Research Article
Open Access

Comparison of Perinatal outcome in pregnant patients with one abnormal value in OGTT as compared to more than two values as per the IADPSG criteria

Abstract

Background: To study the association of gestational diabetes mellitus and adverse perinatal outcome.

Materials and methods: 296 pregnant patients were enrolled in the study and at 24-28 weeks 75 grams OGTT was done and 40 patients were diagnosed as GDM after satisfying the criteria. For comparison the study group was divided in to two groups. Group 1 which included the patients which had only one abnormal value in OGTT, Group 2 which included patients with ≥ 2 abnormal values in OGTT. All these patients were followed till post delivery for perinatal outcome in terms of birth weight, neonatal hypoglycaemia, hyperinsulinemia using cord blood serum C – peptide levels, caesarean delivery for CPD, respiratory distress syndrome, birth trauma, shoulder dystocia and perinatal mortality.

Results: In the study group 15 babies out of 40(37.5%) were LGA (large for gestational age). In group 1, 6 out of 20 babies (30%) were LGA whereas in group 2, 9 out of 20 babies (45%) were LGA. 6 out of 40 babies (15%) had hypoglycemia. In group 1 the incidence of hypoglycemia was 2 in 20 (10%) and in group 2 it was 4 in 20 (20%). The mean cord blood C-peptide level in this study was 2.12±2.17 and elevated levels were seen in 11 out of 40 patients (27.5%). In group 1, it was in 4out of 20 cases (20%) and 7 out of 20 cases (35%) in group 2. Birth injury was seen in 1 baby, 2 had asphyxia and 4 had respiratory distress. Hypocalcaemia, hyperbillirubinemia, polycythemia, sepsis and NICU admission were seen in 5,6,6,3 and 6 babies respectively, neonatal mortality in none.

Conclusion: Adverse perinatal outcome including LGA babies were encountered with lower threshold cut-offs and single deranged value of blood sugars , in particular with fasting blood sugar values.

Keywords: gestational diabetes mellitus, perinatal morbidities, LGA babies, neonatal hypogylycemia, cord serumc peptide levels

Volume 7 Issue 4 - 2018

Gunjan Chaudhary, Chitra Raghunandan, Kanika Chopra

Department of Obstetrics and Gynaecology, Sir Ganga Ram Hospital, India

Correspondence: Kanika Chopra, department of obstetrics and gynaecology, Lady Hardinge Medical College, New Delhi, India. Email kank2kanu@yahoo.co.in

Received: June 17, 2018 | **Published:** September 21, 2018

Abbrevations: GDM, gestational diabetes mellitus; LGA, large-for-gestational-age; OGTT, glucose tolerance test; NICU, neonatal intensive care unit; CPD, cephalopelvic disproportion

Introduction

Gestational diabetes mellitus is fast becoming an important heath issue in India. Traditionally quoted prevalence figures are around 5-7% and the prevalence of GDM directly reflects that of type 2 diabetes in a given population and therefore can be expected to be on the rise. With newer diagnostic thresholds the prevalence in the general population may be up to 18%.[1] Out of 1-14% of pregnancies which are complicated by diabetes mellitus majority (88%)[2] are gestational diabetes mellitus. There is growing evidence that elevated plasma glucose concentrations or hyperglycemia, below what is currently considered GDM are also pathological to fetus.[3] Uncontrolled maternal GDM exposes the fetus to an abnormal glucose load, leading to a compensatory increase in fetal insulin secretion. The resulting hyperinsulinemia often leads to excess fetal growth and these large -for-gestational-age (LGA) fetus face a significantly increase risk for morbidity at the time of vaginal birth such as shoulder dystocia[4] brachial plexus injury and new born asphyxia. Consequently, most obstetricians prefer to deliver LGA infants via caesarean section.[5] Fetus exposed to a high intrauterine glucose environment also have elevated risks for a number of other complications upon delivery, including neonatal respiratory distress syndrome, cardiomyopathy, hypoglycaemia, hypocalcemia, hypomagnesia, polycythemia and hyperviscocity.[6] Armed with the knowledge gained over years and the acute awareness that GDM in pregnancy is associated with poor fetal outcomes and the recent proposition that even milder forms of hyperglycemia are associated with LGA babies and adverse perinatal outcome, the need of the hour is to correctly diagnose the biochemical changes at the right time. This will help to achieve a good metabolic control and improve the perinatal as well as maternal outcome.

Materials and methods

296 patients underwent 2-hour 75 grams OGTT at 24 to 28 weeks

of pregnancy and 40 were diagnosed as gestational diabetes mellitus as per IADPSG criteria. For comparison the study group was divided in to two groups. Group 1 which included the patients which had only one abnormal value in OGTT and Group 2 which included patients with ≥ 2 abnormal values in OGTT. All these women were kept under intense surveillance till delivery. Cord blood serum C-peptide levels were estimated using DRG C-PEPTIDE ELISA KIT (EIA1293) which is an enzyme linked (solid phase) immunoassay for the quantitative in vitro diagnostic measurement of C-Peptide. A cord- blood serum C-peptide value > 1.7microgm/dl was defined as hyperinsulinemia. The birth weight of babies was estimated using the weighing machine & baby was examined to rule out any birth injury. Birth weight > 90th percentile was defined as macrosomia as per Lubchenco's chart. Apgar score was calculated, any symptoms of respiratory distress like RR ≥60 (tachypnea), retractions, nasal flaring or any grunting and cyanosis were noted. Birth asphyxia was defined as Apgar score ≤ 3 at≥10 minutes and cord pH <7. Babies' dextrose levels were monitored serially at1, 4,8,12 & 24 hours of birth to look for any hypoglycemia. In the study hypoglycemia is defined as any dextrose level less than< 45 mg/dl within first 24hrs of birth. The babies were also followed up for any perinatal morbidity such as hypocalcemia, hyperbilirubinemia, polycythemia, sepsis and any NICU admission. In the study hypocalcemia was defined as ionic calcium <4 mg/dl. Polycythemia was defined as venous hematocrit of at least 65%. Hyperbilirubinemia was defined as per AAP chart. Also, perinatal outcomes such as caesarean delivery for CPD, respiratory distress syndrome, birth trauma, shoulder dystocia and perinatal mortality were studied in association with GDM.

Results

The present study was carried out in the Department of Obstetrics and Gynaecology in Lady Hardinge Medical College & Associated Hospitals, New Delhi. 296 patients were screened at 24-28 weeks of gestation with 75 g Oral Glucose Tolerance Test (OGTT). Those who were diagnosed as GESTATIONAL DIABETES MELLITUS (GDM) after satisfying the criteria were followed up in the antepartum, intra-partum and postpartum period. The mode of delivery was noted and the cord blood was collected after the delivery of the placenta and the samples were processed accordingly. The neonate was followed up for the birth-weight, hypoglycaemia and other perinatal morbidities i.e. RDS, birth trauma, hypocalcaemia, hyperbilirubinemia, polycythaemia, and admission to NICU. They were followed up till the discharge of mother. 40 patients out of 296 were tested positive for GDM which constituted the study group. For comparison the study group was divided in to two groups. Group 1 which included the patients which had only one abnormal value in OGTT and Group 2 which included patients with ≥ 2 abnormal values in OGTT.

The mean age of patients in group 1 was 28.35±5.27, which was comparable to mean age of patients in group 2 which was 29.15±4.21 (p=0.599). The mean parity of patients in both the groups were comparable. In group 1, it was 1.05±0.83 & in group 2, it was 1.05±0.94 (p = 1.00). In group 1, the mean gestational age at delivery was 39.05±1.10 which was comparable to group 2, which was 38.25±1.45 (p =0.056). The mean BMI in the group 1 was 28.35±2.41 and in group 2 it was 29.95±6.59 (p=0.316). The mean systolic BP in group 1 was 122.50± 11.22 mm Hg and for group 2 it was 130.05±12.42 mm Hg (p=0.051). The mean diastolic BP in group 1 was 77.75±8.17 mm Hg and for group 2 it was 81.95±11.53 (p=0.192). Hence, both the groups were comparable in demographic characteristics and clinical parameters as depicted in Table 1 & Table 2 shows that in the total of 40 patients, 20 had only one value deranged, 16 had two values deranged and 4 had all three-values deranged. Among the women who had only one value deranged, only fasting value was deranged in 11, only 1sthr value was deranged in 4 and only 2ndhr value was deranged in 5. Only 1 (2.5%) baby had birth injury, 2 (5%) babies had birth asphyxia, 6 (15%) babies had hypoglycaemia, 4 (10%) babies had respiratory distress, 5 (12.5%) had hypocalcaemia, 6 (15%) had hyperbilirubinemia, 6 (15%) had polycythaemia, 6 (15%) had NICU admission and 3 (7.5%) babies had sepsis. No neonatal mortality was observed as seen in Table 3 & Table 4 shows the incidence of LGA babies in the study group. In the group 1, 6 out of 20 (30%) were LGA babies in comparison to group 2 in which 9 out of 20 babies (45%) were LGA (p=0.327) and the difference was not statistically significant. In group 1, 4 babies were LGA out of 11 (36.36%) in which only fasting value was deranged, 1 out of 4 babies (25%) was LGA in which only 1st hr value was deranged and 1 out of 5 babies (20%) was LGA in which only the 2nd hr value was deranged. In the group 1, 2 babies out of 20 (10%) had hypoglycaemia whereas in group 2, 4 out of 20 babies (20%) had hypoglycaemia (p=0.376) and the difference was not statistically significant. In group1, hypoglycaemia was noted only in babies of patients who had fasting value deranged and the incidence was 2 babies out of 11 (18.18%). No hypoglycaemia was observed in the neonates whose mother had either only 1st hr value or 2nd hr value deranged as seen in Table 5 & Table 6 shows the incidence of elevated cord blood C- peptide levels (>1.7µg/dl) in the study group. In the group 1, 4 out of 20 cases (20%) had elevated cord blood C-peptide levels and 7 out of 20 cases (35%) had elevated cord blood C-peptide levels in group 2 (p=0.288), however the difference was not statistically significant. In the group 1, 3 out of 11 cases (27.27%) had elevated cord blood C-peptide levels among the patients having only deranged fasting value. Those who had 1st hr value deranged value none of the babies had elevated cord blood C-peptide levels and in the 2nd hr value deranged 1 in 5 cases (20%) had elevated cord blood C-peptide levels. In group 1, 8 out of 20 (40%) had caesarean delivery and 10 out of 20 (50%) patients had caesarean delivery (p=0.525) in group 2, however the difference was not statistically significant. In group 1, 11 out of 20 (55%) had NVD and in group 2, 9 out of 20 (45%) had NVD (p=0.527). In group 1 and group 2, 1 out of 20(5%) patients had instrumental vaginal delivery (p=1.00).

Table 1 Demographic and clinical parameters with one or more than one abnormal blood sugar values

	Number of values Deranged		P Value
	Group 1 (N=20) Mean ± SD	Group 2 (N=20) Mean ± SD	
Age	28.35 ± 5.27	29.15 ± 4.21	0.599
Parity	1.05 ± 0.83	1.05 ± 0.94	1
Gestational Age	39.05 ± 1.10	38.25 ± 1.45	0.056
Bmi	28.35 ± 2.41	29.95 ± 6.59	0.316
Sbp	122.50 ± 11.22	130.05 ± 12.42	0.051
Dbp	77.75 ± 8.17	81.95 ± 11.53	0.192

Citation: Chaudhary G, Raghunandan C, Chopra K. Comparison of Perinatal outcome in pregnant patients with one abnormal value in OGTT as compared to more than two values as per the IADPSG criteria. *MOJ Womens Health.* 2018;7(5):137–141. DOI: 10.15406/mojwh.2018.07.00184

Table 2 Frequency of abnormal blood sugar values in study group & frequency of single abnormal blood sugar value in study group

Number of value Deranged	Frequency	%
1	20	50
≥2	20	50
Total	40	100
N=20 FASTING	1 HR	2HR
11	4	5

Table 3 Neonatal morbidities in study group

Neonatal Morbidity	Frequency(N=40)	%
Birth Injury/ Shoulder Dystocia	1	2.5
Birth Asphyxia	2	5
Hypoglycemia	6	15
Respiratory Distress	4	10
Hypocalcemia	5	12.5
Hyperbillirubinemia	6	15
Polycythemia	6	15
Nicu Admission	6	15
Sepsis	3	7.5
Neonatal Mortality	0	0

Table 4 Incidence of lga babies

Number of Values Deranged	N	LGA babies>90th Percentile		Non – LGA		
		Number of cases	%	Number of cases	%	P value
Fasting	11	4	36.36	7	63.63	
1st Hr	4	1	25	3	75	
2nd Hr	5	1	20	4	80	
Group 1	20	6	30	14	70	0.327
Group 2	20	9	45	11	55	

Table 5 Incidence of neonatal hypoglycaemia

Number of Values Deranged	N	No of babies having hypoglycemia		No hypoglycemia		P value
		Number of cases	%	Number of cases	%	
Fasting	11	2	18.18	9	81.8	
1st Hr	4	0	0	4	100	
2nd Hr	5	0	0	5	100	
Group 1	20	2	10	18	90	0.376
Group 2	20	4	20	16	80	

Citation: Chaudhary G, Raghunandan C, Chopra K. Comparison of Perinatal outcome in pregnant patients with one abnormal value in OGTT as compared to more than two values as per the IADPSG criteria. *MOJ Womens Health.* 2018;7(5):137–141. DOI: 10.15406/mojwh.2018.07.00184

Table 6 Incidence of elevated cord blood c-peptide levels (>1.7µg/dl)

Number of Values Deranged	N	No of babies having cord blood C-peptide level>1.7 µg/dl		No of babies having cord blood C-peptide level<1.7 µg/dl		P Value
		Number of cases	%	Number of cases	%	
Fasting	11	3	27.27	8	72.72	
1st Hr	4	0	0	4	100	
2nd Hr	5	1	20	4	80	
Group 1	20	4	20	16	80	0.288
Group 2	20	7	35	13	65	

Discussion

This observational study was carried out in the Department of Obstetrics and Gynaecology in Lady Hardinge Medical College & Associated Hospitals, New Delhi and included 296 pregnant patients. This study involved using lower threshold cut offs and single value deranged criteria (IADPSG Criteria)1 for diagnosing gestational diabetes mellitus and study of its association with adverse perinatal outcome and also compared the fetal outcomes with one value and more than one values deranged in 75g OGTT. Thus, the study group was divided in 2 groups for ease of comparison, in group1 there were patients who had one value of blood sugars deranged and in group 2 more than two values of blood sugars deranged as per the IADPSG criteria. Our study revealed numerous remarkable findings. In the present study, shoulder dystocia/birth trauma was observed in 1 out of 40 patients (2.5%) and birth asphyxia was observed in 2 out of 40 patients (5%). In the HAPO study[7] birth trauma was observed in 1.3% cases and in Atlantic DIP study[8] the prevalence of shoulder dystocia was 1.2%. The incidence in all the studies was comparable. Respiratory distress was observed in 4 out of 40 (10%) in our study, whereas in a study by Wahi P et al.[9] the RD was 3.23% whereas the prevalence of neonatal respiratory distress, in Atlantic DIP study was 3.6% .In the present study, hyperbillirubinemia was observed in 6 out of 40(15%) babies whereas in HAPO study hyperbillirubinemia was observed in 8.3% cases and in the Atlantic DIP study the prevalence of neonatal jaundice was 5.8%. There were 6 out of 40(15%) NICU admissions in the study group whereas in HAPO study the NICU admission rate was 8% and in the Atlantic DIP study it was 26%. There was no neonatal mortality in any of the studies. Hypocalcemia was observed in 5 out of 40(12.5%), polycythemia in 6 out of 40(15%) & sepsis in 3 out of 40 (7.5%) babies in our study group.

LGA is one of the common morbidities associated with babies of GDM mothers. The possible explanation for this hyperinsulinemia causes increased IGF's (Insulin like Growth Factors) which stimulate fetal growth and it also causes deposition of fat and glycogen. They are at a high risk of respiratory distress, birth asphyxia, shoulder dystocia, birth trauma and neonatal hypoglycemia. LGA babies in the present study were decided as per Lubchenco's chart. The babies weighing >90th percentile for a particular gestational age were labelled as LGAs. In the study group 15 babies out of 40(37.5%) were LGA. In this group 1, 6 out of 20 babies (30%) were LGA whereas in group 2, 9 out of 20 babies (45%) were LGA. In group 1, when only fasting value was deranged 4 out of 11 babies (36%) were LGA and in isolated 1sthr value deranged, 1 out of 4 babies(25%) was LGA and when only the 2ndhr value was deranged , 1 out of 5(20%) babies was LGA. The difference between group1 and group 2 was not statistically significant (p=0.288) which suggested that even single value deranged with lower cut-offs could be associated with LGA babies. In a study by Zsuzsa et al.[10] the risk of LGA babies was 20.1% when the fasting sugar levels were between 91.8 mg/dl – 99 mg/dl and the incidence of LGA babies was 28.7%, when fasting exceeded 99 mg/dl. According to the HAPO study proposed threshold of 92 mg/dl for fasting plasma glucose, identified 8.3% of the HAPO population and 19.5% of the babies were large for gestational age. Adding the 1 hour threshold of 180 mg/dl identified an additional 5.7% of the population who did not have an elevated fasting value and a total of 16.5% of identified pregnancies delivered babies with LGA. Adding the 2 hour threshold of 153 mg/dl identified an additional 2.1% of the population, and a cumulative total of 16.2% with LGA. In the Atlantic DIP study the incidence of LGA babies was 22.6% when GDM was diagnosed by IADPSG criteria. The incidence of LGA babies was almost comparable in all the studies. This observation also suggested that fasting hyperglycemia was associated with higher incidence of LGA babies.

Neonatal hypoglycaemia is usually seen in babies who have hyperinsulinemia. This can be explained by the Pederson Maternal Hyperglycemia–fetal hyperinsulinimia hypothesis. Usually the raised maternal glucose near term or during labour can evoke hyperinsulinemic response. Hypoglycemia is caused by hyperinsulinemia due to hyperplasia of fetal pancreatic beta cells consequent to maternal-fetal hyperglycemia. Because the continuous supply of glucose is stopped after birth, the neonate develops hypoglycemia because of insufficient substrate. Stimulation of fetal insulin release by maternal hyperglycemia during labour significantly increases the risk of early hypoglycemia in the infants. Perinatal stress may have an additive effect on hypoglycemia due to catecholamine release and glycogen depletion. In present study group 6 out of 40 babies (15%) had hypoglycemia. In group 1 the incidence of hypoglycemia was 2 in 20 (10%) and in group 2 the incidence was 4 in 20 (20%). In the group 1, the incidence was highest in the group which had only fasting value deranged that is 2 out of 11 (18.18%). In the individual 1st hr value and 2nd hr value deranged, no incidence of hypoglycemia was observed. The difference between group1 and group 2 is not statistically significant (p=0.376) which suggests that even single value deranged with lower cut-offs could be associated with neonatal hypoglycemia. The observation also suggests that mothers with only

fasting hyperglycemia have relatively higher incidence of neonatal hypoglycaemia. The clinical neonatal hypoglycemia in HAPO17 study was 2.1%. The prevalence of neonatal hypoglycemia was 2.4% in the Atlantic DIP study.

C-peptide is a 31 amino-acid residue peptide which is released when pro-insulin is cleaved to form insulin. So, C-peptide is secreted in equimolar amounts as that of insulin and is a surrogate way of quantifying the insulin secretion. Increased cord blood C-peptide levels suggest hyperinsulinemia which is responsible both for LGA babies and neonatal hypoglycemia. The mean cord blood C-peptide level in this study was 2.12±2.17, whereas in the HAPO study the mean C-peptide level was 1.0±0.6. The difference could be due to the fact that the HAPO included the participants with normal glucose tolerance also. Elevated cord blood C-peptide levels was seen in 11 out of 40 patients (27.5%) in our study. In group 1, elevated cord blood C-peptide levels were seen in 4 out of 20 cases (20%) and 7 out of 20 cases (35%) in group 2. In group 1, 3 babies out of 11 cases (27.27%) had elevated cord blood C-peptide levels with only fasting value deranged, 1 out of 5 cases (20%) had elevated cord blood C-peptide level in cases with only 2nd hr value deranged and no cases observed in patients with 1sthr value deranged. There was no statistical difference between the group 1 and group 2(p=0.288) which suggests even single value deranged with lower cut-offs could be associated with elevated cord blood C –peptide levels .The observation also suggests that mothers with fasting hyperglycemia had elevated cord blood C-peptide levels. In HAPO study, the C–peptide level above 90th percentile was seen in 8.4%.

Conclusion

Adverse perinatal outcome including LGA babies were encountered with lower threshold cut-offs and single deranged value of blood sugars, in particular with fasting blood sugar values.

Thus, the single step OGTT with lower threshold value cut offs and single abnormal value for diagnosis of GDM as advocated by IADPSG seems to be effective because of its association with adverse fetal outcome. However, this study needs to be done on large pregnant women population with GDM."

Acknowledgements

None.

Conflict of Interest

The author declared that there is no conflict of interest.

References

1. Metzger BE, Gabbe SG, Persson B, et al. International association of diabetes and pregnancy study groups recommendations on the diagnosis and classification of hyperglycemia in pregnancy. *Diabetes Care.* 2010;33(3):676–682.
2. Engelgau MM, Herman WH, Smith PJ, et al. The epidemiology of diabetes and pregnancy in the US. *Diabetes Care*. 1995;18(7):1029–1033.
3. Landon MB, Mele L, Spongy CY, et al. The relationship between maternal glycemia and perinatal outcome. *Obstet Gynecol.* 2011; 117(2 pt 1):218–224.
4. Gottlieb AG, Galan HL. Shoulder dystocia an update. *Obstet Gynecol Clin North Am.* 2007;34(3):501–531.
5. Jones CW. Gestational diabetes and its impact on neonate. *Neonatal Netw.* 2001;20(6):17–23.
6. Pettit DJ, Knowler WC. Long term effects of the intrauterine environment, birth weight, and breast-feeding in Pima Indians. *Diabetes Care.* 1998;21:B1:38–41.
7. HAPO study cooperative research group. Hyperglycemia and adverse pregnancy outcome. *New Eng J med.* 2008;358(19):1991–2002.
8. O'Sullivan EP, Avalos G, Dennedy MC et al. Atlantic Diabetes in Pregnancy (DIP): the prevalence and outcomes of gestational diabetes mellitus using new diagnostic criteria. *Diabetologia.* 2011;54:1670–1675.
9. Wahi P, Dogra V, Jandial K, et al. Prevalence of gestational diabetes mellitus and its outcomes in Jammu region. *J Assoc Physicians India.* 2011;59:227–230.
10. Zsuzsa Kerenyi, Gyula Tamas, Mika Kivimaki, et al. Diabetes Care. 2009;32(12):2200–2205.