

Characteristics of Pre-gestational and Gestational Diabetes: A Comparison of Maternal and Fetal Outcome

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Abstract

Background: Pregnancy is a diabeto-genic condition, which is why pregnancy with diabetes is one of the common medical and endocrinological disorder encountered in obstetrics. Diabetes Mellitus complications during pregnancy has become more common worldwide. About 0-4% of all pregnancies are complicated by diabetes mellitus and 90% of those are GDM. **Aim of the study:** This study was conducted to find out the maternal and fetal outcome of the pregnancies complicated by pre-gestational and gestational diabetes mellitus. **Material & methods:** This was a cross-sectional analytical study which was conducted in the Department of Obstetrics and Gynecology Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka. In this study, a total of 225 patients were selected using purposive sampling technique. There were three groups of pre-gestational diabetic, gestational diabetic and non-diabetic control, designated as Group A, Group B, Group C accordingly; and each consists of 75 patients. Duration of data collection was one year (July 2016 to June 2017). Information collected from all pregnant women (After 28 weeks of gestation) using a questionnaire made for recoding all relevant parameters under study, after proper counseling and taking written consent of the patient or her legal guardian. **Results:** History of GDM was significantly more common among patients with pre-GDM (38%) and GDM (18%) compared to controls. History of abortion, IUFD and congenital anomaly were significantly higher among pre-GDM mothers than GDM mothers and controls ($p < 0.05$). History of deliveries with macrosomia and still birth was distributed similarly across the groups ($p > 0.05$). Pre-GDM and GDM patients had significantly higher number of patients with HbA_{1c} $> 6.5\%$ than controls. Mean FBS and PPBS was significantly higher in pre-GDM & GDM patients than control ($p < 0.05$). APGAR score was < 7 in significantly higher number of pre-GDM and GDM babies than controls ($p < 0.05$). Mean Weight of the babies was significantly lower among pre-GDM patients than GDM patients ($p < 0.05$). Among pre-GDM patients and GDM patient's cases of birth asphyxia, Hypoglycemia, hyperbilirubinemia and congenital anomalies were significantly higher than controls ($p < 0.05$). **Conclusion:** Interventions such as preconception care for women with pre-gestational diabetes, screening for early diagnosis, patient education, multidisciplinary approach and good metabolic control maintained throughout the pregnancy is the key to successful fetomaternal outcome.

Keywords: Diabetes, Pregnancy, Pre-Gestational and Gestational Diabetes, Maternal and Fetal Outcome.

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INTRODUCTION

Gestational diabetes mellitus (GDM) is defined as a carbohydrate intolerance which occurs for the first time during pregnancy and disappears by the end of the puerperium [1]. If diabetes mellitus is diagnosed before pregnancy, it is classified as pregestational diabetes mellitus (PGDM). A mild increase in glucose levels during pregnancy can

adversely affect both the mother and fetus. Increased incidences of pre-eclampsia, preterm delivery, miscarriage, fetal malformation and perinatal mortality and morbidity have been reported in diabetic pregnancies in comparison to the general population [2]. World Health Organization (WHO) defined gestational diabetes as "carbohydrate intolerance resulting in hyperglycemia of variable severity with

onset or first recognized during pregnancy” [3]. The prevalence of pre-gestational diabetes mellitus (Pre – GDM) in Saudi Arabia is 4.3% and gestational diabetes mellitus (GDM) is 24.3% [4]. While in Bangladesh, almost 9.7% of pregnancies are affected by GDM [5]. Diabetes is a major public health problem in India with prevalence rates reported to be between 4.6% and 14% in urban areas, and 1.7% and 13.2% in rural areas. India has an estimated 62 million people with type-2 diabetes mellitus (DM); this number is expected to go up to 79.4 million by 2025 [6]. The pregnancy specific hormone such as Human placental lactogen, cortisol, prolactin increases the insulin resistance. This diabetogenic stress causes production of more insulin as a compensatory mechanism. When this balance is inadequate gestational diabetes occur. The risk factors for gestational diabetes mellitus are age > 30 years, family history of diabetes mellitus, obesity, history of macrosomia, glycosuria, previous unexplained neonatal death, unexplained recurrent abortion, Previous congenital malformations, history of hydramnios, history of stillbirth, history of gestational hypertension and history of pre-eclampsia. Teenagers of mother who drank alcohol were less likely to have gestational diabetes mellitus [7, 8]. Gestational diabetes can lead to miscarriage, premature delivery, congenital malformations, altered fetal growth, unexplained fetal demise, hydroamnios and other neonatal complications. Uncontrolled diabetes mellitus in pregnancy leads to preeclampsia, diabetic ketoacidosis, diabetic nephropathy, diabetic retinopathy, neuropathy in mothers. Macrosomia is one of the major effects of GDM [9, 10]. Gestational diabetes leads to macrosomic infant (birth weight exceeds 4500 gram) due to excessive fat deposition on shoulders and trunk which predisposes them to shoulder dystocia or caesarean delivery. The HAPO study demonstrate that maternal hyperglycaemia even at a level below that diagnostic of DM is associated with increased birth weight and macrosomia. An increase in morbidity during pregnancy with a likelihood of developing diabetes in future is associated with maternal hyperglycaemia. This also has a direct impact on the developing foetal pancreas and remains a risk factor for developing DM in future [11-13]. Higher incidence of congenital anomaly is associated with poor glycemic control at the time of conception or during organogenesis [14]. Congenital malformations in the form of diabetic embryopathy especially anencephaly, microcephaly, congenital heart disease and caudal regression syndrome directly proportional to elevation of A1C during first 10 weeks of pregnancy [15]. In long standing pregestational diabetes there are some micro vascular and macro vascular complications. This vasculopathy causes uteroplacental injuries which leads to IUGR and develop maternal hypertension. In pregnancy there may be acceleration of some end organ disease like retinopathy, nephropathy, diabetic ketoacidosis. These are the life threatening condition for the mother as well as the fetus. There also may be risk of death due diabetic cardiomyopathy.

Interventions such as preconception care for women with pre-gestational diabetes, screening for early diagnosis, patient education, multidisciplinary approach, (including obstetrician, dietician, endocrinologist, neonatologist and anaesthesiologist) and good metabolic control maintained throughout the pregnancy is the key to successful feto-maternal outcome. This study was conducted to find out the maternal and fetal outcome of the pregnancies complicated by pre-gestational and gestational diabetes mellitus.

METHODS

This was a cross-sectional analytical study which was conducted in the department of Obstetrics and Gynecology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka. In this study, a total of 225 patients were selected using purposive sampling technique. There were three groups of pre-gestational diabetic, gestational diabetic and non-diabetic control, designated as Group A, Group B, Group C accordingly; and each consists of 75 patients. Duration of data collection was from July 2016 to June 2017. Information collected from all pregnant women (After 28 weeks of gestation) with diagnosed GDM and Pre-GDM and symptoms signs suggestive of GDM and Pre-GDM later confirmed by relevant investigation (FBS, 2h PPBS & HbA1C) admitted during the study period in obstetric ward in Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka using a questionnaire made for recoding all relevant parameters under study, after proper counseling and taking written consent of the patient or her legal guardian. Data were analyzed using SPSS software and p value <0.05 was considered as statistical significant.

Inclusion Criteria

- Gestational age >28 weeks
- All the diagnosed case having GDM & Pre-gestational DM and non diabetic control patients admitted for delivery in Bangabandhu Sheikh Mujib Medical University (BSMMU).
- Singleton pregnancy

Exclusion Criteria for Pre-GDM & GDM mothers:

- Multiple Pregnancy
- Patient with any medical or surgical illness i.e. renal disease, liver disease & endocrine disorder that may affect the blood sugar level
- Non-compliant patient

Exclusion criteria for control mothers:

- Multiple Pregnancy.
- Patients with any medical or surgical illness i.e. renal disease, liver disease, endocrine disorder that may affected the blood sugar level.
- Non –compliant patient.
- Not willing to participate.

RESULTS

Table-1: Socio-demographic profile of participants (n=225)

Variables	Group A		Group B		Group C		P value
	Pre-GDM (n=75)		GDM (n=75)		Control (n=75)		
	N	%	N	%	N	%	
Age (in year)							
<25	3	4	12	16	14	18.6	0.069 ^{ns}
25-29	49	65.33	44	58.6	44	58.7	
≥30	23	30.67	19	25.4	17	22.7	
Mean±SD	28.62±2.11		27.90± 2.04		27.56± 2.65		0.064 ^{ns}
Education							
Illiterate	6	8.2	6	8	11	14.7	0.886 ^{ns}
Below SSC	41	54.6	44	58.5	31	41.3	
SSC	17	22.6	17	22.3	17	22.7	
HSC	7	9.3	7	9.2	15	20	
Graduate and Above	4	5.3	1	2	1	1.3	
Occupation							
Housewife	63	84	60	80	66	88	0.860 ^{ns}
Service Holder	5	6.7	3	4	3	4	
Day Laborer	6	8	8	10.7	4	5.3	
Others	1	1.3	4	5.3	2	2.7	
Socio-economic status							
Lower	35	46.7	36	48	45	60	
Middle	31	41.3	30	40	24	32	
Higher	9	12	9	12	6	8	
Residence							
Rural	54	72	54	72	62	82.7	0.464 ^{ns}
Urban	21	28	21	28	13	17.3	
Family history							
Present	53	70.7	49	65.3	8	10.7	<0.001 ^s
Absent	22	29.3	26	34.7	67	89.3	

P value determined by Chi- squared test and ANOVA as appropriate. Ns= Non Significant:= Significant.

Table Shows that age distribution among the study groups were similar ($p>0.005$), mean age of Group A (28.62 ± 2.11), Group B (27.90 ± 2.04) and Group C Was (27.56 ± 2.65) years. Most of the participants were educated below SSC (respectively 54.6%, 58.5% and 41.3% in pre-GDM, GDM and controls), were housewives (84%, 80% and 88%

respectively), came from rural area (72%, 72% and 82.7%) and were from lower socioeconomic class (46.7%, 48% and 60% respectively). These distributions were statistically similar across the groups. Both pre-GDM and GDM mothers has significantly higher number of positive family history then control mothers ($p<0.001$).

Table-2: Glycemic profile of patients (n=225)

Variables	Group A		Group B		Group C		P value
	Pre-GDM (n=75)		GDM (n=75)		Control (n=75)		
	N	%	N	%	N	%	
HbA ₁ C							
<6.5%	32	42.7	46	61.3	75	100	< 0.001 ^s
≥6.5%	43	57.3	29	38.7	0	0	
Mean±SD	6.95±0.72		6.21 ±0.78		4.59±0.59		<0.00 ^s
FBS (mmol/l)							
Mean±SD	6.88±1.07		6.63±1.24		3.68±0.58		< 0.001 ^s
PPBS(mmol/l)							
Mean±SD	11.87 ±2.01		12.11 ±2.43		5.56±0.77		< 0.001 ^s

P value determined by Chi- squared test and ANOVA as appropriate. ns= Non Significant: s = Significant.

Table shows that Pre-GDM and GDM patients had significantly higher number of patients with HbA_{1c} >6.5% than controls. Mean FBS and PPBS was significantly higher in pre-GDM & GDM patients than control ($p<0.05$).

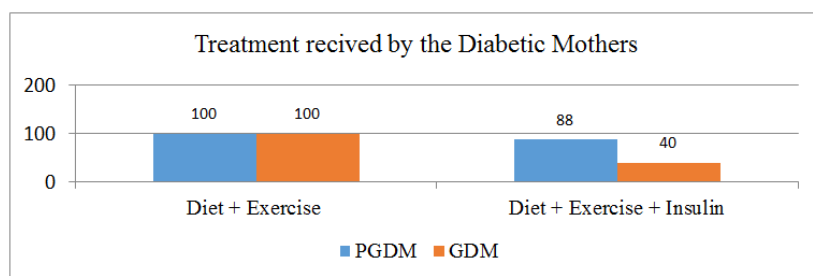


Fig-1: Treatment received by diabetic mothers. (n=100)

Figure shows that all of the diabetic mothers received diet and exercise. Among them 88% pre-GDM and 40% GDM mothers received insulin along with diet and exercise.

Table-3: Obstetric profile of participants. (n=225)

Variables	Group A		Group B		Group C		P
	Pre-GDM (n=75)		GDM (n=75)		Control (n=75)		
	N	%	N	%	N	%	
Parity							
Primi-parous	20	26.7	9	12	15	20	0.206ns
Multi-parous	55	73.3	66	88	60	80	
Gestationam Age Delivery (week0							
28-32	12	16	2	2.7	0	0	0.045ns
33-36	22	29.3	15	20	5	6.7	
>36	41	54.7	58	77.3	70	93.3	
Mean±SD	36.06 ± 2.71		37.34± 1.12		38.46±1.13		0.001 ^s
Past obstetric history							
H/O GDM	19	38	9	18	4	8	0.001 ^s
H/O HTN	9	18	4	8	5	10	0.266 ^{ns}
H/O congenital anoaly baby	5	10	1	2	0	0	0.026 ^{ns}
H/O macrosomia	4	8	1	2	0	0	0.068 ^{ns}
H/O IUFD	7	14	1	2	0	0	0.014 ^{ns}
H/O stillbirth	1	2	0	0	0	0	0.365 ^{ns}
H/O abortion	10	20	3	6	2	4	0.015 ^s
ANC							
Regular	58	7.3	48	64	42	56	0.046 ^s
Irregular	14	18.7	23	30.7	27	36	
None	3	4	4	5.3	6	8	

P value determined by Chi- squared test and ANOVA as appropriate. ns= Non Significant: s = Significant

Table shows that among pre-GDM patients 73.3% were multi-para, among GDM patients 88% patients were multi-para and among control 80% were multipara ($p>0.05$). Gestational age at delivery was significantly lower among pre-GDM mothers than GDM mothers and controls ($p<0.05$). History of GDM was significantly more common among patients with pre-GDM (38%) and GDM (18%) compared to

controls. History of abortion, IUFD and congenital anomaly were significantly higher among pre-GDM mothers than GDM mothers and controls ($p<0.05$). History of deliveries with macrosomia and still birth was distributed similarly across the groups ($p>0.05$). ANC follow-ups were significantly more regular in both diabetic mothers than control ($p<0.05$).

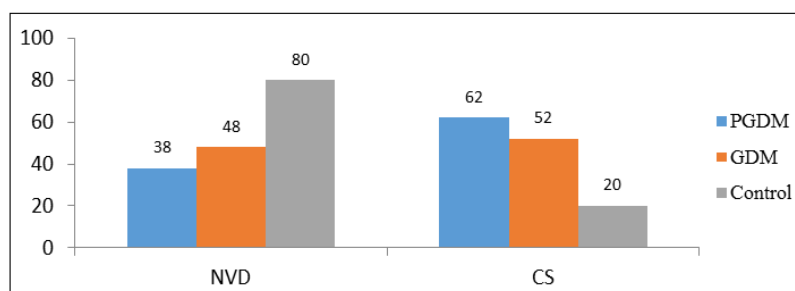


Fig-2: Mode of delivery of patients

Figure shows that mode of delivery was delivery in respectively 38%, 48%, 80% of PGDM, Caesarian section in respectively 62%, 52% and 20% of PGDM, GDM and control mothers; and vaginal GDM and control mothers.

Table-4: Maternal outcome. (n=225)

Variables	Group A		Group B		Group C		P value
	Pre-GDM (n=75)		GDM (n=75)		Control (n=75)		
	N	%	N	%	N	%	
Antepartum complications							
Pre – eclampsia	5	10	8	16	4	8	0.056 ^{ns}
UTI	6	12	8	16	4	8	0.469 ^{ns}
Vulvovaginitis	10	20	3	6	0	0	0.001 ^s
Polyhydramnios	11	22	3	6	0	0	< 0.001 ^s
PROM	6	12	8	16	1	2	0.564 ^{ns}
Preterm delivery	23	46	11	22	3	6	< 0.001 ^s
Intrapartum Complication							
Cervical tear(VD)	3	6	4	8	1	2	0.397 ^{ns}
Perineal Tear(VD)	3	6	4	8	1	2	0.397 ^{ns}
Instrumental delivery	0	0	2	4	0	0	0.876 ^{ns}
Postpartum Complication							
PPH	6	12	5	10	2	4	0.339 ^{ns}
Mastitis	4	8	3	6	0	0	0.143 ^{ns}
Caesarian	5	10	13	26	0	0	<0.001 ^s
Wound	35	70	19	38	9	18	<0.001 ^s
Infection							
UTI	10	20	13	26	1	2	0.003 ^s

P value determined by Chi- squared test; ns = non-significant, s= Significant.

Table shows that preeclampsia. Urinary tract infection and premature rupture of the membrane were higher in gestational diabetes mellitus as compared to

overt diabetes among women. Rate of LSCS were higher in gestational diabetes. Wound Infection rate is higher in Pre-GDM.

Table-5: Fetal outcome. (n=225)

Variables	Group A		Group B		Group C		P value
	Pre-GDM (n=75)		GDM (n=75)		Control (n=75)		
	N	%	N	%	N	%	
live birth	71	94.6	72	96	75	100	0.344 ^{ns}
Still birth	4	5.4	3	4	0	0	
Apgar score at 5 min							
≤ 7	45	60	20	26.6	8	10.6	<0.001 ^s
≥ 7	30	40	55	73.4	67	89.4	
Birth weight of neonate (kg)							
<2	18	24	4	5.3	3	4	0.001 ^s
2-4	57	76	63	84.1	70	93.3	
>4	0	0	8	10.6	2	2.7	
Mean ± SD (gram)							
Need for NICU							
No	42	56	53	70.7	67	89.3	<0.000 ^s
Yes	33	44	22	29.3	8	10.7	
Perinatal Complications							
Birth asphyxia	19	38	8	16	3	6	<0.001 ^s
Hypoglycemia	11	22	5	10	2	4	0.019 ^{ns}
Hyperbilirubinemia	8	16	6	12	0	0	0.017 ^{ns}
Congenital anomaly	1	2	0	0	0	0	
Perinatal Death	2	4	1	2	0	0	0.566 ^{ns}

P value determined by Chi- squared test ANOVA as appropriate; ns = non-significant, s = Significant.

Table shows that Pre-GDM, GDM and control mothers had respectively 94%, 96%, 100% live births. Distribution was similar across groups ($p > 0.05$). APGAR score was < 7 in significantly higher number of pre-GDM and GDM babies than controls ($p < 0.05$). Mean Weight of the babies was significantly lower among pre-GDM patients than GDM patients ($p < 0.05$). Among pre-GDM patients and GDM patient's cases of birth asphyxia, Hypoglycemia, hyperbilirubinemia and congenital anomalies were significantly higher than controls ($p < 0.05$).

DISCUSSION

This study reflects the maternal and fetal outcome in pregnant women with pregestational and gestational DM. In this study most of the patients belonged to age group 25- 29 years. Mean age of Group A was (28.62 ± 2.11), Group B was (27.90 ± 2.04), Group C Was (27.56 ± 2.65) years. Group A patients had slightly higher age than Group B and Group C, but there was no significant difference among the groups ($p > 0.05$). In a study of Clausen et al, shows that increasing age of the patients of GDM had been described as a risk factor for pregnancy complication maternal age was higher in overt diabetes than that of GDM in the study of Wahabi *et al.*, [16, 17]. A study done by Mustary and her colleagues [18] showed that maternal age was higher in PGDM (26.67 ± 4.57) than that of GDM (26.04) which is similar to our study. Mean age of diabetic mothers as relatively higher than control. The similar findings were observed in some other studies which may be due to the fact that, increasing maternal age is one of the risk factors [19, 20]. Regarding obstetric parameters in represented that most of the mothers were multipara and there was no difference across groups in relation to parity ($p > 0.05$); this finding is similar to some other studies [21-23]. Chanu *et al.*, [24] showed that higher parity carried a significant risk for developing GDM. Majority of the control mothers came from rural area in this study. More diabetic mother came from urban than control mothers. This finding is similar to that of Chanu *et al.*, [24] who revealed that 79% of GDM mothers came from urban area and 72% of Non-diabetic mothers came from rural area. Most of the pre-GDM, GDM and control mothers were educated below SSC (54.6%, 58.5%, and 41.3% respectively). Literacy was relatively higher in diabetic mothers than non-diabetic controls. Concordant to this study Chanu *et al.*, [24] found that GDM was higher among literate women. Higher number of diabetic mothers (pre - GDM and GDM both) came from higher socio- economic condition than control mothers. Although the difference was not statistically significant, but a similar finding was reported [25]. Regarding glycemic profile of the patients in that there were significant ($p < 0.001$) differences between fasting and 2 hours post prandial blood glucose level among diabetic and non -diabetic control group of patients. But no significant difference was found between Group A and Group B. Fasting

blood glucose level were 6.88 ± 1.07 mmol/L and 6.63 ± 1.24 mmol/L and 2 hours post prandial blood glucose level were 11.87 ± 2.01 and 12.11 ± 2.43 mmol/L in pre -GDM and GDM patient respectively. Mustary *et al.*, [26] showed similar result which is consistent with our study. In UK Corrado *et al.*, [27] showed diabetic patient had higher mean fasting glycaemia than GDM patients, which was inconsistent with the present study. HbA1c level was significantly high in both diabetic group than control group. Poor glycaemic control was related to the development of complications. In this study it was found that majority of diabetic patients were treated by diabetic diet and exercise. Insulin was added with diet and exercise in 88% patients with pre - GDM and 40% patients with GDM. In a study done by Corrado *et al.*, [27] found that pre -GDM patient (78.1%) required more insulin than GDM (14.0%) patients . This finding is consistent with my study. Mean gestational age at delivery was significantly lower in pre- GDM patients than GDM patients and control (36.06 ± 2.71 , 37.34 ± 1.12 , and 37.46 ± 1.13 weeks respectively). This indicates that, earlier termination of pregnancy in diabetic patients was needed. Study conducted by Abu- Heiza *et al.*, [28] found a mean gestational age of 38 ± 2.1 and 38.6 ± 5.9 weeks in pre-GDM and GDM mothers. History of GDM IUFD and abortion were significantly higher among pre-GDM and GDM patients than control groups. In addition to above mentioned complications history of congenital anomaly was also significantly higher among diabetic mothers than non-diabetic mothers. This is similar to the findings of Mustary and colleagues [29] which might be because many of pre-GDM patients could possibly had continuation of diabetes after previous episode of GDM. In a study done by Fareed *et al.*, [30] found that past history of GDM was significantly more common among diabetic mother than non-diabetic mother. This result was consistent with my study. In this study showed that, maternal complications were more in PGDM than GDM and control group and was statistically significant ($p < 0.001$). The incidence of pre eclampsia in pre - GDM and GDM was 10% and 16% respectively and in non- diabetic control patient it was 8%. Similar result was observed in Akalaghi and Hemedi [31] and Fareed & Siraj [32]. In a study done by Garner *et al.*, [33] observed that diabetic patients were complicated with PE in 9.9% compared with 4.3% in non- diabetic controls. PE in diabetes seems to be correlated with endothelia dysfunctions, insulin resistance and poor glycaemic control in pregnancy. Incidence of neonatal hypoglycaemia and hyperbillirubinaemia was higher in PGDM than GDM patient in this study, which is dissimilar to the findings of Elango *et al.*, [34]. In this study we found infant malformation in Pre GDM mothers. In the study of Dheffield *et al.*, [35] found that the incidence of infant malformation rate in women with pregestational DM was significantly high than women without diabetes (6% vs 1.5%). Teratogenic effect of diabetes arises early on in pregnancy. Fetal

exposure to maternal hyperglycemia in the case of pregestational diabetes is prolonged and severe, hence, may be more pathogenic than with gestational DM. In this study we found that perinatal mortality was higher in infant of both diabetic patients (pre GDM & GDM) in comparison to infant of non-diabetic control mothers (4%, 2%, 0%) respectively. In the UK, Dunne & Brydon [36] showed similar result which are very close to our study. Fetal birth weight although within normal limit but macrosomia was significantly higher in infant of GDM mothers ($p < 0.001$) than infant of pre GDM and controls mothers. In a study Abu- Heija *et al.*, [37] showed that fetal birth weight was higher in PGDM mothers than GDM mothers, which was inconsistent with the present study. Need of NICU admission was significantly more common in babies of diabetic mothers than non –diabetic mothers ($p < 0.000$). Similar to the findings of Abu Heija [37] it was more common in babies born to PGDM mother than GDM mothers. Birth asphyxia was significantly more common among infants of PGDM mothers among other complications reported. Birth asphyxia was found higher in the study of Sultana *et al.*, [38] and Mustary *et al.*, [29]. Lack of education, infrequent follow-up and non-compliance of patient poses difficulty in better glycaemic control. In comparison to control group maternal and fetal complications were significantly more common in diabetic mothers. Also, this study found that the maternal and perinatal outcome of pregestational diabetes mellitus were less favorable than those of gestational diabetes mellitus.

LIMITATIONS OF THE STUDY

The study was conducted at a very short period due to time constrain & fund limitation. Which is why it might not reflect overall situation of our country. Most of the study subject who had normal vaginal delivery was discharge after 24 to 48 hours of delivery. So long term follows up were beyond the scope of the study.

CONCLUSION AND RECOMMENDATIONS

Awareness about outcome of DM and its long term sequelae should be created among the general people. Role of stringent control of blood sugar is advised to reduce complications. Further Population based study is necessary to infer the findings over the general population.

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