

Association of the Serum Glucose Level with Fetal-Maternal Complications of Gestational Diabetes with Insulin Therapy

Tayyebeh Jahed Bozorgan and Mandana Manzouri Lashgari

Department of Obstetric & Gynecology, Mahdih Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran

Received: 30 Aug. 2010; Received in revised form: 7 Sep. 2010; Accepted: 15 Sep. 2010

Abstract- Gestational diabetes mellitus (GDM) is one of the important problems in pregnant women. This study conducted to determine association the level of serum glucose with fetal-maternal complications of gestational diabetes with insulin therapy. This study has been conducted as an Existing Data Study, so medical records of all pregnant women with GDM that have been treated with insulin during 2 years of study has been selected using census. The information was obtained using, medical records data. Mean level of serum glucose before and after treatment in different times according to correct level of serum glucose did not show statistical significant ($P>0.05$). Apgar score, time of stay in NICU, weight at the birth, base on correct level of serum glucose did not show statistical significant ($P>0.05$). Gestational age at the delivery, stay in hospital, diagnosis and fetal-maternal complications between two groups did not show statistical significant ($P>0.05$). It seems we can with screening and diagnostic GDM with suitable control of level of serum glucose and insulin therapy reduce incidence of fetal-maternal complications.

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Acta Medica Iranica, 2011; 49 (7): 442-446.

Keywords: Blood glucose; Pregnancy complications; Gestational diabetes mellitus; Insulin

Introduction

Gestational diabetes mellitus (GDM) is one of the main problems in pregnant women that, if untreated in pregnant women predisposes fetal death and morbidity. General prevalence of diabetes in pregnancy is 1-14% which includes 90% of GDM cases (1). The prevalence of GDM is strongly linked to maternal race and culture. In at risk women the risk of recurrence of GDM in later pregnancies has been reported 68% (2). Race is among the factors that affects diabetes complications in the pregnancy (3,4).

GDM is associated with increased risk of obstetric complications and prenatal mortality that controlling blood sugar and keeping it close to normal limit during pregnancy can reduce the prevalence of maternal, fetal and neonatal complications. Study of Kwik *et al.* in 2007 showed that in untreated GDM the incidence of macrosomia, shoulder dystocia, preeclampsia and urinary tract infections is significantly more than the treatment group (5). Due to the importance of good blood sugar control in reducing fetal and maternal morbidity, this study aimed to determine the relationship between blood glucose levels and maternal and fetal

complications in gestational diabetes treated with insulin.

Materials and Methods

In this study, which was conducted according to the information in patients' file, the files of all pregnant women referred to Mahdih Hospital (Tehran, Iran) during 2004-2006 with the diagnosis of gestational diabetes mellitus (GDM) and treated with insulin for glycemic control were evaluated. Information of each patient evaluated and recorded by obstetrics and gynecology resident according to the attached information. All required information included demographic data, maternal complications (type of delivery, preeclampsia, urinary tract infections, ...) and fetal complications (intrauterine death, fetal hypoglycemia, birth weight, Apgar score at birth, macrosomia, RDS, admission at NICU, Shoulder dystocia, ...) were obtained using information in the mothers' file.

Insulin therapy protocol

According to this protocol, blood glucose levels in under control GDM patients for different times were

Corresponding Author: Mandana Manzouri Lashgari

Department of Obstetric & Gynecology, Mahdih Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran
Tel: +98 261 3403006, Fax: +98 261 3400177, E-mail: mandana_manzouri@yahoo.com

considered normal if having the features of Table 1 (6). Insulin intake at different gestational age has been determined as follows (7). Total dose of daily intake of insulin:

- 0.7 U/kg in the first trimester
- 0.8 U/kg in the second trimester
- 0.9 U/kg in the third trimester

Dose of daily injection of insulin twice a day is as follows:

- 2/3 of total dose in the morning before breakfast
- 1/3 of total dose at night before dinner

Considering the indications, total insulin dose was set in this way:

- 2/3 of total dose in the morning: 2/3 NPH and 1/3 Regular

- 1/3 of total dose at night: 1/2 NPH, 1/2 Regular

Then all the data were entered in to the prepared sheets. All data encrypted and were analyzed by SPSS V. 16 software. The mean and standard deviation of quantitative variables and frequency of qualitative variables were calculated. Comparison of quantitative variables between the two groups was done by t-test and to compare qualitative variables between groups chi-square test was used. If necessary, the Fisher test was used. Significant level was considered 0.05.

Table 1. Blood glucose levels in under control GDM patients

Normal range	
90-70	FBS) mg/dl(
120>	2hpp) mg/dl(

Table 2. Demographic data of mothers and infants

age	29.05 ± 4.05
Pregnancy N.	2.5 ± 1.3
Pariety N.	1.1 ± 1.1
Living child	0.6 ± 0.8
Gestational Age	37.4 ± 1.8
Gestational Age at diagnostic	21.2 ± 9.8
Weight of infant at birth	3124.05 ± 612.5
Duration of mother hospitalization	15.2 ± 9.1
Stay at NICU	4.5 ± 5.3

Table 3. Comparison of fetal complications based on blood glucose level

	Corrected (n=33)	Uncorrected (n=7)	P Value
Polyhydramnius	0 (0%)	1 (3%)	0.641
RDS	10 (30.3%)	1 (14.3%)	0.389
Hypoglycemia	2 (6.1%)	0 (0%)	0.504

Table 4. Comparison of fetal complications based on gestational age

	Term (n=34)	Preterm (n=6)	P Value
Polyhydramnius	1 (2.9%)	0 (0%)	0.641
RDS	8 (23.5%)	3 (100%)	0.01
Hypoglycemia	2 (5.9%)	0 (0%)	0.504

Table 5. Comparison of Apgar score based on blood glucose level

	Corrected (n=33)	Uncorrected (n=7)	P Value
First minute	8.8 ± 0.6	9 ± 0	0.641
Fifth minute	9.8 ± 0.5	10 ± 0	0.01

Results

Demographic and therapeutic information of mothers and infants is given in table 2. In this study, blood sugar was corrected in 33 (82.5%) individuals and was not corrected in 7 (17.5%) cases. Insulin dose received by the mother was accordance with the protocol in 12 cases (30%), in 19 (47.5%) individuals increasing in dose was required and 9 cases (22.5%) needed the reduction in dose. 21 of newborn s (51.4%) were boys and 19 (48.6%) were girls. Type of delivery in 2 patients (5%) was vaginal and in 38 cases (95%) was cesarean section. Comparison of fetal complications according to corrected blood glucose level is brought in table 3 that no significant difference was found between the groups. In the subjects there was a significant relationship between gestational age and respiratory distress syndrome. Comparison of fetal complications according to gestational age is demonstrated in Table 4.

Table 6. Comparison of maternal complications based on blood glucose level

	Corrected (n=33)	Uncorrected (n=7)	P Value
UTI	2 (6.1%)	0 (0%)	0.504
Preterm labor	6 (18.2%)	0 (0%)	0.221
Preeclampsia	4 (12.1%)	1 (14.3%)	0.875

Table 7. Comparison of type of delivery based on blood glucose level

	Corrected (n=33)	Uncorrected (n=7)	P Value
NVD	2 (6.1%)	0 (0%)	0.504
Cesarean	31 (93.9%)	7 (100%)	

Table 8. Comparison relevant data to mother based on blood glucose level

	Corrected (n=33)	Uncorrected (n=7)	P Value
Gestational age at terminate of pregnancy (week)	37.3 ± 2.0	37.8 ± 0.8	0.557
Gestational age at diagnostic (week)	21.8 ± 9.1	18.3 ± 12.6	0.394
Duration of hospitalization (day)	15.9 ± 8.9	11.8 ± 9.9	0.291

Table 9. Comparison relevant data to infants based on blood glucose level

	Corrected (n=33)	Uncorrected (n=7)	P Value
Time of stay in NICU	4.7 ± 5.7	3.3 ± 2.8	0.574
Weight at birth	3103.5 ± 650.8	3230.0 ± 380.0	0.650

Table 5 shows the comparison of first and fifth minute infants' Apgar based on corrected maternal blood glucose level that no significant difference between the groups was found. Comparison of maternal complications according to corrected blood glucose level is given in Table 6. Comparison the type of delivery based on corrected maternal blood glucose level is seen in Table 7. Table 8 shows the comparison of mean gestational age at the time of termination of pregnancy, gestational age at the diagnosis and duration of maternal hospitalization based on corrected maternal blood glucose level. Findings indicate that there is no significant difference between corrected and uncorrected groups in three variables of gestational age at the time of termination of pregnancy, diagnosis and duration of maternal hospitalization. Comparing the mean duration of hospitalization at NICU, infants' birth weight according to corrected maternal blood glucose level is given in Table 9.

Discussion

In this study, treatment success rate and correction of blood sugar was 82.5%. In this group the dose of insulin intake to correct blood sugar as compared with the values determined in the treatment protocol required to be increased in 42.4% of patients. It seems that more than 0.8 unit/kg increase in the total dose of NPH and Regular at 18-26 weeks of pregnancy, 0.9 unit/kg at 26-36 weeks and 1 unit/kg at 40-36 weeks led to more effective correction of blood glucose in pregnant women with gestational diabetes. According to previous studies carried out insulin therapy to is the most common treatment to achieve corrected blood sugar level and traditionally NPH and Regular insulin is used in diabetic pregnant women (8). For correction of maternal blood glucose during pregnancy, oral anti hyperglycemia agents including glibenclamide (9), metformin (10),

acarbose (11) is also used. On the other hand insulin analogues are associated with the desired therapeutic effect, the minimum crossing from the placenta and no teratogenic complications during pregnancy (12-16). In this study, the number of pregnancies, number of abortions, number of living children, age at the time of termination of pregnancy, gestational age at the time of diabetes diagnosis, duration of maternal hospitalization and maternal blood glucose level showed no significant relationship. Also the mean duration of hospitalization at the NICU, the first and fifth minute Apgar score and birth weight showed no significant relationship with maternal blood glucose level. Duration of hospitalization in infants of these women at NICU was about 4 days which showed no relationship with maternal blood sugar level. In this study the first and fifth minute Apgar score was above 7 that showed no significant relationship with maternal blood sugar level. in Berkowitz *et al.* study, the Apgar score and hospital admission showed no relationship with glycemic control (17). Cousin L's study found no significant relationship between Apgar score and maternal blood glucose level (18). In the contrary Persson and Hanson reported that the risk of low Apgar score and less than 7 in the fifth minute in diabetic pregnant women increases three times (19). In the present study 2.5% polyhydramnios, 27.5% respiratory distress syndrome and 5% fetal hypoglycemia were reported as the complications of fetal preterm and term deliveries that showed no significant relationship with maternal blood glucose level and probably is due to leaving the study by one third of the patients. In the contrary gestational age showed a significant relationship with respiratory distress.

Also the most common complication in this study was between the two groups of fetal respiratory distress syndrome. However, in none of the cases still birth and neonatal shoulder dystocia was reported and probably

due to the low number of samples has not been reported. This finding has also been approved in Cousin L (18) and Yang X (20) study and the risk of respiratory distress syndrome in these patients has been mentioned five times higher. In this study, fetal hypoglycemia was reported in two cases of corrected gestational diabetes that both were observed along with respiratory distress syndrome in term infants. It is necessary to note that in both cases the maternal blood sugar was within normal limit one hour before the delivery. While in Hossein nejad's study fetal hypoglycemia in GDM group was higher than Non GDM and in GDM group 15% fetal hypoglycemia was reported (21). In this study, one case of polyhydramnios was reported in uncorrected group. Ahkter J's study reported polyhydramnios in 4.6% of the cases (22). In previous studies polyhydramnios and fetal hypoglycemia was reported at higher levels in diabetic pregnant women who had uncontrolled blood sugar (5,19,22-24). Three complications of macrosomia, preeclampsia and preterm labor were remained as the main and common complications despite the standard blood glucose control in Sun WJ *et al.* study although the maternal and fetal complications had been decreased (23). In Kwik M *et al.* study macrosomia and shoulder dystocia was significantly higher in untreated diabetic pregnant women. While these complications showed no significant differences between the treated groups and that of with normal blood sugar (5). Ahkter J *et al.* reported that generally in mothers who had gestational diabetes and mothers who already had diabetes mellitus neonatal complications included 13.1% fetal macrosomia, 7.1% intrauterine growth retardation and 5.3% intrauterine death. Also the fetal complications in mothers with uncontrolled blood sugar were higher (22). Considering the importance of polyhydramnios, respiratory distress syndrome and fetal hypoglycemia complications and low incidence of these complications in diabetic pregnant with uncorrected blood sugar it is recommended to conduct a study with larger sample size to confirm these findings. In this study, maternal complications included 5% urinary tract infections, 15% preterm labor, 12.5% preeclampsia and 95% of cesarean section that showed no significant relationship with maternal blood glucose level. In this study, the most common maternal complications was cesarean section that the most common cause was 13 cases of repeated cesarean, 10 cases of high risk pregnancies, 6 cases of respiratory distress, 5 cases of breech presentation, 1 case of twin pregnancy, 2 cases of macrosomia and 1 case of fetus transverse lie. In this study, a significant relationship was seen between blood glucose level and cesarean section rate. Previous studies have also

reported higher incidence of preeclampsia in uncontrolled diabetic pregnant (5,22-24). Kwik M *et al.* reported that preeclampsia was significantly higher in untreated diabetic pregnant while these complications show no significant difference between the treated group and that of with normal blood sugar. Cesarean section rate, labor induction, and gestational age during delivery showed no significant difference between the three groups of normal blood sugar, treated and untreated (5). Ahkter J *et al.* reported that generally in mothers who had gestational diabetes and mothers who already had diabetes mellitus maternal complications included 19% preeclampsia, 4.6% polyhydramnios and 3.4% threatened abortion. Also the maternal complications in mothers with uncontrolled blood sugar were higher (22). In Malinowska-Polubiec *et al.* study two-thirds of deliveries was vaginal delivery and one third was cesarean section that the most common causes was asphyxia and CPD. In the present study blood glucose level showed no significant relationship with preterm labor and all cases of preterm labor were among the patients with corrected blood glucose. In Sun WJ *et al.*'s study preterm labor is still a major and common complication despite the glycemic control (23). In the study done by Malinowska-Polubiec *et al.* the rate of preterm labor, preeclampsia and urinary tract infection has been decreased with blood sugar control. Increasing the rate of cesarean section in mothers with uncorrected blood sugar has been also supported by Persson B *et al.* study (19) but in the contrary Cousin L's study stated that the increased risk of cesarean is not associated with hyperglycemia (18). According to the obtained results in this study it is recommended to obstetrics and gynecologists to screen diabetic pregnant women and pay special attention to the diagnosis of gestational diabetes and reduce the incidence of maternal and fetal complications to the minimum by accurate and appropriate control of blood glucose and insulin therapy in diabetic pregnant women. Also control these patients after pregnancy in terms of overt diabetes to prevent this complication in subsequent pregnancy. In the present study the cause of obtained insignificant relationship between maternal blood glucose level and fetal and maternal complications was the limited and insufficient. Number of evaluated patients that this was the limitation of the present work. Therefore considering the fact that in Obstetrics and Gynecology, maternal and neonatal health and reducing maternal and fetal complications is of great importance it is recommended for future studies to design a prospective cohort with a larger sample size for confirming the obtained results of this study.

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