

Research Article

Neonatal Complications of Gestational Diabetes Mellitus

Dr. Vaishali M Paunikar¹, Dr. D Rajashree²

¹Associate Professor, MNR Medical College, MNR Nagar, Narsapur Road, Sanga Reddy, Medak Dist - 502 294, Telangana, India

²Associate Professor, Mallareddy Medical College for Womens (MRMCW), Jeedimetla, Hyderabad, Telangana, India

***Corresponding author**

Dr. Vaishali M Paunikar

Email: dr.bvaishali@gmail.com

Abstract: Impact of gestational diabetes mellitus(GDM) on maternal and fetal health is a major concern since prevalence of GDM is increasing worldwide. Present study aims at identifying the magnitude of increased perinatal risks due to GDM. Nine hundred antenatal women of gestational age 24 weeks and above were screened for GDM using 50g glucose challenge test followed by oral glucose tolerance test(OGTT). Based on American Diabetes Association(ADA) criteria, 30 women were diagnosed with GDM, followed up till their deliveries and the fetal outcome was studied. Data regarding the perinatal complications associated with GDM was recorded. The study findings revealed an increased risk of fetal macrosomia(13.33%), neonatal hypoglycemia(13.33%), respiratory distress syndrome(RDS) in 10%, polycythemia(3.33%), hyperbilirubinemia(13.33%), hypocalcaemia(3.33%), small for gestational age babies(SGA) in 10%, intra-uterine deaths(IUD) in 3.33% and still births(3.33%). Thus, an early intervention through good glycemic control in diagnosed cases of GDM can lower the perinatal complications and improve the fetal outcome.

Keywords: GDM, macrosomia, SGA, hypoglycemia, polycythemia, RDS, hyperbilirubinemia, hypocalcaemia, still births, IUD

INTRODUCTION

Normal growth and development of fetus is dependent on adequate maternal nutrition, normal maternal metabolism, good placental transfer and proper utilisation of substrates by fetus. Many metabolic changes occur in normally pregnant women due to placental hormones which modify her use of ingested substrates so that critical fetal fuels are always abundant in her blood stream for placental transfer. Certain maternal diseases modify this unique adjustment and result in fetal growth abnormalities such as macrosomia or growth retardation in addition to loss of infant life. One of such diseases is Gestational Diabetes Mellitus(GDM).

GDM is a glucose tolerance disorder that occurs or is diagnosed for the first time during pregnancy[1]. Pregnancy is a special situation in which potential effects on fetus are of paramount importance and should be clearly identified by clinician and managed with care. Carbohydrate intolerance in a pregnant woman is associated with obstetric problems and increased perinatal risks. Perinatal risks include congenital abnormalities, fetal macrosomia, birth trauma, neonatal hypoglycemia, respiratory distress

syndrome(RDS), polycythemia, hyperbilirubinemia, hypocalcaemia and death[2]. Early detection and management can modify the course of disease and reduce excess perinatal morbidity and mortality.

MATERIAL AND METHODS

The present study was a hospital based study conducted at Gandhi Hospital, Secunderabad. Nine hundred antenatal women of gestational age 24 weeks and above attending the outpatient department of Obstetrics and Gynecology were initially screened for the study. All antenatal women were screened using two-step process which has been the most commonly used screening approach for diagnosing GDM[3, 4]. Initially, these women were subjected to glucose challenge test with 50g oral glucose without any preparation and plasma glucose levels were measured 1 hour after ingesting glucose. Plasma levels ≥ 135 mg/dl was considered as positive. Women with positive test then underwent a 100-g, 3-hour oral glucose tolerance test (OGTT) and plasma glucose levels were measured at 0 hour, 1 hour, 2 hour and 3 hour. The threshold values used for the OGTT were: fasting ≥ 95 mg/dl, 1-hour ≥ 180 mg/dl, 2-hour ≥ 155 mg/dl, and 3-hour ≥ 140 mg/dl, based on the ADA criteria [5]. Those with

two abnormal values were diagnosed with GDM. Multiphase sampling technique was used. Out of 900, 30 women were diagnosed with GDM and followed up till their deliveries and the fetal outcome was studied. All women diagnosed with GDM were treated in a similar manner throughout the study period with dietary modification and/or insulin depending on their plasma glucose values. A pre-designed, pretested, semi-structured questionnaire was administered to each patient. Questionnaire included information about age, weight, height, parity, obstetric history and family history of diabetes. General physical examination and relevant laboratory investigations were also done. Subjects were instructed to undergo self-monitoring of glucose, urine analysis of glucose, proteins and ketone bodies, daily B.P recording and report weekly to antenatal clinic. Non-stress test was done twice a week. Weekly ultrasound for biophysical profile of fetus and fundus examination was also done. Timing of delivery was determined based on fetal maturity. Subjects were briefed about the study protocol and informed consent

was taken. Clearance from Institutional Ethical Committee was taken.

Following delivery, gestational age calculation was done to assess macrosomia in fetus which was calculated by Ballard’s Modification of Dubowitz scoring for gestational age[6]. Based on gestational age and birth weight, they were classified as macrosomia or large for gestational age(LGA), small for gestational age(SGA) and appropriate for gestational age(AGA). Hypoglycemia was diagnosed by blood glucose levels less than 40mg/dl. Blood glucose estimation was done at 0, 1, 2, 3 and 6hrs for 48 hrs. Polycythemia was assessed by PCV values more than 65%.Hypocalcaemia was diagnosed with serum calcium levels less than 7ml/dl. RDS was assessed by Downe’s score[7]. Hyperbilirubinemia was assessed by Kramer’s rule and serum bilirubin levels more than 12mg/dl[8]. Data was tabulated and percentage distribution of neonatal complications was recorded.

RESULTS

Table 1: Characteristics of mothers with GDM

S.no	Risk factors	No. of cases with GDM	
1	Age	20-25yrs	09
		>25 yrs	21
2	Gestational age at diagnosis	24-32 weeks	20
		>32 weeks	10
3	Parity	Primipara	08
		Multipara	22
4	Family history of diabetes	Positive	19
		Negative	11
5	Previous history of GDM	Positive	20
		Negative	10
6	Previous history of still birth/IUD	Positive	07
		Negative	23

Table 2: Percentage distribution of neonatal complications of GDM

S.no	Complications	No. of cases	Percentage
1	Hypoglycemia	04	13.33
2	Hyperbilirubinemia	04	13.33
3	Respiratory distress syndrome	03	10
4	Macrosomia	04	13.33
5	Small for gestational age babies	03	10
6	Polycythemia	01	3.33
7	Hypocalcemia	01	3.33
8	Still births	01	3.33
9	Intra-uterine death (IUD)	01	3.33

DISCUSSION

Production of placental counter regulatory hormones which have a blocking effect on insulin produced, termed as insulin resistance is the cause of GDM[9]. Fetal glucose concentration is controlled primarily by maternal blood glucose concentration via transplacental transport. As there is absence of any significant glucose

production in fetus in contrast to hepatic production in mother, there is no regulatory pathway in fetus. Difference between adult and fetus demonstrate that fetal homeostatic capability is substantially reduced compared to that of an adult, putting the fetus at risk in case of alterations in maternal glycemc status.

Before the discovery of insulin, perinatal mortality was about 75%. After the introduction of insulin, there is a dramatic decline in maternal mortality and an improved perinatal outcome. The present study revealed an increased risk of fetal macrosomia(13.33%), neonatal hypoglycemia(13.33%), hyperbilirubinemia(13.33%), respiratory distress syndrome(RDS) in 10% (Table 2) which is similar to the results found in a study by Abdulbari Bener et al conducted in Qatar[10]. Pregnancies complicated by GDM have few short term effects on developing fetus including risk of birth trauma and long term effects of obesity and development of type II diabetes mellitus.

Macrosomia is defined as fetal weight >90th percentile for gestational age or $\geq 4,000$ g[11]. Maternal diabetes is an independent risk factor for fetal macrosomia. In maternal hyperglycemic states, basal membrane GLUT-1 expression and activity on fetal side is upregulated by 50% providing a means for increasing transplacental glucose flux with microvillous membrane GLUT-1 expression on maternal side unaffected. Hence, maternal hyperglycemia leads to fetal hyperglycemia resulting in increased production of growth factors such as insulin, IGF-1, insulin-like growth factor binding protein-3 with subsequent increase in fetal growth or macrosomia[2]. Complications associated with macrosomia like birth trauma, shoulder dystocia, brachial plexus injury etc. was not seen owing to the decision of elective caesarian section.

Neonatal hypoglycemia is a common, transient complication in neonates of mothers with GDM occurring in 50% of macrosomic infants and in 5–15% of those with optimally controlled GDM[12]. Neonatal hypoglycemia is defined as fetal serum glucose values less than 40mg/dl irrespective of gestational age during the first 12 hours of life. Maternal hyperglycemia causes increased placental glucose transfer to fetus. The fetus by virtue of being exposed to high concentration of glucose in utero responds by fetal β cell hyperplasia which results in fetal hyperinsulinemia[7]. This causes neonatal hypoglycemia after umbilical cord clamping depriving fetus of supply of glucose.

Polycythemia is defined as hematocrit more than 65% at delivery. Polycythemia in the neonate is a result of increased erythropoietin induced RBC production in response to fetal hypoxia. Fetal hyperglycemia and hyperinsulinemia increase fetal basal metabolic rate and oxygen consumption leading to relative hypoxic state. The fetus responds by increasing O₂ carrying capacity through increased erythropoiesis [13]. Also, GDM mothers have increased HbA_{1c} which binds tightly with oxygen making maternal O₂ less

available for placental transfer to fetus leading to neonatal hypoxia[14].

Hyperbilirubinemia is defined as maternal serum bilirubin levels more than 12mg/dl. It is seen as an associated complication of polycythemia and result of an immature bilirubin conjugation system in neonate[14].

Infants exposed to high levels of glucose develop hyperinsulinemia which in turn inhibits enzyme inductive action of cortisol on fetal lungs. This then inhibits type II pneumocytes from producing lecithin. Lecithin is a phospholipid present in surfactant. Lack of lecithin causes poor stabilisation of fetal alveoli during exhalation and development of RDS. Hyperinsulinemia also decreases production of pulmonary phospholipids, phosphatidyl glycerol which is also a component of surfactant[15].

Hypocalcaemia is defined as total serum calcium levels less than 7mg/dl or an ionized calcium level less than 4mg/dl[7]. Hyperglycemia in GDM mothers leads to osmotic diuresis. The loss of water also entails some accompanying loss of electrolytes like calcium and magnesium causing hypomagnesaemia. Magnesium is required for parathyroidhormone(PTH) synthesis and in severe hypomagnesaemia; PTH synthesis is impaired[16]. Thus, a delay in fetal parathyroid hormone synthesis after birth leads to neonatal hypocalcaemia[14].

Cause for small for gestational age(SGA) babies born to mothers with GDM is related to pre-eclampsia which leads to vasoconstriction in placental vessels leading to improper blood supply to growing fetus[2].

Several studies have found an increased rate of stillbirths & intra-uterine deaths(IUD) in untreated GDM[17]. Early diagnosis can have better control of hyperglycemia. 20 GDM women diagnosed before 32 weeks had good glycemic control with no still birth or IUD. Out of the 10 cases diagnosed after 32 weeks, 1 was still birth and 1 IUD indicating late diagnosis leads to slower control of hyperglycemia by which time, damage is already done. Sudden fetal IUD in last week of pregnancy is the classic obstetric accident in diabetic mothers. Fetal hyperglycemia and hyperinsulinemia may cause fetal acedemia and hypoxia leading to sudden death.

Fig1. Shows that incidence of caesarian section was high as compared to normal vaginal delivery in GDM cases. Macrosomia places the infant of a diabetic mother at greater risk for birth trauma due to cephalopelvic disproportion. Elective caesarian section was done to prevent birth canal injuries to mother and to

avoid instances of sudden intrauterine death and still births. Emergency caesarian was done in fetal distress to avoid fetal hypoxia related to uterine contractions in vaginal delivery[17, 18].

In addition to the immediate morbidity associated with delivery and the neonatal period, investigators have expressed concern about long-term outcome in children of diabetic mothers. Hence, long term potential complications related to metabolism, weight and behavior need to be studied through follow up of such children which however remain the limitation of this study.

Compared to expected number of fetal complications according to recorded prevalence in uncontrolled GDM, number of complications observed in study group babies was found to be less which is a sign of good glycemic control in mothers with GDM.

CONCLUSION

Targeting delivery early in term, improved compliance, better glycemic control during pregnancy, improved control at conception, improved neonatal care and early screening for fetal abnormalities all likely contribute to improved outcome.

REFERENCES

1. Tracy L, Setji MD, Ann J, Brown MD, Mark N, Feinglos MDCM; Gestational Diabetes Mellitus. *Clinical Diabetes*, 2005; 23 ;(1): 17-24.
2. Ahuja MMS, Tripathy BB, Sam G P Moses; *Textbook of Diabetes Mellitus*, 1st edition, 2002; 681-714.
3. Kisti P, Fuller MD, Adam F, Borgida MD; Gestational Diabetes Mellitus Screening Using the One-Step Versus Two- Step Method in a High-Risk Practice. *Clinical Diabetes*, 2014; 32(4);148-150.
4. American College of Obstetricians and Gynaecologists: Committee Opinion No. 504: Screening and diagnosis of gestational diabetes mellitus. *Obstet Gynecol*, 2011; 188; 751-753.
5. American Diabetes Association: Gestational diabetes mellitus (Position Statement). *Diabetes Care* 27(Suppl. 1): 2004; S88-S90.
6. Ballard JL, Khoury JC, Wedig KL, Wang L, Eilers-Walsman BL, Lipp R.; New Ballard Score, expanded to include extremely premature infants. *J. Pediatr.*, 1991; 119: 417-423.
7. Singh M; *Care of the Newborn*, 7th edition, 2010; 277-373.
8. Kramer LI; Advancement of dermal icterus in the jaundiced newborn. *Am J Dis Child.*, 1969; 118(3): 454-458.
9. Kuhl C; Insulin secretion and insulin resistance in pregnancy and GDM. Implications for diagnosis and management. *Diabetes*, 1991; 40(Suppl 2): 18-24.
10. BenerA, Najah M Saleh, Abdulla Al-Hamaq; Prevalence of gestational diabetes and associated maternal and neonatal complications in a fast-developing community: global comparisons. *Int J Womens Health*, 2011; 3: 367-373.
11. Mohammadbeigi A, Farhadifar F, Zadeh NS, Mohammadsalehi N, Rezaiee M, Aghaei M; Fetal macrosomia: Risk factors, Maternal and Perinatal Outcome. *Ann Med Health Sci Res.*, 2013; 3(4): 546-550.
12. Darcy Barry Carr MD and Steven Gabbe MD; Gestational Diabetes: Detection, management and implications. *Clinical Diabetes*, 1998; 16(1).
13. Francis B M, MimouniG, Yoram AB; Neonatal Management of the Infant of Diabetic Mother. *Pediat Therapeut.*, 2013; 4: 1.
14. Milašinović L, Hrabovski I, Grujić Z, Bogavac M, Nikolić A; Biochemical and physiological characteristics of neonates born to mothers with diabetes during gestation. *J Med Biochem.*, 2012; 31(1): 47-52.
15. Steven AD, Jeannie MS; The combined effects of insulin and cortisol on surfactant protein mRNA levels. *Pediatric Research*, 1995; 38(4): 513-521.
16. Tandon OP, TripathiY; Best and Taylor's Physiological Basis of Medical Practice. Chapter 54. *Hormonal Regulation of Mineral Metabolism*, 13thed, 2012; 887.
17. Kachhwaha CP, Singh HV; Prevalence of gestational diabetes mellitus and its outcome in western Rajasthan. *Indian J Endocr Metab.*, 2013; 17:677-80.
18. Gasim T; Gestational Diabetes Mellitus: Maternal and Perinatal Outcomes in 220 Saudi Women. *Oman Med J*, 2012; 27(2):140-144.