Dicle Tıp Derg/Dicle Med J
Copyright © Dicle Tıp Dergisi 2009 Cilt/Vol 36, No 4, 235-240

ORIGINAL ARTICLE / ÖZGÜN ARAŞTIRMA

Gestational diabetes mellitus diagnosed in different periods of gestation and neonatal outcome

Gebelik diyabeti ve yenidoğana etkisi

Aqueela Ayaz[1], Shazia Saeed[2], Mian Usman Farooq[3], Muhammad Luqman Ali Bahoo[2], Kashif Hanif[1]

[1]Hera General Hospital, Makkah, Saudi Arabia.[2]Bahawal Victoria Hospital, Bahawalpur, Pakistan.
[3]Al-Noor Specialist Hospital, Makkah, Saudi Arabia.

ABSTRACT

Objective: To evaluate the maternal and neonatal outcomes in women diagnosed as gestational diabetes mellitus (GDM) in different periods of pregnancy.

Materials and Methods: This descriptive observational study was carried out from 1st January 2007 to 31th December 2007 in the department of Obstetrics and Gynecology of a 1300 bedded tertiary care hospital "Bahawal Victoria Hospital" in Bahawalpur, Pakistan. Seventy six pregnant women met the inclusion criteria of diabetes diagnosed on the basis of the Oral glucose tolerance test (OGTT) according to the National Diabetic Data Group. The study subjects were divided on the basis of gestational age at the first time diagnosis of GDM in the current pregnancy into group A (gestational age 13-23 weeks), group B (24-30 weeks) and group C (31-36 weeks).

Results: Out of total study subjects, 19 (25%) were diagnosed as GDM between 13-23 weeks of gestation (early-onset), 25 (32.9%) between 24-30 weeks while 32 (42.1%) diagnosed in the gestational age of 31-35 weeks (late-onset). Pregnancy-induced hypertension 5 (26.3%), polyhydramnios 5 (26.3%) and insulin treatment 13 (68.4%) were higher in women with earlier GDM diagnosis ($p<0.05$). APGAR score at 5-min below seven was seen in 3 (15.8%), large for gestational age in 5 (26.3%), respiratory distress in 6 (31.5%) and pre-term delivery in 5 (26.3%) of the early GDM group. These complications were seen more frequently in the early group compared with late-onset GDM group ($p<0.05$).

Conclusion: Earlier diagnosis of GDM was seem to be associated with less favorable newborn outcome.

Key Words: Gestational diabetes mellitus; maternal outcome; neonatal outcome; period of diagnosis

ÖZET

Amaç: Gebeliğin farklı dönemlerinde gestasyonel diabet tanısı alan kadınlarda anne ve bebek sonuçlarını değerlendirmek

Gereç ve Yöntem: Bu tanımlayıcı gözlemsel çalışma Pakistan'daki 1300 yataklı "Bahawal Victoria Hastanesi" Kadın-Doğum Kliniğinde 1 Ocak-31 Aralık 2007 tarihleri arasında gerçekleştirildi. Oral glukoz tolerans testi sonucuna göre Ulusal Diabet Veri Grubu kriterlerine uyan 76 gebe kadın diabet tanısı aldı. Çalışma grubundaki hastalar gestasyonel diabetin (GDM) ilk tanı anındaki gebelik dönemine göre Grup A (gebelik haftası 13-23 arası), Grup B (24-30 haftalık gebelik) ve Grup C (31-36 haftalık gebelik) olarak alt gruplara ayrıldı.

Bulgular: Toplam çalışma grubundan 19 (%25)'u erken başlangıçlı GDM (13-23 hafta), 25 (%32.9)'u 24-30 haftada, 32 (%42.1)'i 31-36 haftada (geç başlangıçlı GDM idi. Erken başlangıçlı GDM'li grupta gebelik ilintili hipertansiyon 5 (%26.3), polihidramniyos 5 (%26.3), insülin tedavisi 13 (%68.4)'ünde görüldü ve bu oranlar diğer dönemlerdeki hastalardan daha yüksekti ($p<0.05$). Erken GDM grubunda 5. dakikadaki APGAR puanı<7 üç hastada (%15.8), gebelik yaşına göre büyük bebek 5 (%26.3)'inde, solunum sıkıntısı 6 (%31.5)'ında ve erken doğum 5 (%26.3) hastada görüldü. Bu komplikasyonlar erken GDM grubunda geç başlangıçlı GDM grubundan daha sık idi ($p<0.05$).

Sonuç: Erken başlangıçlı GDM daha olumsuz yenidoğan sonuçları ile birlikte gözükmektedir.

Anahtar kelimeler: Gebelik diyabeti, anne sonuçları, bebek sonuçları, tanı dönemi

INTRODUCTION

Gestational diabetes mellitus (GDM) is defined as "any degree of glucose intolerance with onset or first recognition during pregnancy". Its prevalence may range from 1 to 14% of all pregnancies because of diversity of population studied and implementation of different diagnostic tools[1].

Geliş Tarihi / Received: 03.08.2009, Kabul Tarihi / Accepted: 01.09.2009
Yazışma Adresi /Correspondence: *Mian Usman Farooq, Medical Research Officer Health Research Centre Al-Noor Specialist Hospital P.O. Box 6251 Makkah, Saudi Arabia.* Email: drus76@yahoo.com

Gestational diabetes mellitus is associated with maternal and fetal morbidity[2], because maternal glucose level if rise during pregnancy cross the placenta and can lead to fetal hyperinsulinaemia which subsequently causes macrosomia and further increases the risk of shoulder dystocia and/or traumatic delivery. Moreover, infant of diabetic mother has to face threats like hypoglycemia, respiratory distress and jaundice after delivery[3,4]. Furthermore, an elevated glucose during embryogenesis, in formerly undocumented type 2 diabetes mellitus predispose to congenital anomalies[5,6].

It was mentioned in Fourth Workshop Conference on Gestational Diabetes Mellitus that screening in the early gestational period is only recommended for those women who have high-risk characteristics, whereas those at low risk could even pass over screening[7]. However, Bartha in 2000, has reported a worse outcome for women with GDM diagnosed in the first 23 weeks of pregnancy[8]. The typical recommendation is to perform screening between 24–28 weeks of gestation despite the fact that 40% of women with GDM could be detected in the early weeks of pregnancy[9].

We aimed to analyze the maternal and neonatal outcomes in the subjects diagnosed as GDM in different periods of pregnancy.

MATERIALS AND METHODS

This descriptive observational study was carried out from 1st January 2007 to 31st December 2007 (one year) in the department of Obstetrics and Gynecology of a 1300 bedded tertiary care referral teaching hospital in Bahawalpur, Pakistan, the Bahawal Victoria Hospital, with an average annual delivery rate of 2500.

Inclusion Criteria

It covered all singleton pregnant women attending the out patient department of obstetrics and gynecology during the first trimester with one or more risk factors that is age >35 years, body mass index (BMI) >30, with risk factors in past history that is family history of diabetes mellitus in first degree relative, previous history of GDM, repeated miscarriages, unexplained still births and previous macrosomic or congenitally malformed baby were subjected to OGTT and regular follow up especially for research purpose.

Exclusion Criteria

It comprised of all GDM women suffering from some other disorders which directly or indirectly may affect the outcome of pregnancy that is asthma, epilepsy, pre-pregnancy hypertension, thyroid dysfunction, anemia and heart problems. The pregnant women known to have pre-pregnancy diabetes mellitus or having OGTT positive in first twelve weeks of pregnancy were also excluded because pregnant women diagnosed to have GDM in the first trimester are probably to have Type 2 DM[10]. Subjects with poor glycemic control and follow up.

Patients

Out of total (85) high risk cases who visited out patient department in first trimester, nine females were excluded from study because two had OGTT positive in first trimester two had poor glycemic control while five had OGTT positive subsequently but did not have regular follow up. Finally seventy six were enrolled as study subjects. The study subjects were divided on the basis of gestational age at the first time diagnosis of GDM in the current pregnancy into three groups. Group A had gestational age 13-23 weeks, group B had >23-30weeks and group C had >30-36 weeks.

Diagnosis of Gestational Diabetes Mellitus

The Oral Glucose Tolerance Test (OGTT) was done according to the National Diabetic Data Group. After an over-night fasting of 8-14 hours and at least 3 days of unrestricted diet with unlimited physical activity, venous plasma glucose concentrations were measured in fasting, 1 hour, 2 hours and 3 hours samples after giving 100 gm of glucose in 250 ml of water orally. Patient was diagnosed as a case of GDM if two or more readings equaled or exceeded the levels of fasting 105 mg/dL, 1 hour 190mg/dL, 2 hour 165 mg/dL, 3-Hour 145 mg/dL[11]. The woman with negative OGTT in first visit was subjected to same test in subsequent visits.

Management of Gestational Diabetes Mellitus

Dietary control was advised by a registered dietician for all women with GDM. Total calories per day were calculated according to 30-35 cal/kg of body weight and diet charts were given to them. Insulin treatment was initiated and adjusted in subjects with failed dietary therapy (>2 weeks) to maintain the fasting whole blood glucose level between 70-100 mg/dl and two hours post parandial

less than 140 mg/dL according to American Diabetes Association criteria[1].

After adjusting insulin dosage, patients were discharged with instructions to be followed regularly at antenatal clinic with glucose home monitoring (2 levels) and to report immediately in case any complication that is pregnancy induced hypertension, preterm labor, premature rupture of membranes or decrease fetal movement.

Obstetrical Management

Baseline investigations carried out in all the patients at the time of enrollment, that were hemoglobin, blood group and Rh factor, complete examination of urine, ultrasonography. Liver function, serum uric acid and renal functions were advised where indicated. At each antenatal visit, glucose home monitoring (fasting and 2 hours post prandial) record was checked, maternal and fetal well being were assessed and if there was any complication, the patient was readmitted and managed accordingly. Ultrasonography was done early in gestation for fetal anomalies and was repeated if indicated. Elective caesarean section was reserved for those diabetics who had fetal macrosomia and emergency caesarean section was done for obstetrical indications.

During labor and prior to elective caesarean section, euglycaemia was achieved by administering intravenous insulin via an infusion pump together with intravenous dextrose at a rate of 10 g/h, using 10% solution. Maternal plasma glucose levels were monitored hourly and insulin dose adjusted to maintain the blood glucose concentration between 70-110 mg/dl[12]. All the newborn babies were assessed by a pediatrician immediately after delivery. A structured proforma were used to collect data after taking informed consent from subjects.

Outcome measures with outcome and operational definitions

Gestational age was estimated by ultrasound biometry (via CRL measurements in the first trimester of pregnancy) in cases where there was more than 3 days difference from that obtained from the last menstrual period (LMP)[13]. Pregnancy-induced hypertension was defined as a blood pressure >140/90mmHg presenting at gestational age of >20 weeks or the first week after delivery, confirmed as of 6 h later in a woman without a former diagnosis of hypertension, or previous hypertension worsening during pregnancy and requiring additional treatment. Perinatal mortality was defined as any fetal or neonatal death occurring from gestation of 22 weeks through the first 4 weeks after birth[14]. Neonatal hypoglycemia was defined in accordance with Cornblath and Reisner's criteria[15] for capillary blood glucose, which take into consideration both birth weight and prematurity. Neonatal jaundice was defined as hyperbilirubinemia requiring treatment[16]. All types of respiratory distress, including transient tachypnea, were considered. Preterm birth was defined as a birth before 37 complete gestational weeks. Macrosomia was defined as a birthweight of >4000 g. LGA newborns are defined as those with a birthweight of >90th percentile for the corresponding sex and gestational age[17].

Informed consent was obtained from all participants.

Statistical analysis

The non-normally distributed continuous variables were expresed as median (range) and subjected to Kruskal-Wallis analysis of variance. Chi square test was applied to categorical data. P-value <0.05 was considered as significant.

RESULTS

During study period a total of 3550 deliveries were done and total cases diagnosed as GDM were 110 (3.1%). Out of total (76) study subjects, 19 (25%) were diagnosed as GDM between 13-23weeks of gestation, 25(32.9%) between >23-30 while 32 (42.1%) diagnosed in the gestational age of >30-35 (p>0.05). Maternal median age was higher in group B 40 (36-47) than both of remaining groups but age range was wider in group C 38.7 (36-49). Multiparity was more common in Group C 18 (56.3%) but not significant (P>0.05).

Table 1. Maternal features in different groups (N=76)

Variables		Group A (n=19)	Group B (n=25)	Group C (n=32)	p-value
Age (yrs)		34 (30-39)	33 (29-40)	32.7(28-38)	*NS
Parity	0	3 (15.8)	3 (12)	6 (18.8)	
	1	6 (31.6)	10 (40)	8 (25)	NS†
	>1	10 (52.6)	12 (48)	18 (56.3)	
Height (cm)		156 (126-170)	154 (129-172)	151.2 (130-169)	NS*
Weight (kg)		59 (43-69)	66 (52-75)	75.4 (58-86)	<0.05*
BMI (kg/m^2)		23 (19-32)	28 (19-35)	32.1 (20-40)	<0.05*
Hemoglobin (g/dl)		10.2 (8.3-13)	9.8 (8-12.9)	10.6 (8.9-12.4)	NS*
Diagnostic OGTT (mg/dl)	Fasting	120 (88-130)	112 (62-145)	109 (72-138)	<0.05*
	1 hour	214 (99-336)	206 (89-324)	200.5 (111-321)	NS*
	2 hour	190 (109-320)	205 (96-326)	182 (94-280)	<0.05*
	3 hour	144 (60-250)	150 (65-250)	157.5 (40-266)	<0.05*

Results are expressed in median (range) or number (%), NS Not significant
* Kruskal–Wallis ANOVA between periods. †χ^2-test

Table 2. Maternal and fetal outcome in subjects groups (n=76)

Variables			Group A (n=19)	Group B (n=25)	Group C (n=32)	p-value†
Maternal	Pregnancy induced hypertension		5 (26.3)	2 (8)	2 (6.3)	<0.05
	Recurrent Monilial Infection		2 (10.5)	2 (8)	1 (3.1)	NS
	Recurrent UTI		2 (10.5)	1 (4)	1 (3.1)	NS
	PROM		3 (15.8)	3 (12)	4 (12.5)	NS
	Ante partum hemorrhage		1(5.3)	1 (4)	1 (3.1)	NS
	Polyhydramnios		5 (26.3)	3 (12)	2 (6.3)	<0.05
	Insulin Treatment		13 (68.4)	11 (40)	8 (25)	<0.05
	Mode of delivery	Cesarean section	7 (36.8)	5 (20)	5 (15.6)	NS
		Spontaneous	7 (36.9)	11 (44)	15 (46.9)	NS
		Instrumental	3 (15.8)	5 (20)	7 (21.9)	
		Breech	2 (10.5)	4 (16)	5 (15.6)	
Fetal	5 minute APGAR score <7		3 (15.8)	0	1 (3.1)	<0.05
	Large for gestational age		5 (26.3)	3 (12)	3 (9.4)	<0.05
	Macrosomia		3 (15.8)	2 (8)	3 (9.4)	NS
	Shoulder dystocia		3 (15.8)	4 (16)	3 (9.37)	NS
	Perinatal mortality		2 (10.5)	3 (12)	2 (6.3)	NS
	Hypoglycemia		3 (15.8)	2 (8)	1 (3.1)	<0.05
	Hyperbilirubinemia		5 (26.3)	5 (25)	6 (18.9)	NS
	Respiratory distress		6 (31.5)	3 (12)	3 (9.4)	<0.05
	Pre-term Birth		5 (26.3)	2 (8)	3 (9.4)	<0.05

Results are expressed in number (%), NS not significant, †χ^2-test

Basal mass index was highest in Group C with wider range 32.1 (20-40) ($p<0.05$). Group A had higher median fasting glucose level 120 mg/dl in diagnostic OGTT while range was wider in group B that is 62-145 ($p<0.05$). Even though, second and third hours postprandial glucose levels during diagnostic OGTT were significantly different among the groups ($p<0.05$) (Table 1).

In the bivariate analysis evaluating the association between the period of diagnosis and outcomes (Table 2), the period was found to be associated with three out of nine maternal outcomes: pregnancy-induced hypertension 5 (26.3%), polyhydramnios 5 (26.3%) and insulin treatment 13 (68.4%) which were higher in women with earlier GDM diagnosis ($p<0.05$). While discussing the fetal outcomes, the period was found to be associated with four out of eight factors that is 5-min Apgar <7 3(15.8%), large for gestational age 5(26.3%), respiratory distress 6(31.5%) and pre-term delivery 5(26.3%) were more frequent seen in the Group A ($p<0.05$). No differences were found in macrosomia, perinatal mortality, hypoglycemia and hyperbilirubinemia (Table 2).

DISCUSSION

In this study, the incidence of GDM was 3.1%, a figure very less to the 13.9% found in the Chinese population in Australia[18] but consistent with 2-5% in the US[19], and little bit high than 2.8%in Bahrain[20] and 2.7% in Australia[21]. Only a few studies in past had explained the relationship between gestational age at GDM diagnosis and maternal and neonatal outcome. This relationship was first analyzed by Berkowitz in 1992[22] followed by Bartha in 2000[8] and Svare in 2001[23]. On the other hand, some authors had mainly paid attention towards maternal characteristics with GDM diagnosis early in pregnancy, but perinatal outcome was not investigated[9,24]. The formerly mentioned studies were comparable with our results as early diagnosis was related with higher rates of insulin treatment[8,23] and higher or borderline increased hypertension rates[8,22]. Our study results highlighted that earlier diagnosed GDM cases developed not only hypertension and required of insulin treatment but also polyhydramnios was also more frequent in the same group which is contrary to formerly mentioned studies. On the other hand overall insulin therapy was initiated in 42.1% subjects higher than 23.2% used in the study of Moses[25]. We did not measure post-partum glucose levels or tolerance of the subjects as done by Svare[23]. In relation to fetal outcomes, Overall rate of large for gestational age in present study was 11 (14.5%) lesser than (16.7%) found in the study of Lepord and Worda[26] while macrosomia rate 8 (10.5%) was higher than (8%) seen in Moses study[25]. While discussing the study of Malinowska, hyperbilirubinemia (17.3%) were seen infrequently than 21.1% of our study and repeatedly seen the cases of hypoglycemia (15.6%) than our study that is 7.9%[27]. Berkowitz and Svare[21,22] did not focus the dissimilarities in women diagnosed with GDM early in pregnancy. However, Bartha[8] reported an increased rate of hypoglycemia in these infants as noted by us 3 (15.8%) and increased perinatal mortality which was not prominent in our study 2(10.5%) in earlier diagnosed group. In the present paper, we also found more frequent rate of preterm birth, respiratory distress, and 5-min Apgar <7 in earlier diagnosed group.

We concluded that thorough metabolic management and good on the whole outcome, earlier diagnosis of GDM is associated with poor newborn outcome.

REFERENCES

1. American diabetes association. Preconception care of women with diabetes mellitus. Diabetes Care 2003;26:S91-93.
2. Persson B, Hanson U. Neonatal morbidities in gestational diabetes mellitus. Diabetes Care 1998;21(suppl.2):B79–B84.
3. Kjos S, Buchanan T. Gestational diabetes mellitus. N Engl J Med 1999;341:1749-1756.
4. Langer O. Is normoglycemia the correct threshold to prevent complications in the pregnant diabetic patient? Diabetes Reviews 1996;4:2-10.
5. Farrell T, Neale L, Cundy T. Congenital anomalies in the offspring of women with type 1, type 2 and gestational diabetes. Diabet Med 2002;19:322-326.
6. Schaefer U, Songster G, Xiang A, Berkowitz K, Buchanan TA, Kjos SL. Congenital malformations in offspring of women with hyperglycemia first detected during pregnancy. Am J Obstet Gynecol 1997;177:1165-1171.
7. Metzger BE, Coustan DR. Summary and Recommendations of the Fourth International Workshop-Conference on Gestational Diabetes Mellitus. Diabetes Care 1998;21(suppl.2):B161-167.
8. Bartha J, Martinez P, Comino R. Gestational diabetes mellitus diagnosed during early pregnancy. Am J Obstet Gynecol 2000;182:346-350.
9. Meyer WJ, Carbone J, Gauthier DW, Gottmann DA. Early gestational glucose screening and gestational diabetes. J Reprod Med 1996;41:675-679.

10. Bartha JL, Martinez-Del-Fresno P, Comino-Delgado R. Early diagnosis of gestational diabetes mellitus and prevention of diabetes related complications. Eur J Obstet Gynecol Reprod Biol 2003;9:41-44.
11. National Diabetes Data Group. Classification: and diagnosis of diabetes mellitus and other categories of glucose intolerance. Diabetes 1979;28):1039-1057.
12. Gillmer MDG, Hurley PA. Diabetes and endocrine disorders in pregnancy. In: Edmonds DK, editor. Dewhurst's Textbook of obstetrics and gynaecology for postgraduates. 6th ed. Oxford: Blackwell Science 1999. p. 197-209.
13. Goldstein SR. Embryonic ultrasonographic measurements: crown-rump length revisited. Am J Obstet Gynecol 1991;165:497-501.
14. Nasrat AA, Augensen K, Abushal M, Shalhoub JT. The outcome of pregnancy following untreated impaired glucose tolerance. Int J Gynaecol Obstet 1994;47:1-6.
15. Tan YY, Yeo GS. Impaired glucose tolerance in pregnancy – is it of consequence? Aust N Z J Obstet Gynaecol 1996 ;36:248-255.
16. Deerochanawong C, Putiyanum C, Wongsuryrat M, Serirat S, Jinayon P. Comparison of National Diabetes Data Group and World Health Organization criteria for detecting gestational diabetes mellitus. Diabetologia 1996;39:1070-1073.
17. Jacobson JD, Cousins L. A population-based study of maternal and perinatal outcome in patients with gestational diabetes. Am J Obstet Gynecol 1989;161:981-986.
18. Beischer NA, Oates JN, Henry OA, Sheedy MT, Walstab JE. Incidence and severity of gestational diabetes mellitus according to country of birth in women living in Australia. Diabetes 1991;40 (Suppl 2): 35-38.
19. Sermer M, Naylor CD, Farine D, et al. The Toronto Tri-Hospital Gestational Diabetes Project . A preliminary review. Diabetes Care 1998;21(Supplement 2):B33-42.
20. El-Shafei A, Bashmi Y, Norman A. Incidence and severity of gestational diabetes in Bahrain and Australia. Aus NZ J Obstet Gyneacol 1989;29:204-209.
21. Moses RG, Colagiuri S. The extent of undiagnosed gestational diabetes mellitus in New South Wales. Med J Aust 1997;167:14-16.
22. Berkowitz G, Roman S, Lapinski R. Maternal characteristics, neonatal outcome, and the time of diagnosis of gestational diabetes. Am J Obstet Gynecol 1992;167(4 pt 1):976-982.
23. Svare J, Hansen B, Molsted-Pedersen L. Perinatal complications in women with gestational diabetes mellitus. Acta Obstet Gynecol Scand 2001;80:899-904.
24.Super D, Edelberg S, Philipson E, Hertz R, Kalhan S. Diagnosis of gestational diabetes in early pregnancy. Diabetes Care 1991;14:288-294.
25. Moses RG, Griffiths RD. Can a diagnosis of gestational diabetes be an advantage to the outcome of pregnancy? J Soc Gynecol Investig. 1995;2:523-525.
26. Leipold H, Worda C, Gruber CJ, Kautzky-Willer A, Husslein PW, Bancher-Todesca D. Large-for-gestational-age newborns in women with insulin-treated gestational diabetes under strict metabolic control. Review Group(s): Cochrane Child Health Field, Cochrane Metabolic and Endocrine Disorders Group. Source: Wiener Klinische Wochenschrift 2005;117:521-525.
27. Malinowska-Polubiec A, Czajkowski K, Sotowska A. Pregnancy and delivery course in patients with gestational diabetes mellitus. Ginekol Pol 2003;74:1200-1207.