



“ PREGNANCY OUTCOMES IN WOMEN WITH PREEEXISTING AND GESTATIONAL DIABETES MELLITUS”

Endocrinology

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ABSTRACT

Context: Diabetes in pregnancy is increasing and associated with increased risk of complications. There is little data on whether the pregnancy outcomes have changed over time.

Aim: The aim is to compare rates of pregnancy outcomes between women with preexisting diabetes and gestational diabetes (GDM).

Settings and Design: This was a prospective observational study done in women with preexisting diabetes and GDM.

Methods and Material: Baseline characteristics and medical comorbidities were recorded. Women were counseled regarding life style modification (LSM) and glycemic goals. Metformin and/or insulin were used accordingly. Maternal outcomes and neonatal outcomes were assessed.

Results: Out of 183 subjects who were enrolled, 74 (40 %) were women with preexisting diabetes and 109 (60%) were GDM. More than 50% of patients required combination of LSM, metformin and insulin in both groups. Pregnancy weight gain was higher in GDM (11.15±3.48) compared to preexisting diabetes (10.07±3.25; $p < 0.05$). Preterm delivery was more in preexisting diabetes (43.28%) than GDM (25.24%; $p = 0.01$). There were higher miscarriages in preexisting diabetes compared to GDM ($p = 0.02$) whereas intra uterine deaths were similar in both groups. Prevalence of PIH was 26.86% in preexisting diabetes and 15.53% in GDM ($p = 0.08$). Caesarean section rate was 89.55% in preexisting diabetes and 87.37% in GDM. Birth weight was higher in neonates of GDM compared to preexisting diabetes (3.05±0.42 versus 2.88±0.52, $p = 0.02$). There were four neonates with congenital malformations in preexisting diabetes and none in GDM.

Conclusions: The present study in women with Preexisting Diabetes and GDM showed higher miscarriages and higher preterm deliveries in preexisting diabetes. There were high rates of caesarean section, reduced macrosomia and lesser congenital malformations in the present study.

KEYWORDS

Preexisting Diabetes, Gestational Diabetes, Maternal Outcomes, Neonatal Outcomes.

INTRODUCTION:

Diabetes in pregnancy is increasing and the prevalence rates of gestational diabetes (GDM) has varied from 3.8% to 21% in India.^[1,2,3] Diabetes in pregnancy is associated with increased risk of complications for both the mother and the newborn. Hyperglycemia in the period around conception carries a substantially higher risk of congenital anomalies. Studies have demonstrated reduced rates of congenital malformations and perinatal mortality with preconception counseling, optimal glycemic control and treatment of comorbidities prior to and during pregnancy.^[4,5] This awareness over the last decade has the potential to reduce rates of serious outcomes in women with diabetes. There is little data on whether these rates of serious outcomes have changed over time in diabetes complicating pregnancy. The aim of the present study is to compare rates of maternal and neonatal outcomes between women with preexisting diabetes and GDM.

SUBJECTS AND METHODS: This was a prospective observational study done in women with preexisting diabetes and gestational diabetes attending endocrinology outpatient clinic in a South Indian tertiary care hospital from January 2016 to January 2018.

Women were considered to have preexisting diabetes if they were diagnosed before pregnancy or at the first prenatal visit if fasting plasma glucose (FPG) ≥ 126 mg/dl or 2 hour post prandial glucose (2 hr PPG) ≥ 200 mg/dl or HbA1c $\geq 6.5\%$. Women with preexisting diabetes included both Type 1 diabetes and Type 2 diabetes. GDM was diagnosed based on International Association of Diabetes and Pregnancy Study Groups criteria.^[6] Baseline characteristics recorded were maternal age, prepregnancy BMI, duration of diabetes and gestational age of onset of GDM. Medical comorbidities such as hypothyroidism and hypertension were documented. All women had received advice regarding diet and physical activity. Metformin and/or insulin was started when nutritional therapy failed to achieve glycemic goals in GDM. Insulin was initiated in addition to metformin to control hyperglycemia in women with preexisting Type 2 Diabetes. Women with Type 1 Diabetes continued insulin therapy during pregnancy. Glycemic control in preexisting diabetes was assessed based on fasting, preprandial and post prandial glucose either on laboratory or

self monitoring of blood glucose (SMBG) values. Glycemic control in GDM was assessed based on FPG and PPG either on laboratory or SMBG values. Patients were on weekly follow up and dose adjustments were done on a weekly basis.

Study outcomes: Maternal outcomes assessed were pregnancy weight gain, miscarriage, pregnancy induced hypertension (PIH), preterm delivery and caesarean section (CS). Preterm delivery was defined as delivery less than 37 weeks of gestation. Neonatal outcomes assessed were still birth, macrosomia, low birth weight, neonatal hyperbilirubinemia, hypoglycemia, congenital malformations and neonatal death. Macrosomia was defined as birth weight ≥ 4 kg and low birth weight as < 2.5 kg. Neonatal hyperbilirubinemia was defined as serum bilirubin > 12 mg/dl. Neonatal hypoglycemia was defined as plasma glucose < 45 mg/dl.

STATISTICAL ANALYSIS: Data were presented as percentage (%) for qualitative variables, mean and standard deviation for continuous variables. Independent Student's t-test was done for comparison of continuous variables and Chi-square test for frequencies. p value < 0.05 was considered statistically significant.

RESULTS:

A total of 183 subjects were enrolled of which 74 (40 %) were women with preexisting diabetes and 109 (60%) were gestational diabetes. Of those with preexisting DM, 17 (23%) had Type 1 Diabetes and 57(77%) had Type 2 Diabetes. Four GDM patients lost follow up and were excluded from the study. There were seven miscarriages in preexisting diabetes and two in GDM. The remaining 170 subjects were included in the analysis. The baseline characteristics of the subjects were shown in Table 1.

TABLE 1: Baseline characteristics of the subjects.

Parameter	Preexisting DM(n=67)	GDM (n=103)	p value
Age (years \pm SD)	28.15 \pm 5.03	29.08 \pm 3.74	0.171
BMI(kg/m ² \pm SD)	25.19 \pm 5.07	25.20 \pm 3.60	0.992

Duration of DM (years ± SD)	2.79±1.44	-	-
GA of onset of GDM (weeks ± SD)	-	23.04 ±5.03	-
Prevalence of hypothyroidism (%)	40.29% (27/67)	27.18% (28/103)	0.07

Table 2 summarizes the treatment received by the subjects. More than 50% of patients required combination of life style modification (LSM), metformin and insulin therapy. There was no significant difference in the modes of treatment between two groups.

TABLE 2: Modes of treatment received by the subjects.

Parameter	Preexisting diabetes	GDM	p value
LSM alone	0%	4.85% (5/103)	-
LSM + Metformin	6.06% (4/67)	6.79% (7/103)	0.833
LSM +Insulin	28.78% (19/67)	34.95% (36/103)	0.368
LSM + Metformin +Insulin	65.67% (44/67)	53.39% (55/103)	0.111

Maternal outcomes:

The maternal outcomes were shown in Table 3. A total of 163 live births occurred out of 179 pregnancies (91.06%) with a mean gestational period of 36.77±1.67 weeks. Nine (5.0%) subjects had miscarriages in first trimester and there were 7/179(3.91%) intra uterine deaths (IUD) at mean GA of 32.85±2.79 weeks. Pregnancy weight gain was 11.15±3.48 kg in GDM compared to 10.07±3.25 kg in preexisting diabetes ($p<0.05$) while preterm delivery was 25.24% in GDM compared to 43.28% in preexisting diabetes ($p=0.01$).

TABLE 3: Maternal outcomes of Preexisting diabetes and GDM

Parameter	Preexisting DM(n=67)	Gestational DM(n=103)	P value
Pregnancy weight gain (kg)	10.07±3.25	11.15±3.48	<0.05
PIH	26.86%(18)	15.53% (16)	0.08
Preterm delivery	43.28% (29)	25.24% (26)	0.01
Mean GA of delivery (weeks ± SD)	36.16±2.19	36.91±1.68	<0.05
Caesarean section	89.55% (60)	87.37% (90)	0.667
No. of live births	94.02%(63)	97.08%(100)	0.327
No. of IUDs	5.9%(4)	2.9%(3)	0.327
No. of miscarriages	7	2	0.022

Neonatal outcomes:

A total of 166 new borns comprising 160 singleton pregnancies and 3 sets of twins were included in this study. Various neonatal outcomes were shown in Table 4. Congenital malformations observed were patent ductus arteriosus in three neonates and retroperitoneal cyst in one neonate born to women with preexisting diabetes.

TABLE 4: Neonatal outcomes of Preexisting diabetes and GDM.

Parameters	Preexisting DM (n=64)	Gestational DM(n=102)	P value
F/M	31/33	49/53	-
Birth weight in kg	2.88 ±0.52	3.05±0.42	0.02
LBW	18.75% (12)	13.72% (14)	0.38
Macrosomia	7.81% (5)	9.80% (10)	0.65
Hyperbilirubinemia	37.5% (24)	26.47% (27)	0.05
Hypoglycemia	10.93% (7)	10.78% (11)	0.97
Neonatal deaths	1.5%(1)	1.9%(2)	0.84
Congenital anomaly	6.25%(4)	0%	-

DISCUSSION

The incidence, management and complications of Diabetes in Pregnancy are showing changing trends worldwide. A recent study from Scotland showed that women with diabetes in pregnancy are receiving increased interventions during pregnancy.^[1] The present study compared the clinical characteristics, treatment, maternal and neonatal outcomes in women with preexisting diabetes and GDM. The results of the study showed significantly higher preterm deliveries, miscarriages in preexisting diabetes compared to GDM. The incidence of PIH and Hypothyroidism were higher in preexisting diabetes although not statistically significant. In the present study, majority of women with GDM and preexisting diabetes underwent CS. Women with GDM had a higher pregnancy weight gain and their neonates had

higher mean birth weight than those with preexisting diabetes. The incidence of still birth, low birth weight, macrosomia, neonatal hyperbilirubinemia and hypoglycemia were not different between the two groups.

The mean duration of diabetes was 2.79±1.44 years in women with preexisting diabetes and GDM had been diagnosed at a mean gestation of 23.04 ±5.03 weeks. This reflects the early screening practices seen in this region. Maternal age at conception and pre pregnancy BMI were similar in both groups, however the pregnancy weight gain is more in women with GDM. This can be explained by higher awareness in women with preexisting diabetes regarding weight gain and complications. The present study observed PIH in 15.53% of GDM which is similar to earlier Indian studies.^[8,9] However, Neeta Singh et al in their study reported PIH in 6.3% of women with GDM.^[10] The reasons for these differences could be the severity of GDM. The prevalence of PIH in women with preexisting diabetes is generally higher than GDM due to their longer duration of diabetes. In the present study, the rate of PIH in women with preexisting diabetes is 26.86% which is higher than that of GDM but did not achieve statistical significance. This may be due to small sample size of women with preexisting diabetes.

The present study showed significantly higher rate of preterm deliveries in women with preexisting diabetes (43.28%) compared to GDM (25.24%). A study done in France showed similar rate of preterm deliveries in preexisting diabetes (49.4%) as the present study but a lower rate in GDM (8.4%).^[11] The rate of preterm deliveries in GDM were higher in our study when compared to other Indian studies also.^[9,12] This may be due to earlier onset of GDM, severity of GDM.

The rate of CS in this study was 87.3% and 89.5% in GDM and preexisting diabetes respectively. Earlier studies by Prakash et al, Bhat et al and Sreelakshmi et al reported a rate of 45%, 40% and 33% in GDM respectively.^[12,13,14] The high rate of CS is a concern in this study. This could be explained by the severity of diabetes, higher socioeconomic status, preference of mode of delivery by the patient, intervention by obstetrician due to high risk pregnancy. Awareness needs to be improved in preventing CS in women with diabetes.

In our study nearly 88% of women with GDM required Insulin with or without metformin therapy for glycemic control suggesting the severity of hyperglycemia in our GDM cohort. Metformin and LSM were used in 6.79% of GDM and 53.39% of subjects used metformin along with insulin and LSM. The higher metformin usage indicates the changing trend in the management of hyperglycemia in pregnancy.

Neonates of women with GDM were significantly heavier than neonates of preexisting diabetes. The mean birth weight of neonates in GDM was 3.05±0.42 kg which was higher than earlier studies.^[9,12] Though mean birth weight was higher in GDM, macrosomia was seen only in 9.8% neonates which was lower than earlier studies.^[15] Neonatal complications occurred in 48.4% in preexisting diabetes and 37.2% in GDM and overall perinatal mortality (still birth and neonatal death) was 5.5%. Prevalence of still birth was 5.9% in women with preexisting diabetes and 2.9% in GDM. A study from Saudi Arabia reported 3.4% in preexisting diabetes and 0.9% in GDM.^[16]

Congenital malformations reported were Patent ductus arteriosus in three neonates and retroperitoneal cyst in one neonate born to mothers with preexisting diabetes. In this study, there were no congenital malformations observed in neonates of GDM mothers whereas in an Indian study by Kumari et al congenital anomalies were reported in 4.7% of GDM.^[9] A study by J.G.Ray et al showed 2.6% prevalence of congenital anomalies in offspring of mothers with preexisting diabetes and 2.8% in offspring's of GDM mothers.^[17]

The present study highlights changing trends in the management of diabetes in pregnancy like higher metformin usage and higher rate of CS. The low rates of congenital malformations, reduced incidence of macrosomia reflect better management of diabetes in pregnancy.

The limitations of study were small sample size, lack of control group and not measuring HbA1c to assess the severity of Preexisting Diabetes. Parameters like polyhydramnios, premature rupture of membranes and fetal distress were not analyzed.

CONCLUSIONS

The present study comparing pregnancy outcomes in women with

GDM and Preexisting Diabetes showed higher miscarriages and higher preterm deliveries in preexisting diabetes. The high rate of caesarean section in the present study highlights the need to create awareness in patients and obstetricians. Better treatment of diabetes during pregnancy reduced macrosomia and congenital malformations.

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