Gestational Diabetes Mellitus

Is Further Improvement Necessary?

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SUMMARY

The maternal antepartum, intrapartum, and neonatal characteristics of 158 patients with gestational diabetes mellitus (GDM) attending a large teaching hospital between 1979 and 1983 were described and compared with a matched nondiabetic control group. The primary cesarean section rate in patients with GDM (18%) was significantly greater than in the control group (11%, $P < 0.04$). Neonatal macrosomia, as reflected in mean birthweight ($P < 0.04$), the number of neonates weighing > 4 kg ($P < 0.05$) and large-for-gestational-age infants ($P < 0.05$), and the birthweight adjusted for gestational age (K-score, $P < 0.01$) was significantly increased in the diabetic group.

The characteristics of patients with GDM treated with diet alone and diet and insulin together were examined. The insulin-therapy group was characterized by more patients older than 25 yr ($P < 0.01$) and a higher mean birthweight (3743 ± 677 g) ($P < 0.02$) than the diet-alone group. This may reflect an increased magnitude of glucose intolerance in the insulin-treated group. Obese patients with GDM delivered heavier neonates than the nonobese patients with GDM ($P < 0.01$). Although there was no difference between the groups, perinatal mortality was present in this study. These data indicate that the major perinatal morbidity in GDM included increased cesarean section for fetal macrosomia. Early diagnosis with strict diagnostic criteria and rigid antenatal surveillance may result in further improvements in outcome. DIABETES 1985; 34 (Suppl. 2):55–60.

The term gestational diabetes mellitus (GDM) is restricted to pregnant women in whom the onset or recognition of glucose intolerance occurs during pregnancy.[1] As a special patient class, the long-term implications of GDM for the mother are not disputed. For example, O'Sullivan has demonstrated that the development of GDM increases the risk of subsequent overt diabetes.[2] However, other clinical implications of GDM are unclear. Earlier studies have reported a wide range of perinatal mortality rates.[3,4] In contrast, more recent studies have not demonstrated increased perinatal mortality in mothers with GDM.[5–7] This apparent improvement in perinatal mortality may be due to recent improvements in identification, metabolic diabetic control, obstetrical management, and advances in neonatal intensive care. However, all of the reports demonstrated the persisting problems of increased cesarean sections, neonatal macrosomia, and neonatal morbidity.

A uniform pattern of treatment for GDM is even less clear. The first American Diabetes Association Workshop on Gestational Diabetes in 1980 made certain specific recommendations.[8] These recommendations presumably improved clinical care and stimulated interest in diagnosis and therapy. The purpose of this present study was: (1) to describe the experience in treating a large number of patients with GDM at a teaching hospital, and (2) to determine further needs for the care of the GDM mother.

MATERIALS AND METHODS

Background. Cleveland Metropolitan General Hospital is a large tertiary teaching hospital of Case Western Reserve University with a fellowship training program in maternal fetal medicine and a referral center for high-risk patients. The hospital has approximately 3500 deliveries per year consisting of both private and indigent clinic patients. Approximately 48% of the patients are white, 46% are black, and 5% are Hispanic. Data are collected prospectively from mothers and their neonates during the antepartum, intrapartum, and postpartum periods and form the basis for a computerized, databased system. At this hospital, the diagnosis of GDM has been made since 1968 and it has been the accepted

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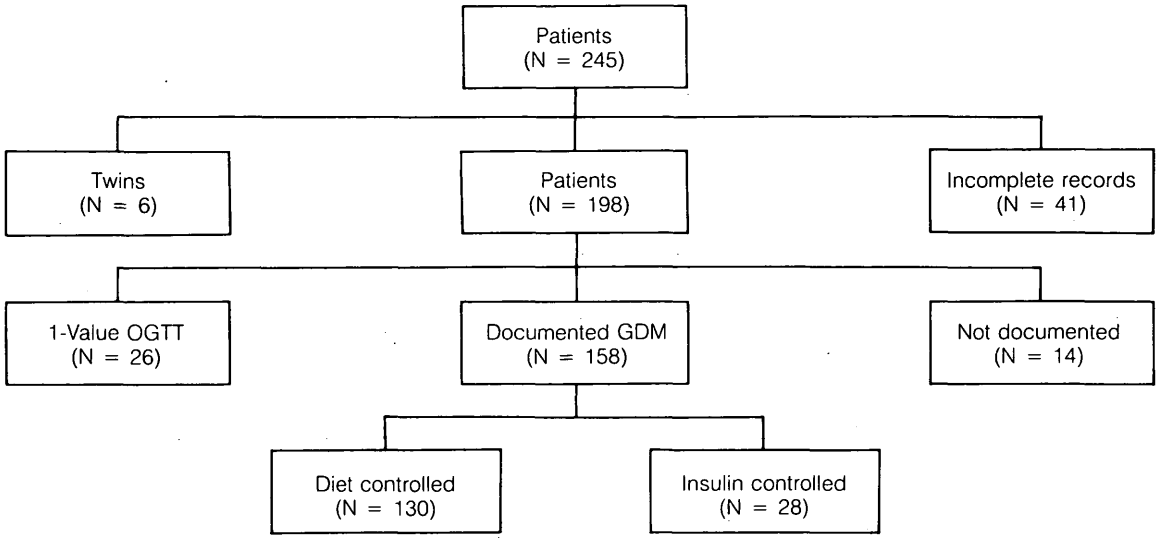
TABLE 1
Details of subjects studied



practice to screen patients with risk factors for diabetes mellitus. However, the guidelines for both patient care and for the identification of patients with GDM have changed throughout this time period.

Protocol. Data for this study were collected from January 1, 1979, to December 31, 1983. The charts were reviewed for all antepartum patients identified as GDM mothers. The diagnosis of GDM was confirmed if the following criteria were met in any of three methods. First, a 1-h, 50-g postprandial glucose screen with a plasma glucose > 200 mg/dl. A second method included a 100-g oral glucose tolerance test (OGTT) based on the criteria of O'Sullivan and Mahan[2] and adjusted for analysis of plasma sample and the glucose-oxidase method as suggested by Carpenter and Coustan.[9] Any two of the following abnormal values were considered diagnostic: fasting glucose > 95 mg/dl, 1-h glucose > 180 mg/dl, 2-h glucose > 155 mg/dl, or 3-h glucose > 140 mg/dl. Finally, a 25-g rapid intravenous glucose tolerance test (IVGTT) and a fractional rate of disappearance of glucose (K_t) less than 1.18/min was also used.[10] Individual patients with multiple gestations, recent ritodrine therapy, or incomplete records were excluded.

A control population was matched for maternal age (< 25 or > 25 yr), maternal race (white, black, or Hispanic), maternal weight (< 200 or > 200 lb), maternal socioeconomic status (private or clinic), and gestational age at the first obstetric visit.

The maternal antepartum, intrapartum, and neonatal characteristics of the GDM and control groups were examined. All neonates were weighed in the nursery immediately after birth. The neonatal gestational age was determined by the Ballard modification of the Dubowitz examination performed on the second day of life.[11] The birthweights were evaluated by the number of macrosomic neonates (> 4 kg); the number of large-for-gestational-age infants (> 90th percentile); and K-score, a standard score for birthweight for each gestational age corrected for the population where the mean is zero, the tenth percentile is −1, and the ninetieth percentile is +1. Neonatal hypoglycemia was defined as two plasma glucose values < 20 mg/dl during the first 48 h after birth in preterm infants or a value < 30 mg/dl thereafter, and in term infants, a value < 30 mg/dl at any time. Neonatal hypocalcemia was defined as the total serum calcium < 8.0 mg/dl in term infants and 7.0 mg/dl in preterm infants at any time in the nursery. Neonatal hyperbilirubinemia was defined as a serum bilirubin > 6.5 mg/dl in term and 3.5 mg/dl in preterm infants at any time.

In assessing the outcome measures, univariate differences were examined by means of contingency table analysis and Chi-square test; continuous variables were tested by Student's *t*-test. A P-value of < 0.05 was considered to be significant.

RESULTS

During the study period, 245 (1.5%) of 16,648 patients were identified as GDM mothers. Of these 245 patients (Table 1), 198 patients had singleton pregnancies with complete antenatal, intrapartum, and neonatal records. Of these 198 patients, 158 patients were documented to have GDM and were successfully matched with controls. Included in this group are 14 patients with a documented abnormal glucose tolerance test in a previous pregnancy. Although their glucose

TABLE 2
Maternal characteristics of patients with GDM

Age (yr)	28.9 ± 6.1*
Nulliparity	45 (28%)
Private service	52 (33%)
Race	
White	83 (53%)
Black	60 (38%)
Hispanic	12 (8%)
Obese (> 200 lbs)	69 (38%)
Gestational age at first obstetrical visit (wk)	18.8 ± 10
Antenatal risk score[12]	16.5 ± 11.8†

*Mean ± SD.
†Total risk score minus 10 points for risk of diabetes.

TABLE 3
Intrapartum characteristics of patients with GDM and control subjects

	Study group (N = 158)	Control group (N = 158)
Prematurity*	24 (15%)	22 (14%)
Preeclampsia	13 (8%)	7 (4%)
Breech presentation	6 (4%)	6 (4%)
Shoulder dystocia	3 (2%)	2 (7%)
Fetal distress	7 (4%)	11 (7%)
Primary cesarean section	29 (18%)	17 (11%)†

Figures are numbers in each category with percentage in parentheses.
*Less than or equal to 37 wk gestation.
†$P < 0.04$.

intolerance was not documented in the index pregnancy, they were considered as gestational diabetic subjects.

The maternal characteristics of the 158 patients with GDM (study group) are shown in Table 2. The mean maternal age was 28.9 ± 6.1 yr with 72% being older than or equal to 25 yr. The racial distribution was 53% white, 38% black, and 8% Hispanic. Obesity was found in 69 (38%) of the patients. In this study group, 130 patients were treated by diet therapy alone and 28 patients treated by diet and insulin therapy.

The intrapartum characteristics of the study and control groups are presented in Table 3. There were no differences between the groups in the incidences of prematurity, preeclampsia, breech presentation at delivery, shoulder dystocia, or fetal distress in labor. The primary cesarean section rate was significantly higher in the study group (18%) than in the control group (11%) ($P < 0.04$).

Neonatal outcomes in Table 4 document the higher mean birthweight in the study group than in the control group ($P < 0.04$). When adjusted for gestational age, the birthweight of the study group was also significantly greater than that of the control group. This is reflected in significant differences in the K-score and the number of macrosomic and large-for-gestational-age infants. Neonatal morbidity occurred in 86 (54%) neonates in the study group, which was not different from the control group. There were no differences in Apgar scores or neonatal trauma. Congenital anomalies in the study group consisted of one neonate with an absent left kidney, one neonate with subaortic stenosis, two neonates with microcephaly, one neonate with a cleft lip and palate, and one neonate with talipes equinus varus. The last two neonates also had a single umbilical artery.

The perinatal mortality rate in the study group (three stillborns and two neonatal deaths) was 3.2% and in the control group (one stillborn and one neonatal death) was 1.3%.

Within the study group, the 130 patients treated by diet therapy alone were compared with the 28 patients treated by diet and insulin therapy (Table 5). The maternal characteristics were similar between the groups except for maternal age, which was greater in the insulin-treated patients. There were no differences in intrapartum characteristics or Apgar scores between the groups. The mean neonatal birthweight in the insulin group was significantly higher than in the diet alone group ($P < 0.02$). The K-score tended to reflect this difference but was not statistically significant. There were no differences in neonatal morbidity or perinatal mortality between the groups.

Within the study group of patients with GDM, there were 62 patients who were obese. The cohort of 62 obese gestational diabetic subjects was compared with the 96 nonobese gestational diabetic subjects and the results of this comparison are shown in Table 6. There were no differences in maternal or intrapartum characteristics between the groups. The obese patients delivered heavier neonates than did the nonobese patients as expressed in mean birthweight, K-score, and the number of macrosomic and large-for-gestational-age infants. There were no other differences in neonatal morbidity.

TABLE 4
Neonatal outcome of patients with GDM and control subjects

	Study group (N = 158)	Control group (N = 158)	P-Value
1-Min Apgar < 7	40	44	NS
5-Min Apgar < 7	8	9	NS
Birthweight (g)	3463 ± 740*	3302 ± 662	<0.04
Neonatal gestational age (wk)	39 ± 1.9	39.2 ± 1.9	NS
K-Score	0.6 ± 1	0.3 ± 0.9	<0.01
Macrosomia†	39 (25%)	22 (14%)	<0.05
Large for gestational age	52 (33%)	35 (22%)	<0.05
Neonatal sex-male	87	79	NS
Trauma	1	1	NS
Hypoglycemia	4	2	NS
Hypocalcemia	0	0	NS
Hyperbilirubinemia	80	67	NS
Respiratory distress	1	2	NS
Admission to NICU	18	18	NS
Neonate discharged after mother	12	15	NS
Perinatal mortality	5	2	NS

*Mean ± SD.
†Birthweight > 4 kg.
NS, Not significant.

TABLE 5
Patients with GDM: comparison of those treated by diet alone and those treated by diet and insulin

	Diet (N = 130)	Diet + insulin (N = 28)	P-Value
Maternal			
Age (yr)	28.6 ± 6.5*	30.4 ± 3.7	NS
Parity	1.6 ± 1.6	1.9 ± 1.4	NS
Obesity	47 (36%)	15 (54%)	NS
Private service	40 (31%)	12 (43%)	NS
Race			
White	69 (33%)	14 (50%)	NS
Black	50 (38%)	10 (36%)	NS
Hispanic	10 (8%)	2 (7%)	NS
Gestational age at first obstetrical visit (wk)	18.3 ± 10	20.6 ± 10	NS
No. > 25 yr	87 (67%)	26 (93%)	<0.01
Intrapartum			
Prematurity	21 (16%)	3 (11%)	NS
Preeclampsia	10 (8%)	3 (11%)	NS
Fetal distress	7 (5%)	0	NS
Primary cesarean section	23 (18%)	6 (21%)	NS
Neonatal			
1-Min Apgar < 7	31 (24%)	4 (14%)	NS
5-Min Apgar < 7	7 (5%)	0	NS
Birthweight	3402 ± 742	3743 ± 677	<0.02
Dubowitz	39.0 ± 0.9	39.0 ± 1.3	NS
K-Score	0.5 ± 0.9	0.9 ± 1.1	NS
Macrosomia	26 (20%)	10 (30%)	NS
Large for gestational age	38 (29%)	11 (39%)	NS

*Mean ± SD.
NS, Not significant.

DISCUSSION

This study represents a review of recent experience with GDM at a large teaching hospital. Our approach was to describe the maternal, intrapartum, and neonatal characteristics of gestational diabetic subjects and then to compare this population with a matched, nondiabetic control group to determine if there is a need for improvement in the outcome of GDM pregnancies.

The results of this study indicate that patients with GDM deliver larger neonates than do nondiabetic patients, even when adjusted for gestational age. This finding was associated with a significantly higher primary cesarean section rate in the gestational diabetic population, which was almost twice as high as the control population. However, it must be noted that beyond 40 wk there is a greater incidence of inductions and that neonatal size may not be the only reason for the increased cesarean section rate. Similar findings of neonatal macrosomia (20%) and an increased primary cesarean section rate (21%) were present in a large study of 261 gestational diabetic subjects reported from Los Angeles County Hospital[4] as well as in other studies.[6,7] The overall neonatal morbidity that occurred in 54% of the neonates of mothers with GDM was not different than in the control group. The incidence of neonatal morbidity was higher than in the previous studies, but may reflect differences in definitions or populations. Nevertheless, macrosomia is a consistent finding in GDM, even though it is not necessarily associated with increased neonatal morbidity.

Some findings in the current study are not in agreement with previous studies. First, perinatal mortality was evident in our study as well as in the other large study.[4] The two recent studies of 68 and 45 patients with GDM reported no perinatal mortality.[6,7] This difference may be accounted for by differences in populations, the sample size, type of obstetrical care (private versus clinic), definition, etc. Nevertheless, the results of two large studies (one 14 yr old[4] and the present study) indicate that perinatal mortality exists in GDM. Although the numbers (5) are too small to make definitive conclusions, our data suggest the possibility of a greater risk of perinatal mortality in patients with GDM, but the trend is not significant. Second, congenital anomalies were identified in six neonates, although none of these anomalies were responsible for the perinatal mortality. As embryogenesis is complete by the seventh postconceptional week, and carbohydrate intolerance of GDM manifests itself late in gestation, the frequency of congenital malformations might be expected to be low. In spite of this, we observed six neonates (4%) with congenital anomalies. This may be due to the presence of subtle abnormalities of glucose metabolism in GDM women early in gestation. Nevertheless, congenital anomalies have been reported in GDM and several studies have demonstrated a significant increase of congenital anomalies in infants of gestational diabetic women.[7,13] However, other studies have not supported this increase in frequency.[14,15] In our study, no congenital anomalies were identified in the control group, but these results were not confirmed by a neonatal chart review and, hence, a comparison cannot be made at the present time.

The characteristics of the patients with GDM who required insulin therapy were studied. The patients treated with insulin therapy were older than patients treated by diet alone. Although this difference may be due to a greater degree of glucose intolerance in patients requiring insulin, the additional risk of neonatal macrosomia emphasizes the need to

TABLE 6
Patients with GDM: comparison of obesity and nonobesity

	Obese (N = 62)	Nonobese (N = 96)	P-Value
Maternal			
Age (yr)	29.3 ± 5.4*	28.7 ± 6.5	NS
Parity	1.9 ± 1.4	1.5 ± 1.7	NS
Private service	19 (31%)	33 (34%)	NS
Antenatal risk score†	15.0 ± 11.6	14.3 ± 11.6	NS
Gestational age at first obstetrical visit (wk)	18.8 ± 9.9	18.7 ± 10.2	NS
Insulin therapy	15 (24%)	13 (14%)	NS
Intrapartum			
Prematurity	7	17	NS
Preeclampsia	4	9	NS
Fetal distress	3	4	NS
Primary cesarean section	12 (19%)	17 (18%)	NS
Neonatal			
1-Min Apgar < 7	12	23	NS
5-Min Apgar < 7	1	6	NS
Birthweight (g)	3667 ± 682	3331 ± 750	<0.01
Dubowitz (wk)	39.2 ± 1.7	38.9 ± 2.1	NS
K-Score	0.8 ± 1.1	0.4 ± 0.9	<0.05
Macrosomia	23 (37%)	13 (14%)	<0.001
Large for gestational age	27 (44%)	22 (23%)	<0.01
Hypoglycemia	1	3	NS
Hyperbilirubinemia	34	46	NS
Respiratory distress	1	0	NS
Admission to NICU	7	11	NS
Perinatal mortality	1	4	NS

*Mean ± SD.
†Total score minus 10 points for diabetes and 5 points for obesity.
NS, Not significant.

continue glucose monitoring during the antenatal period, especially in older patients.

The effects of obesity as a risk factor were studied within the group of patients with GDM by comparing the obese and nonobese patients. The obese patient with GDM delivered heavier neonates than did the nonobese gestational diabetic subject. This difference may be due to a greater degree of glucose intolerance in the obese gestational diabetic group. One additional finding in our study was that the obese gestational diabetic group had only one perinatal mortality, while the nonobese gestational diabetic group had four perinatal mortalities. Although this finding may not be significant, it suggests the need for further study in this area.

Our data indicate that the problem of neonatal macrosomia and maternal morbidity from an increase in cesarean section persists in patients with GDM. Even though specific obstetrical recommendations on the treatment of GDM and improvements in neonatal care have been developed, these problems remain; therefore, there is room for improvement. Although better screening methods, early diagnosis, and treatment with more rigid antenatal surveillance may alter these consequences, this study also demonstrated poor record keeping and an inherent difficulty in identification and documentation of GDM due to confusion in the literature with regard to specific values required for screening and diagnosis. A uniform, consistent, and universal method of screening, diagnosis, and treatment is needed before improvement in the outcome of GDM can occur. It is evident that with clear guidelines less confusion would result.

ACKNOWLEDGMENTS

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REFERENCES

[1] National Diabetes Data Group: Classification and diagnosis of diabetes mellitus and other categories of glucose intolerance. Diabetes 1979; 28:1039–57.

[2] O'Sullivan, J. B., and Mahan, C. M.: Criteria for the oral glucose tolerance test in pregnancy. Diabetes 1964; 13:278–85.

[3] O'Sullivan, J. B., Charles, D., Mahan, C. M., and Dandrow, R. V.: Gestational diabetes and perinatal mortality rate. Am. J. Obstet. Gynecol. 1973; 116:901–904.

[4] Gabbe, S. G., Mestman, J. H., Freeman, R. K., Anderson, G. V., and Lowensohn, R. I.: Management and outcome of class A diabetes mellitus. Am. J. Obstet. Gynecol. 1977; 127:465–69.

[5] Khojandi, M., Tsai, A. Y.-M., and Tyson, J. E.: Gestational diabetes: the dilemma of delivery. Obstet. Gynecol. 1974; 43:1–6.

[6] Gyves, M. T., Rodman, H. M., Little, A. B., Fanaroff, A. A., and Merkatz, I. R.: A modern approach to management of pregnant diabetics: a two-year analysis of perinatal outcomes. Am. J. Obstet. Gynecol. 1977; 128:606–16.

[7] Lavin, J. P., Lovelace, D. R., Miodovnik, M., Knowles, H. C., and Barden, T. P.: Clinical experience with one hundred seven diabetic pregnancies. Am. J. Obstet. Gynecol. 1983; 147:742–52.

[8] Summary and Recommendations, The American Diabetes Association Workshop–Conference on Gestational Diabetes. Diabetes Care 1980; 3:499–501.

[9] Carpenter, M. W., and Coustan, D. R.: Criteria for screening tests for gestational diabetes. Am. J. Obstet. Gynecol. 1982; 144:768–72.

[10] Silverstone, R. A., Solomons, E., and Rubricius, J.: The rapid intravenous glucose tolerance test in pregnancy. J. Clin. Invest. 1961; 40:2180–89.

[11] Ballard, J. L., Novak, K., and Driver, M.: A simplified score for assessment of fetal maturation and newly born infants. J. Pediatr. 1979; 95:769–74.

[12] Hobel, C. J., Hyvarinen, M. A., Okada, D. M., and Oh, W.: Prenatal and intrapartum high-risk screening. I. Prediction of the high risk neonate. Am. J. Obstet. Gynecol. 1973; 117:1–9.

[13] Pedersen, L. M.: Pregnancy and diabetes. A Survey. Acta Endocrinol. 1980; 94 (Suppl. 238):13–19.

[14] Haukkamaa, M., Nilsson, C. G., and Luukkainen, T.: Screening, management and outcome of pregnancy in diabetic mothers. Obstet. Gynecol. 1980; 55:596–602.

[15] Simpson, J. L., Elias, S., Martin, A. O., Palmer, M. S., Ogata, E. D., and Radvany, R. A.: Diabetes in pregnancy. Northwestern University series (1977–1981). I. Prospective study of anomalies in offspring of mothers with diabetes mellitus. Am. J. Obstet. Gynecol. 1983; 146:263–70.