THE PREGNANT NATAL INDIAN DIABETIC*

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In 1961, Campbell[1] put forward his concept of the 'insulin-independent young diabetic' on the grounds that certain pregnant Natal Indian diabetics remained ketosis-free without requiring insulin. Similar observations were noted by me and others during the course of obstetrical duties at the King Edward VIII Hospital, Durban, and the 'clinical impression' developed that these patients differed in many respects from their Caucasian counterparts.

Therefore the aim of this contribution was to clarify the clinical picture and presentation of the pregnant Natal Indian diabetic, based on experience gained during the past 4½ years.

MATERIAL AND METHODS

Proved diabetics and patients with significant prediabetic or latent diabetic histories (unexplained perinatal loss, family history of diabetes, large babies, hydramnios and glycosuria) were requested to attend the antenatal clinic, where modified glucose-tolerance tests were performed. The method employed is based on the assessment of the 2-hour blood-sugar level following a glucose load of 100 G. Patients with blood-sugar levels of 140 mg./100 ml. or more were admitted for further study; those with results between 120 and 140 mg./100 ml. were referred for repeat tests a fortnight later, and those with values below 120 mg./100 ml. were regarded as having normal carbohydrate tolerance.

On admission all patients had confirmatory glucose-tolerance tests (values above 140 mg./100 ml. were regarded as positive), renal function (blood urea and uric acid estimations plus microscopic, chemical and bacteriological examination of the urine) and lipid studies (serum cholesterol) in addition to the usual antenatal haematological investigations—full blood counts, Wassermann reaction and Rh grouping. Particular emphasis was placed upon the detection of complications such as diabetic ketosis, pre-eclamptic toxaemia, hydramnios and renal and vascular disease.

The patients studied were all of the same socio-economic status and had similar religious affiliations.

During the 4½-year period November 1963 - May 1967, approximately 300 patients were admitted for further investigation; 166 of these were positively identified as being diabetic. Unfortunately, 42 of these patients absconded while still on treatment and were therefore lost to the series. The observations and conclusions of this study are based on the clinical picture presented by the remaining 124 pregnant Natal Indian diabetics.

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Clinical Presentation

Of the 124 patients, 35 had had diabetes for one or more years before becoming pregnant. The remaining 89 were all diagnosed during the current pregnancy. The reasons for the investigation of the latter group are summarized in Table I.

TABLE I. PRESENTING FEATURES OF 89 RECENTLY DIAGNOSED DIABETICS

Symptoms		*No.*
Family history of diabetes		18
History of big babies		7
Symptoms of diabetes (polyuria, pruritus vulvae, polydipsia, polyphagia)		7
Glycosuria		33
Poor obstetrical history		12
Coincidental with		
Anaemia	2	
Infertility	2	
Heart disease	1	
Pyelitis	2	
Arthritis	1	
Sarcoidosis	1	
Molar pregnancy	1	
Hypertension	1	11

The majority of the investigations were based on the presence of sugar in the urine. However, although 72 of the 124 patients in the series exhibited glycosuria, a significant finding was that 54 positively established diabetics were aglycosuric—an incidence of 35·5%. This confirms the impression that Natal Indian diabetics develop glycosuria at a much later stage of the syndrome compared with other races, probably because of an elevated renal threshold to sugar.[3] Conversely, the statement that 'if a Natal Indian has sugar in his urine he is almost certainly a diabetic'[2] must be treated with caution during pregnancy, for many patients diagnosed in this way have, on full investigation, been found to be in normal carbohydrate balance. During the period of study several pregnant diabetic Natal Indians (diagnosed on urinalysis alone and all on treatment) had been referred for obstetrical management, but on glucose-tolerance studies were found to be normal.

The need for postprandial blood-sugar assessment of all diabetic suspects is thus apparent, and it is rather surprising that this method is not projected into everyday practice, particularly in population groups where this syndrome is known to have a high incidence. The reliability and simplicity[2] of certain diagnostic techniques, e.g. the

use of Dextrostix, ensure the practicality of this procedure.

A strong correlation exists between disordered carbohydrate metabolism and a family history of diabetes. Although this feature was the presenting feature in only 18 of the recently diagnosed diabetics, further questioning elicited a positive family history in 61 (49%) of the 124 patients in the series. This figure correlates very closely with the family history incidence of 47·8% and 45·6% quoted by Campbell from surveys conducted among Indian populations[2,3] and that of 41% quoted by Joslin for Caucasian diabetics.[4]

Beaser,[5] in a study of the clinical characteristics of early diabetics, noted that whereas most juvenile diabetics had manifest symptoms at the time of diagnosis, the same was true for only 34% of adult diabetics. Of the 89 recently diagnosed diabetics, only 7 (7·7%) were investigated because of complaints of excessive thirst, pruritus and polyuria. On direct questioning, however, 52 patients complained of polyuria, 46 of polydipsia, 28 of pruritus vulvae and 12 of polyphagia. In most instances the symptoms were only of mild to moderate severity.

The lack of symptoms has 2 unfortunate consequences, in that it leads to underestimation of the severity of diabetes in the pregnant Natal Indian, and, secondly, many patients refuse hospitalization and treatment (especially with insulin) because they are relatively symptom-free.

The significance of a history of having had large babies (weighing 10 lb. or more) was first documented by Skipper[6] in 1933 and subsequently confirmed by others.[7,8] They demonstrated that the birth of large babies (especially if they increased progressively in weight) heralded the development of diabetes in the mother. Because of the unreliability of the histories of most of the patients in our series, cognizance was only taken of those patients who could relate the precise weight of their previous offspring. It is therefore possible that the 7·8% incidence of a history of large babies is too conservative.

The increased perinatal wastage in pre- and overt diabetes is equally well recognized and was the reason for 13·5% of the diabetics of recent onset being investigated.

Age. The mean age of the patients studied was 30·3 years (range 17 - 43 years). Of these, the majority (40·3%) were in the 26 - 30-year age-group, while more than half of the patients were aged 30 or less (Table II).

TABLE II. AGE DISTRIBUTION IN 124 PREGNANT NATAL INDIAN DIABETICS

Age in years:	*20–25*	*26–30*	*31–35*	*36–43*
Number of patients	16	50	28	30
%	12·9	40·3	22·6	24·2

Campbell classifies a patient up to the age of 35 years as being a young diabetic and, on this basis, the majority of our patients must therefore be regarded as such.

It is interesting to note that the reported age for the emergence of diabetes in East Pakistani Indians is soon after the age of 40,[4] while the results of a survey among Tongaat Village dwellers (Natal Indians) illustrated that only 3·2% of the diabetics detected were aged 29 years or less.[9]

Parity. The female Natal Indian diabetic has normal fertility—only 8 of the patients (6·4%) were pregnant for the first time. Of the remainder, 76 had had 1 - 4 children (61·4%), 35 were grandmultiparae (28·2%) and 5 had had 10 or more children (4%).

It should be noted that 2 of the recently diagnosed pregnant diabetics presented with histories of infertility, but it is felt that this feature is purely coincidental and does not reflect a behaviour pattern of the female Natal Indian diabetic.

Weight. Although assessment of weight during pregnancy can be notoriously unreliable, a comparison between normal pregnant controls and pregnant diabetics at equivalent stages of pregnancy has indicated that the pregnant diabetic conforms to the description of being 'short and fat with frequent buffalo-hump obesity'.[9] Although they are of short stature (mean height 5 ft), 70·8% weighed more than 130 lb. and 30% weighed more than 160 lb. The percentage in the pregnant controls was 44·2 and 18·6% respectively (Table III).

TABLE III. COMPARISON OF HEIGHT AND WEIGHT BETWEEN 100 NORMAL PREGNANT CONTROLS AND 124 PREGNANT NATAL INDIAN DIABETICS

Measurement	*Controls*	*Diabetics*
Mean height	5 ft 1 in.	5 ft
Weight		
% below 130 lb.	55·8	29·2
% above 130 lb.	44·2	70·8
% above 160 lb.	18·6	30·0

It is tempting to speculate that the obesity and insulin-independence of the Natal Indian diabetic are due to the presence of increased amounts of circulating insulin, which is inhibited in muscle by insulin antagonists, but not in adipose tissue. This reaction would be catalysed by the high carbohydrate content of their diet.

In support of this concept is a recent preliminary communication[10] from New Delhi which has indicated that of 15 young (mean age 23 years) ketoacidosis-resistant diabetic Indians, 6 had normal levels of insulin-like activity, whereas higher than normal levels were found in 9 cases.

Ketosis. The reported incidence of acidosis in African diabetics varies from 12 to 22%,[11] but the Natal Indian diabetic is remarkably free from this complication.[9] Thus, 11 patients (8·8%) developed ketosis at times during their pregnancy, but in only one case was the acidosis associated with any degree of severity. The average incidence of ketosis occurring during diabetic pregnancy in Whites is approximately 16·7%.[12] Of the 11 patients with acetonuria, only one was associated with perinatal loss (as opposed to an average of 30·1% in the literature), but even in this case it is highly unlikely that the acidosis had any part in the resulting stillbirth, as the acetonuria was only present on admission when the patient was 20 weeks pregnant, and did not recur. She was fairly well controlled on tolbutamide for the remainder of her pregnancy and delivered vaginally at 37 weeks.

A noticeable feature in the Natal Indian diabetic before 1963 was the high incidence of acetonuria—33·3% compared with 8·5%. It was subsequently noted that although acetonuria was detected in the presence of moderate degrees of glycosuria, the addition of carbohydrate to

the diet resulted in a decrease in the frequency of acetonuria without significantly affecting the degree of diabetic control.

Hirsutes. The Natal Indian diabetic is said to be extremely hirsute, as significantly more diabetic women have moustaches and side-burns than non-diabetic women.[13]

In the present series, this particular feature was recorded in 73 patients, 36 of whom were found to exhibit excessive hair growth—a figure far above that of 15% found in control non-diabetic Indian females.[12] It has been suggested that the reason for the hirsutes is excessive adrenocortical function.

Duration of diabetes. The duration of diabetes in the 35 known diabetics is reflected in Table IV, from

TABLE IV. DURATION OF DIABETES IN 35 'ESTABLISHED' PREGNANT NATAL INDIAN DIABETICS

Duration of diabetes	*No. of patients*	%
Less than 1 year	8	22·9
1 - 5 years	21	60·0
5 or more years	6	17·1

which it may be gathered that the pregnant Natal Indian, as seen in Durban, has a characteristically short history. It is pertinent to note, however, that there is no significant relationship between the duration or age of onset of diabetes and the foetal mortality.[14-16]

Special Studies

Adrenocortical function. A recent study[17] has indicated that the urinary excretion of 17-hydroxycorticoid is greater in the pregnant Natal Indian diabetic compared with pregnant non-diabetic controls. The mean values for the diabetic subjects were 11·7 mg./24 hours and 12·6 mg./24 hours, respectively, compared with 9·3 mg./24 hours and 11·0 mg./24 hours in the control group.

These findings may be of even greater significance if the statement is true that Natal Indian diabetics behave in an abnormal fashion to normal levels of circulating adrenal hormones.[9]

Further observations which arose from the study of adrenocortical function in the pregnant Natal Indian diabetic are:

(*i*) the importance of assessing patients individually, as only some diabetics will have evidence of excessive adrenocortical activity;

(*ii*) that abnormal values should always be based on a comparison with normal values obtained in the same racial group;

(*iii*) when adrenocortical hyperactivity is found to be the cause of abnormal carbohydrate metabolism, 'true' control cannot be achieved by suppressing the blood-sugar level;

(*iv*) adrenocortical function during pregnancy should always be studied in conjunction with oestrogen assays, since the level of free and therefore biologically active cortisone is directly related to the degree of binding with an oestrogen-induced globulin.

Oestrogen metabolism. Boulle[18] recently investigated 5 pregnant Natal Indian diabetics and found that the total oestrogen excretion was well below the normal curve of non-diabetic Indian controls (Fig. 1). Although the results of this study are too small for statistical analysis, the observed trend correlates with that obtained in the literature, for it has been ascertained that the average oestriol excretion value in the diabetic is lower than that of the non-diabetic.[19,20] These findings may be related to the observations of Plotz and Davis[21] that the elevated levels of androsterone and etiocholanolone in diabetic pregnancies are due to the absence of an enzyme responsible for their conversion to oestrogen.

Lipid metabolism. There is sufficient clinical evidence to correlate the degree of atherosclerosis with abnormal fat, carbohydrate and oestrogen metabolism,[22] although doubts were entertained as to whether the shortness of the gestational period permitted much vascular damage. However, a recent report from the Joslin Clinic[23] has indicated that maternal vascular disease in diabetes is far more common than was previously acknowledged. Thus, acute atherosis with deposition of lipid in the intima of the large decidual vessels and arteriolar disease characterized by hypertrophy, onion-skinning and hyalinization, was recorded in no fewer than 20 - 50% of specimens taken from pregnant diabetics with and without other evidence of angiopathy.

The study of lipid metabolism in the present series was confined to the assessment of serum cholesterol. The mean level during the second trimester was 237 mg./100 ml. (range 150 - 400 mg./100 ml.), and that of the third trimester 235 mg./100 ml. (range 130 - 410 mg./100 ml.). The values obtained are therefore well within the normal range, while the progressive increase in cholesterol associated with pregnancy was not observed.

It is unfortunate that the study was restricted to serum cholesterol estimations, for a recent report has confirmed[24] that serum cholesterol *per se* is not the only factor involved in the aetiology of degenerative arterial diseases, since the serum levels of beta-lipoproteins and other lipid fractions may be of equal importance. In this regard, it is pertinent to note that whereas no significant difference could be established between serum cholesterol values in Indian and Bantu diabetics, the mean total serum lipids were higher among female Natal Indian diabetics than those observed in Indian and Bantu female and male diabetics and controls.[25]

The need for an intensive investigation of lipid metabolism in the pregnant Natal Indian diabetic has been emphasized recently[22] and is based on the close relationship that exists between vascular disease, oestrogen and fatty acid metabolism.

The Natal Indian diabetic is particularly prone to vascular disease. Thus Cosnett[26] found that 26·6% of 207 diabetics had retinopathy, 15% had diabetic nephropathy and 9·2% had peripheral vascular disease. Further studies[9] have shown that the presence of diabetic angiopathy bears no relationship to the clinical duration of diabetes; that angiopathy often precedes the clinical diabetic state; that ketosis is by no means a prerequisite for the development of severe and often lethal vascular disease; and that retinopathy is more common and advanced in those Indians who have been treated with insulin.

Since maternal vascular disease is known to have an unfavourable influence on the course of diabetic preg-

nancy, fundoscopic and radiological examinations were performed. Despite the predisposition of this racial group to vascular disease, it is rather surprising to note that, of the 43 records available, only one patient had evidence of diabetic retinopathy (this pregnancy resulted in a live-birth), while no radiological evidence of calcification of the pelvic or iliac vessels has as yet been detected.

However, in a series of 900 diabetic pregnancies, White[27] noted that 41% had evidence of vascular disease, and the incidence of retinopathy during pregnancy has been found to vary between 15 and 32% in some series.[32] It is my opinion that further research into the vascular status of the pregnant Natal Indian diabetic is mandatory and will help to clarify the so-called 'unexplained stillbirth'.

Uric acid metabolism. McKechnie[28] recently observed that a definite relationship existed in Natal Indians between hyperuricaemia and abnormal carbohydrate tolerance. Since these levels are also elevated in persons with atherosclerosis[29] and therefore presumably liable to decreased placental perfusion, it was decided to record the uric acid levels at regular intervals during pregnancy to establish whether a relationship existed between this fraction and the severity of the diabetes, the degree of diabetic control, the development and severity of pre-eclamptic toxaemia and the perinatal mortality.

A preliminary study of serum uric acid levels in 40 aglycosuric Indians showed that normal values for women were 3·7 ± 0·5 mg./100 ml., and that values above 6 mg./100 ml. should be regarded as abnormal.[28] Using the above criterion, no relationship was observed between serum uric acid and the 'severity' of diabetes or the degree of diabetic control.

However, a progressive rise in the uric acid was associated with a poor foetal prognosis. Thus, pregnancies with mild toxaemia and a serial rise in uric acid were more liable to result in neonatal deaths and stillbirths than pregnancies with a similar degree of toxaemia and a consistently normal uric acid level (Table V).

TABLE V. RELATIONSHIP BETWEEN SERUM URIC ACID, PRE-ECLAMPTIC TOXAEMIA AND FOETAL MORTALITY IN PREGNANT NATAL INDIAN DIABETICS

Case No.	*Severity and response of toxaemia*	*Serial uric acid (mg./100 ml.)*	*Result (weights in lb. and oz.)*
146	165/100 oed. + alb. + 120/ 90 oed. nil alb. nil	3·9; 4·7; 5·3; 6·5	Neonatal death —5/4
132	160/ 90 oed. + alb. + 120/ 80 oed. nil alb. nil	3·1; 3·2; 3·0	Alive—6/12
7	150/110 oed. + alb. nil 150/110 oed. nil alb. nil	2·4; 3·1; 4·1; 5·2; 7·8	Alive—7/9 (cerebral)
294	150/110 oed. + alb. + 150/110 oed. nil alb. +	6·1; 6·1; 7·2; 9·1	Stillborn—8/10

It is therefore suggested that the serum uric acid is a useful guide in the management of the pregnant diabetic, and that importance should be attached to a progressive rise in the serum concentration of this fraction.

A less definite relationship was noted between serum uric acid and the development of pre-eclamptic toxaemia, as only 3 of the 12 patients who developed toxaemia had elevated levels.

Complications Commonly Associated with the Pregnant Diabetic

Abortions. Based on a recent survey of the literature,[12] the incidence of spontaneous abortions in diabetes has been estimated at 10%, a figure similar to that quoted for non-diabetic pregnancies.[30]

The single patient of my series who aborted reflects a similar tendency, but a completely different view is obtained when the past histories of these patients are taken into consideration. The incidence of abortion in 60 non-diabetic controls was 8·3%, as opposed to 23·6% in the 89 recently diagnosed diabetics and 22·8% in the 35 established diabetics, a difference of marked statistical significance (Table VI).

TABLE VI. COMPARISON OF PREVIOUS OBSTETRICAL HISTORIES IN NORMAL CONTROLS, 'RECENTLY DIAGNOSED' AND 'ESTABLISHED' DIABETIC NATAL INDIANS

Group	*Abortions*	*Neonatal deaths*	*Stillbirths*
Normal controls	8·3%	1·6%	3·3%
'Recently diagnosed' diabetics	23·6%	7·8%	25·8%
'Established' diabetics	22·8%	17·1%	34·3%

Jackson[31] conducted a survey in women who had had 3 or more abortions, and found that 17% had evidence of abnormal glucose-tolerance curves. He concluded that the examination of women who had had repeated abortions, without apparent reason, would therefore not disclose any latent diabetics.

However, in view of the marked difference exhibited between the controls and the diabetic Natal Indians, it is suggested that miscarriage in this population group (especially if repeated) is a valid indication for a glucose-tolerance test.

Hydramnios. The incidence of hydramnios will depend in large measure upon the astuteness of the observer and the criteria used for diagnosis. Although Driscoll and Gillespie[32] maintain that all diabetics have more amniotic fluid than do non-diabetics, a survey of the literature has indicated that the average incidence is 19%, a figure far in excess of the usually quoted 1 : 1,200 found in normal pregnancies (Table VII).

TABLE VII. COMPARISON BETWEEN COMPLICATIONS IN THE PREGNANT NATAL INDIAN DIABETIC AND THE WORLD LITERATURE*

Complication		*Natal Indian*	*Literature*
Ketosis	Incidence	8·8%	16·7%
	Perinatal loss	9·0%	30·1%
Coma	Incidence	0·8%	7·2%
	Perinatal loss	Nil	64·5%
Hydramnios	Incidence	19·3%	19·0%
	Perinatal loss	16·6%	39·0%
Toxaemia	Incidence	9·7%	25·0%
	Perinatal loss	25·0%	23·0%
Insulin requirement		Insulin-independent	Requirement increased
Vascular disease		? infrequent	++ Has been recorded in 20–50%

*As adapted from Kyle.[12]

Analysis has shown that 24 patients exhibited evidence of an excessive amount of liquor—an incidence of 19·3%. The presence of hydramnios bore no relation to the duration or severity of the diabetes, but was associated with 2 neonatal deaths and 2 stillbirths—a 16·6% perinatal mortality rate. The average foetal loss associated with hydramnios (as quoted in the literature) is 34%.[32]

Pre-eclamptic toxaemia. The criteria adopted for the diagnosis of pre-eclamptic toxaemia were two or more of the following signs: a blood pressure above 140/90 mm.Hg, oedema and proteinuria.

Despite irregular and infrequent attendance by many of the patients, only 12 (9·7%) of our diabetics developed toxaemia, an incidence which is considerably lower than the average figure of 20%.[32] All the 12 toxaemic pregnancies were classified as mild (blood pressure less than 160/110 mm.Hg, oedema +, albuminuria +), yet the perinatal mortality rate in this group was 25%, the comparative mortality quoted in the literature being 23%.[32]

Therefore, although pre-eclamptic toxaemia is an infrequent complication in the pregnant Natal Indian diabetic, it has a serious effect on the outcome of the pregnancy. Consequently pre-eclamptic toxaemia in the diabetic warrants close attention and careful supervision.

Pyelonephritis. Midstream specimens of urine were collected from all the patients for microscopic, chemical and bacteriological study. Based on the results of these investigations, together with blood urea estimations and special renal function tests (when indicated), it was found that 10% of the patients had evidence of chronic glomerulonephritis, 15% had pyelonephritis and 23·8% had asymptomatic bacteriuria (the presence of 100,000 or more organisms/ml.). Of the organisms isolated from culture of the urine, *E. coli* was the predominant bacterium in 76·1% of cases and *B. proteus* in 13·4%, while the remaining 10·5% was divided between haemolytic streptococci, *B. aerogenes* and non-haemolytic streptococci. Unfortunately, renal biopsies were not performed and the incidence of subclinical diabetic nephropathy could therefore not be assessed.

In spite of the high incidence of urinary tract involvement, no correlation could be found between infection, prematurity and perinatal mortality. None of the patients had evidence of impaired renal function.

The above results are in agreement with reports from the literature[32] and add considerable weight to the statement of Simms[33] that a pregnant diabetic should be assumed to have bacteriuria (with or without pyelonephritis) until proved otherwise.

DISCUSSION

The argument has often been put forward that the diabetes exhibited by the pregnant Natal Indian is either mild or merely indicative of a temporary disturbance in carbohydrate balance. Thus, although these patients are young, they behave in a pattern similar to the maturity-onset diabetic in that they are asymptomatic, rarely develop acidosis, are often well controlled on dietary restriction alone and are virtually independent of insulin. Furthermore, the pregnant Natal Indian usually gives a diabetic history of short duration and rarely develops toxaemia; and whereas the incidence of hydramnios is closely correlated with that in the literature, the associated foetal mortality rate is considerably lower. Finally, although the non-pregnant Natal Indian appears to be particularly prone to vascular disease, for some unaccountable reason her pregnant counterpart appears to be relatively free from this complication.

It would therefore seem reasonable to conclude that the pregnant Natal Indian diabetic does in fact exhibit a metabolic disturbance which varies both in presentation and severity from that in Caucasians (Table VII).

This conclusion, however, poses a pertinent but controversial question, namely: how do you assess the severity of diabetes in pregnancy?

The following 2 case histories serve to illustrate how the unpredictable behaviour-pattern of the Natal Indian diabetic precludes a satisfactory answer to this problem.

Case 1

A 36-year-old Indian was admitted on 23 September 1964 to the obstetrical unit at King Edward VIII Hospital, in coma. On examination she was found to be approximately 32 weeks pregnant, grossly ketotic and dehydrated. She had a blood pressure of 160/100 mm.Hg and a pulse rate of 130/min. A blood-sugar reading taken shortly after admission was 408 mg./100 ml., while the CO_2 combining power was 12·1 mEq./litre. Her electrolytes were normal.

She was resuscitated with sodium bicarbonate, intravenous fluids and insulin—given both intravenously and intramuscularly—and responded to this treatment within 6 hours. Good diabetic control was achieved within 48 hours on therapy with soluble insulin, prescribed according to the degree of glycosuria.

Three days later she was taken off all antidiabetic therapy as satisfactory diabetic control was maintained on dietary restriction alone. Apart from a moderate degree of hypertension (160/90 mm.Hg), she had hydramnios, diabetic retinopathy and a fairly pronounced urinary tract infection. The hypertension responded to treatment with guanethidine, and the pyelitis to therapy with suitable antibiotics.

Her previous obstetrical history indicated that she had had 3 previous pregnancies, the last 2 being terminated by caesarean section and resulting in a neonatal death and a stillbirth. The diagnosis of diabetes was established subsequent to her last pregnancy, during which time she had been on treatment with chlorpropamide.

On 28 October, when she was 37 weeks pregnant, an elective caesarean section was performed under general anaesthesia and a live 8-lb. male infant delivered with an Apgar rating of 10.

She made an uneventful recovery and her glucose-tolerance test on the 10th postpartum day showed a fasting blood-sugar level of 100 mg./100 ml. and a 2-hour value of 225 mg./100 ml. There was no glycosuria.

This patient (who had evidence of vascular disease) was the only one in the series who presented with diabetic coma. Yet despite a moderate degree of hypertension and hydramnios, she was delivered of a live child. The case further serves to illustrate characteristics commonly seen in the pregnant Natal Indian diabetic, namely, the high renal threshold and, in spite of an obviously severe metabolic disorder, the independence of insulin.

Case 2

A 22-year-old Indian female was admitted to the lying-in ward with a history of 'having had diabetes for one year'. On examination she was found to be 33 weeks pregnant, with a moderate (1%) degree of glycosuria but no acetonuria. She was normotensive and had no evidence of hydramnios or diabetic retinopathy. Her glucose-tolerance test showed a fasting blood-sugar level of 72 mg./100 ml. and a 2-hour value of 171 mg./

100 ml. She was well controlled on dietary restriction alone, her postprandial blood-sugar levels varying between 140 and 166 mg./100 ml.

Despite fairly close supervision, foetal movements disappeared when she was 37 weeks pregnant, and shortly thereafter she was delivered of a stillborn male infant weighing 10 lb. 2 oz.

Thus a stillborn infant resulted from a diabetic pregnancy characterized by a mild disturbance in carbohydrate metabolism, without the complications of ketosis, hydramnios and hypertension.

The underlying disorder must therefore be considered to be severe if the gestation results or is liable to result in a perinatal death, irrespective of whether the mother exhibits symptoms, is subject to the so-called complications of diabetes or is dependent on insulin for diabetic control.

The above results, together with the experience gained in the management of these patients, would justify the classification of the metabolic disorder in the pregnant Natal Indian diabetic as being 'severe'. The patient is not interested in semantics—she wants a live child!

SUMMARY AND CONCLUSIONS

A study of 124 pregnant Natal Indian diabetics is presented, based on the experience gained during the past 4½ years.

Glycosuria was found to be an unreliable index of abnormality as no fewer than 35·5% of patients in the series presented without glycosuria. It is therefore suggested that postprandial blood-sugar estimations be substituted for urinalysis and that every gravid patient should be screened by this method during each of the 3 trimesters.

The pregnant Natal Indian diabetic rarely presents with significant symptoms. The typical appearance of a patient is one of shortness, obesity and marked hirsutes.

Although these patients are young, they behave in a pattern similar to the maturity-onset diabetic; as ketosis is rare, they are often well controlled on dietary restriction alone; and they usually give a diabetic history of short duration. The pregnancies are infrequently complicated by toxaemia and, whereas the incidence of hydramnios is closely correlated with that in the literature, the associated perinatal mortality is considerably lower. Renal tract infection was found to be an extremely common complication.

Hormonal studies have indicated that the pregnant Natal Indian diabetic has increased adrenocortical activity together with impaired oestrogen biosynthesis. Whereas uric acid estimations were not related to the severity of diabetes or the degree of diabetic control, a progressive rise in this fraction was associated with a poor foetal prognosis. Serial estimations of uric acid are therefore recommended as a guide in the management of the pregnant diabetic. No abnormalities in lipid metabolism were noted.

Despite a 'moderate' metabolic disturbance, the perinatal mortality of the diabetics of recent onset and short duration, as judged by their previous obstetrical history, was considerably greater than that of normal controls. The 'severity' of the diabetes should be based on the liability of a particular pregnancy to result in a perinatal death, irrespective of whether the patient is subject to the so-called complications of diabetes, or is dependent on insulin for diabetic control. On this basis, the pregnant Natal Indian diabetic may be classified as 'severe'.

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REFERENCES

1. Campbell, G. D. (1960): Brit. Med. J., **2**, 537.
2. Leading Article (1965): Lancet, **2**, 578.
3. Campbell, G. D. (1961): Med. Dig. (Bombay), **29**, 714.
4. Joslin, E. P., Root, H. F., White, P. and Marble, A., eds. (1959): *The Treatment of Diabetes Mellitus*, p. 211. Philadelphia: Lea & Febiger.
5. Beaser, S. B. (1948): New Engl. J. Med., **239**, 765.
6. Skipper, E. (1933): Quart. J. Med., **2**, 353.
7. Allen, E. (1939): Amer. J. Obstet. Gynec., **38**, 982.
8. Kriss, J. P. and Futcher, P. H. (1948): J. Clin. Endocr., **8**, 380.
9. Campbell, G. D. (1963): S. Afr. Med. J., **37**, 1195.
10. Ahuja, M. M. S. (1965): Lancet, **1**, 1254.
11. Gelfand, M. and Forbes, J. I. (1963): S. Afr. Med. J., **37**, 1208.
12. Kyle, G. C. (1963): Ann. Intern. Med., **59**, suppl. 3, p. 18.
13. Campbell, G D. and McKechnie, J. (1961): S. Afr. Med. J., **35**, 1009.
14. Oakley, W. (1953): Brit. Med. J., **1**, 1413.
15. Long, W. N., Hartman, W. L., Futcher, P. H. and Eastman, N. J. (1954): Obstet. and Gynec., **3**, 160.
16. Parkin, G. M. (1958): Med. J. Aust., **1**, 622.
17. Notelovitz, M. (1967): M.D. thesis, University of the Witwatersrand.
18. Boulle, T. P. (1967): Personal communication.
19. Frandsen, V. A., Pedersen, J. and Stakeman, G. (1962): Acta endocr. (Kbh.), **40**, 400.
20. Greene, J. W., Smith, K., Kyle, G. C., Touchstone, J. C. and Dubring, J. L. (1965): Amer. J. Obstet. Gynec., **91**, 684.
21. Plotz, E. J. and Davis, M. E. (1962): Clin. Obstet. Gynec., **5**, 346.
22. Notelovitz, M. (1967): S. Afr. J. Obstet. Gynaec., **5**, 9.
23. Driscoll, S. G. (1965): Med. Clin. N. Amer., **49**, 1053.
24. De Waal, V. M., Rademeyer, L. J. and Booyens, L. J. (1967): S. Afr. Med. J., **41**, 106.
25. Hathorn, M. K. S., Gillman, T. and Campbell, G. D. (1961): Lancet, **1**, 1314.
26. Cosnett, J. E. (1959): Brit. Med. J., **1**, 187.
27. Joslin, E. P., Root, H. F., White, P. and Marble, A., eds. (1959): *The Treatment of Diabetes Mellitus*, chapt. 27. Philadelphia: Lea & Febiger.
28. McKechnie, J. K. (1964): S. Afr. Med. J., **38**, 182.
29. Eidlitz, M. (1961): Lancet, **2**, 1045.
30. Jeffcoate, T. N. A. (1962): *Principles of Gynaecology*, 2nd ed., p. 209. London: Butterworth.
31. Jackson, W. P. U. (1964): *On Diabetes Mellitus*, p. 158. Springfield, Ill.: Charles C. Thomas.
32. Driscoll, J. J. and Gillespie, L. (1965): Med. Clin. N. Amer., **49**, 1025.
33. Simms, E. A. H. (1962): Clin. Obstet. Gynec., **5**, 462.