

NEONATAL COMPLICATIONS IN INFANTS BORN TO DIABETIC MOTHERS-A STUDY ON IRAQI

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ABSTRACT

Background: Diabetes Mellitus during pregnancy has important consequences on both mother and infant, it consider one of the leading causes of maternal and fetal morbidity and mortality. It has been confirmed that adverse maternal and neonatal outcomes highly related to poor glycemic control and therefore confirmed on the importance of antenatal care and effective treatment. **Objectives:** To evaluate obstetric complications and infant outcomes in women with diabetes mellitus in Iraq. **Materials and Methods:** A total of (60) Iraqi mothers suffering from diabetes mellitus; either gestational or pre-gestational diabetes mellitus; with their living neonates (60) were included in this

study during their admission to the maternity wards in several hospitals in Baghdad, Iraq. We collect the data regarding maternal and neonatal complications and correlate them with glucose level and birth weight. **Results:** 60 diabetic mothers included in the study with FBG 200.88 ± 83.16 , AFI was 22.02 ± 4.09 , 27% of cases had polyhydramnios, 30% were preterm and 83% delivered by cesarean section. 42% of neonates were macrosomic and 58% of cases were hypoglycemic with FBG 39.35 ± 12.43 , serum bilirubin concentration was 9.54 ± 3.80 . Tachypnea reported in 40% of cases while prematurity reported in 30% of cases. Neonatal hypoglycemia is significantly correlated with maternal hyperglycemia as well as neonatal macrosomia and tachypnea is significantly correlated with neonatal hypoglycemia ($p < 0.05$) while correlation with serum bilirubin concentration was non-significant. A significant differences ($p < 0.05$) between macrosomic and non- macrosomic neonates in body weight, hypoglycemia and tachypnea while for jaundice, polyhydramnios and cesarean delivery were non-significant. **Conclusion:** Pregnant women with diabetes mellitus have increased

incidence of obstetric and neonatal complications, which found to be related to poor glycemic control.

KEYWORDS: Diabetic Mother, Neonatal complications, Macrosomia, Iraq.

INTRODUCTION

Pregnancy complicated with diabetes mellitus; either gestational or pre-gestational; carries significant risks for both mother and infants since outcomes of such pregnancy remain substantially worse than that of general gestational population.^[1-3] As it reported in the summary and recommendations of the fourth and fifth International Workshop-Conference on Gestational Diabetes Mellitus, uncontrolled hyperglycemia on the pregnant will increase the risk of wide range of complications like preeclampsia, cesarean delivery and future type 2 diabetes. In the fetus or neonate, the disorder is associated with higher rates of perinatal mortality, macrosomia, birth trauma, hyperbilirubinemia, and neonatal hypoglycemia.^[4-6]

Recent Hyperglycemia and Adverse Pregnancy Outcome (HAPO) study described a strong continuous association between maternal glucose concentrations and increasing neonatal abnormalities.^[7] Many studies confirmed on the importance of treatment and perinatal care of diabetic mothers to ensure optimal control for their glucose level in order to lower serious perinatal outcomes among infants.^[8-11]

In Iraq, diabetes mellitus spread widely in the recent days, so we need to educate the community; pregnant women especially; for its complications due to high rates of neonatal abnormalities have been reported.^[12] For this we designed a study to estimate the association between diabetes mellitus and adverse pregnancy and neonatal outcomes in Iraq.

MATERIALS AND METHODS

A total of (60) Iraqi mothers suffering from diabetes mellitus; either gestational diabetes mellitus or pre-gestational diabetes mellitus; with their living neonates (60) were included in this study during their admission to the maternity wards in several hospitals in Baghdad, Iraq for the period from November 2015 to March 2016. Maternal characteristics extracted from the database include age, parity (primipara or multipara), type of diabetes (gestational or pregestational), fasting blood glucose (FBG) measured just before delivery, type of delivery (cesarean delivery or normal vaginal delivery), amniotic fluid index (AFI) and gestational age

(pre-term or full-term). While neonatal characteristics (recoded within first 24-48 hours) were birth weight, fasting blood glucose, serum bilirubin concentration and respiratory rate.

Results were expressed as means with standard deviations (SD) or as percentages using SPSS and Microsoft Excel for the statistical analyses. One way analysis of variance (ANOVA) and chi-square were used to compare the complications of macrosomic with non-macrosomic neonates. Pearson correlation was done to identify the link between maternal/ neonatal FBG with neonatal outcomes. P-value of <0.05 was considered significant.

RESULTS

Characteristics of mothers and neonates are shown in table 1. From 60 diabetic mothers included in the study 15 (25%) of cases had pregestational diabetes (PGDM) and 45 (75%) were gestational diabetes (GDM). Large percent (83%) of diabetic mothers were delivered by cesarean section while only (17%) delivered by normal vaginal delivery. Mean FBG just before delivery was (200.88 ± 83.16), AFI was (22.02 ± 4.09) while (27%) of cases had polyhydramnios (AFI>25cm).

Regarding neonates, 25 (42%) of cases were macrosomic (body weight >4000g) and 35 (58%) were non-macrosomic. (58%) of cases were hypoglycemic with FBG (39.35 ± 12.43), mean serum bilirubin concentration was (9.54 ± 3.80). Tachypnea (respiratory rate >60 breath/min) reported in (40%) of cases while prematurity (Gestational age (GA) <37 wk) reported in (30%) of cases.

Table 2 shown that neonatal hypoglycemia is significantly correlated with maternal hyperglycemia ($p<0.05$) as well as neonatal macrosomia and tachypnea is significantly correlated with neonatal hypoglycemia while correlation with serum bilirubin concentration was non-significant.

Comparison between macrosomic and non- macrosomic neonates in the observed complications, as shown in table 3, resulted in significant differences ($p<0.05$) in body weight, hypoglycemia and tachypnea while for jaundice, polyhydramnios and cesarean delivery were non-significant.

Table 1: Demographic and clinical characteristics of mothers and neonates

Characteristics	No. (%) or mean \pm SD
No. of mothers	60
Maternal age (y)	31.87 \pm 6.86
Maternal FBG (mg/dl)	200.88 \pm 83.16
AFI (cm)	22.02 \pm 4.09
Polyhydramnios ^a	16 (27%)
Primipara	6 (10%)
Multipara	54 (90%)
Cesarean Delivery	50 (83%)
Normal Vaginal Delivery	10 (17%)
Pregestational DM	15 (25%)
Gestational DM	45 (75%)
No. of Neonates	60
Neonatal FBG (mg/dl)	39.35 \pm 12.43
Hypoglycemia ^b	35 (58%)
Birth weight (g)	3283 \pm 1.11
Macrosomia ^c	25 (42%)
Mean Respiratory Rate	53.10 \pm 15.86
Tachypnea ^d	24 (40%)
Neonatal serum bilirubin conc. (mg/dl)	9.54 \pm 3.80
GA <37 wk	18 (30%)
GA \geq 37 wk	42 (70%)

^a Polyhydramnios; AFI >25cm.^[13]

^b Hypoglycemia; FBG \leq 40mg/dl (both in the term and premature infants).^[14]

^c Macrosomia; body weight \geq 4000g.^[15]

^d Tachypnea; respiratory rate > 60/min.^[16]

Table 2: Correlation between maternal / neonatal FBG with neonatal complications

Variables	Maternal FBG	Neonatal FBG
	Pearson Correlation (p-value)	Pearson Correlation (p-value)
Hypoglycemia	-0.313* (0.015)	-
Macrosomia	0.151 (0.248)	-0.244* (0.036)
Tachypnea	0.077 (0.558)	-0.260* (0.025)
Jaundice	0.143 (0.275)	-0.063 (0.595)

*Correlation is significant at the 0.05 level.

Table 3: Complications of macrosomic compared with non-macrosomic neonates

Parameters	Macrosomic neonates (n=25)	Non- Macrosomic neonates (n=35)
Mean Weight (g)	4424 \pm 0.35**	2444 \pm 0.59
Hypoglycemia	35.72 \pm 8.08**	44.08 \pm 11.93
Tachypnea	59.29 \pm 16.6*	48.94 \pm 14.31
Jaundice	9.68 \pm 3.68	8.74 \pm 3.81
Polyhydramnios	22.2 \pm 3.18	21.89 \pm 4.68
Cesarean Delivery	23 (92%)	27 (78%)

* Significant difference between the groups at the 0.05 level.

** Significant difference between the groups at the 0.01 level.

DISCUSSION

Neonatal hypoglycemia consider as a serious problem and maintaining blood glucose level is very important for neonates as it is confirmed that the persistent early and prolonged hypoglycemia results in brain damage and mental retardation.^[17] The mechanism of hypoglycemia in neonates of diabetic mothers is neonatal hyperinsulinism. These babies are generally large for gestational age, because of the anabolisant effect of insulin.^[18] Our study, confirmed by Edwin et al. study demonstrated a direct correlation between neonatal and maternal glucose level that is mean whenever maternal glucose increase neonatal glucose will decrease, we also reported elevated maternal glucose before delivery as some studies indicate that normoglycemia should be encouraged on the day of delivery as maternal hyperglycemia at this stage increases the incidence of neonatal hypoglycemia.^[19,20]

Macrosomia or excessive birth weight have reviewed by perinatologist as obstetric problem that could increase risks of labor and newborn complications.^[21,22] Previous studies have shown association of fetal macrosomia with many adverse maternal and neonatal health outcomes since it can result in birth trauma and damage to the mother and infant.^[23-25] Our findings are similar to other studies which reported that neonatal hypoglycemia occur significantly more often in macrosomic than in non-macrosomic infants^[26,27], in addition women having macrosomic infants had a higher frequency of cesarean deliveries.^[28,29] Further we found that neonatal macrosomia is in part related to maternal glucose level and as it is directly correlated to neonatal hypoglycemia which is in agreement with most authors^[30,31], others stated that the severity of macrosomia increase when mother's diabetes is poorly controlled.^[32]

Transient tachypnea and respiratory difficulties have been reported in the newborns are obviously not related to prematurity; as non-significant cases of tachypneic infants were preterm; Jeanna et al. demonstrated that timing of fetal pulmonary maturation is linked to the level of maternal glucose and adequate glucose control may lower the risk of fetal pulmonary immaturity^[33], as we found in our study that respiratory rate is correlated with neonatal hypoglycemia. But a recent study by Fung et al. demonstrated an independent effect of diabetes on the respiratory complications although they reported a high incidence of transient tachypnea of these newborn.^[34]

Bilirubin level in present study recorded high rates within the first 24 hours of infant's life which confirms that jaundice very commonly affects infants of diabetic mothers^[35], but we did not found a significant correlation with glucose level or neonatal weight. Some authors demonstrated that increased bilirubin production related to poor maternal diabetic control with resultant macrosomic infant in association with elevated maternal levels of glycosylated hemoglobin and fetal hypoxia.^[36]

Polyhydramnios, a common maternal complication in diabetic pregnancy, it has been proved that amniotic fluid volume increase as a result of increased amniotic fluid glucose concentration.^[37] In the present study although a small percent of cases had polyhydramnios with non-significant correlation for amniotic fluid volume and glucose level or birth weight, Joy et al. study reported that polyhydramnios may be related to birth weight at the highest centile and increase with poor glycemetic control that could be partly explain our result.^[38]

CONCLUSION

Pregnant woman with diabetes mellitus will experience a multiple perinatal as well as neonatal complications and the severity will increase with poor glycemetic control. Mother may expose to preterm delivery and/or elective cesarean delivery. Infant may experience birth injuries, respiratory distress, hypoglycemia, hypocalcemia, hyperbilirubinemia and macrosomia. Uncontrolled diabetes has profound effects on embryogenesis, organogenesis, and fetal and neonatal growth, and evidence increasingly indicates that some of these effects are lifelong. Preconception control of diabetes and monitoring throughout pregnancy are important in reducing the impact of diabetes on the fetus and newborn.

REFERENCES

1. Chia YT1, Chua S, Thai AC, Yeoh SC, Kek LP, Selamat N, Ratnam SS. Obstetric outcome of pregestational diabetic pregnancies. Singapore Med J, 1995; 36(5): 498-500.
2. Langer O, Yogev Y, Most O, Xenakis EM. Gestational diabetes: the consequences of not treating. AM J Obstet Gynecol, 2005; 192: 989-97.
3. Reece EA. The fetal and maternal consequences of gestational diabetes mellitus. The Journal of Maternal-Fetal & Neonatal Medicine, 2010; 23(3): 199-203.
4. Naylor CD, Sermer M, Chen E, Sykora K. Cesarean Delivery in Relation to Birth Weight and Gestational Glucose Tolerance. JAMA, 1996; 275(15): 1165-1170.

5. Metzger BE, Coustan DR. Summary and recommendations of the Fourth International Workshop-Conference on Gestational Diabetes Mellitus. The Organizing Committee. *Dia. Care*, 1998 Suppl; 2: B1617.
6. Metzger BE, Buchanan TA, Coustan DR, Leiva AD, Dunger DB, Hadden DR, et al. Summary and recommendations of the Fifth International Workshop-Conference on Gestational Diabetes Mellitus. *Diabetes Care*, 2007; Suppl 2: S25160.
7. The HAPO Study Cooperative Research Group. Hyperglycemia and adverse pregnancy outcomes. *N Engl J Med*, 2008; 358: 1991–2002.
8. Walkinshaw SA. Pregnancy in women with pre-existing diabetes: management issues. *Semin Fetal Neonatal Med*, 2005; 10: 307–15.
9. Crowther C, Hiller J, Moss J, McPhee A, Jeffries W, Robinson J. Effect of treatment of gestational diabetes mellitus on pregnancy outcomes. *N Engl J Med*, 2005; 352: 2477- 2486.
10. Victor HG, Niki BI, Debbie JR, et al. The Impact of Glycemic Control on Neonatal Outcome in Singleton Pregnancies Complicated by Gestational Diabetes. *Dia Care*, 2007; 30(3): 467–470.
11. Numan NH. Infants of diabetic mothers: an Iraqi Teaching Hospital experience. *J Fac Med Baghdad*, 2011; 53(3).
12. Kalhan S, Peter-Wohl S. Hypoglycemia: Per GO, Dorte MJ, Peter D, Steen R, Ulrik SK. Maternal and neonatal outcomes in pregnancies complicated by gestational diabetes. *The Journal of Maternal-Fetal & Neonatal Medicine*, 2010; 28(14).
13. Pri-Paz S1, Khalek N, Fuchs KM, Simpson LL. Maximal amniotic fluid index as a prognostic factor in pregnancies complicated by polyhydramnios. *Ultrasound Obstet Gynecol*, 2012; 39(6): 648-53.
14. Dorina RB, Valentin B, Doina T. Neonatal Hypoglycemia. The Incidence of the Risk Factors in Salvator Vuia Obstetrics-Gynecology Hospital, Arad. *Tmj*, 2009; 59(1): 77-80.
15. Behrman RE, Kliegman R, Jenson HIB. *Nelson textbook of pediatrics*. 17th ed. Philadelphia, Pa: Saunders, 2004; 556.
16. Carlo WA, Ambalavanan N. Respiratory tract disorders. In: Kliegman RM, Stanton BF, St Geme JW, Schor NF (eds). *Nelson Textbook of Pediatrics*. 20th ed. Philadelphia, PA: Elsevier, 2016; chap. 101.
17. Kalhan S, Peter-Wohl S. Hypoglycemia: What is it for the neonate? *Am J Prenatal*, 2000; 17: 11-4.

18. Gomella TL, Fabien GE, Karin EZ. Neonatology: management, procedures, on-call problems, diseases and drugs. Lange Medical Books, 2004; 262-7.
19. Norman GS, Susan MS, John MM. Neonatal Morbidity among Infants of Diabetic Mothers. *Diabetes Care*, 1978; 1(6): 340-350.
20. Edwin D, Sandeep G. Glucose levels in newborns with special reference to hypoglycemia: A study from rural India. *J Clin Neonatol*, 2014; 3(1): 35-38.
21. Hod MM, PFriedman SSchoenfeld AOvadia J. Gestational diabetes mellitus: a survey of perinatal complications in the 1980s. *Diabetes*, 1991; 40: 74-78.
22. Kjell H, Jouko P, Per B. Suspected big baby: a difficult clinical problem in obstetrics. *AOGS*, 2002; 81(3): 185-194.
23. Sheree LB, Greg RA, Hamisu MS, Mary AP. Macrosomic births in the United States: Determinants, outcomes and proposed grades of risk. *Am J Obstet Gynecol*, 2003; 188(5): 1372–1378.
24. Stotlanda NE, Caugheya AB, Breed EM, Escobar GJ. Risk factors and obstetric complications associated with macrosomia. *Inter J Gynecol Obstet*, 2004; 87(3): 220–226.
25. Astrid RB, Kaja IH, Anne KD, Lorentz MI. Macrosomia: mode of delivery and pregnancy outcome. *AOGS*, 2010; 89(5): 664-669.
26. John LK, John PC, Donna MY, Ashraf T, Suzanne BR, Ilene S, Michael FE, Shailini S, Raymond KN. Diabetic pregnancy and perinatal morbidity. *Am J Obstet Gynecol*, 1978; 131(5): 560-580.
27. Inge ME, Harold WV, Gerard HAV. Risk of complications of pregnancy in women with type 1 diabetes: nationwide prospective study in the Netherlands. *BMJ*, 2004; 328(7445): 915.
28. Casey BM, Lucas MJ, Mcintire DD, Leveno KJ. Pregnancy outcomes in women with gestational diabetes compared with the general obstetric population. *Obstet Gynecol*, 1997; 90(6): 869-73.
29. Hong JU, Yogesh C, Tim D, Peter O. Fetal macrosomia and pregnancy outcomes. *ANZJOG*, 2009; 49(5): 504-509.
30. Michael TG, Harvey MR, Brian AL, Avroy AF, Irwin RM. Modern approach to management of pregnant diabetics: a two-year analysis of perinatal outcomes. *Am J Obstet Gynecol*, 1977; 128(6): 606- 616.
31. Neiger R. Fetal macrosomia in the diabetic patient. *Clin Obstet Gynecol*, 1992; 35: 138- 150.

32. William WH. Care of the Infant of the Diabetic Mother. *Diabetes and Pregnancy*, 2012; 12(1): 4-15.
33. Jeanna MP, Oded L. Does maternal diabetes delay fetal pulmonary maturity? *Am J Obstet Gynecol*, 1993; 168(3) 1: 783-786.
34. Fung GPG, Chana LM, Hoa YC, Tob WK, Chana HB, Laoc TT. Does gestational diabetes mellitus affect respiratory outcome in late-preterm infants? *Early Human Development*, 2014; 90(9): 527–530.
35. Maisels MJ. Neonatal Jaundice. *Pediatrics in Review. Pediatr. Rev.* 2006; 27: 443-454.
36. Keith JP, Stephen AL, Steven JG. Hyperbilirubinemia in Infants of Diabetic Mothers. *Pediatrics*, 1980; 66(3): 417-419.
37. Jodi SD, Lawrence N, Donald DM, PhD, Kenneth JL, Correlation between amniotic fluid glucose concentration and amniotic fluid volume in pregnancy complicated by diabetes. *Am J Obstet Gynecol*, 2000; 182(4): 901–904.
38. Joy YV, Sarah HP, Alessandro G, Catherine YS. Amniotic fluid index and birth weight: Is there a relationship in diabetics with poor glycemic control? *Am J Obstet Gynecol*, 2006; 195(3): 848–850.