Neonatal Short-Term Outcomes of Gestational Diabetes Mellitus in Saudi Mothers: A Retrospective Cohort Study

R. Al-Khalifah, A. Al-Subaihin, T. Al-Kharfi, S. Al-Alaiyan, Khalid M. AlFaleh

Department of Pediatrics, College of Medicine, King Saud University, Neonatology Section, King Faisal Specialist Hospital and Research Centre, Riyadh, Saudi Arabia

ABSTRACT

Background: Gestational diabetes mellitus (GDM) affects up to 10% of all pregnancies and results in significant maternal and neonatal morbidities. Objectives: Our main objective was to investigate retrospectively the rate of neonatal intensive care unit (NICU) admissions and significant neonatal complications in pregnant mothers with gestational diabetes. Materials and Methods: A retrospective cohort study was conducted. The medical records of King Khalid University Hospital (KKUH) were reviewed from January till December 2007. All pregnant women with GDM along with their offsprings were included and matched with healthy pregnant women. The primary outcome was the rate of NICU admission, hypoglycemia, birth weight and length of hospital stay. Results: A total of 766 mothers (419 GDM mothers and 347 controls) with their term babies were included. Infants born to GDM mothers had significantly higher risk of NICU admissions [OR 2.7 (95% CI 1.5, 4.9), P value 0.0004], longer hospital stay and higher rates of hypoglycemia. Newborns of GDM mothers had higher rates of perinatal distress and macrosomia; however, the difference did not reach statistical significance. Conclusion: GDM remains a significant morbidity to newborns resulting in increased intensive care admission, prolongation of hospital stay and higher rates of neonatal hypoglycemia. More efforts to assure early recognition and strict sugar control during pregnancy are still needed.

Key words:
Gestational diabetes mellitus, hypoglycemia, large for gestational age, macrosomia, neonatal intensive care unit

INTRODUCTION

Gestational diabetes mellitus (GDM) is defined as glucose intolerance of variable degree with onset or first recognition during pregnancy. Three to ten percent of all pregnancies are complicated with abnormal glycemic control, GDM accounts for 80% of them. In Saudi Arabia, abnormal glycemic control affects 8.9-12.5% of all pregnancies based on the region and the diagnostic criteria used. Even with a well-developed antenatal care services, GDM carries a significant burden on individuals as well as health care services through its multiple complications affecting both the mother and her baby. These complications include obstetrical morbidities, perinatal mortality, increased rates of neonatal intensive care unit (NICU) admissions due to hypoglycemia, macrosomia, respiratory distress syndrome (RDS), jaundice, polycythemia, electrolyte imbalance and birth trauma. Other postnatal complications affecting newborns of diabetic mothers include transient myocardial hypertrophy, impaired left ventricular relaxation, congenital malformations with cardiovascular defects ranking on the top of the list followed by musculoskeletal and central nervous system (CNS) anomalies. Other long-term complications include a wide range of neuropsychological dysfunctions in the form of lower total developmental score, attention deficit disorder, and hyperactivity.

The main objective of our study was to investigate, retrospectively, the rate of NICU admissions and the significant neonatal complications in pregnant women with gestational diabetes.

MATERIALS AND METHODS

A retrospective case-control study was conducted at King Khalid University Hospital (KKUH) -tertiary care center- during the period of January till December 2007. Charts were identified through medical records. All pregnant women diagnosed with GDM along with their term infants were included. A number of randomly selected healthy pregnant women with their newly born infants were also included.

Access this article online

Quick Response Code: www.jcnonweb.com

DOI: 10.4103/2249-4847.92241
identified. They were selected based on timing of delivery i.e., each healthy mother who gave birth after GDM mother in a 1:1 fashion. Cases who were excluded from the cohort included women with chronic DM, out born infants, women delivering preterm (<37 weeks GA) and those who were not followed up at KKUH during their pregnancy were excluded. The Ethics Board at KKUH approved this study.

The diagnosis of GDM was made by the obstetricians based on abnormal fasting blood sugar and oral glucose tolerance test (OGTT) diagnosed after 24 weeks of pregnancy. Mothers were followed up regularly and blood sugar control was achieved with either diet or insulin. After delivery, infants were admitted to the newborn nursery unless they required intensive care. Glucose monitoring was performed for all infants of GDM mother and high risk infants-like infants with intrauterine growth restriction (IUGR). The monitoring was done by hemoglucocheck that started within the first 3 hours of birth at the newborn nursery, then before each feed until the blood glucose is stable for two subsequent readings. The same protocol was followed if the newborn required admission to the NICU. Hypoglycemia was defined as glucose level below 2.6 mmol/L measured by hemoglucocheck. A single reading of glucose level below 2.6 mmol/L was treated with feeding if possible otherwise the baby was admitted and IV dextrose was initiated with close monitoring.

Maternal data included; age, number of deliveries and abortions, mode of delivery, fasting blood glucose level, 2 hours OGTT level and other maternal comorbidities such as hypertension, hyperthyroidism, hypothyroidism and asthma. Neonatal data included; sex, birth weight, length, head circumference, Apgar score at 1, 5, 10 minutes, details of NICU admission if the baby was admitted, length of NICU stay, neonatal complications with details of hypoglycemia, jaundice, respiratory distress, CNS, cardiac anomalies, metabolic abnormalities and birth trauma.

### Statistical analysis

Data were entered electronically using Social Sciences statistical software package. Data were presented as mean (SD) for centrally distributed data and median (interquartile range) for skewed data. Continuous variables were assessed between the two groups using Student t-test. Binary data were analyzed utilizing χ² or fisher exact test as appropriate. We chose a convenient sample of all GDM mothers and their matched control during the study period.

### RESULTS

A total of 1532 chart were retrieved from the medical records, 419 GDM mothers and 347 controls with their term babies. Maternal demographics and parity for both groups are shown in Table 1. The mean age for the mothers was 33.5 and 28.9 years for GDM and normal group, respectively. Women with gestational diabetes were noticed to have a significant higher risk of abortions with lower parity order as compared to normal women; this observation could indicate the presence of genetic or environmental association that

| Table 1: Maternal characteristics |
|----------------------------------|
| Outcome variable                | GDM (N=419) | Normal (N=347) | P value | OR (95% CI) |
| Maternal age years – mean±SD     | 33.5±5.7    | 28.9±6.1       | <0.001  | (-5.4,-3.8)* |
| Fasting blood sugar (mmol/L)- mean±SD | 5.1±0.8 | 4.7±0.55       | <0.001  | (-0.6,-0.25)* |
| Oral glucose tolerance test (mmol/L)- mean±SD | 8.6±2.3 | 6.2±1.2       | <0.001  | (-2.9,-1.8)* |
| Parity-delivery ≥20 weeks        |             |                |         |             |
| Median                          | 2           | 4              | <0.001  | –           |
| Interquartile range              | 2-6         | 0-4            |         |             |
| Abortions- no. (%)              |             |                |         |             |
| 0                               | 211 (50.3)  | 239 (68.9)     | –       | –           |
| 1                               | 112 (26.8)  | 63 (18.1)      | <0.001  | 2.0 (1.4,2.9) |
| 2                               | 58 (13.8)   | 30 (8.6)       | 0.002   | 2.2 (1.3,3.6) |
| ≥3                              | 38 (9.1)    | 15 (4.3)       | 0.001   | 2.9 (1.5,5.6) |
| Obstetrical outcomes-no. (%)    |             |                |         |             |
| Cesarean                        | 99 (23.8)   | 66 (19.0)      | 0.12    | 1.3 (0.93,1.9) |
| Assisted                        | 12 (2.9)    | 9 (2.6)        | 0.87    | 1.2 (0.46,3.1) |
| Maternal medical comorbidities-no. (%) |         |                |         |             |
| Asthma                          | 30 (7.2)    | 26 (7.5)       | 0.99    | 0.96 (0.54,1.7) |
| Hypertension                    | 21 (5.0)    | 7 (2.0)        | 0.04    | 2.6 (1.02,6.7) |
| Hyperthyroidism                 | 4 (0.95)    | 3 (0.9)        | 0.60    | 1.1 (0.21,2.5) |
| Hypothyroidism                  | 23 (5.5)    | 16 (4.6)       | 0.69    | 1.2 (0.6,2.4) |
| Others                          | 30 (7.2)    | 22 (6.3)       | 0.75    | 1.1 (0.6, 2.1) |

*Mean difference 95% CI; GDM – Gestational diabetes mellitus; OR – Odds ratio; CI – Confidence interval
needs further study. As expected the mean OGTT and the mean fasting glucose were significantly higher in GDM group (fasting blood glucose 5.1±0.8 versus 4.7±0.55 mmol/l, \(P<0.001\)) and (2 hours OGTT 8.6±2.3 versus 6.2±1.2 mmol/l, \(P<0.001\)). Both groups had similar delivery routes. GDM mothers were more likely to have higher blood pressure compared to normal mothers; we believe this is mainly due to the observational nature of our study. Other medical comorbidities were equal between both groups.

The baseline demographics of the newborns are shown in Table 2. Both groups had equal distribution of gender and number of singletons. There was no significant statistical difference in the means of birth weight, length and head circumference. The mean birth weight was 3.3 kg and 3.19 kg for newborns of GDM and normal mothers, respectively. The number of large for gestational age newborns was doubled in the GDM group as compared to normal group; however this did not reach significant statistical difference mostly due to small sample size. The number of small for gestational age newborns was equal between the two groups.

Neonatal outcomes are shown in Table 3. Newborn infants delivered in both groups had equal Apgar score. The number of infants needed NICU admission was significantly higher for infants born to GDM mothers compared to infants born to normal mothers [OR 2.7 (95% CI 1.5, 4.9), \(P<0.001\)]. Of those admitted to NICU, infants born to GDM mothers had longer hospital stay compared to newborn infants born to normal mothers (6 days versus 3 days, \(P=0.03\)).

### Table 2: Neonatal baseline characteristics

| Outcome variable | GDM (\(N=419\)) | Normal (\(N=347\)) | \(P\) value | OR (95% CI) |
|------------------|-----------------|---------------------|-------------|-------------|
| Male sex – no. (%) | 211 (51.2) | 187 (54.5) | 0.40 | 0.87 (0.65, 1.2) |
| Singleton – no. (%) | 408 (99) | 333 (97.9) | 1 | - |
| Birth weight – no. (%) | 13 (3.2) | 12 (3.6) | 0.98 | 0.91 (0.38, 2.2) |
| Small for gestational age \(^a\) | 20 (5.0) | 9 (2.7) | 0.17 | 1.9 (0.8, 4.5) |
| Birth length – no. (%) | 112 (27.3) | 99 (28.4) | 0.72 | 0.94 (0.68, 1.30) |
| Large for gestational age \(^b\) | 15 (3.6) | 7 (2) | 0.21 | 1.78 (0.71, 4.45) |
| Birth head circumference – no. (%) | 105 (25.5) | 95 (27.7) | 0.62 | 0.91 (0.65, 1.3) |
| Small for gestational age \(^c\) | 13 (3.2) | 7 (2.0) | 0.50 | 1.53 (0.56, 4.3) |
| Large for gestational age \(^d\) | 51 (12) | 15 (4.3) | <0.001 | 3.74 (1.86–7.50) |

\(^a\) Birth weight below the 10\(^{th}\) percentile; \(^b\) Birth weight above the 90\(^{th}\) percentile; \(^c\) Birth length below the 10\(^{th}\) percentile; \(^d\) Birth length above the 90\(^{th}\) percentile; \(^e\) Birth head circumference below the 10\(^{th}\) percentile; \(^f\) Birth head circumference above the 90\(^{th}\) percentile; GDM – Gestational diabetes mellitus; OR – Odds ratio; CI – Confidence interval

| Outcome variable | GDM (\(N=419\)) | Normal (\(N=347\)) | \(P\) value | OR (95% CI) |
|------------------|-----------------|---------------------|-------------|-------------|
| Admission to NICU – no. (%) | 41 (10) | 20 (5.8) | <0.001 | 2.7 (1.5, 4.9) |
| Length of NICU stay (days) | | | | |
| Median | 6 | 3 | 0.03 | - |
| Interquartile range | 4-9 | 2-6 | - | - |
| Apgar score – mean±SD | | | | |
| 1 min | 7.7±0.8 | 7.7±0.8 | 0.64 | –0.47 (–0.15, 0.09) |
| 5 min | 9.1±4.4 | 8.9±0.6 | 0.34 | –0.95 (–0.7, 0.24) |
| Causes of NICU admission– no. (no./total NICU admission no. %) | | | | |
| Hypoglycemia | 15 (36) | 4 (20) | 0.04 | 3.19 (1.05, 9.71) |
| Perinatal distress | 8 (19) | 2 (10) | 0.19 | 3.4 (0.66, 20.9) |
| Respiratory distress syndrome \(^g\) | 4 (9) | 6 (30) | 0.54 | 0.55 (0.13, 2.2) |
| Others | 14 (34) | 8 (40) | 0.12 | 1.9 (0.85, 4.5) |
| Neonatal complications – no. (%) | | | | |
| Hypoglycemia \(^c\) | 51 (12) | 15 (4.3) | <0.001 | 3.74 (1.86–7.50) |
| Jaundice \(^a\) | 97 (23) | 80 (23) | 0.55 | 1.02 (0.95–1.10) |
| Respiratory complications \(^h\) | 11 (2.6) | 10 (2.8) | 0.45 | 0.40 (0.38–4.33) |
| CNS complications \(^i\) | 2 (0.5) | 2 (0.5) | 0.17 | 0.10 (0.004–2.70) |
| CVS anomalies \(^i\) | 10 (2.3) | 5 (1.4) | 0.82 | 1.16 (0.30–4.46) |

\(^a\) Respiratory distress syndrome: the presence of respiratory distress signs till 4 hours of age with the need for supplemental oxygen for more than 4 hours; \(^b\) Hypoglycemia not requiring NICU care; \(^c\) Jaundice requiring phototherapy; \(^d\) Respiratory complications: meconium aspiration, transient tachypnea of the newborn, etc; \(^e\) CNS complications: seizures, hypotonia; \(^f\) mean difference 95% CI; GDM – Gestational diabetes mellitus; NICU – Neonatal intensive care unit; CNS – Central nervous system; CVS – Cardiovascular system; OR – Odds ratio; CI – Confidence interval
Hypoglycemia was the main cause of NICU admission for newborns of GDM mothers. These babies were more likely admitted to NICU for IV dextrose than newborns of normal mothers [OR 3.19 (95% CI 1.05, 9.71)], P value 0.04]. Moreover, infants of GDM mothers were more likely to experience hypoglycemia at the newborn nursery than infants born to normal mothers (OR 3.74, P<0.001). In a multivariate analysis, infants who developed hypoglycemia were larger for their gestational age, [OR 16 (95% CI 2.4, 110)]. Other causes of NICU admission were similar between both groups.

Although newborns of GDM mothers have double the risk of cardiovascular anomalies; it didn't reach statistical significance. Other neonatal outcomes namely respiratory complications, CNS complications, jaundice requiring phototherapy, birth trauma and biochemical abnormalities were not significantly different between the two groups; this lack of significance could be explained by the small sample size.

**DISCUSSION**

In this retrospective case-control study, we have shown as previously reported that around 10% of infants born to GDM mothers are admitted to NICU for various reasons mainly hypoglycemia and perinatal distress, since we lack the differentiation of special care, high dependency, and intensive care unit in our institute, a comparison to international standards couldn't be made to assess whether our infants born to GDM utilize more resources or not. Nevertheless, the rate of 8-10% is comparable to most recent reports in the literature. This rate is double the admission rate and the length of hospital stay of newborns of unaffected mothers, which causes tremendous burden over health care system.

A strong association has been observed in multivariate analysis; infants who developed hypoglycemia were larger for their gestational age. This augments the published results of hyperglycemia and adverse pregnancy (HAPO) study that showed strong continuous associations between cord C-peptide levels, neonatal hypoglycemia and excessive size at birth. Despite having similar rates of NICU admission, hypoglycemia and utilizing similar definition for macrosomia, the macrosomia rate in our study was lower than reported literature. This observed difference can be explained by different genetic, demographic and maternal metabolic factors that are known to affect fetal growth. Nonetheless; this difference can be simply due to the natural limitation of our study design to identify with precision mothers with normal and abnormal blood glucose levels in their respective groups. Other well-known fact is the effect of using different cut limits- the World Health Organization criteria or American Diabetes Association criteria- on the diagnosis of GDM; thus we may have undiagnosed mothers with GDM who were assigned to the normal group.

Maternal hyperglycemia is in favor of fetal overgrowth and macrosomia. This overgrowth can be one of the controllable complications with good antenatal care. Recently, two clinical trials subjected pregnant women with varying degrees of abnormal glucose tolerance test to either active management of their hyperglycemia or routine antenatal care; both trials showed a significant reduction in the rate of macrosomia in the treatment group but no effect on the rate of hypoglycemia. Moreover, good maternal glycemic control can reduce the risks of shoulder dystocia, cesarean delivery, and hypertensive disorders.

The rate of RDS was not increased in the offspring’s of GDM mothers included in our study. This in a way can be explained by good glycemic control. A comprehensive review by Piper in 2002 underlined the importance of glycemic control. Diabetic women with good glucose control (mean blood glucose <5.9 mmol/L) had babies with lung maturation similar to that of non-diabetic women. Other important factor that could explain our observation is the exclusion of preterm deliveries that have been shown to be associated with GDM.

Firm conclusion could not be made with regard to biochemical abnormalities, birth trauma and multiple pregnancies mostly due to small numbers presented.

Our study is unique since it’s the first regional study that focuses on neonatal outcomes. Our data is comparable to international figures. Our study had few limitations mostly due to its retrospective nature. The maternal nutritional status, availability of laboratory data, data reflecting treatment goal achievement such as fasting glucose level post initiation of therapy were unavailable. Our data is also limited since it represents a single center experience.

Gestational diabetes poses a special mixture of metabolic factors; key player essentially in terms of preventive strategies. Respectable number of research papers emphasized the importance of maternal blood glucose control, yet other metabolic factors are awaiting more exploration. Lately, two retrospective studies showed a significant higher fasting serum triglyceride levels in the second and third trimester in GDM mothers. This observational was even stronger for mothers who gave birth to macrocosmic babies. Preventative future strategies must take serum triglyceride levels essentially into their focus.

**CONCLUSION**

Gestational Diabetes Mellitus remains a significant
morbidity to newborns resulting in increased intensive care admission, prolongation of hospital stay and higher rates of neonatal hypoglycemia. More efforts to assure early recognition and strict sugar control during pregnancy are still needed.

REFERENCES

1. Metzger BE, Coustan DR. Summary and recommendations of the Fourth International Workshop-Conference on Gestational Diabetes Mellitus. Diabetes Care 1998;21 Suppl 2:B161-7.

2. King H. Epidemiology of glucose intolerance and gestational diabetes in women of child bearing age. Diabetes Care 1998;21 Suppl 2:9-13.

3. Egelgau MM, Herman WH, Smith PJ. The epidemiology of diabetes and pregnancy in the US. Diabetes Care 1995;18:1029-33.

4. Al-Hakeem A. Pregnancy outcome of gestational diabetic mothers: Experience in a tertiary center. J Family Community Med 2006;13:355-9.

5. Ardawi MS, Nasrat HA, Jamal HS, Al-Sagaaf HM, Mustafa BE. Screening for gestational diabetes mellitus in pregnant females. Saudi Med J 2000;21:155-60.

6. Khwaja SS, Al-Suleiman SA, Al-Sibai MH. Screening for gestational diabetes in a teaching hospital in Saudi Arabia. Aust N Z J Obstet Gynaecol 1998;38:209-11.

7. Al-Shawaf T, Akiel A, Moghbraby SA. Gestational diabetes and pregnancy in women of child bearing age. J Obstet Gynaecol Res 1999;25:333-8.

8. Metzger BE, Lowe LP, Dyer AR, Trimble ER, Chaovarindr U, Deerochanawong C, et al. Hyperglycemia and adverse pregnancy outcomes. N Engl J Med 2008;358:1991-2002.

9. Metzger BE, Persson B, Lowe LP, Dyer AR, Cruickshank JK, Välimäki I. Impaired left ventricular diastolic function in newborn infants of mothers with pregestational or gestational diabetes with good glycemic control. Early Hum Dev 2004;77:13-22.

10. Halliday HL. Hypertrophic cardiomyopathy in infants of poorly-controlled diabetic mothers. Arch Dis Child 1981;56:258-63.

11. Vanuca RC, Vunucicib SJ. Hypoglycemic brain injury. Semin Neonatol 2001;6:147-55.

12. Metzger BE, Lowe LP, Dyer AR, Trimble ER, Chaovarindr U, Coustan DR, et al. Hyperglycemia and adverse pregnancy outcomes. N Engl J Med 2008;358:1991-2002.

13. Crowther CA, Hiller JE, Moss JR, McPhee AJ, Jeffries WS, Robinson JS. Effect of treatment of gestational diabetes mellitus on pregnancy outcomes. N Engl J Med 2005;352:2477-86.

14. Di Cianni G, Miccoli R, Volpe L, Lencioni C, Ghio A, Giovannitti MG, et al. Maternal triglyceride levels and newborn weight in pregnant women with normal glucose tolerance. Diabet Med 2005;22:775-80.

15. Crowther CA, Hiller JE, Moss JR, McPhee AJ, Jeffries WS, Robinson JS. Effect of treatment of gestational diabetes mellitus on pregnancy outcomes. N Engl J Med 2005;352:2477-86.

16. Al-Rowaily MA, Abolfotouh MA. Predictors of gestational diabetes mellitus in a high-parity community in Saudi Arabia. East Mediterr Health J 2010;16:636-41.

17. Vannuccia RC, Vannucib SJ. Hypoglycemic brain injury. Semin Neonatol 2001;6:147-55.

18. Al-Khalifah R, Al-Subaihin A, Al-Kharfi T, Al-Alayian S, Al-Faleh KM. Neonatal short-term outcomes of gestational diabetes mellitus in Saudi mothers: A retrospective cohort study. J Clin Neonatol 2012;1:29-33.

Source of Support: Nil, Conflict of Interest: None declared.