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RESEARCH ARTICLE

Pregnancy outcome in gestational diabetes mellitus under treatment and its correlation with hba1c at 36 weeks

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ABSTRACT

Brain Objectives: To observe pregnancy outcomes in gestational diabetes mellitus (GDM) under treatment.

Methods: Pregnant mothers diagnosed with GDM (N=40) age: 27.44 ± 7.91 yr; body mass index, BMI: 26.88 ± 4.16 kg/m²; mean±SD) on the basis of WHO 2013 criteria were compared for pregnancy outcome irrespective of gestational age. HbA1c was measured in all mothers. Gestational hypertension, preeclampsia, premature rupture of membrane (PROM), hydramnios, recurrent urinary tract infection (UTI), recurrent moniliasis, intrauterine growth retardation (IUGR), intra uterine death (IUD), mode of delivery, birth weight, birth injury, neonatal hypoglycemia, hyperbilirubinemia, respiratory distress syndrome (RDS), congenital anomaly were recorded at every trimester.40 mothers(GDM on MNT =9, GDM first started on MNT then converted to Insulin treatment =13, GDM on Insulin=18) could be followed for outcomes to the end of pregnancy. All the GDM mothers were offered standard treatment throughout pregnancy period.

Results: HbA1c monitoring (less than or equal to 5.7% in 15; 5.7% to 7% in 20; 7.1% - 8% in 2; more than 8% in 3).Outcome events in GDM with associated co-morbidity: preeclampsia- 7; Hypothyroid – 5; Long period infertility – 7; Anemia – 3; PCOS-6; Recurrent GDM -1; PROM-7; hydramnios-4; recurrent UTI-8; recurrent moniliasis- 2; Labour Naturalis- 7; Instrumental Delivery -2; Caesarean section- 31; small for gestational age (SGA)-7; large for gestational age (LGA)- 6; IUGR- 2; neonatal hypoglycemia-2; hyperbilirubinemia-1; RDS- 1 and birth injury-0, congenital anomaly-2,Preterm delivery- 6; caesarean section-31, Perinatal mortality - 1

Conclusions: With proper treatment and good Glycemic Control adverse events on fetal outcome are relatively less in GDM.

Key words: GDM, HbA1C monitoring, Glycemic control, Pregnancy outcome

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INTRODUCTION

Gestational diabetes mellitus (GDM) is increasing among the South Asians (Nusrat-Sultana et al., ?; Sandesh-Panthi et al., 1999). India is considered as the capital of Diabetes. GDM is associated with adverse pregnancy outcomes. However, whether standard treatment at outset makes any difference is not well studied. Several studies world wide including the land mark Hyperglycemia and Adverse Pregnancy Outcome study (HAPO study) did not assess the adverse outcomes in light of this point (Hyperglycemia and Adverse Pregnancy outcome, 2008). As GDM is associated with significant metabolic alterations, increased maternal and perinatal morbidity and mortality, it is imperative to screen pregnant mothers for GDM (Farooq et al., 2007). Many studies have observed various complications of GDM without regard to the emphasis of treatment during pregnancy (American Diabetes association, 2003; Ghosh and Sudip, 2012).

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A multicenter, randomized trial observed statistically significant decrease in the relative risks of several outcomes like macrosomia, large for gestational age (LGA) and shoulder dystocia with standard treatment for GDM. Additionally the risks for perinatal mortality, birth trauma were also reduced in treated women (Landon *et al.*, 2009). Present study was carried out to evaluate the pregnancy outcomes in GDM mothers on treatment with MNT, Insulin and Glycemic control monitored by HbA1C and Institutional delivery is offered to all. Mode of delivery planned wisely to avoid both maternal and perinatal mortality and morbidity . NICU admission for all babies are done soon after delivery to monitor for RDS, hypoglycemia, hyperbilirubinemia and anomaly screening.

MATERIALS AND METHODS

Study subjects: It was a prospective cohort study carried out during June 2017 to July 2018 by GDM study group of Dept. of Obstertic and Gynaecology, GRH, Madurai on pregnant mothers diagnosed with GDM (n=40, age: 27.44±7.91yr; body mass index, BMI: 26.88±4.16 kg/ m2) for pregnancy outcome irrespective of gestational age. Informed written consent was taken from each of the mothers.

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Study design: Pregnant women diagnosed as GDM by oral glucose tolerance test (OGTT) were randomly selected and included in the study irrespective of their associated obstertric complications, as well as HbA1c were done to monitor the glycemic control. The GDM group received standard treatment with concomittent diabetolist monitoring with MNT, insulin, and few with MNT were transferred to Insulin, and doses of Insulin was adjusted according to blood glucose level and were followed till delivery. Their pregnancy outcomes were recorded.Demographic, anthropometric measures,glycaemic status as well as adverse pregnancy outcomes e.g. hydramnios, recurrent monilial infections, recurrent urinary tract infection (UTI), preterm delivery, preeclampsia, macrosomia, birth injury etc. in light of the experience with GDM by our obstetricians were recorded. GDM mothers were advised regular antenatal check-up. At the end of every trimester clinical and biochemical parameters and ultrasound imaging for pregnancy profile was done. All the mothers were advised for hospital delivery.Prior to commencement of this study the research protocol was approved by Institutional Review Board (IRB).

Analytic method: Blood glucose was measured by glucose oxidase peroxidase method. HbA1c was measured by high performance liquid chromatography (HPLC)

RESULTS

Among the GDM mothers 6 were >30 years, 16 were having BMI >27 kg/m2 and 3 BMI >30 kg/m2. GDM was diagnosed in II trimester in 20 members and early III trimester in 16 members and late III trimester in 4 members. 7 mothers had H/O long period of infertility and among them 3 conceived after infertility treatment and 4 had spontaneous conception. Family history positive in 19 members. Associated comorbidities like PCOs in 6 members, 5 were hypothyroid taking Tablet Thyroxine after obtaining endocrinologist opinion., 7 had pre eclampsia and 3 had anemia, 1 had recurrent GDM, 9 had recurrent urinary tract infection (UTI), 6 had recurrent moniliasis, intrauterine growth retardation (IUGR)-2. Mode of delivery- Labour naturalis-7, Instrumental delivery-2 and CS-31. Among these SGA-7, LGA-6, birth injury- nil, neonatal hypoglycemia-2, hyperbilirubinemia -1, Congenital anomaly-2(small ASD-1, Small muscular VSD-1), respiratory distress syndrome-1, and that baby died on POD 4.

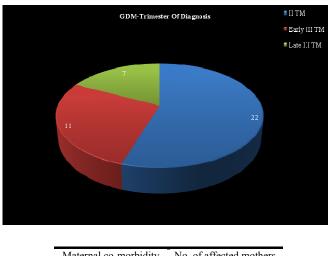
DISCUSSION

Our study was intended to observe the outcomes in GDM mother on treatment. The study revealed that a number of maternal as well as complications with infants in GDM are higher. The frequency of preeclampsia was higher though not statistically significant. Similar findings were also observed by some authors though treatment was not offered in their studies (Ghosh and Sudip, 2012; Preeti et al., 2011). In GDM group, 4 mothers developed premature rupture of membrane (PROM) which was statistically significant though under treatment. While few studies observed statistically significant higher frequency of PROM in GDM mothers without standard treatment, others did not (Farooq et al., 2007; Preeti et al., 2011). Another study in India showed significant number of PROM among GDM mothers on treatment (Dasari and Habibullah, 2011). Previous history of spontaneous abortion was found in 4 mothers in study group which was similar to

other studies (Farooq *et al.*, 2007; Duran *et al.*, 2014). Recurrent UTI was more frequently found in GDM group and is statistically significant (Farooq *et al.*, 2007). Mothers with GDM are nine times more likely to have vaginal infections (Enmanuel *et al.*, 2004).

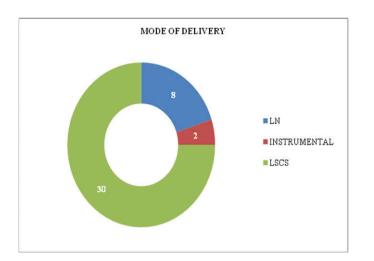
HbA1C Level (%) at 36 weeks	No. of GDM mothers
Below 5.7	15
5.7-7 - Good Control	20
7.1-8 - Fair Control	2
>8 – Poor Control	3

In the context of fetal outcomes neonatal hypoglycemia, hyperbilirubinemia, congenital anomalies, macrosomia, LGA, SGA, IUGR were studied. The HAPO study observed continuous linear associations between hyperglycemia and hyperbilirubinemia. They found stronger association between maternal hyperglycemia with hyperbilirubinemia but weaker with neonatal hypoglycemia though HAPO included those mothers with minimal hyperglycemia without standard treatment (Hyperglycemia and Adverse Pregnancy outcome, 2008). Our study observed increased frequency of both neonatal hypoglycemia and hyperbilirubinemia in GDM mothers (Masoud *et al.*, 2012; Carmelo *et al.*, 2013).

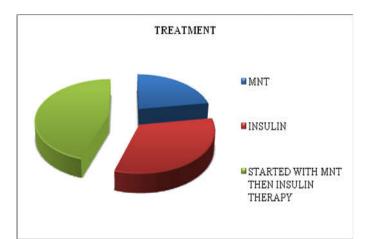


Maternal co-morbidity	No. of affected mothers
Hypothyroid	5
Long period infertility	7
Hypertensive disorders	7
Anemia	3

A study in India found significantly high frequency of neonatal hypoglycemia as well as hyperbilirubinemia (Joy and Sivakumar, 2012). The congenital malformations among offspring of women with diabetes are not uncommon (Casson et al., 1997). In our study, 5% neonates developed congenital anomalies which were not significant as they are non lethal minor anomalies. Similar findings were observed in several studies conducted in Pakistan, India and Saudi Arabia (Farooq et al., 2007; Preeti et al., 2011; Gasim, 2012). This study demonstrated that 15% babies are LGA (Hyperglycemia and Adverse Pregnancy outcome, 2008). In another study high fasting plasma glucose (FPG) was strongly associated with LGA neonates and/or macrosomia, and primary cesarean section (Riskin-Mashiah et al., 2009). Conversely, an outcome study in Jammu region showed birth weight was not significantly higher among infants of GDM mothers with good glycemic control (Preeti et al., 2011).



Around 15% of the deliveries in the present study were preterm and corroborated to other studies (Farooq et al., 2007; Theresa et al., 2001). GDM was positively related to the higher rate of caesarean section which was shown in HAPO study (Hyperglycemia and Adverse Pregnancy outcome, 2008). Other studies in Canada, Pakistan also showed similar type of evidence (Farooq et al., 2007; Kevin et al., 2006). This study showed significant number of caesarean section among the GDM mothers to prevent perinatal mortality and morbidity. A multicentre randomized trial concluded that even very mild alterations in glucose tolerance can result in these adverse outcomes which can be prevented by simple but aggressive control of blood sugars (Mark et al., 2009). In this regard, all the GDM mothers were treated with lifestyle intervention as well as insulin as required.22.5 % treated by life style modification and MNT; while 45% of our GDM mothers required insulin in addition to lifestyle intervention; 32.5% were shifted from MNT to Insulin therapy. Other studies showed higher percentage of insulin requirement (Duran et al., 2014; Kevin et al., 2006).



Baby weight	Total no: of neonates
SGA	7
LGA	6
IUGR	2
AGA	25

Neonatal complications	No: of neonates affected
Hypoglycemia	2
Hyperbilirubinemia	1
Rds	1
Congenital anomaly	2
Sepsis	Nil

It is important to mention that GDM mothers were provided with standard treatment and overall adherence to treatment was good. This might be the reason behind no adverse outcomes. While conducting this study on our pregnant population we confronted multiple obstacles in maintenance of good adherence to regular follow-up. Moreover, periodic follow-up for the status control by life style and insulin (where applicable) could not be meticulously maintained owing to lack of compliance in many patients (Many patients are from rural areas which is far away from our institition, which hinders the regular follow up, hence glycemic control) which might have influence over the outcome to some extent. This also hindered the assessment over correlation between glycemic status, compliance for treatment and pregnancy outcome..

Details of mothers with poor glycemic control HbA1C > 8 %

	Locality	Ga at Diagnosis	An visit	Insulin dose at delivery time
Patient i	Rural	24 w	Regular	Inj regularinsulin 18-12-12 Inj nph 12
Patient ii	Rural	16 w	Irregular	Inj lispropen 22-15-9
Patient iii	Urban	20 w	Regular	Inj regularinsulin 15-12-8 Inj nph 12 T.metformin 1 bd

Baby outcome of GDM mothers with poor glycemic control HbA1C > 8 %

	Mode of delivery	Baby	Anomaly	Complications
Patient i	LN	SGA	Small ASD	-
Patient ii	LSCS	IUGR	-	RDS, died on POD 4
Patient iii	LSCS	LGA	-	Hypoglycemia

Conclusion

This study showed that with proper treatment and good glycemic control adverse events on fetal outcome were relatively less in GDM mothers. In patients requiring high dose of insulin and poor, uncompliant - the glycemic levels never become normal. Hence the HbA1C level at 36 weeks denotes poor fetal outcome. So, in conclusion, patients requiring high dose of insulin are under corrected, hence fetal outcome is poor in this group. Early diagnosis, appropriate insulin dosage, life style modification and Hb A1C level less than 8%, scores good fetal outcome without any neonatal morbidity and mortality.

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