

Pregnancy in Diabetes Complicated by Vascular Disease

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SUMMARY

Over 50 years of experience with pregnancy in diabetic women is reviewed. In particular, the maternal and fetal survival in mothers with either microvascular or macrovascular disease is considered. This includes White classes E, F, R, RF, H, and T. In this group of patients with vascular disease, maternal survival during pregnancy is virtually 100 per cent with the exception of class H (ischemic heart disease). Fetal survival has steadily improved throughout the time period examined, but is still considerably below that of pregnancies occurring in women without vascular disease. Long-term maternal survival is adversely affected by the first decade after delivery. *DIABETES* 26:953-55, October, 1977.

The entire experience of the Joslin Clinic with the problems of pregnancy that complicate diabetes covers a period of over three quarters of a century—the 78 years between 1898 and 1975 (table 1). Not every pregnancy failed in the pre-insulin era. In a small series, 10 cases treated from 1898 to 1917, viable fetal salvage was 40 per cent and maternal survival was 66 per cent. The immediate favorable influence of the insulin era on the course of pregnancy in diabetes and on diabetes per se was more significant in respect to maternal experience than it was to fetal. Fetal survival rose only from 40 to 54 per cent during that period, whereas maternal survival rose from 66 to 99 per cent in the same interval. The entire Joslin Clinic obstetric experience of patients treated in the interval of 1898 to 1975 consists of 2,232 viable cases reaching the 28th week. Fetal survival rose from 54 to 86 per cent between the years 1938 and 1958, and from 1958 to 1974 it rose to 90 per cent. The highest survival rate occurred in 1975—100 per cent for maternal and 94 per cent for fetal survival—virtually matching the nondiabetic maternal and fetal survival of the Boston

Hospital for Women. All deliveries of our patients since 1950 have taken place at the Boston Hospital for Women. From 1936 until 1950, Joslin Clinic patients were delivered at the Faulkner Hospital and, prior to 1936, at the New England Deaconess Hospital. A detailed study of outcome in 1975 by class is shown in table 2. Although mortality was low (one infant each in classes B, C, D, E, and F), it is striking to note the almost universal incidence of fetal distress or serious neonatal morbidity in class F. Furthermore, each insulin-dependent class contributed one fatality, even though class F is the smallest numerically. Because of the over-all favorable results with pregnancies in diabetic women followed in recent years, it seemed pertinent and desirable to retrospectively evaluate the highest-risk cases, namely, those with vascular disease. The classes chosen for this study were class R, with proliferating retinopathy; class F, with diabetic nephropathy; class RF, with both retinopathy and nephropathy; and class E (not sought today), with macroangiopathy as evidenced by calcified vessels in the pelvis. Usually these changes are recognized by intravenous pyelography or total vascular surveys and are, of course, not sought during pregnancy. Two new classes, as yet small, are added: class H, for arteriosclerotic heart disease (four cases), and class T, for pregnancy after renal transplantation. This latter class was added by Tagatz et al. at the University of Minnesota. They reported a successful course and outcome in one such patient.¹

RESULTS

A total of 416 cases were reviewed in this report (table 3): class R, 82 cases; class F, 185; class RF, 83; class E, 62; class H, 4; class T, one previable. These 416 cases are divided into two periods: The earlier period, from 1924 to 1962, consists of 271 cases, and the period from 1963 to 1975 consists of 145 cases. The findings in the earlier group have been reported previously² and are included here.

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TABLE 1
Pregnancy and diabetes—Joslin Clinic (viable cases)
1898 to 1975

Dates	Cases (no.)	Fetal survival (%)	Maternal survival (%)
1898-1917	10	40	66
1924-1938	128	54	
1938-1958	900	86	
1958-1974	1,119	90	
1975	75	94	
Total	2,232		

TABLE 2
Joslin diabetic pregnancies, 1975
perinatal survival rate: 94.4 per cent

N	Class	Fetal distress	Neonatal serious	Morbidity mild
6	A	0	0	1
10	B	2	1	5
33	C	4	2	21
17	D	5	2	12
5	F	2	3	1
71 Reaching 20 weeks' gestation				
Spontaneous abortion rate: 15%				

TABLE 3
Viable fetal survival—vascular series 416 cases

Class	1924-1962		1963-1975	
	No.	Survival (%)	No.	Survival (%)
R	34	74	48	84
F	126	65	59	72
RF	53	54	30	81
E	58	76	4	100
H	0	—	4	75
T	0	—	(1 previable)	—
Total	271		145	

The maternal survival in the early group, 1924 to 1962, was nearly 100 per cent. This favorable result indicated that young women with diabetes could achieve motherhood with safety. However, their chances for delivering liveborn, surviving infants were not only less than the 97 per cent viable survival of the general population but also less than the very high survival in diabetes without vascular lesions. In the two series reported here, fetal survival rose in all classes that appeared in both series. In class E, fetal survival rose from 76 per cent in 58 cases to 100 per cent in a very small series of four cases. In class F the survival rose from 65 per cent in 126 cases to 72 per cent in 54 cases. In class RF the rise was from 54 per cent in 53 cases to 81 per cent in 30 cases. In the very small class H (four cases) fetal survival was 75 per cent. The only class-T pregnancy was terminated in the previable

period. In only one class was maternal survival threatened. Of the four patients in class H only one mother survived. One young woman died undelivered. Two died within the four-week period after delivery. The only maternal survivor in this group was a patient who had had coronary bypass surgery performed three months prior to her pregnancy. Two of the three children survived their mothers. The experience of the other three young women indicates the need for careful evaluation of the cardiac status in those patients with diabetes of long duration and with an early age of onset. The pregnancy of one patient in class T was terminated. Only live, related-donor kidneys have a long survival in diabetics,³ and she possessed the only one that matched, and she had a living son with multiple anomalies that were not of functional significance.

DISCUSSION

The course of pregnancy in this vascular group differed from the usual course in diabetes in several aspects. When intrauterine deaths occurred, they tended to occur earlier than the 36th week. The characteristics of the placenta in this group had been described as revealing panvascular changes including medial hyalinization and stenosis of the arteriolar lumens.⁴ Decidual and placental ischemia are inferred. Hyalinosis occurred in 50 per cent and atherosclerosis in 20 per cent. In the renal groups, classes F and RF, the placenta was small. The effect of the maternal and placental vascular complications on the growth and development of the fetus was also evident. In contrast to the experience with infants of mothers without vascular lesions, fetal macrosomia did not occur. These infants were less cherubic in appearance and only moderately obese. The frequency of hyperbilirubinemia and the respiratory-distress syndrome paralleled their degree of prematurity. The frequency of congenital anomalies was comparable to the series as a whole, 13 per cent. The course of maternal diabetes was less intensified in this complicated series. The expected large increase in insulin over the prepregnancy level did not occur. Stable and even decreased doses of insulin were obtained in 40 per cent of the cases. A possible explanation for the decreased requirement for insulin in these patients is the impairment of function in structures such as the kidney⁵ or placenta,⁶ responsible for the degradation of insulin. Some pregnancies were interrupted because of decreasing renal function. No patient, however, required hemodialysis during pregnancy.

Many of these patients received female sex hormone therapy. This was discontinued after the demonstration by Leavitt of adenosis of the vagina in 23 per cent of the daughters of mothers so treated.⁷ Yalom et al. report a decrease in masculinization, measured by aggression, and a tendency toward femininity in the sons of mothers so treated.⁸ In an earlier study, 58 offspring of the first group shown in table 3, ages 11 to 25, were recalled. Five per cent had overt diabetes; 17 per cent had positive glucose tolerance tests. A greater number of congenital anomalies were observed in the slightly older group, namely, 26 per cent. Maternal internal environment did not seem to influence the tendency to diabetes in the offspring. The rate of overt diabetes and chemical diabetes in the offspring of diabetic fathers was 19 per cent, but the offspring of diabetic fathers do not show an increase in the rate of congenital anomalies that is seen in the offspring of mothers with diabetes. A follow-up of mothers in group 1 of the series, delivered between 1924 and 1962, was done in 1963.¹⁰ At that time, the average age of the patients (mothers) was 35 and the average duration of diabetes was 23 years. 32 of the 144 women who had had the 271 pregnancies had died (22 per cent). The average survival since their pregnancy was eight years. Therefore, one child in five had lost a mother before reaching 10 years of age. This impressive mortality is felt not to differ from the expected outcome of patients with diabetes that is complicated by vascular disease who were not pregnant. In a retrospective review of patients with diabetic nephropathy¹¹ the mortality was even higher. This is consistent with the outcome in our group, since retinopathy usually precedes nephropathy. Those patients with only retinopathy would be expected to have a longer survival than those who already had nephropathy.

Pedersen et al. have published data from a large retrospective survey of their diabetic pregnant population. Their results were similar to ours. The over-all fetal survival from 1966 to 1972 of 90 per cent is the same as our experience from 1958 to 1974. They found a 44 per cent mortality in class F, which includes White classes F, R, and RF, from 1946 to 1965 and a 19 per cent mortality from 1966 to 1972. If our results are similarly expressed (by grouping classes F, R, and RF) we find a 36 per cent mortality from 1924 to 1962 and a 22 per cent mortality from 1963 to 1975.¹²

CONCLUSION

Maternal survival from pregnancy is practically assured except in those with ischemic heart disease. Viable fetal survival in the series as a whole has reached that of women without diabetes delivered in the same hospital, but not if vascular disease is present. Immediate fetal survival in all cases has resulted from many factors, including improved insulins, antimicrobial agents, and specific tests applicable to pregnancy in diabetes for assessment of fetal health. Maternal survival was adversely affected in one small group with unrecognized ischemic heart disease. Subsequent maternal survival is significantly decreased by the first decade after delivery.

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