# THE OBSTETRICIAN AND THE FOETUS OF THE DIABETIC MOTHER*

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The obstetrician's contribution to the improved perinatal survival resulting from diabetic pregnancies centres on antenatal supervision and hospitalization, planned termination of the pregnancy before the expected date of confinement and improved methods of delivery.

Of these three facets, it is the decision of when to induce labour which is most liable to error, and which therefore constitutes the weakest link in the obstetrician's therapeutic armamentarium.

The following contribution is based on the experience gained in the personal supervision of over 150 pregnant diabetics and is presented with the primary object of describing certain features regarding the diabetic baby. The treatment differs in many respects from generally accepted practice, and is intimately bound with the obstetrician's dilemma of when and how to deliver the pregnant diabetic.

## THE SMALL DIABETIC BABY

Although most pregnant diabetics are seen at an early stage of pregnancy, the same is not true of the Natal Indian diabetic. Late and irregular attendance at the antenatal clinics, together with illiteracy, frequently results in inconsistencies between the menstrual history and the clinical assessment of the expected duration of the pregnancy. Consequently, the tendency to correlate the estimated size of the baby with gestational maturity became the accepted practice in our unit. This, however, posed 2 queries, namely, does foetal maturity equate with foetal size; and, are diabetic babies always large?

In 1947, McBurney[1] drew attention to the undernourished full-term baby, and demonstrated that it was incorrect to call a baby 'premature' simply because its birthweight was low. The World Health Organization Expert Committee[2] subsequently recommended that babies with birthweights of 5½ lb. or less should in future be called 'low birthweight babies' rather than premature babies, thus confirming the concept of a gestationally mature baby which appears small according to the date.[3-5]

Recognition of this condition is of importance for the following 3 reasons:

(*a*) It occurs frequently—no fewer than 35% of low birthweight babies born during the recent perinatal mortality survey[6] were found to be gestationally mature.

(*b*) The perinatal death rate of such infants is high, 'the major component being stillbirth and intra-uterine death of the fade-out variety'.[3]

(*c*) Whereas a clinical cause for poor growth can be found in over 80% of prematurely born babies, only 40% of pregnancies with babies that are small according to the date have some clinically detectable abnormality.[7]

By contrast, the pathognomonic picture of the diabetic baby is one of a premature, but large overweight infant.

Although this is true for the majority of diabetic babies, Hsia and Gellis,[8] and White[9] have noted a decrease in birthweight with the progression of the severity and duration of maternal diabetes, while Pederson[10] has more recently confirmed that some diabetic babies can be described as small according to dates. It must be emphasized, however, that this decrease in birthweight is not related to that following prolonged hospitalization[11] but is attributed to panvascular lesions which are clinically detectable and definable according to varying grades of severity.[9]

In our unit I have noted a similar trend—particularly in pregnancies complicated by severe toxaemia—but regard as of even greater significance the fact that babies that are small according to dates are frequently born to mothers without any obvious evidence of vascular disease or complications associated with diabetes.

Thus, of 92 proved diabetics (see Table I) who had received no treatment other than bed rest and dietary restriction alone, no fewer than 16·3% gave birth to infants weighing less than 6 lb.

TABLE I. BIRTHWEIGHT OF GESTATIONALLY MATURE INFANTS BORN TO 92 DIABETIC MOTHERS ON NO TREATMENT

| | *5 - 6 lb.* | *6 - 7 lb.* | *7 - 8 lb.* | *8 - 9 lb.* |
|---|---|---|---|---|
| Number | 15 | 22 | 30 | 25 |
| Percentage | 16·3 | 23·9 | 32·6 | 27·2 |

These babies were delivered between the 37th and 38th weeks of gestation, and, with the exception of one stillbirth resulting from an abruptio placentae, all were born alive.

The significance of the diabetic baby which is small according to dates is best appreciated when one considers the perinatal mortality rate in relation to birthweight.

Of the 167 Natal Indian diabetics delivered during the past 4 years (see Table II), 36 babies weighed less than 6 lb., 41 were between 6 and 7 lb., 45 between 7 and 8 lb., and 45 weighed more than 8 lb. The respective perinatal

TABLE II. PERINATAL MORTALITY IN RELATION TO BIRTHWEIGHT: AN ANALYSIS OF 167 DIABETIC PREGNANCIES

| Birthweight (lb.) | < 6 | 6 - 7 | 7 - 8 | 8 > |
|---|---|---|---|---|
| Number | 37 | 41 | 45 | 45 |
| Stillbirths and neonatal deaths | 11 | 1 | 3 | 5 |
| Perinatal loss % | 30·5 (13·8 corrected) | 2·4 | 6·6 | 11·1 |

death rates (with the numbers involved in parenthesis) were 30·5% (11); 2·4% (1); 6·6% (3); and 11·1% (5). However, of the 11 infants below 6 lb. who died, 2 were definitely born prematurely according to dates; one died as a result of abruptio placentae; 2 were associated with severe toxaemia and one with maternal hyperpyrexia due to recurrent pyelonephritis.

The remaining 5 (or 13·8%) were either stillborn or were associated with gross foetal distress resulting in neonatal death. In no instance was there any significant factor which could have accounted for the perinatal death. Thus, in our series the perinatal loss of the babies that were small according to dates, resulting from pregnancies which were otherwise clinically normal and of calculated

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maturity, exceeded that of the typical diabetic baby which is large in relation to the date—13·8% versus 11·1%.

*Why are Diabetic Babies Small?*

Acceptance of this concept is of little practical value, if the underlying cause cannot be explained or determined.

Reference to the non-diabetic small infant reveals histological maturity of the vital pulmonary and renal structures, the small birthweight being due to a low total infant weight associated with a correspondingly small placenta.[32] The pathogenesis of these infants—while not conclusively established—is said to be due to impairment in the maternal vascular supply.[4] As mentioned earlier, a similar situation exists among the long-term diabetic mothers with panvascular lesions.[9]

However, a recent report from the Joslin Clinic[33] established that maternal vascular disease in pregnant diabetics is far more common than was previously acknowledged. No fewer than 20 - 50% of decidual biopsy specimens taken from diabetic subjects (with or without other clinical evidence of vascular disease) were found to have angiopathic changes. There is therefore little reason why the same cannot hold true for the Natal Indian diabetic who produces a small diabetic baby, particularly when one appreciates that the Natal Indian diabetics, as a group, are prone to vascular disease.[34]

*Can the Small Diabetic Baby be Predicted?—A Hypothesis*

It is known that characteristic vascular changes occur in the intimal lining of vessels taken from biopsy specimens of ear-lobes in diabetic and prediabetic subjects.[35] If it can be shown that similar lesions in pregnant diabetics reflect equivalent changes in the pelvic vasculature, a practical and accurate diagnostic method would be available for use, both as a clinical guide and as a yardstick for prognosis.

Thus, on the basis of positive biopsies of skin or muscle, it will be possible to predict which diabetic women are liable to produce small diabetic babies so that planned termination of pregnancy will not be withheld because of a clinically small baby.

Study into this aspect is to be initiated in the near future.

## THE LARGE DIABETIC BABY

*Blood-Sugar Level and Foetal Size*

Foetal overgrowth and overweight are nevertheless the characteristic features of the foetus and infant born to the diabetic mother. Of the many theories regarding the pathogenesis of these features, the maternal hyperglycaemia/foetal hyperinsulinism theory is probably the most popular.[10] Expressed in simple terms, this hypothesis suggests that maternal hyperglycaemia results in foetal hyperglycaemia, and that the latter causes hypertrophy of the foetal islet tissue with insulin hypersecretion. This allows for greater foetal utilization of glucose and augments the deposition of glycogen and fat. In support of this theory Pederson[10] found that the birthweight of infants born to mothers with low blood-sugar levels was (on an average) 150 G less than that of infants whose mothers were poorly controlled.

However, Hagbard[16] and Jackson[17] do not accept this theory, as islet cell hypertrophy is often demonstrable in infants born to mothers many years before diabetes is recognized, while poorly controlled diabetics do not necessarily produce large infants with islet hypertrophy.

This has also been my experience and is illustrated by typical examples.

An infant born to patient A.C. weighed 9 lb. 15 oz. at birth. The maternal blood-sugar level varied between 130 and 150 mg./100 ml. and the patient was well controlled on 20 units lente insulin per day.

A second infant resulted from a poorly controlled diabetic pregnancy with postprandial blood-sugar levels usually above 200 mg./100 ml., the patient (N.N.) requiring 200 units of insulin per day. The infant weighed 6 lb. 15 oz. at birth. Gestational ages were the same in both instances and there was no clinical evidence of vascular disease in either patient.

Many similar examples have been noted and it is therefore my opinion that elevated maternal blood-sugar levels *per se* do not necessarily account for foetal overgrowth. Conversely, it would be logical to conclude that the foetal size is more closely related to the factor(s) which is responsible for the maternal hyperglycaemia, and not vice versa. The cause for the foetal overgrowth can therefore be expected to differ with the aetiology of the underlying metabolic disturbance in individual patients. In this regard it is pertinent to note that the degree of diabetic control (as judged by postprandial blood-sugar levels) did not influence the adrenocortical function of our pregnant diabetics with proved hyperactivity.[18]

*Lipid Metabolism and Birthweight*

Whereas disagreement exists as to the cause of diabetic embryopathy, it is now generally agreed that these infants are fat rather than oedematous. Osler,[19] for example, found a 38 - 46% increase in the subcutaneous fat layer.

During a recent random-sample therapeutic trial,[18] it was noted that the birthweights of infants born to mothers on treatment with the sulphonylureas were significantly lower than those whose mothers had received either insulin or no specific antidiabetic therapy (Table III).

TABLE III. COMPARISON OF BIRTHWEIGHT OF INFANTS BORN ON A RANDOM-SAMPLE THERAPEUTIC STUDY

| *Treatment* | *Normal controls* | *Rastinon* | *Diabinese* | *Insulin* | *Diet* |
|---|---|---|---|---|---|
| Number | 200 | 29 | 26 | 28 | 24 |
| Mean weight (lb.) | 6·38 | 6·58 | 6·99 | 7·65 | 7·50 |
| SD | 1·20 | 1·05 | 1·31 | 2·12 | 1·03 |

'F' test for statistical significance $P = <0{\cdot}01$ $(F = 9{\cdot}69)$.

The mean birthweight of the babies whose mothers had received tolbutamide was 6·58 lb., as compared with 6·99, 7·65 and 7·50 lb. for patients treated with chlorpropamide, insulin and dietary restriction alone.

The significance of these results may be related to the conclusions of a recent study (based on well-documented experimental work) which suggested that the elevated maternal free fatty acids commonly found in diabetic pregnancies led to a greater net transfer of free fatty acids into the foetal circulation, and that this was responsible for the increased body-fat content of the diabetic baby. If these findings are extrapolated to human beings, a plausible explanation for the observed lower weight of the infants born to sulphonylurea-treated mothers can be established, as the sulphonylureas have recently been found to induce a significant decrease in the net release of fatty acids from adipose tissue.[20]

If, in addition, a recent hypothesis[21] regarding the pro-

duction of foetal arteriosclerosis and metabolic acidosis subsequent to increased maternal free fatty acid metabolism is proved to be correct, the indications for the use of the sulphonylureas should be extended to include all pregnant diabetics, since the sulphonylureas are known to cross the placental barrier, and would exert their beneficial antilipid effect in the foetus.

It is well documented that typical 'diabetic-like' babies are delivered many years before the onset of overt diabetes and that elevated free fatty acid levels are frequently found before demonstrable abnormalities in carbohydrate metabolism.[22] Furthermore, the concentration of the plasma free fatty acids normally rises during pregnancy,[22] while both growth hormone[22,23] and cortisone[24] (factors which are increased during pregnancy) increase plasma free fatty acids.

Abundant evidence therefore exists to stimulate a reappraisal of the role and possible value of the antilipid effect of the sulphonylureas in the treatment of the pregnant diabetic, as control of abnormal lipid metabolism may help to reduce the incidence of the so-called 'unavoidable foetal death'.[25]

## CLINICAL MANAGEMENT

The clinical importance of the small diabetic baby lies in the fact that size does not necessarily correlate with the foetal maturity and that an unwarranted prolongation of its intra-uterine existence, in an attempt to deliver a larger baby, will frequently result in perinatal loss.

The obstetrician's dilemma therefore resolves to one of assessing foetal maturity and growth as against placental function and reserve.

### *Foetal Maturity*

*Clinical assessment.* Early and frequent attendance at antenatal clinics usually allows for accurate assessment and follow-up of the duration of pregnancy. However, when this is not available, reliance must be placed on abdominal palpation, in order to determine both the height of the fundus and foetal size.

Whereas the most reliable method of assessing foetal size in the non-diabetic subject is to gauge the weight according to the size of the presenting vertex, the same does not hold true for the diabetic. Abdominal palpation frequently leads to an underestimation of the baby's expected weight, for the brain of the diabetic infant is known to be smaller than that of the gestationally equivalent normal baby.[13] We have been cognizant of this feature for some time and therefore advocate that allowance be made for this discrepancy; a combined abdominal and pelvic examination allows for greater accuracy in this respect and is particularly helpful in the presence of hydramnios.

*Radiological assessment.* Although the accuracy of the radiological assessment of foetal maturity has been questioned in recent times, we still employ and advocate the procedure, for apart from being a guide to maturity it enables one to exclude the presence of skeletal abnormalities and to look for evidence of pelvic vascular calcification.

Our procedure is supported by a recent prospective study[26] which concluded that a distal femoral epiphysis was radiologically detectable in 96% of mature foetuses. When present in association with a visible proximal tibial epiphysis as well, the indication of physiological foetal maturity is even more reliable.[27] Radiological cephalometry, however, is not particularly helpful, for although the biparietal diameter of the foetal head bears a close relationship to the weight, it is only possible to assess the foetal head for this purpose in approximately 33% of cases.[28] We nevertheless regard the presence of a well-developed cortical skull bone as a sign of advanced foetal maturity, cognizant of the fact that it is not in itself a reliable sign of maturity.

### *Foetal Growth*

*Clinical assessment.* The clinical assessment of foetal growth is both difficult and variable. Daily palpation imparts an impression of progressive foetal growth, and it is failure to observe this feature which is often the first detectable sign that foetal growth is retarded. Nevertheless, it remains a clinical guide rather than a reproducible definitive parameter.

*Ultrasonics.* Ultrasonics provides the most effective means of measuring foetal growth, as it can be safely repeated, at frequent intervals, to assess the growth *rate* of the biparietal diameter, and therefore of the infant. For example, failure to progress (in the presence of a clinically small baby) would indicate the need for obstetrical interference. Unfortunately this device is not available at the King Edward VIII Hospital, but it certainly merits further study and use in everyday clinical practice.

### *Placental Function*

It is generally agreed that placental function is best assessed by measuring the oestriol excretion rate.[25,29,30] A recent study[29] has in fact confirmed that:

(*a*) high oestriol levels during pregnancies complicated by diabetes are associated with good foetal prognoses, whereas low levels offer a poor prognosis;
(*b*) oestriol levels can be used for the prediction of the weight of the newborn;
(*c*) they can provide information concerning the growth of the foetus *in utero*;
(*d*) 2 consecutive (daily) falling values are indicative of foetal death and justify immediate termination of the pregnancy.

Since laboratory facilities for the biological estimation of oestrogen are not always available, we hope to correlate the cornification index in our diabetic patients with placental function. Weekly vaginal smears are obtained and screened by the same cytologist. The results are then assessed according to 2 criteria, namely the cornification index itself (below 5% is indicative of good, 5 - 10% satisfactory and 10% or more suggestive of poor placental function) and the serial pattern—a progressive rise in the cornification index being indicative of failing placental activity. This will be correlated with oestriol excretion values.

Insufficient data are at present available to formulate any firm conclusions, but it is hoped that this technique, together with other clinical observations of placental function—such as the bedside assessment of the volume of liquor, daily weight and girth measurements—will form useful adjunctive guides in the management of the pregnant diabetic.

### MODE OF DELIVERY AND PERINATAL LOSS

Vaginal delivery is preferred by some authors as it is said to have the advantage of reducing the incidence of respiratory distress in the infant. It has been our experience, however, that the mode of delivery *per se* does not alter foetal survival, provided that the correct indications are employed. Thus, primary caesarean section is advocated in the presence of complications such as toxaemia, cephalopelvic disproportion, malpresentations, previous caesarean section, poor obstetrical history and an inadequately controlled diabetic state. Evidence of retinopathy, renal or vascular disease, and foetal distress (meconium staining of the liquor or irregularities in the rate and rhythm of the foetal heart rate) is further indication for abdominal delivery.

Induction of labour and vaginal delivery are attempted in both primiparae and multiparae, provided the above features are not present, cephalopelvic disproportion has been excluded and the vertex is well applied to the cervix.

Table IV summarizes the method of delivery and the associated perinatal loss. Equal numbers of patients were

TABLE IV. PERINATAL LOSS AND MODE OF DELIVERY IN 132 NATAL INDIAN PATIENTS

| *Method of delivery* | *Number* | *Live births* | *Still-births* | *Neonatal deaths* | *Perinatal mortality %* |
|---|---|---|---|---|---|
| Vaginal | 66 | 60 | 6 | 0 | 9 |
| Caesarean section | 66 | 57 | 3 | 6 | 13 |

delivered vaginally and by caesarean section (66 in each group). Of infants delivered vaginally, 6 stillbirths and no neonatal deaths were recorded, whereas there were 9 deaths following caesarean section: 3 were stillborn and 6 died neonatally. It might appear that diabetic babies born by caesarean section are more prone to die neonatally than those delivered vaginally. However, 5 of these 6 deaths are directly attributable to causes unrelated to the operative procedure—prolapsed cord, Fallot's tetralogy, placenta praevia, gross foetal distress and prematurity. The sixth neonatal death resulted from a breech delivered by caesarean section, and is the only possible instance where anaesthesia or the operative procedure might have contributed to the perinatal loss.

Fifty-six of the caesarean sections were performed under general anaesthesia without noticeable adverse effect on the infant at birth. The remaining 10 patients were delivered under epidural block or local infiltration plus sedation with pethidine. In one instance, epidural block was followed by such a profound fall in blood pressure that the Apgar rating of the infant at birth was only 2.

A similar result is obtained when the perinatal loss of the small diabetic baby is measured in relation to the mode of delivery (Table V). Thus, the corrected perinatal mortality following caesarean section was 9·1% as compared with 12·5% of those who were delivered vaginally—

TABLE V. PERINATAL MORTALITY RATE OF SMALL DIABETIC BABIES IN RELATION TO MODE OF DELIVERY

| *Mode of delivery:* | *Caesarean section* | *Vaginal* |
|---|---|---|
| Number | 15 | 20 |
| Stillbirths | 1 | 3 |
| Neonatal deaths | 4 | 3 |
| Perinatal loss | 33% | 30% |
| Corrected perinatal loss | 9·1% | 12·5% |

a difference of no statistical significance.

As a result of this experience I feel that both caesarean section and general anaesthesia are perfectly safe for delivery of the diabetic baby, provided that the usual precautions associated with these procedures are observed.


### SUMMARY

A brief résumé of my experience in the antenatal management of the baby of the diabetic mother is presented. As a result it may be concluded that:

(*a*) Diabetic babies need not be large according to dates. The pregnant diabetic produces infants which are frequently gestationally mature but are of low birthweight. The perinatal mortality of these infants is high and is invariably related to an unwarranted prolongation of their intra-uterine existence in an attempt to deliver a larger baby.

(*b*) The pathogenesis of the large diabetic baby is not necessarily related to the maternal blood-sugar level. Closer attention should be paid to the cause of the hyperglycaemia or to abnormalities in lipid metabolism, for the therapeutic consideration of these aspects may help to reduce the incidence of 'unavoidable' foetal deaths.

(*c*) The clinical detection and management of the small diabetic baby and the large diabetic baby are dependent upon close antenatal supervision, clinical acumen, and other ancillary methods of assessing foetal maturity, foetal growth and placental function. The importance of the last 3 factors in determining the time of termination of the pregnancy is emphasized.

(*d*) Provided strict criteria are adopted, the mode of delivery *per se* does not appear to affect the perinatal mortality rate adversely.


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