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Pregnancy Outcome in Gestational Diabetes Mellitus under Treatment

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Abstract

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

Methods: Pregnant mothers (N=191) diagnosed with GDM (n=91, age: 27.44±4.91yr; body mass index, BMI: 26.88±4.16 kg/m^2; mean±SD) on the basis of WHO 2013 criteria were compared with non-GDM (n=100, age: 26.01±4.81yr, BMI: 25.53±3.77 kg/m^2, mean±SD) for pregnancy outcome irrespective of gestational age. HbA1c was also 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. 160 mothers (GDM=75, non-GDM=85) could be followed for outcomes to the end of pregnancy. All the GDM mothers were offered standard treatment throughout pregnancy period.

Results: HbA1c was significantly higher in GDM than that in non-GDM (5.42±0.61 vs. 4.98±0.44%, mean±SD; p<0.001). Outcome events in GDM and non-GDM were: gestational hypertension- 3.6% vs. 2.3% (p=0.621), preeclampsia- 2.4% vs. 0% (p=0.150), PROM- 4.9% vs. 0% (p=0.037), hydramnios- none in any group, recurrent UTI- 12.3% vs. 4.7% (p=0.073), recurrent moniliasis- 0.0% vs. 2.3% (p=0.165), caesarian section- 85.3% vs. 72.9% (p=0.056), small for gestational age (SGA)- 26.4% vs. 36.7% (p=0.246), large for gestational age (LGA)- 1.4% vs. 0%, p=0.246, IUGR- 2.3 vs. 2.5% (p=0.952), neonatal hypoglycemia- 2.7% vs. 0.0% (p=0.130), hyperbilirubinemia- 12.0% vs. 11.8% (p=0.963), RDS- 0.0% vs. 2.4% (p=0.181) and birth injury- 0.0% vs. 1.2% (p=0.346), congenital anomaly- 4.0% vs. 1.2% (p=0.254) and abortion- 1.3% vs. 0.0% (p=0.286). Preterm delivery (12.0% vs. 7.1%, p=0.285) and caesarean section (85.3% vs. 72.9%, p=0.056) were more in GDM.

Conclusions: Despite treatment, adverse events were relatively higher but non-significant in GDM.

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Introduction:

Gestational diabetes mellitus (GDM) is increasing among the South Asians[1,2]. Recently our 'GDM study group' of Department of Endocrinology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka has observed an alarming frequency of 36.6% GDM by WHO 1999 criteria1 and 30.0% by WHO 2013 criteria along with 5.3% diabetes in pregnancy (DIP) in another study[2].

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[3]. As GDM is associated with significant metabolic alterations, increased maternal and perinatal morbidity and mortality, it is imperative to screen pregnant mothers for GDM[4]. Many studies have observed various complications of GDM without regard to the emphasis of treatment during pregnancy[5-8]. 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, neonatal intensive care admission and birth trauma were also reduced in treated women[9].

Present study was carried out to compare adverse pregnancy outcomes between GDM mothers on treatment and mother with normal glycemic status.

Materials and Methods:

Study Subjects:

It was a prospective cohort study carried out during January, 2014 to August, 2015 by GDM study group of Dept. of Endocrinology, BSMMU. Pregnant mothers (N=191) recruited consecutively from GDM clinic and diagnosed with GDM (n=91, age: 27.44±4.91yr; body mass index, BMI: 26.88±4.16 kg/m2, mean±SD) on the basis of WHO 2013 criteria were compared with non-GDM (n=100, age: 26.01±4.81yr, BMI: 25.53±3.77 kg/m2, mean±SD) for pregnancy outcome irrespective of gestational age. Informed written consent was taken from each of the mothers.

Study Design:

At the time of screening oral glucose tolerance test (OGTT) as well as HbA1c were done in all recruited mothers. The GDM group received standard treatment and both the GDM and non-GDM groups 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 & non-GDM mothers were advised for antenatal check-up at the end of every trimester which included clinical and biochemical parameters & ultrasound imaging for pregnancy profile. Majority of the GDM mothers were controlled with diet & exercise but some required insulin. All the mothers were advised for hospital delivery. Total 30 mothers (GDM=16 & non-GDM=14) were lost to follow-up. Prior to commencement of this study the research protocol was approved by Institutional Review Board (IRB).

Analytic Method:

Plasma glucose was assayed by RA-50 analyzer (Dade Behring, Germany). A fixed known concentration for low level (5.21 mmol/l) as well as high level (16.1 mmol/l) was used in every assay run. Inter-assay Co-efficient Variance (CV) for low level was 5.78%, and for high level was 5.59%. HbA1c was measured by the National Glycohemoglobin Standardization Program

(NGSP) certified Bio-Rad D-10TM HbA1c Program 220-0101, USA.

Statistical Analysis:

All data were analyzed by SPSS program (version 22.0). Data were expressed either as mean (+SD/SEM) or as percentage as applicable. Comparison of pregnancy outcome variables between GDM and non-GDM were done by Chi-square test. P values ≤0.05 were considered statistically significant.

Result:

There was significant difference between GDM and non-GDM for age (27.44±4.91 vs. 26.01±4.81 yrs, mean±SD; p=0.044), BMI (26.88±4.16 vs. 25.53±3.77 kg/m2, mean±SD; p=0.020) and family history of DM (45.1% vs. 28.0%, p=0.014) (Table-I).

Complications like preeclampsia (2.4% vs. 0%, p=0.150), gestational hypertension (3.6% vs. 2.3%, p=0.621), spontaneous abortion (1.3% vs. 0.0%, p=0.286), recurrent UTI (12.3% vs. 4.7%, p=0.073), PROM (4.9% vs. 0.0%, p=0.037), preterm delivery (12.0% vs. 7.1%; p=0.285) were relatively higher in the GDM mothers while recurrent monilial infection (0.0% vs. 2.3%, p=0.165), intra-uterine growth retardation (IUGR, 2.3% vs. 2.51%, p=0.952), intrauterine death (IUD, 0.0% vs. 2.3%, p=0.167) were relatively higher in the non-GDM group (Table-II). Of the complications in infants, birth weight (2.91±0.51 vs. 2.80±0.44 kg, mean±SD; p=0.569), neonatal hypoglycemia (2.7% vs. 0.0, p=0.130), hyperbilirubininemia (12.0% vs. 11.8%, p=0.963) and congenital anomalies (4.0% vs. 1.2%, p=0.254) were relatively higher in the GDM mothers. On the other hand respiratory distress syndrome (RDS, 0.0 vs. 2.4%, p=0.181) & birth injury (0.0% vs. 1.2%, p=0.346) were relatively higher in non-GDM mothers (Table-III). On the basis of gestational age, 1.4% babies of GDM mothers were large for gestational age (LGA), but none among non-GDM. Conversely, small for gestational age (SGA) baby were 36.7% in non-GDM mothers while 26.4% in GDM mothers: (p=0.246) (Figure-1). Caesarean section was relatively more in GDM (85.3%, 64/75 vs. 72.9%, 62/85; GDM vs. non-GDM; p=0.056) which is statistically significant (Figure-2). More than 90% mothers were only on lifestyle modifications while 9% mothers required insulin for the control of glucose. As revealed by interrogation compliance to treatment by the GDM mothers. 66% mothers were found to be nicely compliant to the

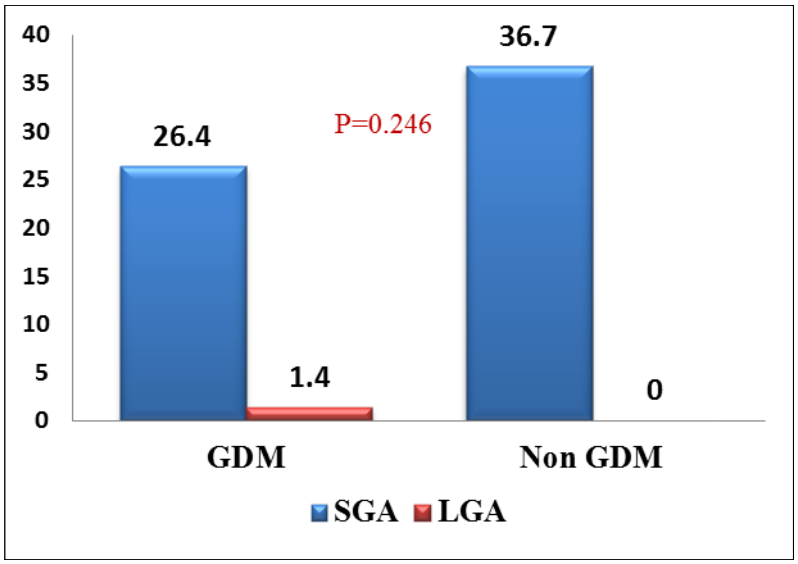

Figure 1: Comparison of birth

SGA- Small for gestational age: < 10th Percentile
LGA- Large for gestational age: >90th Percentile

Table-I: Baseline characteristics of the studied mothers

Variables	All subjects	GDM	Non GDM
N	191	91	100
Age in years (mean ± SD)	26.69±4.90	27.44±4.91	26.01±4.81
BMI in kg/m2 (mean ± SD)	26.18±4.01	26.88±4.16	25.53±3.77
Family history of DM	69 (36.1)	41 (45.1)	28 (28.0)
Occupation			
Housewife	138 (72.3)	60 (65.9)	78 (78.0)
Service	22 (11.5)	16 (17.6)	06 (6.0)
Medical professional	22 (11.5)	11 (12.1)	11 (11.0)
Student	09 (4.7)	04 (4.4)	05 (5.0)
Parity			
Nulliparous	89 (46.6)	43 (47.3)	46 (46.0)
Multiparous	102 (53.4)	48 (52.7)	54 (54.0)
History of abortion			
Yes	57 (29.8)	24 (26.4)	33 (33.0)
No	134 (70.2)	67 (73.6)	67 (67.0)
SBP (mean ± SD) in mm Hg	103.51±10.50	104.62±11.01	102.50±50
DBP(mean ± SD) in mm Hg	65.97±9.55	66.76±10.25	65.25±8.85

GDM: Gestational Diabetes Mellitus
Non-GDM: Non Gestational Diabetes Mellitus
SBP: Systolic blood pressure
DBP: Diastolic blood pressure
DM: type 2 diabetes mellitus
BMI: body mass index

Table-II: Frequency of maternal complications among GDM & Non-GDM

Complications	GDM (n=75)	Non GDM (n=85)	Total (n=160)	p
Preeclampsia	2 (2.4)	0	2 (1.2)	0.15
GTN	3 (3.6)	2 (2.3)	5 (3.0)	0.621
Spontaneous abortion	1 (1.3)	0	1 (0.6)	0.286
Recurrent monilial infection	0 (0.0)	2 (2.3)	2 (1.2)	0.165
Recurrent UTI	10 (12.3)	4 (4.7)	14 (8.4)	0.073
Hydraminos	0	0	0	-
PROM	4 (4.9)	0 (0.0)	4 (2.4)	0.037
IUGR	2 (2.3)	2 (2.5)	4 (2.4)	0.952
IUD	0	2 (2.3)	2 (1.2)	0.167

Table-III Frequency of outcomes among infants of GDM & Non-GDM mothers

Complications	GDM (n=75)	Non GDM (n=85)	p
Birth weight (mean ± SD) in Kg	2.91±0.51	2.86±0.44	0.569
Neonatal Hypoglycemia	2 (2.7)	0	0.13
Hyperbilirubinemia	9 (12.0)	10 (11.8)	0.963
Congenital anomalies	3 (4.0)	1 (1.2)	0.254
RDS	0	2 (2.4)	0.181
Birth injury	0	1 (1.2)	0.346

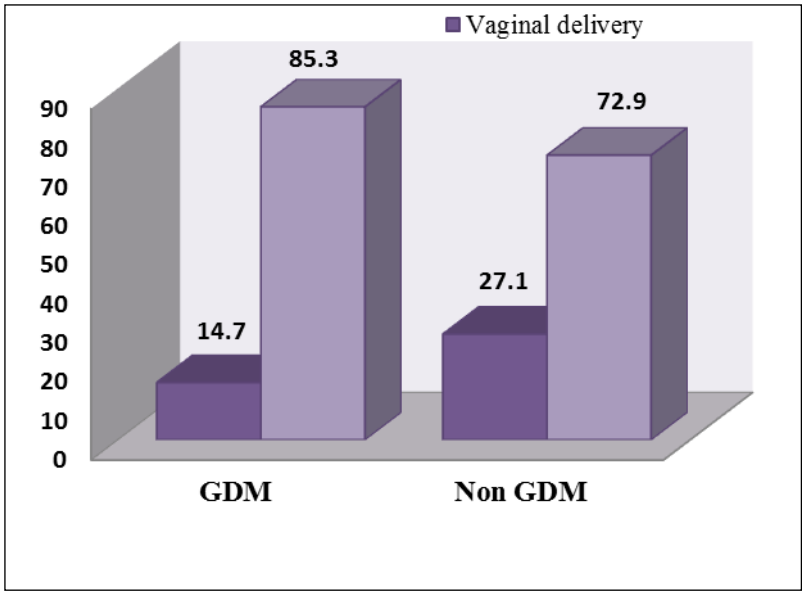

Figure-2: Mode of delivery of studied subjects

advices while 28% were poorly complained & about 5% were non compliant to the advices for control of glucose.

Discussion:

Our study was intended to compare the adverse outcomes in mother and infants between GDM on standard treatment with non-GDM mothers.

The study revealed that a number of maternal as well as complications with infants in GDM are higher than non-GDM. The frequency of preeclampsia and gestational hypertension were higher though not statistically significant. Similar findings were also observed by some authors though treatment was not offered in their studies[8, 10]. 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[4, 10]. Another study in India showed significant number of PROM among GDM mothers on treatment[11]. Spontaneous abortion was found in only one mother of GDM group which was similar to other studies[4, 12]. IUD occurred in two mothers among non-GDM group which was probably due to home delivery without standard obstetric management. Recurrent UTI was more frequently found in GDM group though it was not statistically significant and seems similar to findings of another study[4]. Mothers with GDM are nine times more likely to have vaginal candidiasis as found in Ugandal mothers[13]. But interestingly our study found higher incidence of vaginal candidiasis in non- GDM mothers.

In the context of fetal outcomes neonatal hypoglycemia, hyperbilirubinemia, congenital anomalies, macrosomia were studied between two groups. 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[3]. Our study observed increased frequency of both neonatal hypoglycemia and hyperbilirubinemia in GDM mothers though statistically insignificant. Apropos with this, others also found no significant difference of neonatal hypoglycemia and hyperbilirubinemia between GDM and non- GDM groups[14, 15]. On the contrary, a study in India found significantly high frequency of neonatal hypoglycemia as well as hyperbilirubinemia[16].

The congenital malformations among offspring of women with diabetes are not uncommon[17]. In our study, 4% neonates developed congenital anomalies which were not statistically different between two groups. Similar findings were observed in several studies conducted in Pakistan, India and Saudi Arabia[4, 10, 18]. This study demonstrated that only 1.4% babies are LGA which was not statistically significant[3]. In another study high fasting plasma glucose (FPG) was strongly associated with LGA neonates and/or macrosomia, and primary cesarean section[19]. Conversely, an outcome study in Jammu region showed birth weight was not significantly higher among infants of GDM mothers with treatment[10].

Around 12% of the deliveries in the present study were preterm though statistically insignificant and corroborated to other studies[4, 20]. GDM was positively related to the higher rate of caesarean section which was shown in HAPO study[3]. Other studies in Canada, Pakistan also showed similar type of evidence[4, 21]. This study showed significant number of caesarean section among the GDM mothers. But the rationality behind the caesarean section in each case was not explored.

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[22]. In this regard, all the GDM mothers were treated with lifestyle intervention as well as insulin as required. 9% of our GDM mothers required insulin in addition to lifestyle intervention. Other studies showed higher percentage of insulin requirement[12, 21]. Probably this lower rate of insulin requirement in our study is due to excluding mothers with DIP. 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 significant difference of outcomes between two groups. 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 some cases 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.

Conclusion:

This study showed that frequency of adverse events did not differ significantly between GDM mothers and mothers with normal glycemic status. But most of the adverse events were relatively higher in GDM mothers despite standard treatment.

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