Maternal serum fructosamine values after delivery of macrosomic babies and unexplained stillbirths

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Summary

Measurement of serum fructosamine and haemoglobin A_1 levels and glucose tolerance tests were performed in 75 women in the immediate postpartum period. None had predisposing factors to gestational diabetes. They were divided into three groups: group I consisted of 15 women who delivered an unexplained stillbirth; group II of 30 women who gave birth to babies weighing between 2 500 g and 3 900 g at term; and group III of 30 women who delivered babies weighing ⩾ 4 000 g. There was a significant difference in the mean level of serum fructosamine between the unexplained stillbirth and control groups ($P < 0,001$). Although the HbA_1 values varied in the three groups, there was a significant difference between the unexplained stillbirth group and the macrosomic infant group ($P < 0,05$). All patients had normal glucose tolerance tests.

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Delivery of a macrosomic baby or unexplained stillbirth indicates that the mother may have had abnormal glucose tolerance during pregnancy. Glucose tolerance, however, rapidly returns to normal after delivery in the gestational diabetic, reducing the likelihood of detecting diabetes by standard methods, such as an oral glucose tolerance test, in the pueperium.[1]

Serum fructosamine levels, a measure of keto-amine activity (glycosylated proteins, mainly albumin), have been found to be a good screening test for diabetes.[2] Unlike blood glucose levels, which change rapidly from minute to minute, and glycosylated haemoglobin (HbA_1) values, which give an indication of mean blood glucose level over the preceding 6 - 8 weeks, serum fructosamine levels reflect glycaemia over the preceding 1 - 3 weeks.[3] Estimation of serum fructosamine levels performed immediately after delivery should, theoretically, be able to detect any carbohydrate intolerance present in the last 2 weeks of gestation, whereas the diagnosis of gestational diabetes might be missed by HbA_1 measurement because of its longer half-life.

A study was undertaken to establish serum fructosamine values immediately after delivery in women with no medical complications who had delivered: (*i*) unexplained stillbirths; (*ii*) average-sized babies; and (*iii*) macrosomic babies (> 4 000 g).

Patients and methods

The study was performed at King Edward VIII Hospital, Durban, over a period of 1 year. Informed consent was obtained from 75 black women who had no predisposing factors to gestational diabetes, viz. glycosuria, a family or past history of diabetes, and a history of unexplained stillbirths or neonatal deaths.

Excluded from the study were patients with a haemoglobin level of < 10 g/dl; albumin concentration of < 35 g/l; weight of > 90 kg; positive serological test for syphilis; rhesus negative blood; or a history of hypertension or renal disease. The patients studied were divided into three groups. Group I consisted of 15 patients who delivered an unexplained macerated stillbirth, group II of 30 patients of similar age and parity who had given birth to babies weighing between 2 500 g and 3 900 g at term, and group III of 30 patients who delivered babies weighing ⩾ 4 000 g.

Blood samples were taken after an overnight fast for the measurement of serum fructosamine, glycosylated haemoglobin, and rapid plasma reagin levels, haemoglobin value, blood grouping (ABO and Rh), and liver function tests within 48 hours of delivery.

In addition, a 75 g oral glucose tolerance test (OGTT) was performed. Blood samples for glucose estimation were taken in tubes containing a fluoride oxalate mixture. Plasma glucose levels were measured by the glucose oxidase method using a Centrifichem System 500 analyser. The diagnosis of abnormal glucose tolerance was made according to World Health Organisation criteria.[4]

Serum fructosamine was measured by a colorimetric method using a commercial kit from Roche (Switzerland). The method of Johnson *et al.*,[5] was adapted for the Centrifichem analyser. Glycated protein calibrated with deoxymorpholinofructose was used as the standard. Both the intra- and inter-assay coefficients of variation were < 3%.

HbA_1 was quantitated by cation-exchange chromatography at 22°C. Controls were incorporated in each assay. Both the intra- and inter-assay coefficients of variation were < 10%.

Statistics. Student's unpaired *t*-test and Pearson's correlation coefficient (*r*) were used to quantitate the correlation between relevant variables.

Results

The clinical data are shown in Table I.

Serum fructosamine values are shown in Table II. There was a significant difference in the mean level of fructosamine between the unexplained stillbirth and control groups only (2,27 v. 1,96 mmol; $P < 0,001$).

TABLE I. MEAN (RANGE) CLINICAL DATA

	Group I (N = 30)	Group II (N = 15)	Group III (N = 30)
Age (yrs)	**27**	**25**	**26**
Parity	**2**	**1,5**	**2,5**
Birthweight (g)	**1 490 (500 - 4 600)**	**3 020 (2 500 - 3 250)**	**4 200 (4 000 - 4 600)**

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TABLE II. SERUM FRUCTOSAMINE VALUES (mmol/l)

	Group I	Group II	Group III
Mean	**2,27***	**1,96***	**2,07**
Range	**1,9 - 3,1**	**1,48 - 2,63**	**1,8 - 2,5**

*$P < 0,001$

Plasma glucose results are set out in Table III. All 75 patients in the study had normal glucose tolerance tests. There was a significant difference in the fasting blood sugar values between group I and group II (4,5 v. 3,9 mmol/l; $P < 0,0005$). There was no significant difference between group III and group II. Although the 2-hour blood sugar attained no statistical significance, the mean blood sugar was higher in groups I and III compared with group II.

TABLE III. PLASMA GLUCOSE LEVELS (mmol/l)

	Group I	Group II	Group III
Mean fasting	**4,5***	**3,9***	**4,3**
Range	**3,7 - 5,1**	**3,1 - 5,0**	**3,1 - 5,2**
Mean 2 h	**6,3**	**5,5**	**5,9**
Range	**4,7 - 9,9**	**4,0 - 7,7**	**4,2 - 10,4**

*$P < 0,0005$

Although the HbA_1 values were inconsistent in the three groups (Table IV), there was a significant difference between group I and group III ($P < 0,05$). There was no significant difference between group I and group II or between group III and group II.

TABLE IV. HbA_1 LEVELS (%)

	Group I	Group II	Group III
Mean	**6,4***	**7,0**	**7,7***
Range	**5,2 - 8,3**	**5,6 - 9,1**	**5,6 - 14,9**

*$P < 0,05$

Discussion

There is conflicting evidence regarding the correlation between HbA_1 values and birth weight. Widness *et al.*[6] found a good correlation, whereas Coen *et al.*[7] reported contradictory findings. The present study showed no significant difference between the mean HbA_1 and serum fructosamine levels in groups III and II.

The serum fructosamine level was elevated in 3 patients in group I and in 2 patients in group III, whereas HbA_1 was elevated in 3 different patients in group III. A possible explanation for this discrepancy is that the half-lives of these two substances are very different and hence the two parameters may not strictly conform. This poor correlation between glycosylated haemoglobin and fructosamine level confirms the findings of Ross *et al.*[8]

According to WHO criteria[4] glucose tolerance was normal in all 75 patients. Serum fructosamine values are an index of the mean glucose levels 1 - 3 weeks before delivery. The OGTT may have been normal in the 3 patients in group I who had elevated serum fructosamine levels because of poor placental function. This, however, does not rule out the possibility that the 3 patients may have had glucose intolerance in the predelivery period.

HbA_1 gives a mean glucose reading for the preceding 8 - 12 weeks. The patients with elevated HbA_{1c} in group III may have had normal OGTTs because there are other causes for macrosomia and these may overlap with HbA_1 values in normal patients and known diabetics. Further studies determining the levels of serum fructosamine and HbA_1 in known pregnant diabetics in the post-delivery period are therefore necessary.

It is well known that the fasting plasma glucose concentration is reduced during pregnancy.[9] The difference in the fasting blood glucose in group I and group II may have been as a result of some degree of intolerance in the former.

Although serum fructosamine value gives a good index of mean control in the preceding 1 - 3 weeks,[3] it cannot be used as a screening test for diabetes in the immediate postpartum period, since it does not correlate with birth weight. This is not surprising, since there are other causes for macrosomia. Elevated levels of serum fructosamine in the post-delivery period in the presence of a normal OGTT in patients who deliver unexplained stillbirths does not rule out the possibility that there may have been glucose intolerance.

Since the serum fructosamine assay is in its early stages, we recommend that initially it should be used interchangeably with HbA_1 estimations.

In conclusion, serum fructosamine levels cannot be used as a screening test for diabetes in the immediate postpartum period, since it does not correlate with birth weight. However, it is a good index of the mean control in the preceding 1 - 3 weeks. Elevated levels in the post-delivery period may indicate gestational diabetes.

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