

Maternal and Foetal Outcomes of Gestational Diabetes Mothers Treated with Human Insulin

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ABSTRACT

Background: The most common adverse event that is associated with GDM is that it has led to higher incidence of maternal diabetes mellitus later in life and the major morbidities among the infants born to the diabetic mothers include respiratory distress, macrosomia, polycythaemia, hypoglycaemia, hypocalcaemia, hypomagnesemia, and congenital malformations. As most of the oral hypoglycaemic agents is prone to cause teratogenic effects the most preferred was the insulin therapy and the subcutaneous insulin therapy has been considered as the standard therapy in the management of GDM. **Aim:** To assess the factors associated in the incidence of diabetes among the gestational diabetes mothers and to assess the effect of insulin on them in terms of maternal and foetal outcome. **Methodology:** A prospective study was undertaken among the gestational mothers with diabetes for a period of one year during Jan 2015 – Dec 2015 at the Government Medical College Hospital, Salem. A total of 150 maternal mothers with more than 24 weeks of gestation were included in the study and who had been diagnosed as gestational diabetes mellitus. The insulin used for majority of the patients was novo rapid and it was used four times a day. The outcome parameters which were used for antenatal mothers were their weight gain and the type of complications at the time of delivery whereas for the neonates their birth weight and the necessity for NICU admission were considered as the outcome parameters. **Results:** the risk factors found to be associated with the gestational diabetes among the study population were age more than 30 years, BMI of more than 25, family history both father and mother being diabetic, having a bad obstetric history, primigravida and the mothers who had gained more than 7 kgs in the first two trimesters. majority of the mothers delivered macrosomia babies (29.3%), hypoglycaemia and hypothyroidism was found only in 6% and 5.3% of the new-born babies and 4 were still births and 15 babies were got admitted to NICU for respiratory distress. The pearson's correlation had shown a strong positive correlation between the dose of the insulin given to the antenatal mother and their increase in the weight ($r=0.819$) and a strong negative correlation with the weight of the neonate ($r= -0.532$). **Conclusions:** Gestational diabetes mellitus being associated with maternal and neonatal adverse outcomes, so maintaining adequate blood glucose levels in GDM helps in reducing the morbidity for both the mother and baby. Insulin would be a right choice for treating GDM and when initiated early it prevents most of the complications due to GDM both in the mother and the neonate.

Key words: gestational diabetes mellitus, insulin, maternal outcome, foetal outcome.

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INTRODUCTION

The International Diabetes Federation had reported that currently there are 100 million people living with diabetes throughout the world with an estimated prevalence of 6% among the adults.^[1] The initial study done by the Indian Council of Medical Research on the prevalence of diabetes had quoted a prevalence of 2.3 % in urban areas in 1970's which had now risen to 13 – 20% in 2000 and the numbers had also included gestational diabetes mellitus (GDM). This had alerted the physicians to have a direct and special attention to this population, which is being considered as a vulnerable group especially in developing countries like India.^[2,3]

GDM is defined as glucose intolerance of varying degree which was first recognised during pregnancy with or without remission after pregnancy.^[4] Prevalence of gestational diabetes mellitus varies widely from country to country as many factors related to the race and ethnicity plays a major role in it. Depending on the population studied and the diagnostic test employed based on the WHO and FOGSI guidelines the prevalence had ranged from 2.4 to 21 per cent of all pregnancies.^[5,6] Similarly in India also the prevalence varies due to the wide difference in their living conditions, socio-economic levels and their dietary habits.

The most common adverse event that is associated with GDM is that it has led to higher incidence of maternal diabetes mellitus later in life and the major morbidities among the infants born to the diabetic mothers include respiratory distress, macrosomia, polycythemia, hypoglycemia, hypocalcemia, hypomagnesemia, and congenital malformations and above all those infants are at risk of developing diabetes later in their life.^[7] Perinatal outcomes associated with poor glycemic control in mothers are associated with as high as 42.9% mortality. Appropriate diagnosis and management of GDM can improve maternal and perinatal outcome.^[8,9]

Appropriate diet, alone or associated with physical exercise, does not suffice to control blood glucose levels in pregnant women. The diabetes management in GDM patients usually requires a pharmacological intervention either in the form of oral hypoglycemic drugs or insulin. As most of the oral hypoglycemic agents is prone to cause teratogenic effects the most preferred was the insulin therapy and the subcutaneous insulin therapy has been considered as the standard therapy in the management of GDM.^[10,11] It requires modification based on the patient's body mass index, glucose levels and lifestyle.^[12] Therefore, detailed guidance for dose change of insulin is necessary to ensure the safe self-administration of insulin.

As very few studies had been done on the Indian mothers to assess the effectiveness of insulin therapy on the mothers and neonates and so this study was undertaken in South India to assess the effect of insulin on the outcome of maternal mothers and the neonates among the patients with gestational diabetes mellitus.

Aim: To assess the factors associated in the incidence of diabetes among the gestational diabetes mothers and to assess the effect of insulin on them in terms of maternal and foetal outcome.

MATERIALS AND METHODS

A prospective study was undertaken among the gestational mothers with diabetes for a period of one year during Jan 2015 – Dec 2015 at the Government Medical College Hospital, Salem. A total of 150 maternal mothers with more than 24 weeks of gestation were included in the study and who had been diagnosed as gestational diabetes mellitus based on the Diabetes in Pregnancy Study Group India (DIPSI) guidelines. The study was carried out after

obtaining the clearance from the institutional ethical committee and the informed consent from the patients.

A detailed pre-tested and a semi-structured questionnaire was developed for assessing the factors influenced in the causation of diabetes among the antenatal mothers. The questions related to the family history, dietary pattern, physical activity and the weight gain during the period of pregnancy were included in the questionnaire. The patients were given 75 g oral glucose load in non-fasting state and their blood glucose was assessed at the end of 2 hours and if the value was ≥ 140 mg/dl (DIPSI criteria) the patient was labelled as GDM. For the first two weeks all the patients were advised medical nutrition therapy and once again their fasting and post prandial blood sugar was assessed and when it was found to be higher than the normal and then we advised insulin therapy for all the mothers. The insulin used for majority of the patients was novorapid and for few patients actrapid were used and it was prescribed four times a day, before breakfast, pre-lunch, pre-dinner and at bed time. The dosages of insulin were adjusted based on their sugar levels. All the patients were regularly monitored once in 15 days till the time of delivery. The patients were educated about the warning signs of hypoglycaemia and they were instructed to report to our hospital whenever they experience those warning signs. On every visits the patients fasting blood sugar and the post-prandial blood sugar were assessed and the dose of insulin were adjusted accordingly. The HbA1C levels were also monitored once at the start of insulin therapy and one at the time of delivery.

The mother's weight gain was regularly monitored and they were also screened for hypertension and hypothyroidism. The outcome parameters which were used for antenatal mothers were their weight gain and the type of complications at the time of delivery whereas for the neonates their birth weight and the necessity for NICU admission were considered as the outcome parameters.

The data were entered and analysed by using SPSS version 19 and chi-square test was used for assessing the factors influence for the incidence of gestational diabetes among the antenatal mothers and the pearson's correlation was derived between the dose of insulin and the weight gain of the mother and the new-born weight.

RESULTS

The demographic characteristics of the entire study subjects were shown in Table 1.

It is seen from the table that the majority of the study subjects were in the age group of 26 – 30 years (59.3%) and the majority (80.6%) had the BMI of more than 25. Most of them were primi gravida with education upto primary school and majority belong to the lower middle and upper lower type of socio-economic class.

The risk factors found to be associated with the gestational diabetes among the study population were age more than 30 years, BMI of more than 25, family history both father and mother being diabetic, having a bad obstetric history, primigravida and the mothers who had gained more than 7 kgs in the first two trimesters. All these factors had found

to have the odds of more than 3 and they have a strong statistical significant association ($P < 0.0001$). Among all the factors family history of diabetes was found to have a higher odds (Table 2).

Table 1: Demographic characteristics of the study population.

Demographic variable	Frequency	Percentage	
Age	<20	2	1.3%
	20 – 25	38	25.3%
	26 – 30	89	59.3%
	>30	21	14%
	Mean \pm SD	27.24 \pm 2.16	
BMI	<18.5	3	2%
	18.5 – 24.9	26	17.3%
	>25	121	80.6%
Parity	0	62	41.3%
	1	69	46%
	2	17	11.3%
	3 and above	2	1.3%
Education	Not literate	28	18.6%
	Primary school	70	46.6%
	Middle / high school	51	34%
	Graduate	1	0.6%
	Socio-economic class		
Upper class	Upper class	0	0%
	Upper middle	6	4%
	Lower middle	68	45.3%
Upper lower	Upper lower	71	47.3%
	Lower	5	3.3%

Table 2: Risk factors associated with the incidence of gestational diabetes among the study population.

Variables	Frequency (n=150) (%)	Odds ratio	95% CI for odds ratio		P value
			Lower limit	Upper limit	
Age >30 yrs	78 (52%)	3.94	2.54	4.82	<.0001
BMI >25	121 (80.6%)	4.64	2.96	6.28	<.0001
Family history of father diabetic	36 (24%)	7.12	3.81	10.42	<.0001
Family history of mother diabetic	54 (36%)	6.28	4.65	8.86	<.0001
Family history of both parents diabetic	27 (18%)	6.21	3.98	8.74	<.0001
Bad obstetric history	54 (36%)	6.32	3.39	9.42	<.0001
Primi gravida	62 (41.3%)	3.79	1.65	5.74	<.0001
Weight gain of more than 7 kgs in first 2 trimester	39 (26%)	5.82	2.75	7.92	<.0001

Among the various complications acquired by the maternal mothers the most common was found to be the vaginal candidiasis (38.6%) followed by pre-mature rupture of membranes (18.6%). Out of the entire study subjects only 6 maternal mothers had developed hypertension and 17 had hypothyroidism. The most common mode of delivery in our study population was elective caesarean (59.3%) and 28% had undergone emergency LSCS for causes like maternal and foetal distress (table 3) Of the total babies delivered only 16 babies were delivered as post-dated.

Table 3: Maternal related complications and the mode of delivery among the study subjects.

Maternal complications	Frequency (n=150)	Percentage
Hypertension	6	4%
Hypothyroidism	17	11.3%
Vaginal candidiasis	58	38.6%
Abruptio placenta	16	10.6%
Premature rupture of membrane	28	18.6%
Mode of delivery		
Emergency LSCS	42	28%
Elective LSCS	89	59.3%

The various foetal outcomes were shown in table 4. In that majority of the mothers delivered macrosomia babies (29.3%), hypoglycaemia and hypothyroidism was found only in 6% and 5.3% of the new-born babies and 4 were still births and 15 babies were got admitted to NICU for respiratory distress (Table 4).

Table 4: Foetal outcome among the study population.

Foetal outcome	Frequency (n=150)	Percentage
Still births	4	2.6%
NICU admission	15	10%
Macrosomia	44	29.3%
Hypoglycaemia	9	6%
Hypothyroidism	8	5.3%

The insulin dosage requirement varied from 8 units to 35 units for the maternal mothers and the insulin used were either novorapid or actrapid. Insulin were given before each meal and one shot at bed time. The mean insulin given for each time was shown in table 5.

Table 5: Mean insulin dosage required by the study subjects

Time of giving insulin	Mean	SD	95% CI
Before breakfast	27.8	10.5	23.45 – 31.65
Before lunch	16.5	8.7	13.54 – 18.45
Before dinner	18.5	9.8	15.67 – 21.98
At bed time	15.5	8.6	13.79 – 18.12

The mean time of the start of insulin was 26.5 weeks of gestation and the mean weight of the mothers at that time was 67.78 kgs and the insulin were continued till the time of delivery and the mean weight of the mothers at delivery was 78.89 kgs and their difference in the weight gain was 8.79 kgs, which was found to be significant increase in the weight. The mean weight of the new-born was 3.26 kgs, which was found to be high than the national average which is 3 kgs (table 6).

Table 6: Weight of the mother and the new-born after the initiation of insulin among the study subjects.

Weight	Mean (kgs)	SD	95% CI
Initial (at start of insulin)	67.78	8.76	63.17 – 71.21
Final (at time of delivery)	78.89	9.21	74.28 – 83.10
Difference in the weight gain	8.79	3.15	6.21 – 10.1
P value	<.0001		
New-born weight	3.26	0.76	2.86 – 3.80

P value derived by applying student T test.

The mean fasting and post-prandial blood sugar parameters had shown a statistically significant improvement in their levels after the initiation of the insulin therapy, which was measured at the time of delivery. The glycated haemoglobin levels (HbA1C) had not shown any significant decrease at the time of delivery as it was not high at the time of initiation of insulin. The reason would be that HbA1C shows only the average of the past 3 months blood sugar and all the mothers who were detected were all the new diabetic patients (Table 7).

Table 7: Comparison of blood sugar parameters at the start of insulin and at the time of delivery.

Parameter s	At the start of insulin therapy		At the time of delivery		P value
	Mean	SD	Mean	SD	
Fasting blood sugar	158.5	16.54	129.3	14.47	<.0001
Post prandial sugar	228.8	18.75	172.5	21.45	<.0001
HbA1C	6.6	1.34	6.4	1.21	0.0871

The pearson's correlation had shown a strong positive correlation between the dose of the insulin given to the antenatal mother and their increase in the weight ($r=0.819$) and a strong negative correlation with the weight of the neonate ($r=-0.532$), which means that as the dose of insulin increased there was reduction in the birth weight and the correlation was found to have strong statistical significance ($p<.0001$) (Table 8).

Table 8: Correlation between the dose of the insulin and the weight of the mother and new-born.

Parameter	Pearson's correlation (r value)	P value
Weight of the mother at delivery	0.819	<.0001
Weight of the neonate	-0.532	<.0001

DISCUSSION

In a multi-centric study where a random survey was performed in various cities in India in 2002-2003 to assess the prevalence of GDM had shown that it was 16.2 percent in Chennai,^[15] percent in Thiruvananthapuram, 12 per cent in Bangalore, 18.8 per cent in Erode and 17.5 per cent in Ludhiana.^[13] So the figures seem to be alarming when compared to the prevalence of GDM in 1990's where it was 6.5% according to a study. The researchers had also suggested that the prevalence might go upto 20% in most of the places in India by 2020 due to the various life style changes. As there are varied outcomes among GDM mothers both in terms of maternal and foetal proper diagnosis and early intervention of GDM becomes the need of the hour.

In the present study the mean age of the GDM patients was 27.2 years and it is almost in par with the studies done by Priyanka Kalra etal¹⁴ and Rajesh Rajput etal¹⁵ and a study done from South India had also showed that age of the mother with more than 25 years are at the risk of developing gestational diabetes and which is true in our patients. In our study majority of the antenatal mothers had

education only upto primary school and they were belonging to either lower middle or upper lower type of socio-economic class but most of the Indian based studies had shown that GDM is more common in upper class mothers with high educational level but due to current urbanization and industrialization the situation had changed where even people living with low economic status also are more prone to develop diabetes.

The current study had shown that increasing age and BMI of more than 25 had strong association in the incidence of GDM and the same was also been observed in earlier studies as well.^[16,17] Family history of diabetes mellitus has been reported to be associated with higher chances of developing GDM^[18,19] and in our study also it had been proven. Interestingly, history of diabetes in mother was more common than the history of diabetes in father (36% vs. 24%). Probably the mothers of GDM women might also have had suffered from GDM in their pregnancies but remained undetected, hence supporting the familial association of GDM. In the present study majority of the mother's with GDM were found to be primi and few of the studies had quoted that GDM was most common in multiparous women but an Indian study done in Haryana did not show any association between the parity and GDM. As previously described in many studies in our study also it was proven that more than 7 kgs of increase in weight in the first 2 trimester are more prone to develop GDM. In our study the most common maternal complication was vaginal candidiasis followed by premature rupture of membranes and the similar type of results was shown in a study done by Priyanka Kalra etal.^[14] In her study she had quoted that hypertension was also more common among the GDM patients but in our study only 4% of the subjects had hypertension. In the present study almost 88% of the deliveries were by LSCS which was much contradicting to the study done by Gajjar etal^[20] were only 19% of the deliveries for GDM mothers were LSCS. The most common reason for LSCS was considering it as a high risk pregnancy.

Among the various foetal outcome reported, macrosomia was the most common in our study and similar type of result was also reported by Priyanka Kalra etal^[14] and Hong etal^[21] but in their studies the overall percentage was less it was only 19% and 9% respectively, but in those studies the incidence of still births, hypoglycaemia and hyperbilirubinemia were high which were very less in the present study.

In the present study it was shown that GDM patients had a significant weight gain after the initiation of insulin therapy and there was also significant positive correlation between the dose of the insulin and the weight gain and this result was almost in par with the study done by Juan Gui etal^[22] on the Chinese population, where he compared the insulin with metformin among the GDM patients and proved that metformin had reduced the weight in GDM patients. In our study we found a statistically significant negative correlation between dose of insulin and the weight of the new-born which was also proven in the study done by

Veciana M et al^[23] and Jovanovic L et al^[24]. Our study had also proven significant reduction in the fasting and postprandial blood sugar levels at the time of delivery when compared to the levels at the start of treatment.

CONCLUSION

The prevalence of GDM currently is in rise in India parallel to the increment in the prevalence of obesity and T2DM. Gestational diabetes mellitus being associated with maternal and neonatal adverse outcomes, so maintaining adequate blood glucose levels in GDM helps in reducing the morbidity for both the mother and baby. Insulin would be a right choice for treating GDM and when initiated early it prevents most of the complications due to GDM both in the mother and the neonate.

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