) was observed. Incidence of C-section, macrosomia, still birth, neonatal hyper-bilirubinaemia and foetal anomalies were also found to be increased.

CONCLUSIONS

The prevalence of GDM in this study is 16%. Majority of women belonged to the expected reproductive age of 25-35 years. Multigravidae showed twice and grand-multigravidae showed five times increased risk of developing GDM. Pregnancy outcome is largely determined by GDM and obesity, alone or in combination. A positive family history and a past history of GDM increase the risk of having GDM in the index pregnancy.

KEYWORDS

GDM, NDDG, ADA, HAPO, NICE, OGTT, WHO, BMI, C-Section

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BACKGROUND

Diabetes is a major cause of maternal morbidity as well as peri-natal morbidity and mortality. In a study conducted in the year 2000, to estimate the global prevalence of diabetes, India was found to have the largest number of diabetics (31.7 million) and by the year 2030, it is estimated to be about 79.4 million.[1]

In 1964, O'Sullivan and Mahan suggested specific criteria to identify women at risk of developing GDM. The criteria was later modified by the National Diabetes Data Group (NDDG) in 1979 and Carpenter and Coustan. In 2000, American Diabetes Association (ADA) recommendation was to use Carpenter and Coustan modification of O'Sullivan and Mahan original values and this resulted in a higher prevalence of GDM.[2] Despite these efforts, there is a lack of consensus on diagnostic threshold.[3,4] In 2008, the result of "Hyperglycaemia and Adverse Pregnancy Outcomes (HAPO)" study was published. This major observational study provided us valuable information regarding the risks of adverse outcome associated with various degree of maternal glucose intolerance. Based on the result of this study, The International Association of Diabetes and Pregnancy Study Group (IADPSGC) proposed new diagnostic criteria in 2010.[1,3,5,6]

The prevalence of GDM may range from 1-14% of all pregnancies. Higher prevalence is noted in African, Asian, Indian and Hispanic women. In India, the prevalence of diabetes is very high, about 1-14% of all pregnancies are complicated by diabetes mellitus and 90% of them are gestational diabetes mellitus (GDM).[7,8] It is known that pregnancy is a diabetogenic condition and insulin sensitivity is reduced by as much as 80%. GDM is defined as glucose intolerance that was not present or recognized prior to pregnancy.[9,10] It does not exclude the possibility that unrecognized glucose intolerance may have antedated or begun concomitantly with the pregnancy.[11,12] Detection of

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GDM during pregnancy provides an opportunity to identify women at risk of short term and long term complications.[1,13]

In 2008, National Institute for Health and Clinical Excellence (NICE) guideline recommended that all women should be assessed for risk factors at the first antenatal visit.[4,14] Women with body mass index (BMI) >30 Kg/$m^{2,}$ previous macrosomic baby, previous GDM and family history of diabetes should be offered a diagnostic test using 75 g 2-hour oral glucose tolerance test (OGTT) at the first visit. Many centers perform a 75-g 2-hr OGTT as both a screening test and a diagnostic test, and most centers in United States rely on a 2-step method described above.[15] The WHO extrapolated the diagnostic cut-off from non-pregnant population for 75-g 2-h OGTT as 140 mg/dl.[16] Studies on pregnant women have shown that women with diabetes have undesirable pregnancy outcomes compared to non-diabetic mothers, the wide spectrum of complications being higher incidence of pre-eclampsia, increased rates of congenital malformations, obstetric complications, still births, macrosomia, increased risk of pre-term delivery, peri-natal morbidity and mortality.[17] These various maternal and fetal complications in diabetic pregnancies can be minimized by early detection of diabetes and strict glycaemic control.[18] A study in Indian population has also shown that tighter glycaemic control can favourably alter adverse outcome parameters in case of gestational diabetes mellitus.[19] Studies done in the second and third trimester of pregnancy have shown that poor maternal glycaemic control is associated with neonatal morbidity.[4,20] Improvement of obstetrics and new-born care in these patients has resulted in a significant reduction in neonatal morbidity and mortality over the last few decades.[21] However, progress has been slow in some areas of clinical management, especially in Indian population. Hence there is a need to create awareness regarding the importance of tight glycaemic control. Thus, adequate screening, strict control of hyperglycaemia and a careful planning for pregnant diabetic women ensure a happy outcome. This study was undertaken to see the prevalence and maternal and foetal outcome of gestational diabetes mellitus in a tertiary care centre.

We wanted to identify the prevalence and foetomaternal outcome of gestational diabetes mellitus in antenatal patients attending IMCH, Government Medical College, Kozhikode.

METHODS

Study Design
Retrospective cohort study.

Study Period
Four hundred cases from 2017.

Study Subjects
Four hundred patients who attended Institute of Maternal and Child Health (IMCH), Department of Ob/Gyn during the study period were selected from the parturition register and data were collected from the case records.

Inclusion Criteria
Four hundred patients with singleton pregnancies were selected consecutively irrespective of age and parity.

Exclusion Criteria
Multifetal gestations
Pre-gestational diabetes mellitus.

Sample Size
Expecting a prevalence of 20%, the minimum sample size required is

$n = 4\ pq/d^2$, where p = 20, q = 60 and d = 20% of p.

n = 400. Hence 400 cases were studied.

Statistical Analysis
Statistical analysis is done using Epi info software. Data is presented as frequency and percentage. Chi square test and Fisher's exact test is used to compare between GDM and non-GDM groups. The comparison of mean is done by T test. Risk is estimated using odds ratio (OR) and relative risk (RR). 95% confidence interval (CI) also is estimated. All tests are two sided and a p value < 0.05 is considered as statistically significant.

Ethical Aspects
Permission is taken from hospital superintendent and department of Ob/Gyn for studying the records.

Methodology
This is a retrospective cohort study conducted in the Department of Obstetrics and Gynaecology, Government Medical College, Kozhikode, in the year 2017. Four hundred consecutive patients who attended the Institute of Maternal and Child Health (IMCH), were selected. The above mentioned population with singleton pregnancy were included, irrespective of age and parity. Patients with multifoetal gestation and those with pre-gestational diabetes mellitus were excluded. Cohort was identified from the parturition register and data were collected from case records of patients under inclusion criteria to find out the test used for diagnosis of GDM (WHO/IADPSG), and mode of management. Other variables studied were age, obstetric score, BMI, HbA1c values, mode of delivery, baby weight and Apgar score. Oral Glucose tolerance test (OGTT) is recommended by World Health Organization (WHO) to diagnose gestational diabetes mellitus. A fasting sample for glucose estimation is collected; following which 75-g oral glucose load is administered followed by a plasma glucose estimation at 2 hour. The normal reference range of serum or plasma glucose is < 140 mg/dl at 2 hours after a 75-g glucose load (WHO). A two-hour value of 140-199 mg/dl is considered impaired glucose tolerance and a value > 200 mg/dl is considered as diabetes.

RESULTS
Out of the 400 patients 64 patients satisfied the criteria for GDM thus giving a prevalence of 16% in our institution. There was no statistically significant difference between

GDM and non-GDM patients with respect to maternal age. Multigravidae had two times increased risk of developing GDM and in grand multi, this is increased to five times. Compared to normal patients, obese group has a significantly high prevalence of GDM. A positive family history has 11 times higher risk of developing GDM. Past history of GDM shows 6 times increased risk of developing GDM in the index pregnancy. Patients with GTT value >= 140 have 6 times increased risk as compared to those with GTT value <140. HbA1c >=5 had almost 5 times increased risk of developing GDM. C-section rates were 1.5 times more in cases with GDM. GDM patients are found to have 70 times more risk for intra-uterine foetal demise (IUD). No significant variation is seen with regard to Apgar at 1 minute. Incidence for low birth weight is also increased and all babies with weight > 4 Kg belonged to the GDM group. Incidence of hyper-bilirubinaemia was 7 times more in GDM patients.

Age (years)	Number	GDM	Non-GDM	OR	95% CI	p Value
<=19	15	0	15	1#		
20-24	175	32	143			0.079
25-35	196	32	164			0.134
>=35	14	0	14			
Total	400	64	336			

Table 1. Age

*statistically significant, # reference category

Gravida	Total	GDM	Non-GDM	OR	95% CI	p Value
Primi	178	18	160	1#		
Multi	197	37	160	2.19	1.14-4.24	0.017*
Grand multi	25	9	16	5.33	1.84-15.34	0.001*
Total	400	64	336			

Table 2. Obstetric Score

BMI	Total	GDM	Non-GDM	OR	95% CI	p Value
< 20	122	0	122			0.0002*
20 – 24.9	203	23	180	1#		
25 – 29.9	42	8	34	1.84	0.69-4.79	0.265
>= 30	33	33	0			< 0.0001*
Total	400	64	336			

Table 3. Body Mass Index (BMI)

Family History	Total	GDM	Non-GDM	OR	95% CI	p Value
No	313	23	290	1#		
Yes	87	41	46	11.24	5.94-21.39	<0.0001*
Total	400	64	336			

Table 4. Family History of DM

Past h/o GDM	Total	GDM	Non-GDM	OR	95% CI	p Value
0	178					
No	152	13	139	1#		
Yes	70	24	46	5.58	2.48-12.7	<0.0001*
Total	400	37	185			

Table 5. Past History of GDM

GTT	Total	GDM	Non-GDM	OR	95% CI	p Value
< 140	363	47	316	1#		
>= 140	37	17	20	5.71	2.64-12.39	<0.0001*
Total	400	64	336			

Table 6. 2-h 75-g OGTT in Second Trimester

HbA1c	Total	GDM	Non-GDM	OR	95% CI	p Value
< 5	204	14	190	1		
>= 5	196	50	146	4.65	2.38-9.19	<0.0001

Table 7. HbA1c

Total	GDM	Non-GDM	RR	95% CI	p Value
400	64	336			
Treatment					
0	0	336			
MNT@	50(78%)	0			
Insulin	14(22%)	0			

Table 8. GDM and Treatment

	Total	GDM (%)	Non-GDM (%)	RR	95% CI	p Value
Type of Delivery						
Spontaneous	184	15(23%)	169(50%)	1#		
Induced	98	40(63%)	58(17%)	2.85	2.16-3.75	<0.0001*
Elective CS	118	9(14%)	109(33%)	0.96	0.56-1.64	0.869
Total	400	64	336			
Pre-Term Labour						
No	328	27(42%)	301(90%)	1#		
yes	72	37(58%)	35(10%)	5.55	3.81-8.09	<0.0001*
Total	400	64	336			
Mode of Delivery						
Vaginal	222	49(77%)	173(51%)	1#		
LSCS	169	15(23%)	154(46%)	1.5	1.22-1.71	0.0005*
Instrumental	9	0	9(3%)			0.21
Total	400	64	336			

Table 9. Maternal Outcome

	Total	GDM	Non-GDM	RR	95% CI	p Value
Baby Outcome						
Live	368	50	318	1#		
IUD@	15	14	1	69.78	9.34-521.3	<0.0001*
NND@	17	0	17			0.144
Total	400	64	336			
Apgar 1 Minute						
9	353	49	304	1#		
< 9	32	1	31	0.22	0.03-1.55	0.1
Birth Weight (Kg)						
< 2.5	50	24	26	6.75	4.25-10.7	<0.0001*
2.5- 4	332	22	310	1#		
>4	18	18	0			<0.0001*
Total	400	64	336			

Table 10. Neonatal Outcome

@Intra-uterine demise @Neonatal death

Complications	Total	GDM	Non-GDM	RR	95% CI	p Value
Nil	281	16	265	1#		
Hypoglycaemia	15	2	13	2.38	0.58 - 9.74	0.229
Hyperbilirubinaemia	61	32	29	6.76	4.53 - 10.08	<0.0001*
Sepsis	20	0	20			0.378
Others	8	0	8			1
Total	385	50	335			

Table 11. Neonatal Complications

Foetal Anomalies	Total	GDM	Non GDM	p Value
Nil	374	39	335	1#
NTD@	4	4	0	< 0.001*
Cardiac	7	7	0	< 0.0001*
Total	385	50	335	

Table 12. Foetal Anomalies

DISCUSSION

The present study included 400 pregnant women from Institute of Maternal and Child Health, Government Medical College, Kozhikode. The prevalence of GDM is between 15-20% in our institution for the past ten years and this study shows it as 16%. In India, the National average of prevalence of GDM is about 10-15% and hence, the magnitude of the problem in pregnancy is large.[22] Our

institution being a tertiary care centre, prevalence is slightly higher than the National average. It is 2-5% in USA according to Deborah L. Conway.[23] The study population had majority of the women in the expected age group of 25-35 years (49%). Advanced maternal age is a considered risk factor and nearly 4% of them were ≥35 years. Of the women studied, 56% were multi gravidae and this correlates well with the general trend as observed in various population based surveys. There was no statistically significant difference between GDM and non-GDM patients with respect to maternal age. Multi-gravidae showed a twice increased risk of developing GDM and it was five times more in grand multi-gravidae.

Of the 400 women studied, 33 had BMI >30 and developed gestational diabetes. The relation between obesity and diabetes is well established.[24] Our study also could derive a similar conclusion. The independent association of GDM and obesity alone or in combination with adverse pregnancy outcome is well established by Hyperglycaemia and Adverse Pregnancy Outcome (HAPO) Study.[25,26] According to HAPO study, 25% of those diagnosed with GDM were obese, though we got it as 10%. In this study, a positive family history of diabetes mellitus gives 11 times higher risk of developing GDM and a past history of GDM increases the risk by 6 times. According to H. Kleinwechter et al, for women of European origin, the recurrence risk of GDM in a subsequent pregnancy is 20-50% and it increases up to 50-84% for ethnicities with high diabetes risk (Asia, Latin America).[27] For diagnosis of GDM, the participants underwent a 2-h 75-g OGTT as per recommendations of WHO.[28] Those women with risk factors such as obesity, first degree family history of diabetes, previous history of GDM and/ macrosomia were subjected to 2-h 75-g OGTT as soon as possible and the remaining patients with low risk received GDM testing between 24 and 28 weeks of gestation.[20] In 2008, National Institute for Health and Clinical Excellence (NICE) guideline recommended that all women should be assessed for risk factors at the first ante-natal visit.[4,14] Participants with a 2-h 75-g OGTT value of ≥140mg/dl showed a six times increased risk for developing GDM as compared to those with value <140 mg/dl in the present study, with a statistically significant P value. Dominic F. H.LI and Vivian C. W. Wong et al found that, when the WHO criteria and the National Diabetes Data Group (NDDG) criteria were compared, the 2-h plasma glucose value after the 100 g load was the most discriminative in differentiating the glycaemic status.[29] According to them, when only the 2-h plasma glucose values were assessed, the WHO test agreed with the NDDG test in the diagnosis of glucose intolerance in 60% of subjects only. Reducing the glucose load from 100 g to 75 g produced a reduced glucose response in 49% of the subjects, with a significant decrease in the area under the glucose response curve.[29]

In a study by Heinz Drexel et al, 86% of the patients required insulin for a tight metabolic control where as 50% of the cases were treated with insulin by frank D. Johnstone et al.[30,31] In our study, 78% of the GDM cases were treated with MNT and only 22% needed insulin for glycaemic control. We had an increased rate of induction of labour (63%) in GDM patients as compared to (17%) in non-GDM group. This is comparable to the findings by D. M. Jensen et al (61% vs. 24%), and Turki Gasim, who also found a significantly increased rate of induction.[32,33] This is in contrast to the findings of Deborah L. Conway et al, who got a much lesser percentage of induction (6.8%).[34] Samuel Lurie and colleagues concluded that elective induction of labour at 38 to 39 weeks of gestation is suggested for insulin-requiring diabetic women in order to reduce the incidence of shoulder dystocia.[35] According to H. Kleinwechter et al, a routine, elective induction of labour in all pregnant women with GDM, say at week 38, does not improve the outcome of the pregnancy for mother or child.[27]

In this study, 14% of the patients underwent elective C- section, which is higher than that obtained by Deborah l. Conway et al (3.8%).[23,34] Overall, 23% of the GDM patients underwent caesarean delivery in this context. A significantly increased C-section rate is reported by Per Glud Oversen et al, Turki Gasim, D. M. Jensen et al (33% vs. 21%), John D. Jacobson et al, K. O. El Mallah et al and in GINEXMAL RCT by Gianpaolo Maso et al.[32,33,36,37,38,39] Summary and Recommendations of the Fifth international Workshop also supported a liberal policy toward caesarean delivery when foetal overgrowth is suspected.[40] A substantially high rate of 62% was obtained by the Prospective population based survey of outcome of pregnancy in diabetic women, which is in contrast to the study by Samuel Lurie et al, in which no increase in C-section rate was demonstrated.[35,41] In our study, the chance for a C-section in GDM group was 1.5 times more than the non-GDM population. Pre-term labour is nearly twice as common among diabetic mothers as in the general hospital population.[42] In our study, pre-term labour occurred six times more in GDM patients than in the non-GDM group (58% vs. 10%), though D C Dutta found it as 20%.[8] Substantial excess of premature births in diabetic pregnancies are reported by the Prospective population based survey of outcome of pregnancy in diabetic women: results of Northern Diabetic Pregnancy Audit, 1994.[41] Similar results are obtained from studies by Turki Gasim and H. Kleinwechter et al.[27,32]

Table 9 shows the neonatal outcome of this study. The risk of still birth was observed as 70 times more in GDM patients. Though Per Glud Ovesen et al observed a comparable still birth rate in GDM and non-GDM groups, a significantly higher still birth rates and perinatal and neonatal mortality was observed by H. Kleinwechter et al, Prospective population based survey of outcome of pregnancy in diabetic women, Mary C M Macintosh et al, Oded Langer MD et al and Heinz Drexel et al.[43,44,] Perinatal mortality rates nearly four times greater than non-diabetics and unexplained foetal deaths were observed by Frank D. Johnstone et al.[30] An increased rate of admission in neonatal intensive care unit (NICU) was also observed by H. Kleinwechter et al, Turki Gasim, D. M. Jensen et al, Per Glud Ovesen et al, Caroline A. Crowther et al and John R Moss et al.[45,46] No significant change in rates of Apgar score at I

minute was noted in this study, while Per Glud Ovesen et al noted that low Apgar score was increased in GDM.[38] All the babies with birth weight >4kg belonged to the GDM group in this study, but there was a significantly increased risk for low birth weight too, which may be partly due to the increased rate of pre-term labour. Frank D. Johnston et al found lower birth weights in patients with impaired glucose tolerance.[30] Macrosomia is identified in studies by H. Kleinwechter et al, Turki Gasim, K. O. El mallah et al, Per Glud Ovesen et al, Summary and Recommendations of the Fifth International Workshop, Gianpaolo Maso et al and Frank D. Johnstone et al. Incidence of macrosomia was doubled (28%) in this study as compared to D. M. Jensen et al, who found it as 14% in GDM patients.

The risk of hyperbilirubinaemia was significantly high and was almost 7 times more in the GDM group. No much difference was observed with reference to hypoglycaemia between the groups. D. M. Jensen et al showed a higher incidence of hypoglycaemia (24%) as compared to 4% in this study. Hyperbilirubinaemia was the main indication for NICU admission, amounting to 64% in GDM patients. Similar results are also obtained by John R Moss et al.[46] Foetal anomalies were not identified in non-GDM patients. Cardiac anomalies ranked first closely followed by neural tube defects (NTD) and both were statistically significant. Similar studies were obtained by Turki Gasim, Prospective population based survey of outcome of pregnancy in diabetic women and Mary C M Macintosh et al. Despite considerable advances in the management of GDM, the rate of congenital malformations has not changed in several decades. Congenital malformations have replaced intra uterine foetal demise (IUD) and respiratory distress syndrome (RDS) as a major cause of morbidity and mortality in infants born to women with diabetes mellitus. The frequency of these malformations has been estimated at 6-10%, which represents a 3-5 fold increase compared with the rate seen in the general population and we had a much higher rate of 17% inclusive of still births.[47]

CONCLUSIONS

The prevalence of GDM in this study is 16%. Majority of women belonged to the expected reproductive age of 25-35 years. Multigravidae showed twice and grand-multigravidae showed five times increased risk of developing GDM. Pregnancy outcome is largely determined by GDM and obesity, alone or in combination. A positive family history and a past history of GDM increase the risk of having GDM in the index pregnancy. There is an increased rate of induction of labour and C-section in GDM group. Risk for pre-term labour and still births increased substantially. Macrosomia and foetal anomalies are identified only in GDM group. Inclusion of a targeted screening for cardiac defects in the current management of pregnant women with diabetes needs to be considered. As the incidence of diagnosed diabetes continues to increase, especially at younger ages, the number of women with diabetes in pregnancy will also continue to rise. Treatment of gestational diabetes reduces serious perinatal morbidity and may also improve woman's health-related quality of life. As these women are likely to develop overt diabetes in the non-pregnant state, and subsequently to develop serious complications of this disease, improving glycaemic control, both during pregnancy and thereafter, should be the priority. Women with GDM still have increased incidence of obstetric and neonatal complications, which could imply that treatment of women with GDM should be tightened. If we take good care of the diabetes, pregnancy will take care of itself.

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