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Diabetes Mellitus and Pregnancy – Management and Results at Rikshospitalet, Oslo, 1970–1977

J. Jervell, N. Moe, J. Skjæraasen, W. Blystad, and K. Egge

Rikshospitalet, Oslo, Norway

Summary. During the years 1970–1977, 234 pregnant diabetics were treated in Oslo. A regimen of close metabolic and obstetric control was used. The total perinatal mortality was 4.3%, and 3.1% in 160 patients followed from before week 28. In 74% of patients mean blood glucose (determined 4 times daily) during the last 5–6 weeks of pregnancy was below 6 mmol/l and in only one patient above 8 mmol/l. There was a low incidence of ketoacidosis (5 patients), pyelonephritis (3 patients), and severe preeclampsia (1 patient), although mild to moderate preeclampsia occurred in 28 patients. Preeclampsia was not associated with foetal loss. Macrosomia was rare. Respiratory distress occurred in 33 infants, in most cases light to moderate. Two foetal deaths were associated with respiratory distress. Progression of retinopathy was frequent, and appearance of or progression of proliferative changes occurred in 15 patients with retinopathy before pregnancy. Loss of visual acuity was rare, and reading vision was not lost by any patients. Induced vaginal delivery has been used in half the deliveries during the last years, whereas Caesarean section was preferred during the first years. Mean duration of pregnancy at delivery has been 260 days, 256 days during the first four years, and 262 days during the last four.

Key words: Diabetic pregnancy, perinatal mortality, diabetic retinopathy, respiratory distress syndrome, birth weight, delivery methods, White classification.

A regimen of close metabolic and obstetric control has in many centres reduced the previously high perinatal mortality in diabetic pregnancies [2, 3, 4, 8, 10, 11]. The present study reports the experience gained at Rikshospitalet, Oslo, during a regimen of intensive management started in 1970.

Material and Methods

Our study includes all 234 deliveries during the period 1970–1977, where a definite diagnosis of diabetes mellitus had been made prior to pregnancy. Patients in whom abnormal glucose tolerance was found for the first time during pregnancy, were excluded. The patients were subdivided according to a modified White's classification [12.16] based on the situation before pregnancy:

A: Treated by diet alone or diet + oral antidiabetic drugs, no complications.

B: Insulin-treated, diagnosed at age 20 or later, no complications.

C: Insulin-treated, diagnosed before age 20 years, no complications.

D: Patients with non-proliferative retinopathy.

F: Patients with proliferative retinopathy and/or nephropathy.

Pregnant diabetics who had a spontaneous or induced abortion before the 20th week of pregnancy, were also excluded.

Management

Diabetic. Pregnant diabetics were admitted to the obstetric ward for a short stay as soon as contact was established, preferably in the first trimester. They were put on a strict diet of 5 meals, and insulin was given twice daily as a mixture of medium and short acting forms. Thereafter they were controlled as outpatients every week with fasting and noon glucose determinations as well as quantitative morning and evening urine glucose determinations. Insulin dosage was adjusted according to results and hypoglycaemic symptoms. Those patients who for geographical reasons were controlled elsewhere, were admitted to our ward for short periods every month. All patients were hospitalized from gestational week 32–33 until delivery. In this last phase blood glucose levels were determined 4 times daily, and insulin dose adjusted every morning. Our aim was and is to keep blood sugar levels near to normal (4–5 mmol/l) throughout pregnancy.

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Table 1. Perinatal mortality 1970–1977

Modified White's Class	Number of pregnancies (%)		Perinatal mortality n	%	Mean duration of pregnancies (days)
A	12	(5.1)	1	8.3	262
B	40	(17.1)	0	0	259
C	88	(37.6)	1	1.1	263
D	68	(29.1)	4	5.9	258
F	26	(11.1)	4	15.4	252
	234	(100)	10	4.3	260

Of the 10 perinatal deaths 2 occurred in utero before first admission to the obstetric ward at Rikshospitalet. Of the 26 patients in class F, 10 had proteinuria before pregnancy and of these 2 had moderate reduction in renal function. In one severe deterioration of renal function occurred during pregnancy. The perinatal mortality in class F is significantly higher than in classes A–D ($\chi^2 = 8.84$, $p < 0.005$). The mortality in class D and F combined is significantly above that of A, B and C ($\chi^2 = 6.6$, $p < 0.02$)

Table 2. Causes of perinatal death

Intrauterine deaths	
Keto-acidosis	2
Uraemia	1
Malformations[a]	2
Unexpected intrauterine death	2
Intrauterine growth retardation	1
Neonatal deaths	
Respiratory distress syndrome	2
	10

[a] Multiple malformations (White D) – Hydrocephalus (White F)

Table 3. Duration of pregnancy at first admission to Rikshospitalet

			Perinatal deaths	
	n	%	n	(%)
Before week 14	87	37.1	2	(2.3)
Weeks 14–27	83	35.5	3	(3.6)
Weeks 28–34	54	23.1	4	(7.4)
After week 34	10	4.3	1	(10.0)
	234	100	10	(4.3)

Table 4. Mean blood glucose levels during last hospital stay prior to delivery (usually 5–6 weeks). Blood sugar determinations were made 4 times daily

	%
<5.5 mmol/l	47
5.5–6.0 mmol/l	27
6.1–7.0 mmol/l	19
7.1–8.0 mmol/l	6.5
>8 (8.3 mmol/l)	1 patient

Obstetric. The obstetrician, together with the diabetologist, performed the weekly out-patient clinic. During the last stay in hospital the patients were followed by serum HPL and urine oestriol determinations twice weekly, daily if signs of preeclampsia or foetal growth retardation occurred. Ultrasonography was performed weekly. Amniocentesis for determination of lecithin/sphingomyelin (L/S) ratio in the amniotic fluid was performed to assure foetal lung maturity before planned delivery.

Delivery methods changed somewhat during the period. In the beginning Caesarean section was performed in all cases unless spontaneous labour occurred. Latterly, induced vaginal delivery was preferred, Caesarean section being performed only when there was serious retinopathy, previous Caecerean section, or other obstetric complications. Prostaglandin F_2 α was routinely used for induction of labour with a success rate of 78%.

Planned delivery was made 1–3 weeks before term, unless there had been indications for earlier delivery, e. g.; foetal distress or serious progression of retinopathy.

Ophthalmological. The patients were examined by an ophthalmologist before pregnancy or as early in pregnancy as possible. Patients with retinopathy were closely observed throughout pregnancy.

Paediatric. Paediatricians were present at most deliveries. All newborn infants were observed at the paediatric department for at least 24 h after delivery.

Results

Perinatal Deaths

The regimen described above is accompanied by low perinatal mortality (Table 1). Only 2 out of the 10 deaths occurred prior to the first admission. The causes of perinatal deaths are shown in Table 2. There were no maternal deaths.

During the period 1970–1977 there was an increase in the number of patients admitted from 10–20 up to 40 per year. A large proportion of patients were seen from early pregnancy onwards (Table 3). The perinatal mortality increases with increasing duration of gestation upon first admission. This increase, although suggestive, does not reach statistical significance.

Metabolic Control

Table 4 demonstrates the blood glucose control achieved during the last stay in hospital. This stay lasted 5–6 weeks in most cases, although some patients were admitted to the program at a later stage (Table 1). Blood glucose were determined 4 times daily except during week-ends. Mild hypoglycaemic symptoms were frequent. Only rarely, and in most cases in early pregnancy, did severe hypoglycaemia with cerebral symptoms occur (8 patients).

Ketoacidosis was infrequent, occurring in 5 patients only (Table 5). In only 25 patients were

extra admissions needed because of unsatisfactory metabolic control.

Good blood glucose control was always easy to achieve in the modified White's Class A, more difficult in classes B–D, and in class F 6 out of 26 were readmitted for metabolic adjustment during pregnancy.

Other Complications

Pede en [10] has described the so-called prognostically bad signs during pregnancy (PBSP). In our study these were relatively rare (Table 5).

There was a 10.7% occurrence of macrosomia (birth weight above the 97.5 percentile [1]). Table 6 shows the frequency of respiratory distress syndrome and postnatal hypoglycaemia. There was a high frequency of respiratory distress in children whose birth weight was below 2500 g. Mean duration of gestation in this group was, however, only 246 days.

There were 13 children with malformations (Table 7). Six of these had cardiovascular malformations. Eight of the children with malformations were born to mothers who were in the modified White's classes D and F.

Previous Pregnancies

Out of 234 patients 101 were multiparous. Forty of these had given birth in previous pregnancies to one or two children who died in the perinatal period; on this regimen only one perinatal death occurred. In total the 101 multiparous patients lost 3 children in the perinatal period (3.0%).

Retinopathy

The occurrence and/or progression of retinopathy during pregnancy are shown in Table 8. In cases with no signs of retinopathy prior to pregnancy (modified White's Classes A, B, and C) only one patient developed serious retinopathy. The results, however, were less good in cases classified as D or F; 10% and 29% respectively developed serious progression of the retinopathy during the pregnancy. In 6 patients some loss of vision occurred; in no case, however, was ability to read lost. No systematic follow-up has been made. It is, however, our impression that marked regression of retinopathy occurred after delivery in most cases.

Time and Method of Delivery

Table 9 demonstrates the time and the method of delivery of our patients. Figure 1 shows how the methods of delivery have changed during the period. During the period 1970–73 mean duration of pregnancy at delivery was 256 days, during the last 4 years 262 days.

Table 5. The frequency of "Prognostically Bad Signs during Pregnancy" [12]

Modified White's Class	Keto-acidosis		Pre-eclampsia[a]		Pyelonephritis		Neglectors	
	n	(%)	n	(%)	n	(%)	n	(%)
A	0	(0)	1	(8.3)	0	(0)	0	(0)
B	0	(0)	2	(5.0)	0	(0)	0	(0)
C	2	(2.3)	6	(6.8)	2	(2.3)	2	(2.3)
D	2	(2.9)	10	(14.7)	1	(1.5)	0	(0)
F	1	(3.8)	9	(34.6)	0	(0)	0	(0)
All	5	(2.1)	28	(12.0)	3	(1.3)	2	(0.9)

[a] In only one case severe preeclampsia, in no case associated with foetal loss

Table 6. Birth weight, "respiratory distress syndrome" (RDS) postnatal hypoglycaemia and duration of pregnancy in living infants of diabetic mothers

Birth weight (g)	n	RDS[a]		Hypoglycaemia[b]		Mean duration of pregnancy (days)
		n	(%)	n	(%)	
<2500	19	9[c]	(47.4)	2	(10.5)	246
2501–3500	108	13[c]	(12.0)	15	(13.9)	260
3501–4500	96	8	(8.3)	12	(12.5)	263
>4500	6	3	(50.0)	3	(50.0)	251
Total	229[d]	33	(14.4)	32	(14.0)	260

[a] All grades of RDS are included. Most cases were mild to moderate

[b] Hypoglycaemia: Blood glucose below 1.5 mmol/l in the postnatal period. Asymptomatic in all cases

[c] Two deaths from RDS, one in each weight group

[d] Including 3 pairs of twins

Table 7. Malformations and modified White's Class in diabetic pregnancies

Cardiovascular[a]	6 (2C, 2D, 2F)
Hydrocephalus[b]	1 (F)
Blindness	1 (F)
Mesenteric	1 (D)
Achondroplasia	1 (B)
Polydactyly	1 (C)
Bilateral inguinal hernias	1 (A)
Multiple malformations[b]	1 (F)

[a] No perinatal deaths, one death 31 days after delivery

[b] Intrauterine death

Discussion

The present study demonstrates clearly, as has been shown by others [2, 3, 4, 8, 10, 11], that improved results of diabetic pregnancies are possible. Close

Table 8. Occurrence and/or progression of retinopathy during pregnancy

Modified White's Class	n	Mild progression of retinopathy		Serious progression of retinopathy	
		n	(%)	n	(%)
A	12	1	(8.3)	0	(0)
B	40	2	(5.0)	0	(0)
C	88	22	(25.0)	1	(1.1)
D	68	17	(25.0)	7[a]	(10.3)
F	26	10	(38.5)	8[b]	(30.8)

Serious progression is defined as an increase in or appearance of proliferative changes (in practically all cases on the retina), or marked increase in simple retinopathy

[a] Photocoagulation performed during pregnancy in one case

[b] Photocoagulation performed during pregnancy in 3 cases

Table 9. Time and method of delivery of 234 diabetic patients

Duration of gestation (days)	n	Caesarean section		Vaginal delivery	
		n	(%)	n	(%)
<245	16	9	(72)	7	(28)
245–258	60	46		14	
259–272	107	63	(59)	44	(41)
>272	16	9		7	
Unknown	35	19		16	
	234	146	(62)	88	(38)

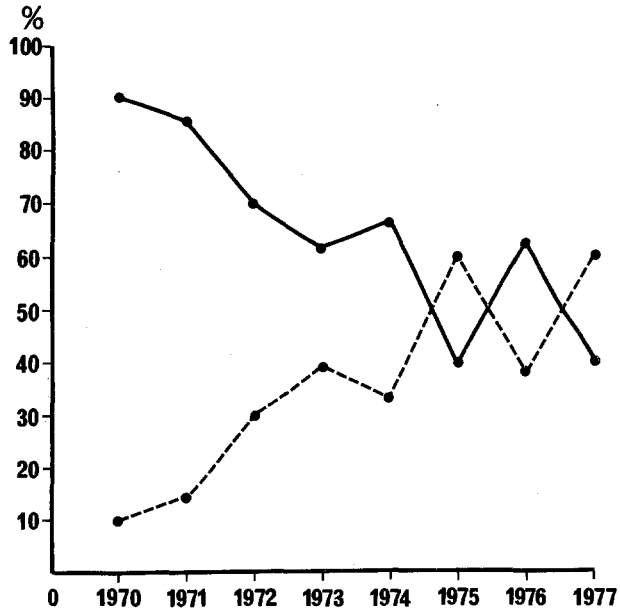

Fig. 1. Changes in delivery methods during the years 1970–1977. ●– – – –● vaginal delivery. ●————● Caesarean section

metabolic control through a greater part of pregnancy is probably the main factor. During the period 1950–1970, when the perinatal mortality at Rikshospitalet, Oslo, was 22%, most of the perinatal deaths occurred before the first admission to the hospital; these were often associated with poor metabolic control and/or preeclampsia [14].

The so-called prognostically bad signs [12] (urinary tract infections, ketoacidosis, and neglectors), were relatively uncommon during the last 8 years. The incidence of preeclampsia was still rather high. In only one case, however, was the condition serious, and in no case associated with foetal loss. Furthermore, the infants rarely had severe hypoglycaemia, or macrosomia. Close metabolic and obstetric supervision thus not only decreases foetal loss, but is also associated with a reduction in Pedersen's prognostically bad signs during pregnancy [12], and with fewer non-fatal foetal complications.

Pregnancy was associated with progression of retinopathy in some cases even when close metabolic control was achieved. In our modified White Classes A, B and C pregnancies, only one case of "serious" progression occurred. Our limited experience indicates that photocoagulation may be used successfully in pregnancy, as shown by others [5]. It is also our impression that progression of retinopathy stops after delivery, and in a number of cases marked regression occurred [6]. Systematic follow-up, however, remains to be done. In a few patients rapid progression of proliferative retinopathy led to the interruption of pregnancy before the 20th week.

It is doubtful if further improvement can be achieved by presently available methods, although self-determination of blood glucose may be used to assure better metabolic control through a greater part of pregnancy [13, 15].

It has been suggested that optimal metabolic control at conception and during the first trimester may prevent malformations. In our study increased frequency of malformations occurred chiefly in the modified White Classes' D and F, where signs of microangiopathy are present before pregnancy. Similar findings have been made by Mølsted-Pedersen et al. [7].

References

1. Bjerkedal, T., Bakketeig, L., Lehmann, E. H.: Percentiles of birth weights of single live births at different gestation periods. Acta Paediatr. Scand. **62**, 449–457 (1973)
2. Drury, M. I., Greene, A. T., Stronge, J. M.: Pregnancy complicated by clinical diabetes mellitus. Obstet. Gynecol. **49**, 519–522 (1977)
3. Essex, N. L., Pyke, D. A., Watkins, P. I., Brudenell, J. M.,

Gamsu, H. R.: Diabetic pregnancy. Br. Med. J. **1973 IV**, 89–93
4. Karlson, K., Kjellmer, I.: The outcome of diabetic pregnancies in relation to the mother's blood sugar level. Am. J. Obstet. Gynecol. **112**, 213–220 (1972)
5. Kohner, E. M., Hamilton, A. M., Tunbridge, W. M. G.: Diabetic retinopathy managed through a pregnancy. Proc. R. Soc. Med. **66**, 442–444 (1973)
6. Korp, W., Lenhardt, A., Levett, R. E., Neubert, J.: Juveniler Diabetes, Schwangerschaft und Retinopathie. Wien. Klin. Wochenschr. **83**, 814–817 (1977)
7. Mølsted-Pedersen, L., Tygstrup, I., Pedersen, J.: Congenital malformations in newborn infants of diabetic women. Correlation with maternal diabetic vascular complications. Lancet **1964 II**, 1124–1126
8. Møller, Eva-Brita: Studies in diabetic pregnancy. Thesis. Studentlitteratur, Lund (1970)
9. Oakley, W.: The evolution of the management of diabetic pregnancy. Postgrad. Med. J. (Suppl. on Diabetes Mellitus) 802–805 (1969)
10. Pedersen, J., Mølsted-Pedersen, L., Andersen, B.: Assessors of fetal perinatal mortality in diabetic pregnancy. Analysis of 1332 pregnancies in the Copenhagen series, 1946–72. Diabetes **23**, 302–305 (1974)
11. Pedersen, J., Mølsted-Pedersen, L., Andersen, B.: Perinatal foetal mortality in 1245 diabetic pregnancies. Secular trends 1946–1971 and variations according to the White and PBSP classifications. Acta Chir. Scand. [Suppl.] **443**, 191–193 (1973)
12. Pedersen, J.: The pregnant diabetic and her newborn. Second edition. Copenhagen: Munksgaard 1977
13. Sönksen, P. H., Judd, S. L., Lowy, C.: Home monitoring of blood glucose. Lancet **1978 I**, 729–732
14. Vangen, O., Molne, K., Bjøro, K.: Diabetes mellitus og svangerskap. Den perinatale mortalitet ved Rikshospitalet, Kvinneklinikken i tiden 1950–1970. Tidsskr. Nor. Lægeforen. **92**, 1313–1317 (1972)
15. Walford, S., Gale, E. A. M., Allison, S. P., Tattersall, R. B.: Self-monitoring of blood glucose. Lancet **1978 I**, 732–735
16. White, P.: Pregnancy and diabetes. Medical aspects. Med. Clin. North Am. **49**, 1015–1024 (1965)

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Dr. J. Jervell
Rikshospitalet
Department of Medicine
Oslo 1
Norway