Early growth retardation in diabetic pregnancy

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Summary and conclusions

Thirty-five insulin-dependent diabetic women with reliable menstrual histories were examined by ultrasonic scanning in the 7th-14th weeks of pregnancy. Judged from crown-to-rump length the fetuses were on average 5.4 days smaller than those in a local normal series. Ten of the fetuses were nine days or more smaller than normal and had a lower mean birth weight than the others, though the mean gestational age was similar. Maternal diabetes was not more severe in this group, but only two of the mothers had attended a special hospital for control of their disease as compared with 19 of the remainder.

Although babies of diabetic mothers are often overweight, there appears to be a subgroup of cases in which fetal growth is retarded early in pregnancy, leading to low birth weight and possibly a higher incidence of congenital malformations.

Introduction

Babies of diabetic mothers are often large and overweight.¹ Clinical and necropsy evidence suggests that the increased weight gain occurs in the last trimester.² We decided to investigate this phenomenon with ultrasound, and, to confirm menstrual history, conducted the first examination in the first trimester. We noticed that the fetuses in early diabetic pregnancy appeared to be smaller than normal more often than could be explained by erroneous menstrual histories. We report here our findings.

Patients and methods

During 1 October 1976 to 31 January 1978, 90 consecutive insulin-dependent diabetic women were examined by ultrasound during pregnancy and gave birth to infants weighing 1000 g or more. From these women we selected the 35 who fulfilled the following criteria: they had regular menstrual cycles of 28-30 days, had not used oral contraceptives for six months before pregnancy, and had been examined by ultrasound at least once during the 7th-14th weeks of pregnancy.

We used a Nuclear Enterprises Disonograph 4102 scanner with the assumed sound velocity set at 1560 m/s. At examination the fetal

crown-to-rump length (CRL) was measured by Robinson's technique.³ He and Fleming⁴ showed that CRL correlates well with gestational age, which may be predicted to within four or five days. We used their normal tables as a reference for the diabetic pregnancies. To validate our scanning and measuring technique we also compared measurements from a preliminary normal series with their normal tables.

The normal series consisted of 62 healthy pregnant women with regular menstrual cycles of 28-30 days who had not used oral contraceptives for at least three months before pregnancy and who after an uneventful pregnancy spontaneously delivered babies of 2500-4500 g at a gestational age of 280 ± 14 days. In each case two to four CRL measurements had been made in the 7th-14th weeks. For every CRL measurement the corresponding gestational age was read from Robinson's tables and compared with the age calculated from the first day of the last menstrual period and the difference (in days) recorded. This difference was obtained for all CRL measurements in each pregnancy and the average calculated, giving the discrepancy in fetal age as estimated by ultrasound and the menstrual age. Fetuses in the diabetic pregnancies had a normal growth rate as shown by the CRL measurements, so that identical calculations could be made in these pregnancies.

Quantitative results were analysed by the Mann-Whitney unpaired rank sum test, and qualitative results by the fourfold table test (Fisher's exact test).

Results

The distribution of differences between "ultrasound" and menstrual age in the normal pregnancies differed significantly from that in the diabetic pregnancies ($P < 0.001$ —table I). In the 62 normal pregnancies the average difference was -1.1 day (range $+4$ to -9 days). Thus our fetal measurements were consistently an average of 1.1 day smaller than Robinson's, though the degree of precision was similar. Our scanning and measuring technique therefore appeared to be adequate.

In the 35 diabetic pregnancies the difference between ultrasound and menstrual age was 6.5 days (range $+3$ to -21 days). Thus these fetuses were on average 6.5 days too small, or 5.4 days too small when compared with our own normal series. Ten fetuses were outside our normal range, being nine days or more too small. These fetuses had a significantly lower birth weight than the remainder ($P < 0.01$) and included twice as many with congenital malformations (table II). Furthermore, significantly fewer of their mothers had attended a special hospital for control of diabetes before conception or in early pregnancy ($P < 0.01$). There was no difference between the two groups in the severity of the diabetes as judged by White's classification.⁵

Discussion

The reliability of the menstrual data was crucial to this study. Thus out of 90 patients we included only 35, who, to our best knowledge, had a reliable menstrual history. From the results we conclude that fetuses in early diabetic pregnancy are on average smaller than normal.

Most of the patients were examined more than once in early pregnancy and showed normal fetal growth rate. Growth retardation must therefore have occurred before the first ultrasound examination in the seventh week or later. Theoretically

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TABLE I—Distribution of differences between "ultrasound" and menstrual age in 62 early normal pregnancies and 35 early diabetic pregnancies

	Difference in age (days)																					Total					
	+4	+3	+2	+1	0	-1	-2	-3	-4	-5	-6	-7	-8	-9	-10	-11	-12	-13	-14	-15	-16		-17	-18	-19	-20	-21
Normal	1	4	2	9	15	15	7	3	3	1		1	1														62
Diabetic		1		3	1	3	4	2	4	2	2	2	1		3					1	1	2			2	1	35

TABLE II—Clinical characteristics in 35 diabetic pregnancies related to fetal size (crown-rump length) in early pregnancy

	Fetal size within normal range	Fetus ≥ 9 days too small
No of mothers	25	10
White's ⁴ classification of severity of diabetes:		
Group B	4	3
Group C	7	3
Group D	13	4
Group F	1	
No of mothers attending special hospital for diabetic control before conception	19	2
Mean difference between "ultrasound" and menstrual age in early pregnancy (days)	-3.1	-15.0
Mean gestational age at delivery (days)	259	256
Mean birth weight (g)	3580	2800
No of mothers delivering infants with congenital malformations	1	2

delayed ovulation might explain the findings, but our patients had a history of regular 28-30-day menstrual cycles, so that a delay in ovulation of up to 20 days is unlikely. Proof might be gained from patients with a known date of ovulation. At present, however, we have basal body temperature measurements on fewer than 10 patients.

We divided the patients into those in whom early fetal size was within our normal range (25 patients) and those with fetuses nine days or more too small (10 patients) (see table II). Contrary to expectation, there was no difference between the groups in the severity of the diabetes. Although the gestational age at delivery differed by only three days, there was a significant difference in birth weight between the two groups. Fetuses that were nine days or more too small in early pregnancy weighed an average of 780 g less than the remainder at delivery. This may be correlated with the difference of 12 days in ultrasound age. Thus a "delay" in early pregnancy beyond our normal range apparently continues throughout pregnancy. Whether the optimum date of delivery should be adjusted accordingly remains an open question.

Twenty-one of the 35 patients (60%) had for various periods—often years—before the pregnancy attended a special hospital in Copenhagen for control of their diabetes—namely, the Steno Memorial Hospital or the Hvidøre Hospital. The remaining patients, often living far from Copenhagen, had had their disease controlled primarily by their family doctors or at local hospitals. Only two of the 10 patients whose fetuses were nine days or more too small in early pregnancy had been controlled at a diabetes hospital compared with 19 of the remainder (table II). Thus diabetes regulation before conception and during early pregnancy might influence fetal growth in early pregnancy. We could not compare the blood sugar values in the two groups during this period, however, since these data were not available.

Infants of diabetic mothers have an increased incidence of malformations. In a large Danish study malformations were found in 8% of infants of diabetic mothers compared with 2.8% of infants in a control series.⁶ Of the 10 infants in our series who were nine days or more too small in early pregnancy, two had gross, fatal malformations (both had multiple lesions including cardiac malformation). In contrast only one of the remaining 25 infants had a congenital malformation (fatal sacral meningo-myelocoele). Although the numbers are too small for conclusions to be drawn, these observations are interesting, since the observed growth retardation apparently occurs during the vulnerable period of organogenesis.

We think that these correlations with birth weight, control of

maternal diabetes at a special hospital, and possibly the incidence of fetal malformations further substantiate our observation of early growth retardation in diabetic pregnancy. We hope to elucidate this phenomenon further in a larger series.

References

¹ Farquhar, J W, *Archives of Disease in Childhood*, 1959, **76**, 34.
² Cardell, B S, *Journal of Obstetrics and Gynaecology of the British Commonwealth*, 1953, **60**, 834.
³ Robinson, H P, *British Medical Journal*, 1973, **4**, 28.
⁴ Robinson, H P, and Fleming, J E E, *British Journal of Obstetrics and Gynaecology*, 1975, **82**, 702.
⁵ White, P, *Medical Clinics of North America*, 1965, **49**, 1015.
⁶ Pedersen, J, *The Pregnant Diabetic and Her Newborn*, p 193. Baltimore, Williams and Wilkins, 1977.

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ONE HUNDRED YEARS AGO On going into the wards of King's College Hospital on Christmas morning, every person and thing wore a joyous aspect. Every patient had a present suitable to his or her age and at least one Christmas-card. The children had their toys laid out before them on the bright counterpanes, which were all new for that day. Many of the presents were articles of clothing, strong and warm. Some of the children had a suit of clothes given them. Plum-pudding was served out at dinner-time, and, except in a few instances, was enjoyed by a large number of the patients. Carol-singing was now commenced in some of the wards, and was continued until the friends of the patients came to visit them. From two till four o'clock, the visitors were allowed in the wards. When these had all left, each ward had arranged in its centre a gaily lighted table adorned with several varieties of eatables, bon-bons, and small flags. All who were allowed to leave their beds sat up to these tables, and those unable to rise had their beds drawn around and ate their meal in ancient Roman style. According to an old custom, as soon as tea was ended, the resident medical officers went round the wards and distributed a "churchwarden" and an allowance of tobacco and whiskey to each male patient, while the females had a little sherry. Cheering and singing could now be heard continuously throughout the building. From five o'clock until past eleven, the sisters went round to every ward singing Christmas carols, and the patients heartily joined in, "Good King Wenceslas" being the chief favourite. On New Year's Day, there was a repetition of the spirits and tobacco, accompanied by singing. (*British Medical Journal*, 1879.)