Pregnancy Outcomes in Diabetic Mothers With Controlled Glycemia: A Case-Control Study

Abstract:

Background: OvertDiabetes mellitus and Gestational diabetes mellitus (GDM) can complicate pregnancy. Early detection and management of the disease should be done to ensure better maternal and foetal outcomes. Our goal is to compare treatment-controlled diabetic women with non-diabetic women to evaluate the pregnancy-related unfavourable outcomes.

Methods and materials: This is a single-centre case-control study with women, from Nellore, Andhra Pradesh, who gave birth between September 2022 and February 2023. A total of 144 patients, including 72 women with diabetes and controlled glycemia (case group, n=72), were compared with non-diabetic women (control group, n=72). Various pregnancy-related outcomes were observed. The student t-test and SPSS were used for statistical analysis to compare

Results: Average ages were 24±4.9 years and 27.83±6.24 years in controls and cases, respectively. Mean pregnancy duration was 268.15±7.1 days in controls and 257.1±31.2 days in cases. The cases had a mean HbA1C of 6.05%, indicating controlled levels. Caesarean births were observed in 75% of cases and 51.3% of controls. While macrosomia (>4 kg) was not observed, 25% of cases had low birth weight (<2.5 kg). Family history, gravidity, consanguinity, newborn sex, APGAR score, nuchal cord, asphyxia, and need for respiratory support did not significantly differ between the cases and controls.However, there was a significant difference ($p<0.05$) in the gestation period, previous neonatal loss, type of previous deliveries, caesarean delivery, baby weight, hyperbilirubinemia, and present neonatal loss between diabetic mothers and non-diabetic mothers.

Conclusion: A well-managed chronic hyperglycaemia was thought to prevent multiple pregnancy-related problems for both the mother and the baby. This study aimed to investigate this point. Though many complications were avoided with controlled glycemia in our study, complications such as caesarean deliveries, preterm births, low birth weight, hyperbilirubinemia, and neonatal loss were more prevalent in cases. This highlights the need for further research, especially in understanding and possibly intensifying glycaemic goals for diabetic mothers.

Key words:

Overt diabetic, Gestational diabetes mellitus, APGAR score, Asphyxia, Hyperglycaemia, Macrosomia.

Introduction:

As per the World Health Organization, diabetes is a persistent metabolic ailment marked by high blood glucose levels that eventually cause severe harm to the heart, blood vessels, eyes, kidneys, and nerves. Due to genetic, environmental, and other underlying aetiologies, diabetes can affect people of all ages [(1)]. Women who have diabetes during pregnancy are the primary focus of our research. Maternal women's blood glucose levels rise during pregnancy in response to the needs of the developing foetus. Unfavourable pregnancy outcomes arise when the body's internal mechanisms fail to regulate these levels appropriately. Diabetes mellitus can complicate pregnancy in women, regardless of whether the patient is overtly diabetic or is diagnosed with gestational diabetes mellitus.

Approximately 540 million individuals worldwide suffer from diabetes. India has 77 million diabetes patients, according to the International Diabetes Federation (IDF) 2021 report [(2)]. In India, 16.55% of people have GDM. Approximately 7% of pregnancies worldwide are affected by GDM. In rural India, the prevalence of Diabetes in pregnancy is 6-9%, while in urban areas, it is 12-21% [(3)]. During pregnancy, the risk of developing glucose intolerance is eleven times higher in Indian women. About 90–95% of pregnant women have diabetes. Pregestational diabetes, with prevalence rates of 0.1-0.3%, accounts for only 10% of cases of maternal diabetes. Pregnancies with previous and current diagnosed diabetes are risky for both the mother and the foetus [(4)].

Pregnancy-related diabetes mellitus (DM) increases the risk of diabetes mellitus for both the mother and her unborn child. Perinatal outcomes were linked to poor glycaemic control in diabetic mothers. In addition to increasing the chance of type 2 diabetes in the future, mothers who have this risk also run the risk of developing cardiometabolic disorders, which include postpartum obesity, metabolic syndromes, hypertension, and cardiovascular disease [(5)].

Many unfavourable foetal outcomes, including macrosomia, shoulder dystocia, birth traumas, hypoglycaemia in neonates, congenital defects, stillbirths, and occasionally elevated neonatal mortality and morbidity, were brought due to diabetes during pregnancy [6]. Obstetric outcomes for mothers include elevated liver enzymes, hypoglycaemia, preeclampsia, caesarean sections, instrumental deliveries, postpartum sepsis, pregnancy-induced hypertension, abortions, and maternal deaths [7,8]. Hence, it is imperative that all medical professionals screen, diagnose, and provide specialized care to pregnant women with diabetes.

The International Association of Diabetes Pregnancy Study Group criteria employs "A Single Step Procedure" (SSP) in order to diagnose GDM [9]. It is not important when the last meal was, this test can be done while fasting or not. When taking the 75g oral glucose test (also known as the glucose challenge test, or GCT), if the plasma glucose level is 7.8 mmol/liter (140 mg/dl), then GDM is diagnosed [9]. In addition to this SSP, measurement of HbA1c, fasting blood sugar (FBS), random blood sugar (RBS), and postprandial blood sugar (PPBS) levels can help to diagnose diabetes in pregnancy.

Treatment for diabetes in pregnancy lowers perinatal complications and enhances health and quality of life, according to the Australian Carbohydrate Intolerance Study (ACHOIS), a randomized trial of GDM treatment for women [10]. For pregnant women diagnosed with diabetes, Medical Nutritional Therapy (MNT) should be initiated. In the event that MNT fails to meet the glycaemic targets (less than 95 mg/dl during fasting and less than 120 mg/dl for two hours postprandial), pharmacotherapy needs to be started. Insulin and oral anti-diabetic medications (OADs) are part of the pharmacotherapy.

There is a lack of information regarding the results of treatment-controlled diabetes in pregnancy, despite the fact that numerous studies on the subject have been conducted throughout India, including those by Mahalakshmi et al [6]in Chennai, Seshiah et al [9]in Chennai, K Ramalingam et al [11]in Guntur and Manni Mohan raj Mahalakshmi et al [12]in Chennai. In order to reinforce the importance of maintaining glycaemic control during pregnancy, our study attempts to determine the impact of diabetes on pregnancy outcomes. Fewer studies in the field show the impact of controlled plasma glucose on pregnancy outcomes. We thought it would be beneficial to share the findings of our investigation and enhance public awareness.

AIMS AND OBJECTIVES

Aims:

- To compare the pregnancy outcomes in treatment-controlled diabetic and nondiabetic mothers attending the obstetrics and gynaecology department in a tertiary care hospital.

Objectives:

- To assess the maternal outcomes in treatment-controlled Diabetes complicating pregnancy.
- To assess the foetal outcomes in treatment-controlled diabetes-complicating pregnancy.

MATERIALS AND METHODS

Study design and setting:

A case-control study conducted at a single centre with women scheduled for deliveries between September 2022 and February 2023 was conducted. A total of 144 patients included in this study were admitted to the tertiary care facility, Narayana Super Specialty Hospital, located in Nellore.

Sample size and study subjects:

Pregnant women in the age group of 18-40 years were enrolled in the study. The cases in this study were the women who underwent an oral plasma glucose tolerance test, were diagnosed with diabetes, and later achieved control of the illness with treatment. The controls in this study were the pregnant women with normal blood glucose levels without diabetes.

The data was collected in all the enrolled mothers at the time of their delivery. Using a data collection proforma, all complications for the mother and fetus during the pregnancy and after delivery were documented.

Statistical Analysis:

IBM Corp., located in Armonk, New York, provided the statistical product services solution IBM SPSS version 23.0, which was used for all data analyses. To compare the means of the two groups, the Student's T-independent test was employed. The

data were shown as percent values and frequencies for categorical variables. For all statistical tests, a two-sided probability of $P < 0.05$ was deemed statistically significant and an ODDs Ratio was calculated.

RESULTS

The research included 144 women in total with 72 women with diabetes with controlled glycemia (Case group) 72 women who were not diabetics and who were pregnant without any complications (Control group). These women were monitored until delivery, and at the time of delivery, data on the maternal and neonatal outcomes were recorded.

The women were from Nellore, Andhra Pradesh, and the neighbouring areas of Nellore. Average age in the Control group was 24±4.9 years while case group was 27.83±6.24 years. In the case group the mean glycated haemoglobin (HbA1c) value was found to be 6.05±0.99%, which indicates the controlled glycemia. Mean pregnancy duration was 257.1±31.2 days in cases, while for the Control group, it was 268.15±7.1 days.

According to the past history of 24 women in the case group, neonatal loss by spontaneous abortion 16 (22.2%) and Medical termination of pregnancy 8 (MTP) (11.1%) were noted. Prior caesarean surgeries were seen in 36 (50%) of the cases. A positive family history of first-degree relative with diabetes was only seen in 6 (8.3%) of cases.

Women with primary gravidity are 26 (36%) vs 29 (40.3%), multi gravidity is 44 (61.2%) vs 40 (55.6%) and grand multi gravidity is 2 (2.8%) vs 3 (4.2%) in Case and Control groups respectively. It was discovered that 75% (54) of mothers with diabetes and 51.3% (37) of the control group had caesarean surgeries in the present birth. Although macrosomia was not observed, Case group showed a notable 25% of low-birth-weight children. Thirty-two (44.4%) infants delivered by the Case group were admitted to neonatal intensive care unit (NICU). Four (5.55%) mothers of the Case group have lost their children.

Family history, gravidity, consanguinity, sex of the newborn, APGAR score, nuchal cord, asphyxia, and need for the respiratory support did not significantly differ between the cases and controls. However, there was a significant difference in previous neonatal loss (odds ratio-2.83; P=0.049), preterm labour (odds ratio-6.215; P=0.001), caesarean delivery (odds ratio-2.85; P=0.013), Baby weight (odds ratio-

2.32; P=0.039), and neonatal loss (P=0.043) between Case and Control groups with more odds towards diabetic mothers. The results were listed in Table 1.

DISCUSSION

This case-control study compared the pregnancy-related outcomes for women with (Case group) and without diabetes (Control group) over a specific period of time, at a single centre. Out of 144 deliveries, 72 were identified as diabetic cases with controlled glycemia. Since the data came from a single centre and the study was a case-control, it's possible that this does not accurately reflect the true frequency**.**

Adverse outcomes for both the mother and the foetus are linked to poor glycaemic control during pregnancy. Risks to women included in this study were miscarriage, caesarean section, preterm labour, preeclampsia, and other risks that were not included in the study are diabetic retinopathy, ketoacidosis, and progression to renal disease. Premature delivery, macrosomia, NICU admissions, respiratory distress, hyperbilirubinemia, neonatal deaths and other risks to newborns were among those covered by the study.

In the Case group with controlled glycemia, the mean HbA1c value is 6.05±0.99%, which is closer to the 6.0% target that was anticipated in our study. The mean HbA1c in the Control group is 5.47±0.26. We found a significant difference (p=0.002) in the mean HbA1c between the Case and Control groups. The study by Buhary et al [(8)].revealed that mothers with diabetes had a mean HbA1C value of 7.7818, which is higher than the value found in our investigation, indicating uncontrolled glycemia. We found no studies on diabetic mothers with controlled glycemia.

According to this study, 97.2% of women in the Case group had regular cycles, while women in the Control group had 91%. None of the studies that we looked at had previously evaluated this parameter. It appears that the menstrual cycle has no impact on or relationship to pregnancy-related diabetes, as most of the Cases had regular menstrual cycles prior to becoming pregnant. We evaluated this parameter as insulin resistance, a risk factor for diabetes, has known association with Poly cystic ovarian syndrome (PCOS) and hypothyroidism, both of which can cause menstrual irregularities.

The Case group of our study had a significantly bad obstetric history of Spontaneous abortions (22.2% Vs 9.7%), MTPs (11.1% Vs 4.1%), and stillbirths (0 Vs 5.5%) when compared to the Control group respectively.

The family history of Diabetes for women was same (8.3%) in the Case and Control groups respectively, which is slightly lower (11.26%) than in cases of diabetes from Ramalingam et al [11]. According to Kumari et al's[7] findings, 22.4% of diabetic women and 10.5% of non-diabetic women (p=0.02) had a family history of diabetes. Our results were not statistically significant when compared to other studies.

Among the Case group, multigravida (61.2%) predominates over primigravida (36%) and grand multigravida (2.8%). Ramalingam et al [11] has shown similarities as they reported 29.5% of primigravida and 69.01% of multigravida.

The mean gestational period in this study was 257.1±31.2 days for women in the Case group and 268.15±7.1 days for women in the Control group (P=0.001). This suggests that the deliveries were earlier in the Case group.

According to this study, 26 (36.1%) women in the Case group and 6 (8.3%) women in the Control group experienced preterm labour (odds ratio-6.215; P=0.001). Similar findings are found in the Mahalakshmi et al [6] study which showed significantly higher preterm births in diabetic women (8.6%) than non-diabetic women (6.9%) (p=0.069).

According to Mahalakshmi et al [6] women in the Case group had a higher overall caesarean section rate of 26.2% compared to 18.7% in women in the Control group. The findings of our study bear some resemblance to those of Mahalakshmi et al [6]. Women with Diabetes in pregnancy had a higher overall caesarean section rate of 75% (54) compared to 51.4% (37) in women without the condition in this study (odds ratio-2.85; P=0.013). In contrast, study by Kumari et al [7] showed a 50% caesarean section rate in women with diabetes mellitus, while women without the disease had 55.5%. This suggests that there is a higher risk of caesarean delivery in Case group, though the risk may not vary based on plasma glucose control.

The mean birth weight was found to be 2.84±0.67 kgs for the neonates born to the Case group. The Ramalingam et al [11] study reports that only 14% of babies born over 4 kg indicate macrosomia and 68.11% of babies born between 2.6 and 3.9 kg. According to our research, 25% of babies born to the Case group weigh less than 2.4 kg, 75% weigh between 2.4 and 4 kg, and there were no newborns with macrosomia. Our study showed a significantly higher odds (odds ratio-2.32; $p<0.05$) of low birth weight in infants born to the case group when compared to controls and without showing the classical complication of macrosomia. We postulate that glycemic control in pregnant mothers may have direct role in prevention of macrosomia.

In the Case group, the neonatal loss was 4 (5.55%), while the Control group experienced no loss. Whereas an intrauterine death (IUD) was not identified in our study, the Mahalakshmi et al [6] study included a 0.3% neonatal IUD in the Case group and a 0.7% IUD in Controls.

According to the findings of ManjuYadav et al [13] 29.63% of NICU admissions are related to the Case group, while 9.5% are related to Controls. According to Buhary et al [8] study, diabetic cases accounted for 21.5% of NICU admissions [8]. In contrast, our study found that 44.4% of NICU admissions were diabetes-related and controls had 55.6%. No increase in NICU admissions was observed in this study.

Asphyxia or respiratory distress is observed in 33.3% of the Case group and 36.1% of the Control group which are not statistically significant. According to a study by Kumari et al [7] respiratory distress syndrome affected 4.7% of the neonates born in case group and 1.6% of the controls. The fact that the respiratory problems in our study did not differ considerably, may be attributed to proper glycaemic control in the Case group.

The APGAR scores at 1st minute were 5.08±1.54 and 4.9±1.35 in Case and Control groups, respectively, which are not statistically significant. The APGAR score at the 5th minute were 7.03±1.24 in the Case group and 7.11±1.88 in the Control group. Similar to our study, Kumari et al [7] results indicated APGAR scores of 8.61±1.36 for diabetics and 8.73±0.82 for non-diabetics at the 5th minute, which were non-significant.

In comparison to controls (15.3%), hyperbilirubinemia is more prevalent in the Case group (33.3%). There was no discernible difference in infants with hyperbilirubinemia between cases (1.6%) and controls (1.2%) according to Mahalakshmi et al [6]. InBlasi I et al [14] 33.3% (4 out of 12) cases shown hyperbilirubinemia, there was an significant risk of hyperbilirubinemia in neonates DM mothers. However, our study had shown higher odds (odds ratio-2.77; $p<0.05$) in the prevalence of hyperbilirubinemia in infants born to the case group.

Out of the 72 women in the Case group, 12 (16.7%) had pregnancy-induced hypertension. This figure is marginally higher than that of the study by Kumari et al [7] which found that 13.5% of diabetic mothers experienced pregnancy-induced hypertension. This suggests that mothers who have diabetes have a very high risk of developing pregnancy-induced hypertension as a maternal complication.

In comparison to control groups, there is no significant difference in the presence of nuchal cord. This may be due to prompt assessment, treatment, and strict monitoring of maternal glycemia.

CONCLUSION

This study aimed to demonstrate the importance of prompt diagnosis, treatment, and close monitoring of hyperglycaemia in diabetic mothers during pregnancy. While maintaining controlled chronic hyperglycaemia can prevent many pregnancy complications, our findings show that few risks still remain elevated.

Preterm births and caesarean deliveries were more common among diabetic mothers despite good glycaemic control. We also observed lower birth weights, higher rates of hyperbilirubinemia, and increased neonatal loss in infants of diabetic mothers. This highlights the need to reevaluate targets for plasma glucose control during pregnancy beyond standard recommendations.

Further large-scale, population-based, and prospective studies on diabetic pregnant women with controlled blood sugars are warranted to discern the possible cofactors which may have significant impact on pregnancy-related complicatons. Our study, while limited to a single centre, adds to the evidence that achieving glycaemic control alone may not be sufficient to normalize all pregnancy risks related to diabetes.

As the burden of gestational and pre-gestational diabetes climbs globally, preventing complications remains a priority. Our findings emphasize the risks associated with any maternal diabetes, controlled or not, and underscore the critical importance of optimal glycaemic control and patient education on diabetes in pregnancy. Tighter glucose targets and additional preventative strategies should be explored to improve outcomes for mothers and babies alike.

Ethical Approval and Consent

The Diabetic and non-diabetic mothers in this study were enrolled with Informedwritten consent after Institutional ethics committee (IEC) approval.

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TABLES

Clinical parameters	Case Group (n=72)	Control Group (n=72)	p	ODDs Ratio
Mother age	27.83±6.24	24±4.9	0.001	
Gestation period	257.1±31.2	268.15±7.1	0.001	
HbA1c	6.05±0.99	5.47±0.26	0.002	
Gravidity				
Primi (first birth)	26 (36%)	29 (40.3%)		0.838
Multi (2-4)	44 (61.2%)	40 (55.6%)	0.761	1.259
Grand Multi (>4)	2 (2.8%)	3 (4.2%)		0.651
Previous caesarean delivery	36 (50%)	19 (26.4%)	0.001	2.793
Prev neonatal loss				
Death	0	4 (5.5%)		0
Medical Termination of Pregnancy	8 (11.1%)	3 (4.2%)	0.049	2.38
Spontaneous Abortion	16 (22.2%)	7 (9.7%)		2.533
Family history ofDM	6 (8.3%)	6 (8.3%)	0.551	1
Pregnancy induced HTN	12 (16%)	0		

Table 1: Clinical parameters of mothers with Treatment controlled DM and Mothers without DM

Pregnancy Outcomes	Case Group (n=72)	Control Group (n=72)	p	ODDs Ratio
Caesarean delivery	54(75%)	37 (51.4%)	0.013	2.85
Baby Birth weight				
Microsomia (≤ 2.4 kgs)	18 (25%)	9 (12.5%)		2.32
Normal (2.4-4 kgs)	54 (75%)	62 (86.1%)	0.039	0.544
Macrosomia (>4 kgs)	0	1 (1.4%)		0
Mean	2.84±0.67	2.945±0.41		
Preterm labour	26 (36.1%)	6 (8.3%)	0.001	6.215
APGAR SCORE 1st min	5.08±1.54	4.9±1.35	0.454	
APGAR SCORE 5th min	7.11±1.88	7.03±1.24	0.753	
Nuchal cord	4 (5.6%)	8 (11.1%)	0.725	0.47
NICU admission	32 (44.4 %)	40 (55.6 %)	0.015	0.64
Asphyxia	24 (33.3%)	40 (55.6%)	0.729	0.4
Respiratory support	26 (36.1%)	26 (36.1%)	0.854	1
Hyperbilirubinemia	24 (33.3%)	11 (15.3%)	0.011	2.77
Neonatal loss	4 (5.55%)	0	0.043	

Table 2: Pregnancy Outcomes of mothers with Treatment controlled DM and Mothers without DM