Maternal and Cord Blood Fructosamine in Normally Pregnant Women During Delivery

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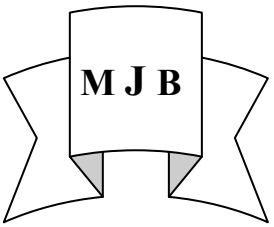

Abstract

To compare between serum fructosamine values in maternal and cord blood and the relationship with birth weight, serum albumin or total protein concentration as well as the influence of albumin or total protein on fructosamine values and the need for correcting their values accordingly using different equations.

Plasma glucose (PG) and serum fructosamine (FAm), albumin and total protein were measured in maternal and cord blood from 20 full-term pregnant women delivered by normal vaginal delivery women. Calculation of corrected fructosamine (FAc) was made according to serum albumin or total protein values using different equations. The pregnant women were attending Al-Batool Maternity Hospital in Mosul during April 2001.

When comparing the maternal and cord blood parameters, there was no significant difference in PG and albumin concentrations, while there was a slight significant difference between them in FAm ($p<0.01$), and a highly significant difference in total protein ($p<0.001$). There was no significant correlation between the weight of the baby and FAm of the maternal blood ($r=0.08$) or cord blood ($r=0.18$). There was also no significant correlation between FAm and albumin in the cord blood ($r=0.31$) or maternal blood ($r=0.07$). After correction, comparison between FAm and FAc showed a slight difference between FAc and FAm in the maternal blood ($P< 0.05$ based on albumin and $p<0.001$ based on total protein). In the cord blood, FAm showed also a highly significant difference from FA ($P< 0.001$). There was no significant difference between FAc in the cord blood and in the maternal blood using all equations.

Cord blood fructosamine was lower than maternal blood fructosamine with no significant correlation was found between weight of baby and maternal fructosamine or cord blood fructosamine. Correction of measured fructosamine accordingly improves its usefulness as an index of glycated protein for assessing glycaemic state.

الخلاصة

تضمنت الدراسة مقارنة بين قيم أمين فركتوزمصل الدم للام ومصل الدم للحبل السري وعلاقتها بوزن الوليد عند الولادة ، وتركيز زلال مصل الدم أو البروتين الكلي ، كذلك مدى تأثير زلال مصل الدم أو البروتين الكلي على قيم أمين الفركتوز ومدى الحاجة إلي تصحيح قيمته وفق ذلك باستخدام معادلات مختلفة معتمدة على تركيز زلال مصل الدم أو البروتين الكلي .

تضمنت الدراسة قياس تركيز سكر العنب لبلازما الدم حال الصوم وأمين الفركتوز والزلال والبروتين الكلي في مصل الدم للحبل السري ومصل الدم للأم (العدد ٢٠) . تم حساب قيم أمين الفركتوز المصحح تبعا لزلال مصل الدم والبروتين الكلي باستخدام عدة معادلات لنساء حوامل أثناء الولادة في مستشفى البتول للولادة في الموصل خلال شهر نيسان ٢٠٠١ . لوحظ عدم وجود فرق احصائي معنوي عند مقارنة تركيز سكر العنب حال الصوم وتركيز زلال مصل الدم في مصل الدم للحبل السري وللأم. بينما ظهر فرق احصائي معنوي عند مقارنة تركيز أمين الفركتوز (ب < ٠،٠١) . وتركيز البروتين الكلي (ب < ٠،٠٠١). مع وجود ترابط غير معتد بين وزن الطفل الحديث الولادة وتركيز أمين فركتوز مصل الدم للأم (ر=٠،٠٨) أو أمين فركتوز مصل الدم للحبل السري (ر=٠،١٨) . أظهرت النتائج وجود ترابط غير معتد بين أمين الفركتوز وزلال مصل الدم في مصل الدم للحبل السري (ر= ٠،٣١) أومصل الدم للأم (ر= ٠،٠٧) . بعد التصحيح أظهرت النتائج وجود اختلاف ذا مغزى احصائي بين أمين الفركتوز المقاس والمصحح في مصل الدم للأم حسب زلال مصل الدم (ب< ٠،٠٥) وحسب تركيز البروتين الكلي (ب< ٠،٠٠١) في مصل الدم للحبل السري ؛ أظهرت النتائج وجود اختلاف ذا مغزى احصائي بعد التصحيح (ب<٠،٠٠١) بينما تبين انه لا يوجد فرق ذا مغزى احصائي بين أمين الفركتوز بعد التصحيح في مصل الدم للحبل السري وللأم.

ان تصحيح أمين الفركتوز طبقا لزلال الدم أو البروتين الكلي يعتبر ضروريا للأستفادة من هذا الفحص في تقدير وزن الجنين في الحوامل السكريين .

Introduction

In pregnant diabetics, poor glycemic control increases the incidence of maternal and fetal complications which is the single most important factor influencing the outcome of pregnancy. Careful plasma glucose control is mandatory because of the adverse effects of hyperglycaemia and ketosis on the fetus. This is particularly important and needs special attention before conception, in early pregnancy and during labour[1].

Johnson *et al.*[2] introduced fructosamine assay into the clinical chemistry literatures in 1983 as a general term for ketoamine reflecting glycated albumin and protein. Fructosamine is the trivial name for 1-amino-1-deoxy-fructose, also called “isoglucosamine” which is a ketoamine derivative of the non-enzymatic post-

translational modification of a sugar (usually glucose) and a protein (usually albumin) which are incorporated during the synthesis of the molecule[3]. Measurement of serum fructosamine can be used in a manner similar to HbA_1c to monitor the average concentration of blood glucose over an extended period of time: about 1-3 weeks for fructosamine and 6-8 weeks for HbA_1c[4,5]. Its value is influenced by the blood concentration of glucose and total proteins[6,7], and during pregnancy it is also related to gestational age[8]. Maintaining maternal glycaemic control within normal, as reflected by HbA_1c or fructosamine, is an important objective in the management of diabetics that focused extra-importance in pregnant women complicated by diabetes mellitus[9,10].

Serum glycated protein includes glycation of all circulating proteins and glycaemic state as well as the state of serum protein and albumin influence its accurate assessment[11]. This is particularly important in patients with hypoproteinemia or with altered metabolism of protein[12]. There is also a potential need for estimating fructosamine during pregnancy where serum albumin or protein may physiologically be affected.

Serum fructosamine concentration depends on the prevailing concentration of glucose and protein mainly albumin. It seems logical to correct the measured fructosamine for expression in term of constant albumin or total protein concentration. However, the need of this correction is controversial and different correction formula have been followed[13-16]. However, many authors warned that increased catabolism and abnormal plasma protein ratios, where the mean half-life is reduced, might affect the value of the measurement and the life span and state of catabolism of the protein is also important[11].

The aim of the current study is to compare between the fructosamine values in maternal and cord blood and the relationship with birth weight or serum albumin or total protein concentration.

Subjects and Methods

Maternal and cord blood samples were collected during delivery from 20 normal pregnant women who were attending Al-Khansa Maternity Hospital in Mosul during April 2001. Their age range was 18-38 with mean±SD of 26.88 ± 5.62 years. They had no history of diabetes mellitus or hypertension. All cases gave birth to

infants at 39-40 weeks and had a normal vaginal delivery.

The sampling of blood was done by antecubital venepuncture during labour from the mother and from the cord of the baby. A sample of 2 ml blood was taken from each lady and divided into two containers: 1. Fluoride-oxalate container: One ml of blood was mixed in fluoride-oxalate container for the estimation of glucose concentration. 2.Plain tube container: Another one ml of blood was collected in plain tube for the estimation of other biochemical parameters (fructosamine, albumin, and total protein).

Plasma glucose (PG) was estimated by enzymatic (glucose-oxidase-peroxidase) method[17] , using a kit supplied by Randox Ltd (England). Serum fructosamine was determined using nitroblue tetrazolium colorimetric method[2], which is based on the reducing ability of fructosamine in alkaline buffer solution, using reagents from Sigma (USA). Serum total protein was determined by biuret method[18], using a kit purchased from Randox (England). Serum albumin was determined by bromocresol green (BCG) dye binding method[19] using a kit purchased from Randox Ltd (England).

Calculation of corrected fructosamine (FAc) was done according to the following equations depending on serum albumin concentration (equations 1, 2, and 3) or total protein (equation 4):

1. FAc_1 = Fam + 0.03 (40 - Albumin concentration g/l)[13]

2. FAc_2 = a decrease or increase in serum albumin concentration of (1g/l) requires: addition or subtraction of (0.023)mmol/l of FAm for albumin < 40 g/l or > 40g/l respectively[14].

3.FAc_3 = FAm x 40/albumin concentration (g/l)[15]

4. FAc_4 = FAm x 70/ total protein (g/l)[16]

The statistical methods were used for the analysis of data included: standard statistical methods, the mean, median, standard deviation (SD), standard error (SE), and skewness. Paired and unpaired student Z-test were used to compare results for various biochemical parameters among subjects of the same group and in the different groups respectively. Linear regression analysis was also performed for finding the relationship between the dependent and independent variables.

Duncan's test was also used to identify group(s) responsible for statistical difference through comparison, following analysis of variance (ANOVA). All values quoted as the mean ± SD. Differences between observations are considered significant at $p \leq 0.05$[20].

Results

The study group composed of 20 full-term pregnant women delivered by normal vaginal delivery. The sampling of blood was done during labour from the mother and from the cord of the baby. The weight of babies was 3.12 ± 0.480 kg (range 2.4-4.4). The results of different parameters (maternal and fetal) are presented in table (1).

Table 1 Comparison between maternal and cord serum parameters (mean ± SD).

Parameters	Maternal (n=20)	Cord (n=20)	Z	p
Glucose (mmol/L)	4.47 ± 0.51	4.38 ± 0.74	0.74	NS
Albumin (g/l)	38.3 ± 3.4	35.7 ± 3.9	1.65	NS
Total protein (g/l)	59.3 ± 4.6	50.6 ± 4.5	4.1	< 0.001
FAm (mmol/l)	1.74 ± 0.31	1.54 ± 0.27	2.4	< 0.01
FAc_1 (mmol/l)	1.79 ± 0.32	1.67 ± 0.33	1.22	NS
FAc_2 (mmol/l)	1.78 ± 0.31	1.64 ± 0.32	1.41	NS
FAc_3 (mmol/l)	1.83 ± 0.37	1.76 ± 0.45	0.98	NS
FAc_4 (mmol/l)	2.1 ± 0.38	2.14 ± 0.37	0.52	NS

When comparing the maternal and cord blood parameters, there was no significant difference in PG and albumin concentrations, while there was a slight significant difference between them in FAm ($p<0.01$), and a highly significant difference in total protein ($p<0.001$).

There was no significant correlation between the weight of the baby and FAm of the maternal blood ($r=0.08$) or cord blood ($r=0.18$). There was also no significant correlation between FAm and albumin in the cord blood ($r=0.31$) or maternal blood ($r=0.07$).

After correction, comparison between FAm and FAc showed a slight difference between FAc_1, FAc_2, FAc_3 and FAm in the maternal blood ($Z= 2.1, 2.01, 2.0$; $p<0.05$). There was also

a highly significant difference between FAm and FAc_4 ($Z = 3.6$; $p<0.001$). In the cord blood, FAm showed a highly significant difference from FAc_1, FAc_2, FAc_3 and FAc_4 ($Z = 3.35, 3.3, 3.2, 3.6$; $p<0.001$). There was no significant difference between FAc in the cord blood and in the maternal blood using all four equations.

The relation between FAm and albumin was studied by linear regression analysis and showed no significant correlation in both, the maternal blood ($r=0.08$) and cord blood ($r=0.30$). No significant correlation was also noted between FAm and total protein in maternal blood ($r = 0.155$) and cord blood ($r = 0.315$).

Discussion

Several studies support the value of the determination of serum glycated protein as a useful parameter for the assessment of the antecedent glycaemic control in patients with diabetes mellitus[21,22,23]. Studies had also stated that serum fructosamine provides an additional complementary screening test for diabetes mellitus including GDM[24,25]. The application of fructosamine in diabetic care during pregnancy requires discrimination values that are both adjusted for gestational age and designed to compensate for the rate of glycation of serum proteins[25]. Maternal diabetic control during pregnancy has a significant influence on fetal growth and poor glycaemic control contributes to the development of fetal macrosomia.

Comparison between the biochemical parameters in fetal and maternal blood of normal pregnant women was done. There were significantly lower values of FAm and total protein in cord blood in comparison with maternal blood. The values of albumin and glucose were also lower but did not reach statistical significance. There was no significant correlation between FAm (fetal and maternal) and the weight of the baby.

In this study, the value of cord blood FAm was 1.54 ± 0.27 mmol/l which is in agreement with that reported by Mousa *et al.*[26] of 1.45 ± 0.16 mmol/l. Comparison of maternal and fetal FAm revealed a significant difference ($p<0.01$) that disappeared following correction using all four equations. When maternal and fetal FAc were compared, no significant difference was obtained when using correction equations based on albumin, while when correction was made according to total protein, a significant difference ($p<0.001$) was

noted. However, when cord blood FAm and FAc were compared, a significant difference ($p<0.001$) was noted using all equations. Hence, correction of fetal FA according to albumin or total protein is required to improve the usefulness of this index of glycated protein.

In comparison with other studies; Nasrat *et al.*[27] and Fadel *et al.*[28], also observed no significant correlation in these parameters in normal pregnant women. However, in pregnant diabetics the relationship between these parameters is different. Mousa *et al.*[26] in their study on 20 pregnant diabetic women showed a good correlation between fetal birth weight and maternal FAm ($r = 0.62$) and between fetal birth weight and cord blood FAm ($r = 0.74$). Hence, it appears that glycated protein is a good determinant of fetal weight in pregnant diabetics[28]. This effect may commence early in pregnancy as supported by Roberts and Baker's[29] finding who reported higher FAm values during the first trimester of pregnancy in mothers of macrosomic infants. Also Robert *et al.*[30] reported that the incidence of fetal macrosomia is increased with FAm levels of more than 2.50 mmol/l at 35-37 weeks gestation. Therefore, it seems that maternal FAm can be of value in predicting fetal macrosomia in diabetic pregnancy and a study is required to determine the cut-off point above which such fetal macrosomia is likely to develop.

In conclusion; cord blood fructosamine was lower than maternal blood fructosamine with no significant correlation was found between weight of baby and maternal fructosamine or cord blood fructosamine. Correction of measured fructosamine accordingly improves its usefulness as an index of glycated protein for assessing glycaemic state.

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