

Effect of Diabetes Mellitus on Neonatal Outcome of Term Pregnancy at a Teaching Hospital of Abbottabad, Pakistan

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ABSTRACT

Introduction: Pregnancies complicated by diabetes are associated with a high rate of miscarriage, preterm delivery, preeclampsia, perinatal mortality and neonatal congenital malformations compared to the background population.

Objective: To determine the effect of Diabetes Mellitus on the neonatal outcome of term pregnancy at a teaching hospital of Abbottabad, Khyber Pakhtunkhwa, Pakistan.

Materials & Methods: This descriptive cross sectional study was carried out in the Department of Obstetrics and Gynecology of Ayub Teaching Hospital, Abbottabad from March to August 2016 on 196 pregnant females diagnosed with either type 1 or type 2 Diabetes Mellitus. They were followed up till delivery and frequency of various adverse neonatal outcomes were recorded in infants born to these diabetic mothers.

Results: The most common adverse neonatal outcome was hypoglycemia (38.78%) followed by low birth weight (21.43%) and macrosomia (17.86%). When the outcome variables were stratified according to Age, BMI, Blood Pressure, Duration and Type of Diabetes Mellitus, only hypoglycemia was found to be significantly associated with type 1 Diabetes Mellitus ($p = 0.002$).

Conclusion: Diabetes Mellitus is associated with a number of adverse neonatal outcomes irrespective of the type of Diabetes Mellitus. Obstetricians need to be aware of recent guidelines for management of Diabetes Mellitus to try to reduce the adverse outcomes in pregnancy.

Keywords: Gestational Diabetes; Hyperglycemia; Macrosomia; Hypoglycemia; Pregnancy; Morbidity; Mortality.

The authors declared no conflict of interest. All authors contributed substantially to the planning of research, data collection, data analysis, and write-up of the article, and agreed to be accountable for all aspects of the work.

INTRODUCTION

The global burden of Diabetes Mellitus (DM) is increasing with time, so much so that it has been estimated to affect more than 360 million human beings by the year 2030.¹ The physiological stress of pregnancy affects the metabolism in both the mother and the fetus and has a diabetogenic effect, even in the non-diabetic woman.² With progression of normal pregnancy, resistance to insulin increases and a stress is put on the pancreatic β -cells reserve which functions to keep blood glucose level to a normal range.² When the pancreatic β -cells fail to keep blood glucose down to a normal level, GDM is said to have developed, defined as impaired glucose tolerance with onset or first recognition during pregnancy.³ At the time of parturition, after the removal of placenta, the glucose homeostasis is restored.

In pregnancy, DM can either be pre-existing (type 1 or 2) or gestational Diabetes Mellitus (GDM). In pre-existing DM, risk factors such as genetic predisposition, family history of type 1 DM and autoimmune disorders are crucial in the development of type 1 DM.⁴ Factors which play a significant role in both type 2 DM and GDM include obesity, unhealthy diets, physical inactivity, family histories of type 2 DM, maternal age and ethnicity.⁵ Other lifestyle changes such as alcohol abuse and smoking have also been implicated in the etiology of type 2 DM.⁶ Depending on the diagnostic criteria, gestational diabetes is diagnosed in 2% to 17.8% of pregnant women.² The prevalence of gestational diabetes in Pakistan has been reported in a range of 3.20% to 3.45% and the total prevalence of Diabetes Mellitus in Pakistan has been reported to be 0.6%.⁷

Pregnancies complicated by diabetes are associated with a high rate of miscarriage, preterm delivery, preeclampsia, perinatal mortality and congenital malformations compared to the background population.¹ It has been shown that pregnancies complicated by type 2 Diabetes Mellitus (T2DM) are associated with worse perinatal mortality and

neonatal mortality than those complicated by type 1 Diabetes Mellitus (T1DM).¹ Diabetes Mellitus, whether type 1 or type 2, can affect pregnancy right from fertilization, through the entire pregnancy period and even after its end. It can predispose the fetus to many alterations in organogenesis, growth restriction and predispose the mother to some diabetes-related complications like retinopathy and nephropathy or accelerate the course of these complications if they are already present. Gestational diabetes generally leads to fetal growth alterations.²

Macrosomia due to Diabetes Mellitus is present in 15-45% of pregnancies, whereas impaired fetal growth is present in 20% of infants born to mothers with Diabetes Mellitus.⁸ Similarly, diabetes is responsible for hypoglycemia in 25-40% of infants born to diabetic mothers.⁸

The present study was conducted to document the effect of Diabetes Mellitus on neonatal outcome of pregnancy. The study would help in identification of neonatal problems associated with Diabetes Mellitus, and identify the burden on neonatal intensive care unit due to Diabetes Mellitus. In future, such studies can help in more vigilant maternal surveillance, prevention and early identification of neonatal problems. The results of this study will help to direct future decisions in the management of pregnant diabetic patients at Ayub Teaching Hospital.

MATERIALS & METHODS

This descriptive cross sectional study was conducted at the Department of Obstetrics & Gynecology, Ayub Teaching Hospital, Abbottabad from 1st March 2016 to 31st August 2016 on patients with GDM and a singleton pregnancy through consecutive non-probability sampling, after obtaining informed consent. Inclusion criteria included all pregnant female patients who presented at term (at least 37 weeks of gestational amenorrhea) with a singleton pregnancy, age between 20 and 40 years of age and diagnosed with Diabetes Mellitus for at least 5 years, pregnant women with pre-term labor, and twin or more fetuses in a single pregnancy. Women diagnosed with hypertension before gestation, eclampsia or pre-eclampsia, women indulging in substance abuse, smoking, alcohol use, and GDM were excluded from the study. Detailed medical and obstetrical history was recorded and a complete physical examination was done.

The patients were followed up till delivery and the neonatal outcomes noted; these included macrosomia (baby born with a birth weight of more than 4,000 grams regardless of gestational age),⁸ impaired fetal growth (infants whose birth weight is below the 10th percentile, when plotted against gestational age on a standard growth curve),⁸ and hypoglycemia (infants who have a random blood glucose level less than 30 mg/dl). All data were recorded on a pre-designed Performa and analyzed in SPSS version 10. Mean \pm SD were calculated for numerical variables like age, birth weight, BMI and blood pressure. Frequencies and percentages were calculated for categorical variables like type of Diabetes Mellitus, macrosomia, low birth weight and hypoglycemia. Neonatal outcomes e.g., hypoglycemia, macrosomia and low birth weight

were stratified among age and type & duration of Diabetes Mellitus, BMI and blood pressure to see the effect modifications. Post-stratification Chi Square test was applied; p value \leq 0.05 was taken as significant.

RESULTS

This study enrolled 196 pregnant women followed till delivery. Table 1 provides demographic data of subjects. The mean age of study participants was 29.53 ± 4.76 years, with age range of 22 to 37 years. The mean systolic and diastolic blood pressures were 135.68 ± 11.11 mmHg and 84.33 ± 4.37 mmHg respectively (BP range systolic 128 mmHg to 145 mmHg and diastolic 80 mmHg to 95 mmHg respectively). Similarly, the mean height was 1.50 ± 0.13 m with range being 1.27m to 1.70m. The mean weight of study participants was 56.17 ± 6.12 kg, with range of 45 kg to 66 kg. The mean body mass index of subjects was 25.53 ± 5.34 , with range of 15.80 to 40.30. Similarly, the mean duration of Diabetes Mellitus in study participants was 7.79 ± 2 years, with range of 5 to 11 years.

Table 1: Descriptive statistics of diabetic mothers (n=196).

Variables	Mean \pm SD	Range
		Minimum - Maximum
Age (years)	29.53 ± 4.76	22 - 37
Systolic BP (mmHg)	135.68 ± 11.11	128 - 165
Diastolic BP (mmHg)	84.33 ± 4.37	80 - 95
Height (meters)	1.50 ± 0.13	1.27 - 1.70
Weight (Kg)	56.17 ± 6.12	45 - 66
BMI	25.53 ± 5.34	15.88 - 40.30
Duration of Diabetes Mellitus (years)	7.79 ± 2.00	5 - 11

The different aspects of diabetes in the subjects and their frequencies are given in Table 2. The majority of subjects (88.78%) had type 2 DM from which they had been suffering for less than 8 years (62.76%). Though most of the subjects (48.98%) were of normal weight based on their BMI, 44.39% were overweight or obese, and 6.63% were underweight.

Table 2: Characteristics of Diabetes Mellitus in mothers (n=196).

Variables	Frequency	Percent
Type of Diabetes		
Type 1 DM	22	11.22
Type 2 DM	174	88.78
Duration of Diabetes		
Up to 8 years	123	62.76
More than 8 years	73	37.24
BMI groups		
Underweight	13	6.63
Normal Weight	96	48.98
Overweight	43	21.94
Obese	44	22.45

The different neonatal clinical features found in 196 diabetic mothers are presented in Table 3. The number of mothers with abnormal neonatal outcomes was 153(78.06%); among their neonates, hypoglycemia was present in 38,77%, Low Birth Weight in 21.43%, and Macrosomia in 17.86%; the number of mothers with normal neonatal outcomes was 43 (21.94%).

Variables	Frequency	Percent
Macrosomia	35	17.86
Low Birth Weight	42	21.43
Hypoglycemia	76	38.77
Total	153	78.06
Normal	43	21.94

When the outcome variables i.e. macrosomia, low birth weight, hypoglycemia were stratified according to age, BMI, blood pressure and duration of Diabetes Mellitus, the results were found to be statistically non-significant except for type of Diabetes Mellitus, where statistically significant hypoglycemia was found to be associated with type 2 Diabetes Mellitus (Table 4).

Neonatal Outcomes	Diabetes Mellitus		Total	p value
	Type 1 (n=22)	Type 2 (n=174)		
Macrosomia				
Yes	6	29	35	0.22
No	16	145	161	
Low Birth Weight				
Yes	7	35	42	0.21
No	15	139	154	
Hypoglycemia				
Yes	2	74	76	0.002
No	20	100	120	

DISCUSSION

The frequencies of macrosomia (17.86%), low birth weight (38.78%), and hypoglycemia (21.43%) in this study are in concordance with the prevalence reported in literature. For example, an earlier study from Nova Scotia reported that the rate of adverse neonatal outcome was 3-9 times greater in infants born to diabetic mothers when compared with infants born to non-diabetic mothers.⁹

In another study from Sweden, researchers concluded that Type 1 Diabetes Mellitus was associated with an increased risk of preterm birth and macrosomia in neonates. In this population based study, the authors had obtained data from medical birth registry. A total of 5,089 type 1 diabetic pregnancies and 1,260,207 control pregnancies were included. Odds ratios were adjusted for group differences in maternal age, parity, BMI, chronic hypertensive disease, smoking habits, and ethnicity. Stillbirth (3.34 [2.46–4.55]), perinatal mortality (3.29 [2.50–4.33]), and major malformations

(2.50 [2.13–2.94]) were more common in type 1 diabetic than control pregnancies. The risk of very preterm birth (<32 gestational weeks) was also higher among type 1 diabetic women (3.08 [2.45–3.87]). The incidence of fetal macrosomia (birth weight ≥ 2 SD above the mean) was increased in the diabetic group (11.45 [10.61–12.36]).¹⁰

A descriptive study on 100 diabetic pregnancies from Faisalabad, Pakistan reported a 33% prevalence of hypoglycemia in infants born to diabetic mothers.¹¹ Eighty patients had GDM, while 20 were found to have Pre Gestational Diabetes Mellitus (PGDM). The study did not report a difference among the effects of Pre-gestational and gestational diabetes on the neonatal outcome of pregnancy. There was no control group either.

Similarly, a study from Bangladesh reported that neonatal hyperbilirubinemia, respiratory distress syndrome and hypoglycemia were common adverse outcomes in infants of diabetic mothers when compared with mothers who had GDM or no diabetes.¹² The researchers studied 100 patients with PGDM and GDM delivering live baby after 37 completed weeks. Diabetic mothers had more macrosomic babies than GDM mothers (14% vs 4%).

A study from Iran reported that pregnancies associated with GDM and PGDM had a higher rate of neonatal complications.¹³ The authors reported that infants born to mothers with PGDM were at increased risk of suffering from respiratory distress syndrome, congenital malformations and hypoglycemia.

A recent study from India reported hypoglycemia (28%) as the most common complication in infants of diabetic mothers followed by macrosomia (20%).¹⁴ The results are somewhat similar to this study where hypoglycemia was detected in 38.78% of infants born to diabetic mothers. However, low birth weight was the second most common neonatal complication in this study.

Post stratification, only neonatal hypoglycemia was found to be significantly associated with T1DM in this study. This association has been reported elsewhere where researchers assessed differences in pregnancy outcomes between T1DM and T2DM.¹⁵ The researchers studied 323 diabetic and 660 matched controls in the aforementioned study. The researchers noted that T2DM women had higher BMI, age and parity with a shorter duration of diabetes and better glycemic control. Preeclampsia occurred more in women with T1DM only. Rates of elective cesarean section were similar between groups but greater than in controls, emergency cesarean section was increased in women with T1DM. Maternal morbidity in T1DM was double that of matched controls, but in T2DM was similar to controls. Babies of mothers with diabetes were more likely to be delivered prematurely. Neonatal hypoglycemia occurred more in T1DM than T2DM and contributed to a higher rate of admission to neonatal intensive care for both groups. Adverse neonatal outcomes including stillbirths and congenital abnormalities were seen in both groups but were more common in T1DM pregnancies. HbA1C values at which these poor outcomes occurred differed between T1 and T2DM.¹⁵

CONCLUSION

Maternal Diabetes Mellitus was associated with a number of adverse neonatal outcomes, the most common being hypoglycemia, low birth weight, and macrosomia.

RECOMMENDATION

The healthcare providers involved in care of diabetic pregnant patients need to be aware of common adverse neonatal outcomes of Diabetes Mellitus for better obstetrical management.

LIMITATIONS

This was a small hospital-based study that enrolled patients attending the OPD or admitted through emergency, hence the results do not reflect the trends in general population. Comparison with neonatal outcomes of non-diabetic mothers was not carried out; the effects of degree of glycemic control on neonatal outcomes of pregnancy was not measured.

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