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A COMPARATIVE STUDY OF THE COMPLICATIONS OF INFANTS OF DIABETIC BETWEEN OVERT DIABETIC AND GESTATIONAL DIABETES IN SOUTH INDIA

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ABSTRACT
Infants of diabetic mothers (IDMs) often have complications associated with fetal hyperinsulinemia induced by maternal hyperglycemia, the incidence of gestational diabetes has significantly increased in the last decades. Infants of diabetic mothers are prone to various neonatal adverse outcomes and present study was investigated that the complications of infants of diabetic between overt diabetic and gestational diabetes. Many of the perinatal complications can be traced to the effect of maternal glycemic control on the fetus and can be prevented or at least reduced through meticulous prenatal and intrapartum care. The morbidities in IDMs was studied and a comparison was made between infants born to women with pregestational diabetes and gestational diabetes. The perinatal outcome was also studied. All consecutive live born babies born to diabetic mothers at Bhaarath Medical college and Hospital between 15th February 2021 to 15th November 2021 were included in the study. IDMs were evaluated for morbidities like macrosomia, birth asphyxia, congenital anomalies, birth inuries, respiratory distress, hypoglycemia, hypocalcemia, hyperbilirubinemia and polycythemia. The neonatal complications in IDMs born to pregestational and gestational diabetic mothers were compared and data was analysed. The perinatal outcome of these IDMs was studied. we conclude that the early intervention and management of pregnancies complicated by diabetes will good neonatal care will result in decreased complications in IDMs and also will improve outcome in this high-risk population.

Key words: Infant of Diabetic Mothers; Diabetes in Pregnancy and Glycaemic Control; Hypoglycemia; Type 2 diabetes

INTRODUCTION

Infants of insulin dependent diabetes mellitus (IDDM) and noninsulin dependent diabetes mellitus (NIDDM), and also gestational diabetic (GDM) women have more perinatal problems than those of normal mothers. These complications have usually been attributed to poor control of hyperglycemia and iatrogenic or emergency preterm delivery.(1) There is a significant correlation between maternal glycemic control and perinatal outcome for the incidence of neonatal hypoglycemia, macrosomia and respiratory distress syndrome.(2) Neonatal respiratory distress, jaundice, hypoglycemia, hypocalcemia, polycythemia, macrosomia, perinatal asphyxia, prematurity, congenital malformation, hyperbilirubinemia, large and small for gestational age, and renal vein thrombosis are seen more in these infants. (3) The neonatal mortality rate is over five times that of infants of nondiabetic mothers; several of these metabolic and morphologic abnormalities can be reversed with fastidious management of the mother. Recent data from several studies have shown that IDMs who have been managed rigorously through pregnancy do not become hypoglycemic and maintain normal rates of glucose

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production and basal metabolism. GDM is usually detected in the second half of pregnancy when placental synthesis of peptide and steroid hormones reach a peak. (4-6) Sacral agenesis syndrome, with agenesis of the sacrum and lumbar spine and hypoplasia of the lower extremities, is almost never seen except in IDMs. Poor maternal control of diabetes at conception is associated with a higher incidence of congenital malformations in infants of IDDM and NIDDM women but not those of women with truly gestational diabetes (e.g., occurrence > 20 weeks' gestation, normal HbA1c concentration and reversible postpartum).(1)

Women with NIDDM are at special risk for fetal malformations because they are frequently asymptomatic and often have unrecognized diabetes; they usually enter prenatal care after embryogenesis is complete. Among many low income older women with NIDDM access to modern diabetic care is unavailable or limited in the United States. This group represents a large pool of one million women of childbearing age at risk for major and minor fetal malformations. (7).The present study was conducted in infants born to diabetic women at Bhaarath Medical College and Hospital. The complications in IDMs were studied and a comparison was made between babies born to mothers with pregestational diabetes and gestational diabetes.

MATERIAL AND METHODS:

All consecutive live born babies born to diabetic mothers at Bhaarath Medical College and Hospital, Chennai during the study period **(**15th February 2021 to 15th November 2021) formed the study population. Data regarding the diabetic status of the mother was obtained from antenatal records. Diabetic mothers were grouped into two categories: Group- I: Pregestational (type I DM and type II DM) Group-II:Gestational DM. The diagnosis of GDM was based on National Diabetes Data (5-7) Group (NDDG) criteria .[NDDG criteria :FBS > 105 mg/ dl,1 hr post prandial value > 190 mg/dl,2 hr post prandial value > 165 mg/dl and 3 hr post prandial value > 145 mg/dl. If two or more values are met or exceeded, the diagnosis of GDM is established]. The glycemic status of the diabetic mothers was ascertained based on the serial estimation of fasting and post prandial glucose levels. Each patient's fasting and 2hr post prandial blood glucose values were averaged, yielding one mean value per patient per blood glucose type (fasting or 2 hr post prandial). Blood glucose control was defined according to American college of obstetricians and gynecologists guidelines: a mean fasting value of < 95 mg/dl or mean 2 hour post prandial value of recommended guidelines (blood glucose controlled or optimal control) and women with blood glucose averages higher than the recommended guidelines (blood glucose not 8 controlled or suboptimal control). Mothers antenatal history included data regarding their socio economic status, urban/rural background, family history of diabetes mellitus (in parents) and ultrasonography findings. HbA1c levels during pregnancy (in I trimester in pregestational DM and at diagnosis in GDM) was estimated. Other associated obstetrical and medical problems were noted. Pregnancy induced hypertension was diagnosed if the systolic BP was more than 140 mm Hg and diastolic BP was more than 90 mm Hg. Hypertension prior to conception was diagnosed if BP was above 140/90 mm Hg before pregnancy. Any infections in the mothers during pregnancy was noted.

INCLUSION CRITERIA:

All consecutive live born infants of diabetic mothers born in Bhaarath Medical College and Hospital, Chennai from 15th February 2021 to 15th November 2021 were included under this study.

Exclusion Criteria:

Stillborn babies of diabetic mothers. Abortions of diabetic mothers.

METHODOLOGY:

Babies born to diabetic mothers were evaluated immediately after birth. Those requiring resuscitation were resuscitated according to National Neonatology Forum protocol for newborn resuscitation. Birth asphyxia was defined as an apgar score of < 6 at five minutes. (9) All babies born to diabetic mothers were then shifted to NICU for monitoring and treatment. At admission, weight was recorded using digital weighing scale (to nearest 10gms). Gestational age assessment was done by modified Ballard score. Macrosomia was defined as either birth weight greater than the 90 centile for gestational (10-11) age or > 4000 gm, independent of gestational age or sex. Small for gestational age was defined as birth weight less than the 10 centile for GA.

Data regarding detailed. Examination of the new born was collected in a preformed proforma. Congenital anomalies were identified clinically and supported by Echocardiography. Respiratory distress was defined as respiratory rate of 60/min and/ or presence of subcostal and intercostal retractions. At admission, blood glucose estimation was done on venous blood sample by glucose oxidase method. Subsequent blood glucose estimation at 1, 2, 3, 6, 12, 24, 36 and 48 hours of postnatal age was done by glucose dextrostix. Infants with blood glucose < 40 mg/dl were subjected to blood glucose estimation by glucose oxidase method. Hypoglycemia was defined as a blood glucose level less than 40 mg/dl in any infant, regardless of gestational age and whether symptomatic or not. (12) Estimation of hemoglobin, hematocrit and serum calcium levels were done in clinical laboratory by automated analyser. Polycythemia was diagnosed if venous hematocrit was greater than 65%. Hypocalcemia was defined as serum calcium level less than 7mg/dl. Bilirubin level estimation was done at the onset of clinical jaundice and repeated if necessary. If jaundice was not clinically

evident, then serum bilirubin estimation was done on day 4 of life. Hyperbilirubinemia was diagnosed based on standard guidelines. (13) Chest x-ray and electrocardiography (ECG) was done for all the babies and findings recorded.

Echocardiography was done for all the infants by an experienced radiologist using standard 2D echocardiography and findings recorded. III. Statistical Analysis Data were analyzed using the SPSS software package, version 11.0 (SPSS Inc. ,Chicago ,Illinois ,USA).Quantitative data were expressed using range, mean, SD, and median, whereas qualitative data were expressed as frequency and percentage .P value was assumed to be statistically significant at 0.05.

Ethical Concern:

Ethical clearance was obtained from the Ethical committee meeting conducted at Bhaarath Medical College and Hospital,Chennai,Tamil Nadu.India.

RESULTS:

Results showed that the distribution of mothers of study sample based on socio-economic status. (Table.2) The most of the mothers were from upper, upper middle and lower middle classes. The highest number of gestational diabetic mothers belonged to upper middle class.

Family history of diabetes mellitus in mothers of the study sample Results indicated that the Family History of DM (in parents of the mothers of the study sample) was present in 39.4% of the mothers of the study population (Table.3.) Maternal glycemic control in pregestational and gestational diabetes mellitus Family History of DM was present in 28.6% of pregestational diabetic mothers and 42.3% of gestational diabetic mothers. Complications seen in infants of diabetic mothers (Table. 4).indicated that the Hypoglycemia was the commonest complication seen in 56 (84.8%) IDMs followed by Respiratory distress in 22 (33.3%) and congential anomalies in 22 (32.4%) IDMs. Hypocalcemia was the least common complication seen in 2 (3.0%) IDM. None of the IDMs sustained any birth injuries. One baby with a major congenital malformation (Syringomyelia) died within 20 minutes of birth. Results Complications seen in infants of diabetic mothers (Table 4).

Table 1: Sector wise distribution of mothers of study sample

Sector	**Number**
URBAN	50 (75.8%)
RURAL	16 (24.2%)
TOTAL	66 (100%)

Table.2: Results showed that the distribution of mothers of study sample based on socio-economic status.

Upper	8 (12.1%)
Upper middle	28 (42.4%)
Lower middle	20 (30.3%)
Upper lower	8 (12.1%)
Lower	2 (3%)
Total	66 (100%)

Table 3: Family history of diabetes mellitus in mothers of the study sample

Family History of DM	**DM- Pregestational**	**DM- Gestational**	**Total**
ABSENT	5 (71.4%)	15 (57.7%)	20 (60.6%)
PRESENT	2 (28.6%)	11 (42.3%)	13 (39.4%)
TOTAL	7 (100%)	26 (100%)	33 (100%)

Table 4:Maternal glycemic control in pregestational and gestational diabetes mellitus

Complication	**Number**
Number Macrosomia (n=68)	14 (20.6%)
Birth Asphyxia (n = 68)	10 (14.7%)
Congenital anomalies (n = 68)	22 (32.4%)
Birth Injuries (n = 68)	00
Respiratory Distress (n = 66)	22 (33.3%)
Respiratory Distress Syndrome (n = 66)	4 (6.1%)
Hypoglycemia (n = 66)	56 (84.8%)
Hypocalcemia (n = 66)	2 (3.0%)
Hyperbilirubinemia (n = 66)	14 (21.2%)

Polycythemia (n = 66)	4 (6.1%)

Discussion:

From 3 to 5% of pregnancies complicated by diabetes mellitus 80 to 90% are gestational diabetes that is defined as glucose intolerance with onset or first recognized during pregnancy.8 The available data suggest that the frequency of diabetes in pregnancy is highly variable, generally reflecting the underlying pattern of NIDDM in this particular population. Different ethnic groups in the same environmental setting experience a widely variable risk. Impaired glucose tolerance is usually more prevalent than diabetes in women of childbearing age. Incidence of GDM is low in the absence of risk factors, suggesting that selective screening programs may be cost-effective. The worldwide epidemic of glucose intolerance predicted by the latest World Health Organization studies will undoubtedly increase the burden of GDM, especially in developing countries.9 Women who are found to have markedly abnormal oral glucose tolerance tests early in pregnancy and elevated hemoglobin A1C concentrations are more likely to have NIDDM rather than GDM even though hyperglycemia was detected for the first time during pregnancy.(6) In true GDM, e.g. evoked by pregnancy, the risk for embryopathy is not increased.(7)

In the present study conducted at Bhaarath Medical College and Hospital,Chennai,, 34 infants born to diabetic mothers formed the study group. 2 infants were born of twin pregnancy to a gestational diabetic mother whose glycemic control was suboptimal and one infant was alive only for 20 minutes after birth. No further investigations could be carried out for this infant. This infant had a major congenital malformation which was diagnosed as Syringomyelia. Syringomyelia was previously thought to be the severe form of caudal regression syndrome but it is now proven to be a different entity. The sex of this anomalous baby could not be determined even after autopsy as no genital organs were identified at autopsy. 68 infants were born to 67 mothers, 14 to pregestational diabetic (type – I and type – II DM) mothers and 54 to gestational diabetic mothers. Most of the diabetic mothers in our study belonged to urban sector. Mothers from upper, upper middle and lower middle classes were more in the present study.

In the present study, In the present study, 30.3% of the mothers had optimal glycemic control during pregnancy and 69.7% had suboptimal control. The number of mothers with suboptimal control was more in the present study. Among pregestational diabetic mothers, 85.7% had suboptimal control and 65.4% among gestational diabetic mothers had suboptimal control.

The important principle is that women with diabetes should start self glucose monitoring before planned conception, and pregnancy should be deferred until glycosylated haemoglobin is relatively normal (12).This is consistent with findings which have shown that components of diabetic serum, β- hydroxybutyrate, somatomedin inhibitor, and D-glucose, act synergistically or additively to produce malformations. These results suggested that several factors in diabetic serum may collectively affect the synthesis of prostaglandins and produce anomalies. A deficiency of myoinositol has also been implicated in the cause of diabetic embryopathy. Organizing action of testosterone on the genitalia involves the arachidonic acid cascade leading to prostaglandins at a critical period of genital development. It appears that the interference with testosterone synthesis or action leads to a teratogenic deficiency of arachidonic acid during this time in the genital analysis. (13) These malformations occur before the seventh week of gestation and apparently result from the mother‘s milieu. There were several hypotheses concerning a possible mechanism for diabetic embryopathy. These included alterations in maternal levels of trace metals such as zinc, enhanced synthesis of proteoglycans, such as hyaluronic acid, abnormally high levels of ketone bodies in poorly controlled diabetic state and partial blockade of glycolysis in the teratogenic action of the glucose isomer, mannose. Because the embryologic processes in the differentiation of the neural tube are similar to those of embryonic palate, it is suggested that the teratogenic pathway of the neural tube and palate in the diabetic embryopathy model may similarly involve the arachidonic acid cascade. If diabetic embryopathy is mediated by a deficiency of prostaglandins in the embryo, supplementation with prostaglandin may be able to prevent the diabetic embryopathy.

The present study, hypoglycemia was the commonest problem observed in IDMs seen in 84.4% of IDMs. The incidence of hypoglycemia in IDMs varies from15-50%. The high incidence of hypoglycemia in the present study may be because cut off level considered for diagnosis of hypoglycemia was 40 mg/dl irrespective of gestational age. In some studies, a lower cut off level has been used to define hypoglycemia in preterm babies and also the cut off level used to define hypoglycemia in general is also less. The rate of congenital anomalies was also high in the present study (32.4%). The reasons could be because all IDMs were subjected to 2D – Echocardiography irrespective of symptoms and so asymptomatic congenital Heart Disease mainly ASD was detected in 10 out of 33 IDMs subjected to ECHO. One infant who had ASD also had VSD and PDA. Another infant who could not be subjected to any investigation, had a major malformation, syringomyelia and the baby died within 20 minutes of birth. Autopsy done on this baby did not detect any cardiac abnormality. The other complications seen in IDMs are comparable to other studies with some differences.

According to WHO the diabetic population will increase until the year 2025 and the major part of this numerical increase will occur in developing countries. There are more women than men with diabetes, especially in developed countries. This report supports the earlier prediction of the epidemic nature of diabetes in the world during the first quarter of the 21st century. It also provides a provisional picture of the characteristics of the epidemic. Worldwide surveillance of diabetes is a necessary first step toward its prevention and control, which is now recognized as an urgent priority (14-19)

The importance of diabetic control before conception is stressed and each woman is advised to have a comprehensive medical assessment, instruction in home blood glucose monitoring, a retinal examination, renal evaluation and nutrition counselling. Frequent supervisory appointments every few weeks at a diabetes center or by a diabetologist are essential to achieve and maintain diabetic control. It usually takes 2-4 months to reach a normal HbAlc concentration along with changes in nutrition and activity that are compatible with the patient's life style, occupation, and quality of life (20)

The current definition of GDM does not allow identifying pregestational diabetes from true GDM. The WHO recently proposed new criteria for the diagnosis and definition of hyperglycemia first detected in pregnancy which distinguishes the more serious diabetes in pregnancy from GDM [21-28]. This is a considerable advance as we say that risks of serious complications for foetus and the neonates are much higher in true diabetes than in GDM. This will help to better understand the burden of hyperglycemia in pregnancy and its relationship with the growing prevalence of T2D. This will also probably allow in the future to determine precisely the risks linked to GDM compared to those linked to T2D. Such distinction will subsequently help better identifying risks in the neonatal period, but also later in life. Indeed, offspring of diabetic and obese women, or macrosomic infants, are more likely to be obese and to have diabetes and cardiovascular diseases in adulthood [29-30]. These long term consequences of diabetes in pregnancy are going to be the burden of further generations.

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