J. Perinat. Med.
9 (1981) 223

Incidence of congenital abnormalities in infants of gestational diabetic mothers

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1 Introduction

The newborns of diabetic mothers are known to suffer from various morbidities including congenital abnormalities [9, 14]. The incidence of abnormality has been reported as from 1.4% to 28.6% for the newborns of diabetic pregnancies [8, 11, 13] and from 1.7% to 7.8% for those of gestational diabetics [2, 10]. Thus, the incidence of malformations in infants of gestational diabetic mothers has been reported as being equal to or as high as four times that of the general population [2, 8, 10, 11, 13]. The reports of malformations in the newborns of gestational diabetics suffer from three important deficiencies: 1) most of them are retrospective, 2) only a few "high-risk" pregnant women are screened for diabetes rather than all pregnant women, and 3) the comparison is usually made between the newborns of gestational diabetics and those of pregnant women in whom a normoglycemic state has not been proven.

This study was undertaken to compare the types and incidence of congenital abnormalities in newborns of gestational diabetics with those of truly normoglycemic pregnant women identified by a three-hour glucose tolerance test.

2 Materials and methods

During the 40 month period from January 1, 1975 through April 30, 1978, four thousand, three hundred and forty (4,340) pregnant women, private patients of a group of six obstetricians,

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were studied. Each patient was counseled by one of two dieticians early in pregnancy. Between 28 and 32 weeks of pregnancy, each was screened with a 50 gram oral glucose load following an overnight fast. As previously reported from this institution, those with a one-hour plasma glucose level greater than or equal to 130 mg% were given a standard three-hour, 100 gram oral glucose tolerance test [3, 4]. Gestational diabetes was diagnosed when two or more of the following plasma glucose levels were met or exceeded: Fasting, 100 mg%; one-hour, 180 mg%; two-hour, 160 mg%; and three-hour, 140 mg%.

The data on congenital abnormalities and gestational diabetes were collected and computerized over the 40 month period. However, for accuracy, the hospital charts of the 4,380 infants were reviewed by two of the authors who did not know which mothers were gestational diabetics. Only those abnormalities noted by the pediatrician during the first hospital stay were included in the study. If there were questions regarding the exact diagnosis, other hospitalizations and pediatrician office records were used for clarification. After the list of abnormalities was compiled, the infant data were matched with maternal data and statistically analyzed.

3 Results

The four thousand, three hundred and forty (4,340) patients who were screened for gestational diabetes delivered 4,380 infants. Of these patients, 23% had an abnormal one-hour glucose screen. After a three-hour glucose screen, 4.9% of the whole population were diagnosed as gestational diabetics, and 18% had a normal GTT. The 215 gestational diabetics delivered 217 infants and the 780 normoglycemic mothers delivered 784 infants (Tab. I).

The incidence of congenital malformations in infants of the total population was 2.6%. This finding is slightly higher than the 2.2% found in infants of mothers with normal GTTs but not statistically significant. However, the incidence of congenital malformations in infants of gestational diabetics was 5.1% (Tab. I). This is significantly different from the incidence in infants of mothers with a normal GTT ($p < 0.05$).

Tab. I. Congenital abnormalities, January 1975 through April 1978

Patient groups	Mothers		# of Abnormalities			
	#	%	Infants #		%	
Total patients	4,340	100%	4,380	114	2.6%	
Normal GTT	780	18.0%	784	17	2.2%	
Abnormal GTT	215	4.9%	217	11	5.1%	

To analyze the significance of the above data, the hypothesis of no difference was tested at the 0.05 level with an X^2 test utilizing the YATES correction for continuity. The test statistics have one degree of freedom. When the ages of mothers with malformed newborns are examined, analysis by t-test indicates there is no statistical difference between the mean age of gestational diabetics (29.0 ± 6.6 years) and that of normoglycemic mothers (24.7 ± 4 years).

Tab. II and Tab. III list the types of congenital abnormalities found in the newborns of mother with normal and abnormal GTTs. Using t-tests, the plasma glucose levels of the gestational diabetics who delivered infants with midline defects were compared to those who delivered infants with non-midline defects. The means of their fasting, one, two, and three-hour levels, as well as the sum of all

Tab. II. Congenital abnormalities in pregnancies with normal GTT

Type	Number	% Percentage
Midline Defects (6)		
Cleft lip and/or palate	4	23.5
Cleft lip only (1)		
Cleft palate only (2)		
Both (1)		
Absent uvula	1	5.9
Chordae of penis	1	5.9
Non Midline Defects (11)		
Congenital heart disease	2	11.8
Ventral septal defect (1)		
Type unknown (1)		
Polydactyl	2	11.8
Hand only (1)		
Feet and hand (1)		
Bilateral trigger thumbs	1	5.9
Congenital hip dislocation	1	5.9
Deformed external ear	1	5.9
Hemoglobinopathies	1	5.9
Lissencephaly	1	5.9
Osteogenesis imperfecta and metatarsus adductus	1	5.9
Poland's syndrome	1	5.9
Total	17	100.0

Tab. III. Congenital abnormalities in pregnancies with abnormal GTT

Type	Number	% Percentage
Midline Defects (5)		
Hypospadias	3	27.3
Hypospadias (2)		
Hypospadias and Hypoplastic Scrotum (1)		
Gastroschisis	1	9.1
KLIPPEL-FEIL Syndrome	1	9.1
Non-Midline Defects (6)		
Hemangioma	2	18.2
Deformed external ear	1	9.1
DOWN's Syndrome	1	9.1
Ductus arteriosus	1	9.1
Polydactyly, hand	1	9.1
Total	11	100.0

four levels, are shown in Tab. IV. Fasting, one, two, and three-hour levels are not significantly different between the two groups. However, the sums are significantly different ($p < 0.01$) (Tab. IV). The difference in the sums appears to be due to the accumulated effect of the two and three-hour plasma levels. This is interesting because the work

of ABELL et al. [1] suggests a relationship between the three-hour plasma glucose levels and small-for-gestation babies.

4 Discussion

There are a number of conclusions one may come to base on these data: 1) the incidence of congenital abnormalities in infants of gestational diabetics is increased about two-fold over normal; 2) the increased incidence of congenital abnormalities in gestational diabetics is related more to maternal glucose abnormality than to maternal age; and 3) the occurrence of midline malformations in infants of gestational diabetics may be related to the severity of the glucose intolerance as measured by the sum of plasma glucose levels at fasting, one-hour, two-hour, and three-hour intervals.

Other studies which have attempted to screen all pregnant women with a one-hour glucose load or a three-hour glucose tolerance test have also shown an incidence of gestational diabetes greater than 1 to 2 percent [5, 6, 12]. Several other investigators have found a similar increased incidence of congenital malformations in infants of gestational diabetics while others have not [7, 9, 15]. The varied definitions and screening criteria for gestational diabetes may partially explain these differences.

Tab. IV. The mean and standard deviation of fasting, hourly and sum of plasma glucose levels in gestational diabetic mothers who delivered malformed infants

# of Mothers	Types of Abnormalities	Fasting	1 Hour	2 Hour	3 Hour	Sum*
5	Midline	87.8 $\pm$ 7.6	186.8 $\pm$ 27.1	188.6 $\pm$ 36.4	173.4 $\pm$ 23.5	636.6 $\pm$ 27.2
6	Non-Midline	87.3 $\pm$ 8.5	185.5 $\pm$ 16.8	164.8 $\pm$ 15.2	141.5 $\pm$ 15.2	579.2 $\pm$ 17.2

$p < 0.01$

Summary

The purpose of this study was to compare the types and incidence of congenital abnormalities in the newborns of gestational diabetics with those found in newborns of truly normoglycemic pregnant women identified by a three-hour glucose tolerance test.

Four thousand three hundred and forty (4,340) pregnant women were screened for gestational diabetes. Between 28 and 32 weeks of gestation, each patient was screened with a 50 gram oral glucose load following an overnight

fast. Those patients with a one-hour plasma glucose level greater than or equal to 130 mg% were given a standard three-hour, 100 gram oral glucose tolerance test as previously reported [3, 4]. Gestational diabetes was diagnosed when two or more of the following plasma glucose levels were met or exceeded: Fasting, 100 mg%; one-hour, 180 mg%; two-hour, 160 mg%; and three-hour, 140 mg%. The data on congenital abnormalities were computerized over a 40 month period and verified through review of the

infants' charts or calls to pediatricians by two of the authors.

Twenty three percent of the 4,340 women had abnormal one-hour glucose screens and were given three-hour glucose tolerance tests. Two hundred fifteen women proved to be gestational diabetics making an incidence of 4.9%. These 215 women delivered 217 newborns of whom 11 (5.1%) had congenital abnormalities. Seven hundred eighty women with normal glucose tolerance tests delivered 784

Keywords: Congenital abnormalities, gestational diabetes.

Zusammenfassung

Vorkommen von angeborenen Fehlbildungen bei Kindern von Müttern mit Schwangerschaftsdiabetes

Ziel der Arbeit war es, die Häufigkeit und Art von angeborenen Fehlbildungen zu untersuchen, bei Neugeborenen von Müttern mit einem Schwangerschaftsdiabetes und bei Neugeborenen von Müttern ohne Schwangerschaftsdiabetes. Es wurde der 3-Stunden-Orale-Glukose-Toleranz-Test benutzt. 4340 Schwangere wurden auf Diabetes untersucht. Zwischen der 28. und 32. SSW wurde bei jeder Patientin eine orale Glukosebelastung mit 50 g Glukose durchgeführt. Nur die Patienten mit einem Blutglukosespiegel von ≥ 130 mg% nach 60 min. wurden weiter untersucht [3, 4].

Die Diagnose eines Schwangerschaftsdiabetes wurde erst dann gestellt, wenn zwei oder mehr von den folgenden Blutglukosewerten erreicht wurden: Nüchtern, 100 mg%, nach 60 min. 180 mg%, nach 120 min. 160 mg%, nach 180 min. 140 mg%. Die Daten der angeborenen Fehl-

Schlüsselwörter: Angeborene Fehlbildungen, Schwangerschaftsdiabetes.

Résumé

Incidence d'anomalies congénitales chez des enfants dont les mères souffrent d'un diabète lié à la grossesse

Le but de cette étude était de comparer les types et incidence des anomalies congénitales des nouveau-nés dont les mères avaient un diabète lié à la grossesse, avec des nouveau-nés dont les mères avaient des glycémies normales (identifié par le test de tolérance au glucose). On a examiné 4340 femmes enceintes de 28–32 semaines, on a administré à jeun par voie orale à chaque patiente 50 g de glucose. Les patients qui, après une heure, avaient une glycémie ≥ 130 mg% ont subi le test de standard de tolérance au glucose [3, 4]. On a diagnostiqué un diabète lié à la gestation quand deux ou plusieurs des glycémies suivantes ont été atteintes ou dépassées: – à jeun, 100 mg%; après 1 h, 180 mg%; après 2 h, 160 mg%; après 3 h, 140 mg%. Les cas d'anomalies congénitales ont été suivis sur une période de 40 mois soit en téléphonant aux pédiatres soit

Mots-clés: Anomalies congénitales, diabète lié à la grossesse.

newborns of whom 17 (2.2%) had congenital abnormalities (Tab. I). This difference is statistically significant ($p < 0.05$). Midline malformations seemed to be related to the severity of the glucose intolerance as exemplified by the sum of the means of the fasting, one, two, and three-hour glucose levels (Tab. IV). There was no statistical difference between the mean age of gestational diabetics (29.0 ± 6.6 years) and that of normoglycemic mothers (24.7 ± 4 years).

bildungen wurden über einen 40-monatigen Zeitraum anhand von Telefongesprächen mit Kinderärzten oder anhand der Krankenakten gesammelt.

Von 4340 Frauen hatten 23% einen erhöhten Blutglukosespiegel nach 60 min. und kamen für weitere Untersuchungen in Frage.

215 (4,9%) hatten nach unseren Kriterien einen Schwangerschaftsdiabetes. Es wurden 217 Kinder geboren, wovon 11 (5,1%) Fehlbildungen aufwiesen. Bei 780 Frauen mit normalem Glukosetoleranztest wurden 784 Kinder geboren. Hier wiesen 17 (2,2%) Kinder angeborene Fehlbildungen auf ($P > 0,05$) (Tab. I). Fehlbildungen kommen offenbar häufiger bei stark erhöhten Blutzuckerwerten vor, wie es dargestellt ist in der Summe der Mittelwerte der Blutglukosespiegel nüchtern, nach 1, 2 und 3 Stunden (Tab. IV). Es gab keinen signifikanten Altersunterschied zwischen den Frauen mit und ohne Schwangerschaftsdiabetes.

par examen clinique. 23% des 4340 femmes avaient une glycémie anormale après une heure et subirent le test de standard. 215 femmes (4.9%) avaient un diabète lié à la gestation selon les critères ci-dessus. Les 215 femmes donnèrent naissance à 217 nouveau-nés, parmi lesquels 11 (5.1%) avaient des anomalies congénitales.

780 femmes qui avaient un test de tolérance au glucose normale donnèrent naissance à 784 nouveau-nés parmi lesquels 17 (2.2%) avaient des anomalies congénitales ($p > 0.05$) Tab. I. Les malformations semblent être liées à l'importance de l'intolérance au glucose, ainsi que le montre la somme des valeurs moyennes des glycémies à jeun, après 1, 2 et 3 heures. (Tab. IV). Il n'y avait pas de différence entre l'âge moyen des femmes souffrant d'un diabète lié à la grossesse et les parturientes à glycémie normale.

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Received March 30, 1981. Revised April 10, 1981. Accepted May 25, 1981.

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