COMPARISON OF MATERNAL AND FETAL/NEONATAL COMPLICATIONS IN GESTATIONAL AND PRE-GESTATIONAL DIABETES MELLITUS

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Abstract- Presence of maternal diabetes mellitus (DM) during pregnancy has important consequences for both mother and child. To determine maternal and fetal/neonatal complications of gestational DM and compare them with pre-gestational DM, a prospective study was performed in 100 diabetic women delivered in our hospital from January 2001 to April 2002. Pregnancy outcome in 27 women with gestational DM and 73 women with pre-gestational DM and their offspring were studied and analyzed. The mean age of women was 28 years, women with gestational DM being slightly older than pre-gestational DM. Mothers with gestational DM were at increased risk of presenting with pre-eclampsia and preterm labor than pre-gestational DM. Frequency of Cesarean section was higher in mothers with pre-gestational DM. Frequencies of abortion and hypoglycemic episodes were similar in gestational DM and pre-gestational DM. Infants born to mothers with pre-gestational DM were at increased risk of suffering from respiratory distress syndrome and congenital malformations but rates of unexplained intrauterine fetal death and large for gestational age were higher in infant of mothers with gestational DM. Gestational and pre-gestational DM are associated with increased risk of maternal and neonatal morbidity. Both gestational and pre-gestational DM pregnancies and the offspring should be monitored and managed identically.

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Key words: Pre-gestational diabetes mellitus, gestational diabetes mellitus, maternal complications, neonatal complications.

INTRODUCTION

Diabetes mellitus (DM) complicates 3–5% of all pregnancies and is a major cause of perinatal morbidity and mortality, as well as maternal morbidity (1). Gestational DM, a glucose tolerance disorder of variable severity which occurs or is diagnosed for the first time during pregnancy, constitutes a public health problem because of its frequency (1 to 6% of all pregnancies) and its short and long term consequences for the fetus and/or the mother (2).

DM increases the risk of important adverse outcomes of pregnancy. The greatest perinatal risk in such cases is fetal macrosomia, which has been associated with a higher rate of Cesarean delivery. Major congenital anomalies are the leading cause of perinatal mortality in pregnancies complicated by DM, occurring in 6–12% of all infants (3). In women with type 1 DM who are poorly controlled at the time of conception and during the early weeks of gestation, the incidence of spontaneous abortion and major congenital malformations are increased. These

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anomalies can be prevented by tight control of maternal glycemia before gestation and during the early weeks of pregnancy.

The goal of our study was to evaluate the outcome of pregnancies complicated by DM and to compare maternal and fetal characteristics and outcome in gestational and pre-gestational DM.

MATERIALS AND METHODS

We included a consecutive series of 100 women with pregnancies complicated by DM who referred and cared in the Khorasan Diabetic Research Center and delivered at the Zeinab Hospital from January 2001 to April 2002. We included those diagnosed with either pre-gestational DM (*i.e.* type 1 and type 2 DM) or gestational DM, according to established criteria (4). We obtained informed consent from all patients.

Management of insulin dependent DM during pregnancy was directed towards strict metabolic control using conventional insulin regimens and diet. A similar program was followed for women in whom screening revealed glucose intolerance. Control of maternal blood glucose level, assessment of fetal well-being and fetal maturity, complications of pregnancy and postpartum and modes of delivery were reviewed. We attempted to define factors which could predict optimal maternal and neonatal outcome. Variables included maternal age at delivery, previous obstetrical history (*e.g.* stillbirth, abortion, preterm birth, previous gestational DM, macrosomic neonate delivery, congenital malformations) and past medical history, including presence of DM and familial history of DM. Maternal complications included Cesarean section, pre-eclampsia and preterm labor. Perinatal/fetal data included abortion, intrauterine fetal death and premature labor delivery.

To complete the data set we reviewed the standard antenatal sheets of all women included in the study. We analyzed and compared the data collected on pre-gestational and gestational DM.

RESULTS

From January 2001 to April 2002, a total of 100 women, 73 with pre-gestational 27 with gestational DM, were cared in Khorasan Diabetic Research Center and delivered at our hospital. Of those with pre-gestational DM, 35 had type 1 DM (48%) and 38 had type 2 DM (52%) who were treated with oral hypoglycemic drugs before pregnancy and insulin during pregnancy. Of those discovered during pregnancy, 27 were classified as gestational DM. The mean age of women was 28 years (from 23 to 42), women with gestational DM being slightly older (31.6 vs. 27.2 years).

Risk factors found in the history of pregnant diabetic women included previous large for gestational age (LGA) infant delivery, intrauterine fetal death, abortion and premature labor. History of previous gestational DM was seen only in gestational DM. Familial history of DM was found in both groups but was more frequent in pre-gestational DM. History of congenital malformations were found only in pre-gestational DM and in type 1 diabetic women was 2 times more frequent than type 2 (5.7% vs. 2.8%) (Table1). The risk for Caesarean delivery among women with pre-gestational DM was nearly four times greater compared to gestational DM (34 vs. 9). There was significant difference in the rate of pre-eclampsia between women with gestational DM and pre-gestational DM (22.2% vs. 6.8%) and in type 1 pre-gestational DM was four times more frequent than type 2 DM (11.11% vs. 2.7%). Compared to those with pre-gestational DM, women with gestational DM experienced higher rates of gestational preterm labor (18.5% vs. 10.9%). Infants born to mothers with type 1 pre-gestational DM were also at increased risk for preterm birth (13.8% vs. 8.1%) (Table 2).

Table 1. Characteristics of singleton women with gestational (group 1) and pre-gestational (group 2) diabetes mellitus

Characteristic	Group 1	Group 2
Maternal age (years)	31.6(4.3)	27.2(3.6)
Prior preterm delivery (<37 weeks)	3 (11.1%)	9 (12.3%)
Previous IUFD	4 (14.8%)	16 (21.9%)
Prior LGA delivery	10 (37%)	19 (26%)
Prior abortion	7 (25.9%)	33 (45.2%)
Prior gestational diabetes	9 (33.3)	0
History of familial diabetes	10 (37%)	16 (21.9%)
Prior congenital malformation	0	3 (4.1%)

Abbreviations: IUFD, Unexplained intrauterine fetal death; LGA, large for gestational age.

Table 2. Maternal outcomes in women with gestational (group 1) and pre-gestational (group 2) diabetes mellitus

Maternal outcomes	Group 1	Group 2
Cesarean section	9 (33.3%)	34 (46.5%)
Preterm delivery	5 (18.5%)	8 (10.9%)
Preeclampsia	6 (22.2%)	5 (6.8%)

*Data are given as number (percent).

Fetal complication included abortion, intrauterine fetal death and premature labor. Abortion was particularly common with similar frequencies in pre-gestational and gestational DM (21.9% vs. 22.2%). Unexplained intrauterine fetal death was nearly two times more frequent in gestational DM compared to pre-gestational DM (14.8% vs. 8.2%). Preterm labor was more frequent in gestational DM compared to pre-gestational DM (18.5% vs. 10.9%).

Neonatal complications included congenital malformations, macrosomia, respiratory distress syndrome (RDS) and hypoglycemia. The rate of neonatal RDS was significantly higher among the offsprings of women with pre-gestational DM compared to gestational DM (13.6% vs. 3.7%). Hypoglycemic episodes were more frequent in pre-gestational DM compared to gestational DM (21.9% vs. 18.5%).

There were overall 10 congenital defects detected at birth in our study. The number of anomalies that may have resulted in either spontaneous or therapeutic termination before birth was not available. Nine (12.3%) anomalies were seen in the offsprings of mothers with pre-gestational DM, of whom 4 had type 1 DM (11.1%) and 5 type 2 DM (13.5%). The remaining one congenital anomaly was seen in the offspring of a mother with gestational DM (3.7%). LGA infants were nearly two times more frequent in gestational DM compared to pre-gestational DM (14.8% vs. 6.8%). Fetal/Neonatal outcomes are presented in table 3.

Table 3. Fetal/Neonatal outcomes in women with gestational (group 1) and pre-gestational (group 2) diabetes mellitus

Fetal/Neonatal outcomes	Group 1	Group 2
Abortion	6 (22.2%)	16 (21.9%)
Premature labor	5 (18.5%)	8 (10.9%)
Unexplained IUFD	4 (14.8%)	6 (8.2%)
Hypoglycemic Episode	5 (18.5%)	16 (21.9%)
Respiratory distress syndrome	1 (3.7%)	10 (13.6%)
Congenital malformation	1 (3.7%)	9 (12.3%)
Large for gestational age	4 (14.8%)	5 (6.8%)

Abbreviation: IUFD, Unexplained intrauterine fetal death.
* Data are given as number (percent).

DISCUSSION

DM is one of the most common medical complications of pregnancy. A review of the literature over the last two decades indicates that the incidence of gestational DM varies from 0.15 to 12.3%. Between 0.2 and 0.3% of pregnancies occur in women with insulin dependent DM. When not diagnosed or treated properly, DM in pregnancy is associated with adverse maternal and fetal outcomes such as high perinatal wastage, congenital anomalies, macrosomia and neonatal, childhood and adult complications (5).

We studied the pregnancy outcomes of 27 women with gestational and 73 women with pre-gestational DM. After controlling for multiple risk factors, including previous LGA infants, fetal death, congenital malformations, abortion, preterm labor, familial history of DM and gestational DM, we observed that women with pre-gestational DM were at increased risk for operative delivery (four times higher than gestational DM). In other studies, similar to the results of our study, frequency of Cesarean delivery has been found to be higher in pre-gestational DM compared to the gestational DM (6, 7). The incidence of pre-eclampsia in our study was high (11%), similar to findings of Lavin *et al.* who found that pre-eclampsia is significantly increased (8).

The different thresholds of glucose in diabetic pregnant women are associated with fetal complications such as stillbirth, spontaneous abortion, congenital anomalies, fetal macrosomia, and metabolic and respiratory complications (9). In our study, the overall incidence of abortion was high (22%), higher in type 2 diabetic women compared to type 1 and gestational DM (31.5% vs. 11.4% and 22.2%). The incidence of congenital anomalies in offsprings of diabetic mothers has been reported as 6-9% (10). In our study, it were higher (11%) and four times more frequent in pre-gestational compared to gestational DM (12.5% vs. 3.6%), while none occurred in those with pre-conceptional counseling. The cause of the higher incidence of congenital anomalies in our study could be poor glucose control in diabetic women, or few pre-conceptional counseling. Macrosomia continues to be a problem,

with a rate of occurrence of 25% compared with none-diabetic mothers. The rate is inversely proportional to glycemic control (11). The rate of LGA in our study was 14.3% in gestational DM and 6.9% in pre-gestational DM, compared to 16% and 37% in Ray *et al.* study. The probable cause of low incidence of LGA in pre-gestational DM in our study is poor control of DM in the pre-conceptional period and presence of vascular disease. In our study we found RDS in pre-gestational DM with a rate 13.9%, four times higher than gestational DM (3.6%) and more common in type 2 DM (21.9%) compared to type 1 DM (7.9%). Clinical studies investigating the effect of maternal diabetes on fetal lung maturation have produced conflicting data. With the introduction of protocols that have emphasized glucose control and antepartum surveillance until lung maturity has been established, RDS has become a less common finding in the IDM (12). In our study, the rate of preterm birth was 11.1% in pre-gestational and 17.9% in gestational DM.

Despite dramatic decrease in incidence of unexplained stillbirth, this complication still occurs in pregnancies of patients who do not receive optimal care (13). In our study rate of fetal death was 8.3% in pre-gestational DM and 14.3% in gestational DM. Hypoglycemia is another neonatal complication in infants of diabetic mothers with overall rate of 5 to 15 percent with near physiologic control of maternal glucose levels (12). In our study, hypoglycemia occurred with high rates in pre-gestational (22.2%) and in gestational DM (17.9%).

Since poor glycemic control in early pregnancy in insulin-dependent DM is associated with an increased risk for spontaneous abortion and congenital malformations, clinical management of diabetic pregnant woman includes pre-conception consultation to improve the pregnancy outcome. The availability of a variety of new insulin's formula, the insulin pump and self-monitoring of blood glucose have revolutionized the care of the pregnancy complicated by DM. Pre-gestational DM is also associated with adverse fetal and maternal outcomes. Studies suggest that optimal control of DM before and during pregnancy minimizes these risks. In conclusion, the presence of maternal DM during pregnancy has important consequences for both mother and child. Women with DM are at increased risk for pre-eclampsia and Caesarian delivery, while their infants tend to experience higher rates of macrosomia, premature labor and hypoglycemic episodes. It is important to increase the rates of pre-pregnancy planning and to optimize glycemic control before pregnancy. In many cases there has been a long interval between diagnosis of DM and pregnancy, so all women with DM should receive counseling at frequent intervals about pregnancy and the importance of planning. Women who plann their pregnancies have improved outcomes, with decreased rate of Caesarean section, better glycemic control and better neonatal Apgar scores (14). Thus, preconception care, intensive regulation of maternal glucose metabolism and fetal surveillance throughout pregnancy are critical.

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