PREGNANCY COMPLICATED BY DIABETES MELLITUS

A STUDY IN COMBINED OBSTETRIC AND PAEDIATRIC MANAGEMENT

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(RECEIVED FOR PUBLICATION FEBRUARY 27, 1959)

Diabetes mellitus in association with pregnancy is an infrequent finding. The present paper gives the results of a series of 94 cases delivered in the Leeds Maternity Hospital during the period January 1, 1947, to August 31, 1958, inclusive. These results are the collective responsibility of a team consisting of an obstetrician, a physician experienced in diabetes mellitus, a paediatrician and their assistants. The results reflect also the value of highly skilled nursing care of the newly born baby.

Clinical Material

In the period during which the 94 women with diabetes mellitus were admitted there were 22,574 deliveries in the hospital. A large proportion of the mothers with diabetes mellitus were referred from the diabetic clinic at the Leeds General Infirmary.

Management

Obstetric. The obstetricians concerned do not hold identical views about management but in general apply the principles advocated by Peel (1955). Pregnancy is usually terminated at 36 or 37 weeks because of the liability of foetal death *in utero* to occur in the last weeks of pregnancy and because of the higher incidence of pre-eclampsia when pregnancy is allowed to continue to term. Only 24 patients were delivered at or after 38 weeks. Occasionally section or induction is performed earlier than the thirty-sixth week, the usual indication being pre-eclampsia. When premature labour begins spontaneously before 36 weeks vaginal delivery is awaited.

It would be incorrect to say that primigravidae have always been delivered by section. During the last three years however, section was performed on all primigravidae not delivered before 36 weeks. In multiparae with a satisfactory obstetric history, trial is given to vaginal delivery after induction usually not later than 37 weeks. A subsequent

decision to perform section may be determined by the occurrence after induction of delay in going into labour, of slow labour or of foetal distress.

Paediatric. Importance is attached to postural drainage at the time of delivery but the stomach is not aspirated as a routine. During the early years of the study infants were nursed in open cots and use of an incubator was limited to babies with evidence of respiratory embarrassment, hypothermia or pronounced frailty. This policy was abandoned in 1953. Since then all newly born babies of diabetic mothers have been nursed for an initial period varying from 24 hours to one week in an incubator with the objects of providing optimum conditions for clinical observation and of favouring constancy of body temperature. Increased humidification of the air is employed only when there are signs of severe, persistent or progressively worsening respiratory distress suggestive of 'hyaline membrane disease'. Oxygen therapy is reserved for infants with sustained or intermittent attacks of cyanosis and infants with persistent respiratory distress. Intra-gastric administration has not been employed on any occasion. Premature infants are given $\frac{1}{2}$ mg. Synkavit i.m. soon after birth.

Feeding is commenced as a routine on the second day of life, use being made of a bottle, a Belcroy or oesophageal tube according to the strength and capabilities of the infant. Human milk obtained from the mother or hospital banked breast milk is given for a minimum period of two weeks. The amounts of milk offered the infant are calculated on a basis of weight and estimated gestation. In general an infant receives each day $1\frac{1}{2}$ oz. of milk per lb. (0.45 kg.) of body weight by the end of the first week and $2\frac{1}{2}$ oz. per lb. body weight at the end of the second week of life. Reluctance to feed is not regarded as an adequate reason for reducing the amount of milk offered. In these circumstances oesophageal feeds are given by skilled nursing staff.

Antibiotics are employed in the presence of established infection but not as a prophylactic measure.

Results

(1) **Maternal Mortality.** There was one maternal death in the series. The patient was sent by her family doctor to book at 19 weeks, and the presence of maternal diabetes was first discovered at the ante-natal clinic. Referred back to her doctor for ante-natal care she was next seen when admitted to hospital in diabetic coma at 27 weeks. At the time of admission the blood sugar was 0.55 % and the urine contained a considerable amount of acetone and albumin. Despite treatment anuria developed and death occurred on the day following admission without the mother having been delivered. At post-mortem examination cortical necrosis of the kidneys was found.

(2) **Foetal Loss According to Treatment.** The results are summarized in Table 1. There was no

The total foetal loss was 25 in the series of 94 pregnancies. Seven of the 27 infants of patients who had pre-eclampsia did not survive, the rate of foetal loss among these mothers approximating closely to that for the whole series.

The highest foetal mortality occurs in the spontaneous labour group. There were eight stillbirths. Of these two occurred at or before 32 weeks and another was born at 36 weeks but had been dead for several weeks. These were probably unpreventable. Four babies died *in utero* at or after 36 weeks, their weights being 4 lb. 13 oz., 6 lb. 9 oz., 7 lb. 8 oz. and 8 lb. 2 oz. Earlier termination of pregnancy might have saved some and possibly all of these four babies. Caesarean section had been decided upon for the smallest of these babies but was delayed to allow the infant to increase in size. Unfortunately the foetal heart sounds disappeared two days before the date fixed for section. Trauma accounted for the eighth stillbirth. The baby presented by the brow, the outlet being described as contracted. Delivery was by mid-forceps after conversion to an occipito-posterior position.

Intra-uterine death had occurred before induction of labour was carried out in all the three stillbirths associated with this procedure. One died at 32 weeks. Another was born at 38 weeks, death having occurred at some unrecorded time previously. The third was to have had caesarean section but this was delayed because the patient had multiple abscesses and there was difficulty in controlling the diabetes. Meanwhile the foetal heart disappeared at 37½ weeks. Unfortunately none of the stillborn babies was submitted to post-mortem examination.

Three neonatal deaths occurred among infants in the spontaneous labour group. Autopsies were carried out on all three. The cause of death was shown to be due in one to severe haemolytic anaemia recognized during life and not attributable to rhesus incompatibility, and in another to gross developmental anomalies involving the heart and great vessels. Death of the third baby resulted from extensive intracranial haemorrhage secondary to bilateral tentorial tears, after delivery at 35 weeks, episiotomy having been omitted.

Thirty-five patients in the total series were delivered by caesarean section. There were three neonatal deaths in this group. Death in one infant was due to massive bilateral suprarenal haemorrhage, and in the other two babies was associated with the presence of hyaline membrane widely distributed throughout the lung structures.

(3) **Neonatal Mortality.** As already indicated there were six neonatal deaths in a total of 75 live

TABLE 1

MATERNAL DIABETES MELLITUS: FOETAL LOSS
ACCORDING TO OBSTETRICAL TREATMENT

Obstetrical Treatment	Total	Living*	Still-born†	Died	Abortion
Spontaneous labour ..	24	13	8	3	—
Spontaneous abortion ..	4	—	—	—	4
Died undelivered ..	1	—	—	—	1
Induced abortion (hysterectomy) ..	3	—	—	—	3
Induced labour ..	29	26	3	—	—
Caesarean section ..	35	32	—	3‡	—
Total ..	96	71	11	6	8
Less§ ..	2	2			
	94	69			

* A child is regarded as liveborn if he breathes or shows other signs of life after complete expulsion from his mother at any stage of pregnancy.

† A child who has issued from his mother after the twenty-eighth week of pregnancy but has not at any time after being completely expelled from his mother breathed or shown any other signs of life is considered to be stillborn.

‡ A fourth child died aged 6½ weeks from congenital heart disease.

§ Two patients, both of whose babies survived, are included against both 'Induced labour' and 'Caesarean section'. Both patients required section because the response to puncture of the membranes was unsatisfactory: abnormal uterine action developed in one, and ketosis in the other.

example of multiple pregnancy. Sixty-nine infants survived the neonatal period. Eleven babies were stillborn and six died post-natally. There were seven abortions including three induced surgically, and the undelivered foetus of the mother who died.

births. Death took place within 18 hours of birth in all except the baby with haemolytic anaemia, who died aged 38 hours. Of the six infants the estimated gestation period was 36 weeks in the case of two and between 33 and 35 weeks in the case of the remaining four. One baby was not weighed. Birth weights of the remaining five infants averaged 5 lb. 13 oz., the smallest being 3 lb. 12 oz. and the largest 7 lb. 15 oz.

(4) Neonatal Morbidity. Congenital anomalies were noted in 10 liveborn babies. They consisted of developmental errors involving the heart (five), the facial appendages (one), microphthalmia (one), the urinary tract (one), the feet (one) and the skin (one). Congenital heart disease was associated in one case with hydrocephalus and absence of the right tibia and fibula. The urinary tract anomaly consisted of a recto-vesical fistula in a baby with gross talipes and extensive hirsuties. The skin anomaly consisted of a strawberry naevus. There was no apparent connexion between the duration or severity of the maternal diabetes and the occurrence of foetal anomalies. In all 10 mothers of babies with developmental errors, the diabetes had been effectively controlled before and during pregnancy. Control had been dietetic in four, and dietetic combined with insulin in six mothers. The duration of the maternal diabetes ranged from two months to 17 years and the age at onset from 13 to 33 years.

Localized bruising or petechiae were noted in 24 infants. In the majority the bruising was evident within 24 hours of birth but in a few it appeared at any time during the first three or four days of life. There were a few instances of bruising in situations known to have been subjected to slight but not abnormal pressure, but there was no history of local pressure in the majority of cases.

Superficial infection was noted in 31 babies. The eye and/or skin was involved in 28, the secretory glands in two, and the mouth in one. Ophthalmia in one infant was due to *Esch. coli* and the single example of buccal infection was monilial. *Staphylococcus aureus* was isolated in the remaining 29 babies. There was no example of deep or generalized infection.

Neuromuscular hyperexcitability commencing within 36 hours of birth was a feature of the clinical picture in 35 infants in the series. In its severest form the hyperexcitability presented as clinical tetany and was associated with a serum calcium level of less than 8 mg. per 100 ml. in 10 cases investigated biochemically. Convulsions occurred in two of these cases. In no baby were there symptoms due to hypoglycaemia.

Enlargement of the liver was a common finding. It was present in 48 infants. The degree of enlargement was considerable, the lower border of the organ being at or almost at the level of the umbilicus with the infant in the recumbent position. Precise measurement was not possible but, in assessing enlargement, the upper level of liver dullness was determined as a routine and account was taken of the extent to which the lungs had expanded. The consistence of the enlarged organ was invariably firm. Liver enlargement was found in the majority of the babies with superficial bruising and/or superficial infection and the infants showing marked reluctance to feed.

Enlargement of the liver was a feature of the majority of infants with a 'Cushing appearance'. The term 'Cushing appearance' refers to associated large size (macrosomia) having regard to the estimated gestation period; pendulous cheeks and heavy 'moon facies'; unusual coloration, consisting of a mulberry tinge giving place to what has been described as a 'sunset glow'; and generalized hypotonicity. This picture was present at birth in different degrees in 61 babies. In four cases the picture became increasingly obvious during the three or four days following birth. Disappearance of the Cushing characteristics was gradual and preceded by reduction in the size of the liver. The time taken for complete disappearance of the high coloured 'moon facies' varied from 10 days to four weeks. Cushing features were present in all the infants with evidence of neuromuscular excitability.

Fourteen infants (seven females and seven males) lacked the Cushing appearance. There was no abnormal clinical sign in 11 of these babies. Superficial infection was present in two infants, and acute respiratory embarrassment together with enlargement of the liver in one.

(5) Birth Weights of Liveborn Babies. Seventy-four of the 75 liveborn babies were weighed at birth. Birth weights varied from 2 lb. 13 oz. to 10 lb. 9 oz. and averaged 7 lb. 2 oz.

(6) Post-natal Weight Loss. Maximum weight loss in the first week of life ranged from 2 to 17% of the birth weight, averaging 7.8% for the 72 babies for whom adequate weight records were made. The day on which weight loss reached its maximum differed, varying from the second to the fifth day of life.

(7) Follow-up of Infants Surviving the Neonatal Period. Fifteen infants were followed up for a maximum period of six months, 25 for one year,

20 for three years and eight for five years. Follow-up took the form of clinical examination in 55 cases and of written enquiries sent to family doctors in 13 cases. Three children with congenital heart disease were alive at the age of 3 years. One infant died in hospital aged 6½ weeks from congenital heart disease first detected a few days after birth. Another child was found to be suffering from diabetes mellitus at the age of four years. A child suspected at the age of 8 months of being mentally defective was found to be deaf. Impaired hearing was suspected in another infant early in the second year of life. Deafness was confirmed and found to be severe by otologists in both these cases. Naevi not present at birth were found within six months of birth in four babies.

Otherwise the development of infants followed up in the series was found to be normal. The health histories of these babies were in no way unusual. Four infants in whom a clearly defined cardiac murmur of doubtful significance had been detected repeatedly in the first two weeks of life were found in the course of follow-up examination to be healthy and without any evidence of cardiac disease.

Discussion

The results of the management of pregnancy complicated by maternal diabetes mellitus are a measure of the effectiveness of teamwork by the obstetrician, physician, paediatrician and nursing staff. Control of the diabetes in the mothers in this study was undertaken by physicians with long experience of the condition. Pedersen, Bojsen-Møller and Poulsen (1954) have emphasized the particular importance of long term antenatal care. Our results serve to underline Miller's (1956) statement that the most meticulous regulation of carbohydrate metabolism and the best of pre-natal care are unable to reduce perinatal mortality to a level comparable to that in the non-diabetic population. Different opinions have been expressed concerning the relative merits of spontaneous delivery following induction and delivery by caesarean section. In our series there was no significant difference in mortality between the two methods, but no conclusion can be drawn from this observation as treatment was selected on the principles already described.

The highest mortality occurred among babies born following spontaneous delivery. Of the eight stillbirths it is possible at least that four might have been prevented had pregnancy been terminated earlier; and of the three neonatal deaths, one might have been avoided had episiotomy not been omitted.

Congenital anomalies were present in 10 babies.

Miller (1956) comments upon the inadequacy of recorded findings and on the absence of statistics for purposes of comparison in a contemporary group of infants born to non-diabetic mothers. He recommends that the frequency and nature of anomalies found in the infants of diabetic mothers should be compared with the findings 'in concurrent non-diabetic populations preferably treated at the same institution as the diabetic group'. Table 2 sum-

TABLE 2
INCIDENCE OF ANOMALIES OF ALL DEGREES IN LIVE-
BIRTHS OF ALL DEGREES OF MATURITY

Anatomical Location	Liveborn Children of	
	Non-diabetics (22,196)	Diabetics (75)
Skin and related structures ..	131 (0·6%)	1
Mouth and jaw	61 (0·3%)	1
Limbs	198 (0·9%)	1
Spine and skull	97 (0·4%)	
Cardio-vascular	74 (0·3%)	5
Alimentary	41 (0·2%)	
Genito-urinary	72 (0·3%)	1
Mongol	29 (0·1%)	
Achondroplasia	1	
Fibrocystic disease	2	
Eye	3	1
Lungs	2	
Reticulo-endothelial	2	
C.N.S. (intracranial)	3	
Total	716 (3·0%)	10

marizes the developmental errors found in other babies liveborn in the Leeds Maternity Hospital during the period January, 1947, to August, 1958. Livebirths excluding babies of diabetic mothers during this period numbered 22,196. Of these babies 716 (3%) had congenital anomalies. A comparison of these figures with the finding of abnormalities in 10 infants of the present series is not inconsistent with the view held by some authorities that anomalies occur with more than usual frequency in the babies of diabetic mothers.

Among livebirths in the present series congenital anomalies contributed directly to a fatal outcome in only two babies. In each case the anomaly was cardiac. One of the deaths occurred in the second month of life. Anomalies considered to be primary causes of death among the 22,196 liveborn babies delivered between January, 1947, and August, 1958, are summarized in Table 3. They total 106 of which

less than one-third were related to the cardiovascular system. There was only one example among the babies of diabetic mothers of anomalous development of the central nervous system; this is the more striking considering the predominance of meningocele in Table 3. Contrary to the

TABLE 3

NUMBER OF ANOMALIES CONSIDERED TO BE THE PRIMARY CAUSE OF DEATH WITHIN TWO WEEKS OF BIRTH IN BABIES OF ALL DEGREES OF MATURITY BUT EXCLUDING BABIES OF DIABETIC MOTHERS

Cardio-vascular	30
Renal	9
Alimentary	8
Spine and skull	51
C.N.S. (intracranial)	3
Ichthyosis	1
Pulmonary	2
Diaphragm	2
Total	106

experience of Peel and Oakley (1950) and, despite the fact that all babies were examined within a few hours of birth and again within the 36 hours preceding discharge from hospital, a strawberry naevus was found in only one infant.

Prospects of neonatal survival are necessarily subject to the influence of premature birth. There were 75 liveborn infants. The estimated gestation period was less than 34 weeks in three, between 34 and 38 weeks in 53, and 38 weeks or more in 18 babies. The corresponding figure for one baby was uncertain. Of the six infants who died within 38 hours of birth (and representing all the neonatal deaths in the total series) the estimated gestation period was 36 weeks in the case of two, and between 33 and 35 weeks in the case of the remaining four. During the period January, 1950, to August, 1958,* approximately 1,610 infants with a birth weight of $5\frac{1}{2}$ lb. or less and with an estimated gestation period of between 30 and 38 weeks were delivered in the Leeds Maternity Hospital. Of these infants 185 (11.6%) died in the hospital. In so far as these figures warrant tentative conclusions and recognizing that they apply only to the work of one particular hospital it seems that in the present series the risks of death due to premature birth were not increased as a result of maternal diabetes. This tentative conclusion is of special significance in that it pro-

vides suggestive evidence in support of the view already expressed that pregnancy might have been terminated earlier in some of the cases delivered spontaneously.

On balance we feel that in our series there has been a tendency to delay interference with pregnancy too long. It is probable that had pregnancy always been terminated at 35 weeks more babies might have been born alive and, in the absence of serious congenital anomalies, would have had good prospects of healthy survival. This view is in accord with those of Bachman (1952) and Peel (1955). The latter states that 'delivery at or before the thirty-sixth week reduces greatly the incidence of intra-uterine death without producing a corresponding rise in the neonatal death rate'.

Nevertheless the need remains for caution in early management by those responsible for the care of the infant of a diabetic mother. Experience in the present series agrees with that of Peel that the majority of deaths occur within a few days of birth. Indeed features of our series are that there was only one late fatality and that other deaths occurred not merely early but very early. Cardiac anomalies, vascular crises and hyaline membrane disease accounted for all the deaths. Both examples of fatal hyaline membrane disease occurred in infants delivered by caesarean section. No death was attributable or contributed to by infection. This is the more striking in view of the high incidence of infection in the series. The occurrence of 31 cases of superficial infection in 75 newly born babies of diabetic mothers compared very unfavourably with the incidence of approximately 8.5% of similar infections among all newly born infants in the hospital over the period January, 1947, to August, 1958.

Another feature of infants with infection in the series was enlargement of the liver. Clinical enlargement of the liver was present in 48 of the 75 liveborn babies. The enlargement might be evidence of the extramedullary haemopoiesis known to affect particularly the liver in babies of diabetic mothers (Miller and Wilson, 1943) although recorded postmortem findings do not suggest that the weight of the liver is significantly increased (Cardell, 1953; Warren and LeCompte, 1952). Alternatively the liver enlargement may reflect the abnormal glucose metabolism suggested by the asymptomatic hypoglycaemia detectable in the early days of life in many infants of diabetic mothers. There seems to be justification for suspecting that the offspring of diabetic mothers are liable to hepatic dysfunction. If this is accepted the tendency to bruising could be related to the disturbed function of the liver. The

* Reliable figures are not available for the years 1947, 1948 and 1949.

occurrence of clinical tetany in a proportion of these babies might be explained by the presence in the newly born infant's circulation of corticosteroids in abnormal amounts as a result of hormonal imbalance in the diabetic mother (Craig, 1958). Excess of circulating cortisone could explain the liability to infection, the Cushing appearance and the enlarged liver.

Initial progress following birth is likely to be slower in babies in whom macrosomia, the Cushing appearance and liver enlargement are pronounced. To judge by the present series progress is not characterized by abnormal weight loss. This observation is in keeping with the recorded findings of Farquhar and Sklaroff (1958) in connexion with the infants of diabetic women who, as in our series, were not subject to delayed feeding. The disappearance of the pseudo-oedema is to be explained not by abnormal fluid loss but by redistribution of body fluids between the intra- and extra-cellular spaces. Cortisone and thyroid have been suggested as adjuvants to treatment (Peel, 1958). We deprecate their use and attach emphasis to simplicity in medical and nursing care.

The results of the follow-up survey are reassuring. They suggest that congenital anomalies with a serious long term prognosis are unlikely to escape initial detection in the early weeks of life. While this is probably correct as a generalization an exception should be made of urinary abnormalities which are notoriously perplexing in early infancy. One child developed diabetes mellitus at the age of 4 years. In other respects the results of the follow-up survey provide no basis for thinking that the subsequent development and health of the babies of

diabetic mothers surviving the neonatal period are in any way prejudiced.

Summary

A series of 94 cases in which pregnancy was complicated by diabetes mellitus is presented.

Obstetrical and paediatric management are outlined.

Foetal loss is discussed in relation to management.

Neonatal morbidity is described with special reference to congenital anomalies, infection, bruising and enlargement of the liver.

The results of a clinical follow-up of infants surviving the neonatal period are summarized.

We are greatly indebted to our senior colleagues on the obstetrical staff of the Leeds Maternity Hospital for permission to include mothers and babies under their care in this series. Dr. R. G. Paley was responsible for the medical supervision of most of the mothers. Assistance in studying maternal records was given by Dr. W. P. Black, and in following-up babies by Dr. A. Bogdan. We wish to pay tribute to the skill of the nursing staff undertaking care of the babies.

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