Maternal and Fetal Outcomes in Diabetic Pregnant Women

Muwafag Hyari MD*, Hala Abu-Romman MD**, Kamel Ajlouni MD*

ABSTRACT

Objective: To assess maternal and fetal outcomes in Jordanian women with known Diabetes Mellitus or Gestational Diabetes.

Methods: A retrospective medical record review was conducted on 234 pregnant women who were followed at the National Center for Diabetes Endocrinology and Genetics and Gynecological Department in Jordan University Hospital between 2004 and 2009. A total of 148 subjects had Gestational Diabetes Mellitus and 86 had known diabetes mellitus (Type 1 = 28, Type 2 = 58).

Results: Caesarean section was more frequent in Gestational Diabetes Mellitus subjects than in Diabetes Mellitus group (47.3% vs. 44.2%). The frequency of pre-term delivery tends to be higher in Diabetes Mellitus group than Gestational Diabetes Mellitus group (9.3% vs. 8.1%). Abortion was more common in Diabetes Mellitus group than Gestational Diabetes Mellitus group (11.6% vs.4%). Macrosomia, hypoglycemia, hypocalcaemia, polycythemia and congenital malformation were more common in Diabetes Mellitus group than Gestational Diabetes Mellitus group.

Conclusion: The results showed that Diabetes Mellitus group witnessed more abortion and pre-term delivery compared to Gestational Diabetes Mellitus groups. The caesarean section was higher in Gestational Diabetes Mellitus compared to Diabetes Mellitus group. Gestational Diabetes Mellitus group had better fetal outcome than the Diabetes Mellitus group, indicating that Diabetes Mellitus (type 1, type 2) in pregnancy is a serious condition.

Key words: Diabetes Mellitus (type 1, type 2), Gestational Diabetes, Maternal and fetal outcomes

JRMS September 2013; 20(3): 56-61 / DOI: 10.12816/0001042

Introduction

Gestational Diabetes Mellitus (GDM) is defined as glucose intolerance that first occurs or is identified during pregnancy.⁽¹⁾ The frequency of this condition is rising and occurs in 1 to 14% of all pregnancies, depending on varying characteristics of the population. Although gestational diabetes mellitus is a recognized marker for an increased risk of subsequent diabetes, its clinical significance with respect to various adverse pregnancy outcomes has been uncertain.^(2,4) Women with gestational diabetes who have very elevated fasting blood glucose levels appear to be at an increased risk for fetal macrosomia and perinatal complications if treatment is not provided.⁽⁵⁾ Type 1 diabetes occurs due to a lack of pancreatic islet beta cells caused by autoimmune destruction and resulting in an absence of insulin; while Type 2 diabetes occurs due to insulin resistance and beta cell dysfunction and is likely to be the result of interactions between genetic, environmental and immunological factors including diet, physical

Correspondence should be addressed to Dr. H. Abu Roman, KHMC, E-mail: drhyari@hotmail.com

^{*}National Centre for Diabetes, Endocrinology and Genetics, Jordan University Hospital, Amman-Jordan

^{**}Department of Community Medicine, King Hussein Medical Center, (KHMC), Amman-Jordan

Manuscript received December 2, 2012. Accepted March 14, 2013

activity and obesity.⁽³⁾ Women diagnosed with diabetes prior to pregnancy (pre-existing diabetes) will experience an increase in insulin demands during pregnancy.⁽⁴⁾ Diabetes can have significant impacts on maternal, fetal and neonatal outcomes. The presence of diabetes can increase the risk of stillbirth by five times, and the risk of neonatal death by three times.⁽⁵⁾ Studies have shown perinatal mortality rates are two to three times higher amongst babies of diabetic women as opposed to the general population. Also higher rates of congenital anomalies in babies of women with diabetes have been reported compared to the general population.^(6,7) The recent Hyperglycemia and Adverse Pregnancy Outcome (HAPO) study, however, described a strong continuous between maternal association glucose concentrations and increasing birth weight, cordblood serum C-peptide levels, and other markers of perinatal complications, even at glucose concentrations below those that are usually diagnostic of gestational diabetes mellitus.⁽⁶⁾

Several professional organizations have recommended screening for gestational diabetes mellitus for most pregnant women despite little evidence that the identification and treatment of mild carbohydrate intolerance during pregnancy confer a benefit.^(1,7) The Australian Carbohydrate in Pregnant Intolerance Study Women (ACHOIS), a large, randomized trial of treatment for gestational diabetes mellitus, concluded that treatment reduces serious perinatal complications and may also improve health-related quality of life.⁽⁸⁾ Despite these findings, the 2008 guidelines of the U.S. Preventive Services Task Force again concluded that current evidence is insufficient to assess the balance between benefit and harm with respect to the screening and treatment of gestational diabetes mellitus.⁽⁹⁾ The objective of this study is to assess maternal and fetal outcomes in Jordanian women with known Diabetes Mellitus or Gestational Diabetes.

Methods

A retrospective medical records review was conducted in all diabetic pregnant women who were followed at the National Center for Diabetes Endocrinology & Genetics and Gynecological Department in Jordan University Hospital between 2004 and 2009. The total number was 234 diabetic pregnant women, 148 subjects had Gestational Diabetes Mellitus (GDM) and 86 subjects had known Diabetes Mellitus (DM) (Type 1 = 28, Type 2 = 58). In the Gynecological Department, all pregnant women with high risk factors or fasting blood sugar > 95mg/dl, oral glucose tolerance test (OGTT) was performed (100-g oral glucose tolerance test in pregnant women, if two or more readings of the followings are abnormal FBS > 95 mg/dl, 1-hr >180 mg/dl, 2-hr > 155 mg/dl, 3-hr > 140 mg/dl, OGTT is considered positive) and patients referred to the diabetic clinic to be followed as GDM patient, if its negative, reassessment at 24 to 28 weeks of gestational age was done. In diabetic clinic fasting blood sugar, one hour post prandial blood glucose (PPBG), HbA1c, blood pressure urine for protein, and fundoscopy were checked. The goal of our management was: FBG < 95mg/dl, 1 hr PPBG < 140mg/dl and 2 hrs PPBG < 120mg/dl., HbA1c (normal nonpregnant reference value 4.2–6.2%).

All pregnant diabetic women (type 1, type 2, and GDM) were followed monthly in the first and second trimester and every two weeks in third trimester. Patients were treated with diet or insulin injection (3 or more injection per day) all pregnant diabetic women delivered in Obstetric Department in Jordan University Hospital. Newborn babies were referred to the neonate care unit. The course of the fetal outcome was assessed regarding hyperbilirubinemia, hypoglycemia, hypocalcaemia, polycythemia, macrosomia and congenital malformation. The course of the pregnancy outcome was assessed regarding cesarean section, pre-term delivery, pre-eclampsia and abortions. Chi-Square analyses were performed to test for differences in proportions of categorical variables between both groups, the significance of observed association was tested by the chi-square test. P<0.05 was considered as the cut-off value for significance.

Results

Maternal features of the study group showed that the ages of GDM and DM (Type 1, Type 2) were nearly similar. The GDM in previous pregnancy was frequently more for current GDM women compared to DM. The family history of DM is more in GDM group than DM group.

Table I: Maternal features of the study group

	GDM (n=148	DM Type 1 (n=28) Type 2 (n=58)	P-value	Total (n=234)
Mean Age	34.5±3.2	33.8±5.4	0.8	34.2 ± 5.6
GDM in previous pregnancy	62(41.9%)	30(34.9%)	0.454	92(43.8%)
Family History of DM	118(79.9%)	66(76.7%)	0.704	184(78.6%)
History of Baby wt > 4 kg	52(35.1%)	18(20.9%)	0.105	70(29.9%)
History of Pre-eclampsia	20(13.5%)	10(11.6%)	0.768	30(12.8%)
History of abortion, Still birth,	82(55.4%)	34(39.5%)	0.0978	116(49.6%)
Intrauterine Fetal Death				

Table II: Diabetic Profile of Both Groups

	GDM group n=148	DM group n=86	P-value
F.B.G* Mean mg/dl ±SD	107.7 + 36.0	122.2 + 41.84	0.050
HbA1c	5.5% + 1.80	6.1% + 1.59	0.099

*FBG<95 mg/dl **HbA1c normal value: 4.2-6.2

	GDM	DM	Total
	n = 148	n=86	n = 234
Caesarian section	70 (47.3%)	38 (44.2%)	108(46.1%)
Pre-eclampsia	16 (10.8%)	6 (6.97%)	22(9.4%)
Polyhydroaminos	4 (2.7%)	2(2.3%)	6(2.6%)
Pre-term labour	12(8.1%)	8(9.3%)	20(8.5%)
Abortion, IUFD& SB	6(4%)	10(11.6%)	16(6.8%)

Table IV: Frequency of fetal outcome in GDM and DM groups

	GDM DM		P value	Total	
	n= 148	n=86		n = 234	
Macrosomia (>4000g)	22 (14.9%)	26 (30.2%)	0.005*	48(20.5%)	
Hypoglycemia (<40 mg/dl)	0	2 (2.33%)	0.13	2(0.85%)	
Hyperbilirubinemia (>103µmol/L)	16 (10.81%)	8(9.3%)	0.7	24(10.25%)	
Hypocalcaemia (< 7 mg/dl)	0	4(4.6%)	0.009	4(1.71%)	
Polycythemia (PCV>65%)	4(2.7%)	8(9.3%)	0.03**	12(5.1%)	
Congenital malformation	4(2.7%)	4(4.6%)	0.32	8(3.40%)	
NOT A 40/050/ CT 1 A4 4 00 DD A 00/050/ CT 1 A2 A 40	1100 0 10/0	50/ GT 1 00 15 1			

*OR: 2.48(95% CI=1.24-4.98),RR: 2.03(95% CI=1.23-3.36) **OR:3.69(95% CI=1.00-15.12), RR: 3.44(95% CI=1.07-11.09)

Table V: Frequency of maternal outcome compared with other international studies

	Our study n= 234	Jensen <i>et al</i> * n= 143	Huddle **n= 354	P value	Collective studies ***
Caesarean	108(46.15%)	46(32%)	178(50.3%)	0.0011	32-45%
Section					
Preterm Labour	20(8.5%)	15(10.5%)	-	0.5	14-33%
Pre-eclampsia	20(8.5%)	28(19.6%)	-	0.001	10-40%
Abortions	16(6.8%)	2(1.3%)	23(6.5%)	0.050	3.8-13.5%

*Jensen DM, et al, (Denmark) Diabetic Medicine 2000; 17:281-286

** Huddle KR (South Africa). Diabetes International 1999; 9(3): 53-55

***Up to Date 10. 1. 2002

Table VI: Frequency of fetal outcome of diabetic mothers compared to other international studies

	Our study	Jensen et al*	Hod et al **	P value	Collective studies
	n= 234	n= 143	n=878		***
Macrosomia	48(20.5%)	20(14.0 %)	157(17.9%)	0.27	9-28%
Hyperbilirubinemia	24(10.25%)	15(10.5%)	145(16.5%)	0.01	11-29%
Hypoglycemia	2(0.85%)	34(24%)	45(5.1%)	0.0000	5-25%
Hypocalcaemia	4(1.71%)	-	48(5.5%)	0.01	4%
Polycythemia	12(5.1%)	-	117(13.3%)	0.0005	5-33%
Congenital malformation	8(3.4%)	34(24%)	26(3.0%)	0.00000	1.7-9.4%

**Huddle KR, (South Africa) Diabetes International 1999; 9(3): 53-55

***Up to Date 10.1. 2002

Frequency of abortion was more among GDM women as shown in Table I. The FBG and HbA1c were less in GDM group compared with DM group as presented in Table II. Table III demonstrates that the percentage of caesarian births, pre-eclampsia, and polyhydroaminos were more among GDM groups, pre-term labour and abortion percentage was more in DM groups. Diabetes mellitus group witnessed higher percentage for macrosomia, hypoglycemia, hypocalcaemia, polycythemia and congenital malformation as illustrated in Table IV. Table V and VI show that the results of this study had similar attitudes compared to other research.

Discussion

The results showed that Caesarean Section (CS) were more frequent in GDM group than in DM group (47.3% vs. 44.2%) (Table III). Percent of CS in both groups was 46.15% which is statistically significant P value (P=0.0011) compared with international studies (Table V). The frequency of pre-term delivery tend to be higher in DM group than GDM group (9.3% vs. 8.1%) (Table III), percent of preterm labor in both groups was 8.5% which is not statistically significant when compared to international studies (P value = 0.5). The abortion was more in DM group than GDM group (11.6 % vs.4%) and this due to uncontrolled BS in type 1DM, type 2 DM before planning for pregnancy, percent of abortion in both groups was (6.8%), which is statistically significant (P value=0.050) compared with international studies (Table V). Pre-eclampsia was defined as blood pressure -140/90mmHg and proteinuria of +2 on a urine protein test strip (equal to 1.0 g/l). Pre-eclampsia more frequent in GDM group than in DM group (10.8%)vs 6.97%) (Table III) which is statistically significant when compared to international studies (P value =0.001) (Table V).

Our study confirms that poor metabolic control before and during pregnancy is associated with prenatal mortality, intra uterine fetal death, still birth and congenital malformations. We found an increased risk of macrosomia, despite earlier delivery in women with type 1 diabetes. One fifth of the diabetic women delivered macrosomic infants (birth weight >4000 g). Macrosomia were (20.5% vs. 9-28%) in our study compared with collective studies which is not statistically significant P value (P=0.27) (Table VI). the outcomes were predated by inadequate maternal self-care (home monitoring of blood glucose) and professional care (preconceptional guidance). Women with adverse pregnancy outcome seemed to have slightly more in DM group than GDM group, hypocalcaemia (< 7mg/dl, normal value 8.2-10.2 mg/dl), polycythemia (PCV > 65%, normal value < 55%) were more in DM group than GDM group, which is statistically significant (P value = 0.0005) compared with international studies (Table VI). Hypocalcaemia were 1.71% compared with collective studies 4% which is statistically Significant (P value=.01) (Table VI). Hypoglycemia (<40 mg/dl) were less in our group than international group 0.85% vs5-25% (Table VI), data suggest that glycemic control need closed observation and good Hyperbilirubinemia control. similar to international studies which are statistically significant (Table VI), hypoglycemia, hypocalcaemia polycythemia and congenital malformation were more in DM group than GDM group. When compared to international studies: our results were similar to these studies in regard to caesarean section, pre-term labour and pre-eclampsia. Abortion rates were higher in our group than the European rates but

approaching the rates from South Africa. As for fetal outcomes; results of our study were nearly similar to other international rates in regard to macrosomia and congenital malformations. Hypocalcaemia and polycythemia were lower than other international rates.

Conclusion

Diabetes mellitus in pregnancy is associated with higher rates of adverse maternal and fetal outcomes than GDM, indicating that DM (type 1, type 2) in pregnancy is a serious condition. Strict glycemic control is of paramount importance in reducing these adverse outcomes. Our data suggest that glycemic control, self-care, and education of the patient still need to be improved significantly and that adequate control using daily glucose monitoring in all patients.

References

- American Diabetes Association. Diagnosis and classification of diabetes mellitus. *Diabetes Care* 2006; 29: Suppl 1:S43-S48
- 2. Jovanovic L, Pettitt DJ. Gestational diabetes mellitus. *JAMA* 2001;286:2516-2518
- O'Sullivan JB, Mahan CM. Criteria for the oral glucose tolerance test in pregnancy. *Diabetes* 1964;13:278-285
- 4. Buchanan TA, Kjos SL. Gestational diabetes: risk or myth? *J Clin Endocrinol Metab* 1999;84:1854-1857
- Langer O, Yogev Y, Most O, Yexakis EMJ. Gestational diabetes: the consequences of not treating. *Am J Obstet Gynecol* 2005;192:989-997
- 6. The HAPO Study Cooperative Research Group. Hyperglycemia and adverse pregnancy outcomes. *N Engl J Med* 2008; 358:1991-2002
- 7. American College of Obstetricians and Gynecologists. ACOG Practice Bulletin: clinical management guidelines for obstetriciangynecologists: Number 30, September 2001 (replaces Technical Bulletin Number 200, December 1994): gestational diabetes. *Obstet Gynecol* 2001;98:525-538
- 8. Crowther CA, Hiller JE, Moss JR, *et al.* Robinson JS. Effect of treatment of gestational diabetes mellitus on pregnancy outcomes. *N Engl J Med* 2005;352:2477-2486
- 9. Screening for gestational diabetes mellitus: US. Preventive services task force recommendation statement. *Ann Intern Med* 2008;148:759-765
- 10. **Metzger BE, Coustan DR.** Summary and recommendations of the Fourth International Workshop-Conference on Gestational Diabetes

Mellitus. Diabetes Care 1998;21:Suppl 2:B161-B167

- 11. Lachin JM, Matts JP, Wei LJ. Randomization in clinical trials: conclusions and recommendations. *Control Clin Trials* 1988;9:365-374
- 12. American Diabetes Association. Nutrition recommendations and interventions for diabetes: a position statement of the American Diabetes Association. *Diabetes Care* 2008; 31:Suppl 1:S61-S78
- 13. Moore TR, Piacquadio K. A prospective evaluation of fetal movement screening to reduce the incidence of antepartum fetal death. *Am J Obstet Gynecol* 1989;160:1075-1080
- 14. **Cowett RM.** Hypoglycemia and hyperglycemia in the newborn. In: Polin RA, Fox WW, eds. Fetal and neonatal physiology. Philadelphia: W.B. Saunders, 1992; 406.
- 15. **Bhutani VK, Johnson L, Sivieri E.** Predictive ability of a predischarge hour-specific serum bilirubin for subsequent significant hyperbilirubinemia in healthy term and near-term newborns. *Pediatrics* 1999;103:6-14
- Alexander GR, Kogan MD, Himes JH. 1994-1996 U.S. singleton birth weight percentiles for gestational age by race, Hispanic origin, and gender. *Matern Child Health J* 1999;3:225-231
- Catalano PM, Thomas AJ, Avallone DA, Amini SM. Anthropometric estimation of body composition. Am J Obstet Gynecol 1995;173:1176-1181
- Gabbe SG, Mestman JG, Freeman RK, et al. Management and outcome of Class A diabetes mellitus. Am J Obstet Gynecol 1977;127:465-469
- Langer O, Rodriguez DA, Xenakis EM, et al. Intensified versus conventional management of gestational diabetes. Am J Obstet Gynecol 1994;170:1036-1046
- Persson B, Hanson U. Neonatal morbidities in gestational diabetes mellitus. *Diabetes Care* 1998;21:Suppl 2: B79-B84
- 21. Hod M, Merlob P, Friedman S, Schoenfeld A, Ovadia J. Gestational diabetes mellitus: a survey of perinatal complications in the 1980s. *Diabetes* 1991; 40: Suppl 2:74-78
- 22. Bancroft K, Tuffnell DJ, Mason GC, *et al.* A randomised controlled pilot study of management of impaired gestational glucose tolerance. *BJOG* 2000;107:959-963
- 23. Garner P, Okun N, Keely E, et al. A randomized controlled trial of stick glycemic control and tertiary level obstetric care versus routine obstetric care in the management of gestational diabetes: a pilot study. Am J Obstet Gynecol 1997;177:190-195
- 24. Naylor CD, Sermer M, Chen E, Sykora K. Cesarean delivery in relation to birth weight and gestational glucose tolerance: pathophysiology or practice style? *JAMA* 1996;275:1165-1170

- 25. Lan KKG, DeMets DL. Discrete sequential boundaries for clinical trials. Biometrika 1983;70:659-663
- 26. McFarland LV, Raskin M, Daling JR, Benedetti TJ. Erb/Duchenne's palsy: a consequence of fetal macrosomia and method of delivery. *Obstet Gynecol* 1986;68:784-788
- 27. Silverman BL, Metzger BE, Cho NH, Loeb CA. Impaired glucose tolerance in adolescent offspring of diabetic mothers: relationship to fetal hyperinsulinism. *Diabetes Care* 1995; 18:611-617.
- 28. Hillier TA, Pedula KL, Schmidt MM, *et al.* Childhood obesity and metabolic imprinting: the ongoing effects of maternal hyperglycemia. *Diabetes Care* 2007;30:2287-2292
- 29. Brody SC, Harris R, Lohr K. Screening for

gestational diabetes: a summary of the evidence for the U.S. Preventive Services Task Force. *Obstet Gynecol* 2003; 101:380-392

- 30. Cousins L. Obstetric complications in diabetic pregnancies. In: Reece EA, Coustan DR, Gabbe SG, eds. Diabetes in women: adolescence, pregnancy, and menopause. 3rd ed. Philadelphia: Lippincott Williams & Wilkins, 2004:351-70.
- 31. Wolf M, Sandler L, Munoz K, et al. First trimester insulin resistance and subsequent preeclampsia: a prospective study. J Clin Endocrinol Metab 2002;87:1563-1568
- 32. Holt RIG. The Hyperglycemia and Adverse Pregnancy Outcomes Trial: answers but still more questions about the management of gestational diabetes. *Diabet Med* 2008; 25:1013-1014