A Study of Birth Weight and Cord Blood Glucose Levels of Neonates in Normal Pregnancy and Pregnancy with Gestational Diabetes Mellitus

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ABSTRACT

BACKGROUND

Gestational Diabetes Mellitus (GDM) is diabetes diagnosed for the first-time during pregnancy. Infants of diabetic mothers are prone to various neonatal adverse outcomes, including metabolic and hematologic disorders, respiratory distress, cardiac disorders, and neurologic impairment due to perinatal asphyxia and birth traumas, among others.

METHODS

This was a comparative study conducted in the Department of Obstetrics and Gynaecology, Institute of Maternal and Child Health, Medical College, Calicut. A total of 200 subjects were included in the study. The subjects were divided into two groups comprising of neonates of healthy 150 pregnant women with no history of GDM. The other group included neonates of 50 pregnant women with GDM. Cord blood sample was collected during delivery. Cord blood glucose was determined by the GOD/POD method. Birth weight of newborn was recorded following delivery. The obtained data was tabulated and analysed using appropriate statistical tests.

RESULTS

The mean birth weight of newborns of women with GDM was 2.96 Kg and mean birth weight of newborns of normal pregnant women was 2.81 Kg. Even though macrosomia was not observed in newborn of GDM in the present study, the birth weight is significantly higher in newborns of women with GDM (p-value <0.05). In newborns of women with GDM, the mean cord blood glucose was 73.74 mg/dL and it was 77.86 mg/dL in newborns of controls. The difference was not statistically significant. There was hyper secretion of insulin from foetal pancreas in women with GDM to maintain normal blood glucose level in the foetus.

CONCLUSIONS

Birth weight of newborns of mothers with GDM was significantly higher than that of controls. Cord blood glucose values of newborns of mothers with GDM and controls show no significant difference.

KEYWORDS

Glucose Tolerance, Gestational Diabetes, Blood Glucose, Pregnancy**,** Birth Weight, Cord Blood.

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BACKGROUND

The foetal and neonatal complications associated with GDM have been known from early times. These include macrosomia, neonatal hypoglycaemia, perinatal mortality, congenital malformations, hyperbilirubinemia, polycythaemia, hypocalcaemia, Respiratory Distress Syndrome and unexplained foetal and neonatal deaths. Perinatal morbidity is increased even in the group of women who have only impaired glucose tolerance.[1]

Macrosomia defined as birth weight >4 kg is a well-documented complication of GDM. The mean birth weight of newborn in GDM mothers and normal controls was statistically significant in epidemiological study conducted in South India.[1] Maternal obesity is an independent and most important risk factor for macrosomia than is glucose intolerance according to Leonardi and Bottoms[2] and Graf et al.[3] Ramachandran et al[4] suggested that it could be explained by the increasing BMI in addition to maternal glucose levels.

Glucose intolerance during pregnancy predisposes the offspring for increased risk for many other complications too. This research tried to find out relationship between neonatal factors and GDM. We wanted to study the relation of birth weight of newborn and cord blood glucose in gestational diabetes mellitus and normal pregnancy

METHODS

The study was conducted in the Department of Obstetrics and Gynaecology, Institute of Maternal and Child Health, Medical College, Calicut.

A total of 200 subjects were included in the comparative study. The subjects were divided into two groups comprising neonates of healthy 150 pregnant women with no history of GDM. The other group included neonates of 50 pregnant women with GDM. Mothers with diabetes, hypertension and renal disease diagnosed before pregnancy were excluded from the study.

A detailed history was taken. Cord blood sample was collected during delivery. Cord blood glucose was determined by the Glucose Oxidase/Peroxidase method (GOD/POD) method. Birth weight of newborn was recorded following delivery. The obtained data was tabulated and analysed using appropriate statistical tests.

Study was approved by Human Ethical Committee and Review Board of Institution. Study subjects (mothers) were counselled separately about the study and a written consent was procured from them.

All statistical data were analysed using SPSS software version 16. Continuous variables were expressed as mean ± standard deviation. Qualitative data was expressed as percentage. Independent t test was used for comparing quantitative data between two groups. Analysis was done to compare birth weight of newborn and cord blood glucose values in GDM and normal pregnancy.

RESULTS

The present study on factors associated with gestational diabetes mellitus was conducted in a total of 200 subjects divided into two groups. One of the groups comprised of 50 neonates of women with GDM and the other included 150 normal neonates of pregnant controls. Birth weight of newborn and cord blood glucose were included as the baseline parameters.

The mean birth weight of newborns of women with GDM is 2.96 Kg and mean birth weight of newborns of normal pregnant women is 2.81 Kg. Even though macrosomia is not observed in newborn of GDM in the present study, the birth weight is significantly higher in newborns of women with GDM (p value <0.05).

	Birth Weight in Kg			
	Primi	**Gravida 2**	**Gravida 3**	**Gravida 4**
GDM	2.9	2.9	3.00	3.04
SD	0.3	0.4	0.40	0.50
CONTROL	2.8	2.85	2.75	2.84
SD	0.4	0.3	0.40	0.50

Table 1. Mean Birth Weight in GDM and Control Groups

Birth Weight of New Born (Kg)		
	GDM	**Controls**
Mean	2.96	2.81
SD	0.38	0.36

Table 2. Comparison of Birth Weight of Newborn of GDM and Normal Pregnant Controls

p value <0.05

In newborns of women with GDM the mean cord blood glucose is 73.74 mg/dL and it is 77.86 mg/dL in newborns of controls. The difference is not statistically significant. There is hyper secretion of insulin from foetal pancreas in women with GDM to maintain normal blood glucose level in the foetus.

Cord Blood Glucose (mg/dL)		
	Newborn - GDM	**Newborn Controls**
Mean	73.74	77.86
SD	14.08	13.66

Table 3. Cord Blood Glucose of Newborns of Women with GDM and Normal Women

p value not significant

DISCUSSION

Macrosomia defined as birth weight >4 kg is a well-documented complication of GDM. The mean birth weight of newborn was found to be 2.96 Kg in GDM and 2.81 Kg in controls in the present study, the difference being statistically significant. An epidemiological study conducted in South India had a similar observation.[1] Maternal obesity is an independent and most important risk factor for macrosomia than is glucose intolerance according to Leonardi and Bottoms[2] and Graf et al.[3] Ramachandran et al[4] suggested that it could be explained by the increasing BMI in addition to maternal glucose levels. The effect of intervention in reducing the incidence of macrosomia has been examined by several investigators.[5] In the present

study also, no newborn was observed to have birth weight >4 kg probably as a result of early detection and management of GDM. However, offspring of mothers with GDM are strongly predisposed to obesity and glucose intolerance regardLess of birth weight.[6]

Macrosomia, defined as birth weight >4000 grams, occurs as a complication in ~20 to 30% of infants of mothers with GDM. Macrosomia and associated complications of delivery are considered to be the most frequent and serious types of morbidity. An incidence of 15 to 45% or a 3-fold increase in incidence of this complication was noted by Moore[7] when compared to normoglycemic controls. Macrosomia results from the delivery of excess glucose, by facilitated diffusion to the foetus as a consequence of maternal hyperglycaemia. A cohort study conducted by Schmidt et al[8] confirmed that GDM predicted a 30% increased risk of macrosomia. This complication affects all foetal organs except the brain.[5] These foetuses are predisposed to shoulder dystocia, increased caesarean section and brachial plexus injuries.[5] They were found to have increased incidence of hypoglycaemia and neonatal jaundice. Birth weight ratio (Birth weight corrected for gestational age) was found to be 1.05 in controls and 1.09 in GDM according to a prospective observational outcome cohort study by Magee et al.[9]

Cord blood glucose values of newborns of women with GDM and controls were compared in the present study. The values were found to be 73.74 mg/dL and 77.86 mg/dL respectively with no significant difference. In GDM, the hyperglycaemia causes hyper secretion of insulin from the foetal pancreas to maintain normal glucose levels. Lee et al[10] have documented altered glucose metabolism in offspring of mothers with GDM ≥ 5 years of age. This suggests that altered glucose metabolism influenced by the intrauterine environment is more likely to occur in offspring of GDM mothers. Further evaluation is required to ascertain as to when it occurs and how can it be ameliorated.

Neonatal hypoglycaemia occurs in infants of diabetic mothers due to hyperinsulinemia. This complication if undetected can lead to coma or even death. An incidence of 9% was reported in a study by Moore.[7] Another cohort study by Barahona et al[11] revealed a high incidence of 24%. Insulin is present in the human pancreas from 11 weeks of gestation and although the pancreatic response to insulin secretagogues is sluggish in normal infants, foetal exposure to high concentrations and large fluctuations of glucose and amino acids such as arginine during poorly controlled diabetic pregnancy appears to produce premature maturation of β cells of foetal pancreatic islets. This causes hyperinsulinemia which may lead to hypoglycaemia within first 24 hours after delivery. High circulating insulin concentrations inhibit glycogenolysis and lipolysis thus depriving the infant of alternative energy sources.[12]

More than a decade ago, Norbert Freinkel postulated that alterations in the maternal metabolic milieu at any time during gestation can influence intrauterine development.[13] The foetal tissues most likely to be affected are neural cells, adipocytes, myocytes and pancreatic β cells. Exposure during early first trimester can lead to intrauterine growth retardation and organ malformations or dysmorphogenesis, described by Freinkel as 'fuel-mediated teratogeneis'. The altered metabolic milieu to which the foetus is exposed can also result in long - term consequences.[13]

Gestational diabetes mellitus is associated with several foetal, neonatal and maternal complications. The normal physiological changes in pregnancy have important implications for women with abnormal glucoregulation. The growth and development of the human conceptus takes place within the metabolic milieu provided by the mother. Freinkel and colleagues introduced the concept of "pregnancy as a tissue culture experience" proposing that the placenta and foetus develop in a medium totally derived from maternal fuels.[6] As all constituents are regulated by maternal insulin, disturbances of secretion and action of this hormone will influence the composition of nutrients to which the foetus is exposed. According to Freinkel's hypothesis, the abnormal maternal mixture of metabolites modifies phenotypic gene expression leading to short and long-term effects in offspring.[6,14]

Congenital anomalies associated with GDM include cardiac anomalies in ~38% including cardiomyopathy, transposition of great vessels, ventricular septal defect, situs inversus, single ventricle and hypoplastic left ventricle. Musculoskeletal anomalies were reported in 15%, commonest being caudal regression. Central nervous system anomalies like anencephaly, encephalocele, meningomyelocele and spina bifida were reported in 10%. The other rare anomalies include renal agenesis, multicystic renal dysplasia, anal or rectal atresia and pulmonary atresia.[5] Periconceptional glycaemic control is the main factor in genesis of diabetes associated birth defects.[5,12,15] Schaefer et al[16] investigated the incidence of congenital malformations in offspring of women with GDM. One or more major congenital malformations were found to occur in 2.9% and minor anomalies in 2.4%. Sheffield and coworkers[17] observed that women with fasting hyperglycaemia diagnosed before 24 weeks had pregnancy outcomes similar to those for pregnant women in classes B through F and R of American College of Obstetricians and Gynaecologists (ACOG). Major malformations were found to occur 3 to 8 times as frequently as against nondiabetics. Barthe et al, Miller et al and Lucas et al[5] had similar conclusions. GDM after first trimester does not appear to increase the risk. A longitudinal study conducted on GDM by Mills et al,[18] 'The Diabetes in early pregnancy Study,' revealed an incidence of 9% of congenital malformations in uncontrolled GDM as against 5% in women with optimized glucose control. Moore[7] reported an incidence of anomalies in 1 to 2% in offspring of GDM with a 4 to 8-fold increased risk when compared to women with normal carbohydrate tolerance. Kitzmiller et al[15] observed one major congenital anomaly in 6.5% of untreated diabetes and 1.2% in the treated group.

Although most foetuses of mothers with diabetes exhibit growth acceleration, growth restriction occurs in pregnancies complicated by pre-existing undetected type 1

diabetes.[15] The most important predictor of foetal growth restriction is underlying maternal vascular disease. Those patients with associated retinal or renal vasculopathies and or chronic hypertension are at risk for growth restriction.[7]

Prematurity is another complication occurring in infants of women with GDM.[5, 12]A prospective cohort study conducted in Iran[19] on perinatal complications associated with GDM revealed a high incidence of prematurity. Svare et al[20] also had similar findings.

Respiratory distress syndrome in infants of mothers with GDM was found to occur with an incidence of ~2%.[7] This complication is due to excessive insulin suppressing the production of surfactant by type 2 alveolar epithelial cells in the foetal lung. This continues to be a relatively preventable complication.[5]

Neonatal hypocalcaemia has been reported in ~1% of offspring of diabetic mothers.[7] Polycythaemia results from increased erythropoietin due to decreased foetal oxygen tension because of hyperglycaemia and hyperinsulinemia. The reported incidence is ~1% and it results in vascular sledging, ischemia and infarction of vital organs like kidney.[5,12] Postnatal hyperbilirubinemia and jaundice occur due to prematurity and polycythaemia and the reported rate is 25 to 30%.[5,7]

CONCLUSIONS

Birth weight of newborn of mothers with GDM is significantly higher than that of controls. Cord blood glucose values of newborn of mothers with GDM and controls show no significant difference.

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