Effect of different intensities of glycemic control on maternal and fetal outcome in women with diabetes in pregnancy

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ABSTRACT

Aims: To compare the feto-maternal outcomes between patients who have achieved different glucose target values after intervention for hyperglycemia in pregnancy.

Methods: A prospective comparative observational study was conducted in the Obstetrics Department of a Teaching Hospital. The main outcome parameters were the values of the fasting blood sugar (FBS) and the postprandial blood sugars (PPBS) obtained from the self-monitoring tests. The patients were grouped into two groups – the tight control group-I and less tight control group-II. maternal and neonatal parameters are compared. Pearson's chi-square test was used for proportions and unpaired t-test was used for numbers after checking for normality of distribution and p-value of <0.05 was taken as statistically significant.

Results: Average values of FBS/PPBS values were lesser in group I (84/120) compared to group II (93/142).The proportion of maternal and fetal complications (hypertensive disorders, polyhydramnios, macrosomia, neonatal hypoglycemia, hyperbilirubinemia, NICU admission) were similar between the two groups. The average gestational age at delivery (38.2 weeks vs 37.7 weeks), the proportion of LSCS (50% vs 66.7%) and neonatal birth weight (2.88 kg vs 2.98 kg) were similar in both groups.

Conclusion: There is no difference in feto-maternal outcome in between well controlled lesser control of blood sugar.

Key words: diabetes mellitus, glycemic control, hyperglycemia, pregnancy

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INTRODUCTION

There is an increasing number of women who are diagnosed with glucose intolerance in the recent decades, which are attributable to a varied list of reasons. This increasing trend is true for both the worldwide trend and in India.[1]

After diagnosis of GDM (gestational diabetes mellitus), the management of hyperglycemia can be medical nutrition therapy, advising physical activity and utilizing oral or injectable hypoglycemic agents based on the degree of the hyperglycemia. The benefits of appropriate control of the hyperglycemia are obvious in terms of reduction of both maternal (polyhydramnios, shoulder dystocia, hypertensive disorders, perineal trauma) and neonatal (large for gestational age, birth trauma, hyperbilirubinemia, hypoglycemia, hypocalcemia) complications.[2]

However, the problems with overzealous and excessive correction of the hyperglycemia can lead to maternal hypoglycemia, small-for-gestational-age babies, overuse of pharmacological agents and psychological strain also.[3]

It is well known that the HAPO (hyperglycemia and pregnancy outcome) study confirmed a linear relationship between maternal blood sugar levels and feto-maternal outcomes.[2] However, the target values for sugar control have not been very clearly defined. Coombs et al mention the need of clinical trial to determine the target glucose level.[3] Prutzky et al also reported the paucity of data regarding this.[4] Thus the objective of this study is to compare the feto-maternal outcomes between patients who have achieved different glucose values after intervention for hyperglycemia in pregnancy.

METHODS

A prospective comparative observational study was conducted in the Obstetrics Department of a Teaching Hospital in Banglore, India. Patients with glucose intolerance (either gestational diabetes or pre-existing) irrespective of gestational age at which diagnosis was made. Irregular follow-up, non-compliance and type I Diabetes Mellitus patients were excluded. The standard diagnostic criteria for diagnosis of GDM (75-gram Glucose Tolerance Test) and protocols for management of GDM were continued as per existing standards, with involvement of endocrinologist when appropriate. Interventions (medical nutrition therapy, oral hypoglycaemic agents or insulin and maintenance of the log of self-monitoring of capillary blood glucose) were continued based on the severity of the sugar values.

The main outcome parameters were the values of the fasting blood sugar and the postprandial blood sugars obtained from the self-monitoring tests. The patients were grouped into two groups – the tight control group (if FBS <90 mg/dl and PPBS <120 mg/dl) and less tight control group (if FBS between 91-95 mg/dl and PPBS 120-140 mg/dl). Sample size estimated was done using the formula $n = \frac{([a + b]^2 [p1q1 + p2q2])}{x^2}$ utilizing p1 (Proportion of subjects with unfavourable outcome in tight control group) as 39%, based on the study by Martis et al.[5]

The maternal parameters (age, parity gestational age at diagnosis, average blood sugar) were compared to ensure comparability between the groups. The

maternal outcomes (gestational age at delivery, polyhydramnios, mode of delivery, maternal hypoglycaemia, occurrence of hypertensive disorders of pregnancy) and neonatal outcomes (hyperglycaemia, hyperbilirubinemia, NICU admission) were compared between the groups. For comparative statistics, Pearson's chi-square test was used for proportions and unpaired t-test was used for numbers, as was appropriate, after checking for normality of distribution' and p-value of <0.05 was taken as statistically significant. Descriptive values were expressed as percentage.

RESULTS

Thirty cases in each arm were taken. There was no significant difference in well controlled and poorly controlled blood sugar groups in terms of age group (p=0.155, Student t-test) and parity (p=0.9) but it was significantly different if diagnosed in third trimester with poor controlled group (p=0.018, Chi-Square Test). The average age (27.9 years vs 29.4 years) and proportion of primigravidae (43.3% vs 40%) were similar in both groups. Expectedly, the FBS/PPBS values were lesser in group I (84/120) compared to group II (93/142). The proportion of patients who were diagnosed in the third trimester was 73% in group I while it was 43% in group II. Those who are diagnosed in the later gestational age, tend to have a more-tight control of sugars, compared to those diagnosed at an earlier gestational age [Table-1].

Table-1: Comparison of Baseline characteristics between the groups

Parameters		Well control group	Lesser control group	Total
Age in year (p=0.155, Student t-test)	<25	7 (23.3%)	3 (10%)	10 (16.7%)
	25-30	16 (53.3%)	14 (46.7%)	30 (50%)
	>30	7 (23.3%)	13 (43.3%)	20 (33.3%)
	Total	30 (100%)	30 (100%)	60 (100%)
	Mean ± SD	27.90±4.72	29.46 ±3.61	28.68 ±4.24
Parity (p=0.9)	Primigravida	13 (43.3%)	12 (40%)	25 (41.7%)
	Multigravida	17 (56.7%)	18 (60%)	35 (58.3%)
	Total	30 (100%)	30 (100%)	60 (100%)
Gestation at diagnosis (p=0.018, Chi-Square Test)	1-12 Weeks	0 (0%)	0 (0%)	0 (0%)
	13-28 Weeks	8 (26.7%)	17 (56.7%)	25 (41.7%)
	29-40 Weeks	22 (73.3%)	13 (43.3%)	35 (58.3%)
Mean values (p=0.001)	Mean FBS	84.46±5.11	93.66±1.12	89.06±5.91
	Mean PPBS	120.36±10.18	142.83±2.61	131.60±13.51

The average gestational age at delivery (38.2 weeks vs 37.7 weeks, p=0.362), the proportion of LSCS (50% vs 66.7%, p=0.296) and neonatal birth weight (2.88 kg vs 2.98 kg, p=0.395) were similar in both the groups [Table-2].

Table-2: Comparison of Delivery outcomes between the groups

Parameters		Group I	Group II	Total
Gestation at delivery in weeks (p=0.362, Student t-test)	28-32	1 (3.3%)	2 (6.7%)	3 (5%)
	33-36	2 (6.7%)	0(0%)	2 (3.3%)
	37-40	27 (90%)	28 (93.3%)	55 (91.7%)
	Mean ± SD	38.20±1.93	37.70±2.26	37.95±2.10
Mode of delivery (p=0.296)	FTND	15 (50%)	10 (33.3%)	22 (36.7%)
	LSCS	15 (50%)	20 (66.7%)	35 (58.3%)
Neonatal Birth weight in Kg (p=0.395, Student t test)	1.0-2.49	5 (16.7%)	3 (10%)	8 (13.3%)
	2.50-3.50	24 (80%)	25 (83.3%)	49 (81.7%)
	3.51-4.50	1 (3.3%)	2 (6.7%)	3 (5%)
	Mean ± SD	2.88±0.49	2.98±0.39	2.93±0.44

The proportion of fetal complications (polyhydramnios, macrosomia, neonatal hypoglycemia, hyperbilirubinemia, NICU admission) were similar between the two groups [Table-3].

Table-3: Comparison of neonatal complications between the groups

Parameters		Group I	Group II	Total
Polyhydramnios at term (p=0.706)	Absent	27 (90%)	25 (83.3%)	52 (86.7%)
	Present	3 (10%)	5 (16.7%)	8 (13.3%)
Neonatal Hypoglycemia (p=0.781)	Absent	21 (70%)	20 (66.7%)	41 (68.3%)
	Present	9 (30%)	10 (33.3%)	19 (31.7%)
Neonatal Hyperbilirubinemia (p=0.436)	Absent	15 (50%)	18 (60%)	33 (55%)
	Present	15 (50%)	12 (40%)	27 (45%)
NICU admission (p=1.000)	Absent	28 (93.3%)	27 (90%)	55 (91.7%)
	Present	2 (6.7%)	3 (10%)	5 (8.3%)
Macrosomia (p=1.000)	Absent	30 (100%)	30 (100%)	60 (100%)

The occurrence of hypoglycaemic episodes (0% vs 10%) and occurrence of hypertensive disorders (6.7% vs 23.3%) was similar between the groups [Table-4].

Table-4: Comparison of maternal complications between the groups

Maternal complications		Group I	Group II	Total
Hypoglycaemic episodes (p=0.237)	Absent	30 (100%)	27 (90%)	57 (95%)
	Present	0 (0%)	3 (10%)	3 (5%)
hypertensive disorders	Absent	28 (93.3%)	23 (76.7%)	51 (85%)

DISCUSSION

Importance of glycemic control: There is a consistent association between high maternal sugar values and the risk of adverse neonatal growth and outcomes, and this risk starts from the early gestational period of the mother. There is good evidence to show that the prompt interventions to reduce the hyperglycemia reduces the adverse effects. Interest regarding strict glycemic control increased when it was shown that it has implications for second trimester screening also.

Rosenn et al had authored an article titled "Glycemic control in the diabetic pregnancy: is tighter always better?" in 2000 which focused on the aspects that there may be higher incidence of complications upon usage of very strict measures to reduce blood sugar. [6]

Poomalar et al have also reviewed the changing trends in management of GDM and noted that though the consensus recommendation remains one of preprandial glucose of less than 96 mg/dl. They also noted that there is very limited evidence that a value of <88 mg/dl (tight control) can yield even better results.[7] However, studies have not taken into account differentiation within the glycemic controlled group, which is the focus of our study.

The importance of glycemic control after a diagnosis of GDM has also been confirmed by multiple studies. For example, Quintero et al have confirmed in a large population-based study that when glycemic control is not good (FBS>95 or PPBS >140), the proportion of neonates with at least one adverse outcome is approximately 65% in the lack of glycemic control group; and the occurrence of at least one adverse outcome was approximately 40% in the less tight control group and around 30% in the tight control group.[8] However, the risk of adverse outcome was only 24% in the good glycemic control group in our study and needs further study on it.

Gestational age at delivery: In our study, the rate of prematurity in both the tight control and the less tight control group was similar (10% vs 7%, p value 0.362). However, our findings are contrary to the findings of the study by Rowan et al who noted that there was an increase in the rate of prematurity (the highest tertile having 13% compared to the lowest tertile having 6%, p value <0.001).[9]

Neonatal birth weight and macrosomia: In our study, the mean birth weight was 2.88±0.49 kg in the non-strict control group and 2.98±0.39 kg in the strict control group, and there was no statistically significant difference between the groups (p=0.395). These findings are comparable to the study by Garner et al, the corresponding values were 3.43±0.57kg and 3.54±0.60 kg.[10] These findings are also comparable to the findings by Hasanein et al, wherein the anthropometric parameters of infants born to GDM mothers, with strict control and non-strict control were both similar.[11] However, the findings of Brown et al showed that there was a higher proportion of LGA infants in the group of patients who had an FBS value of >88 mg/dl, compared to those who had a value of <88 mg/dl, and the difference was statistically significant (p<0.01).[12]

There were no patients with SGA in either group in our study. There is no difference between the outcomes in strict control and non-strict control is contrary to the earlier observations by Metzger et al who had noted that there may be a slight increase in SGA infants when the FBS level drops below 87 mg/dl. Hernandez et al have explained that the target of <95 mg/dl is preferable rather than a target of <91 or <88 mg/dl, justifying this using a statistical reasoning of using a 1SD rather than 2 SD values for identification of LGA or SGA.[13] Hence, it may be stated there does not appear to be a consistent reduction in the neonatal birthweight owing to tight control of sugars. This implies that very tight control of sugars is not to be recommended.

Neonatal hypoglycemia: The frequency of neonatal hypoglycemia was statistically similar between both the tight control group and the non-tight control group (30% vs 33%, p=0.781). This finding is similar to that of Garner et al, who also observed that both the strict and the non-strict groups showed no difference in the rates of neonatal hypoglycemia (p>0.05). Yet again, it implies that very tight control is not to be recommended for the prevention of neonatal hypoglycemia.

Birth trauma: In our study, there was no birth trauma in either group. This is similar to the findings of the study by Garner et al, where there were no cases of birth trauma. This finding is also similar to the findings by Rowan et al, where patients belonging to the highest tertile of sugar values showed a similar rate of birth trauma compared to those of the lowest tertile. (p=0.66). It may be stated that very tight control of sugars may not result in the prevention of birth trauma.[9,10]

Development of hypertension: In our study, there was no difference in the prevalence of hypertensive disorders between the groups (23.3% vs 6.7%, p=0.156). This finding is contrary to the findings of Holmes et al, where those with a higher HbA1c had a higher propensity to develop hypertension (17% vs 11%, p=0.01).[14] In the study by Rowan et al, the group of patients in the highest tertile of fasting blood sugar had a similar rate of

hypertensive disorders compared to the lowest tertile (9.2% vs 3.4%, p=0.39). Hence, it may be stated that the relationship between tightness of control of sugars and development of hypertension is not very clear.[9]

Differentiating which patients need tight control: Selecting which patients to give strict control. In one study by Kjos et al, it was noted that those GDM patients who show a high fetal abdominal circumference can be considered for strict glycemic targets.[15] However, there does not seem to be any consensus regarding the matter. In any case, our study shows that very strict glycemic targets are of not much benefit, as perceived.

CONCLUSION

The strict control and non-strict control appear to yield similar results in this study with small sample size. Thus the further study in a large population is required.

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