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Relevance of Serum Fructosamine and Random Blood Glucose for the Screening of Gestational Diabetes Mellitus

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Abstract: This preliminary study examined the efficacy of serum fructosamine and Random Blood Sugar (RBG) for the screening of Gestational Diabetes Mellitus (GDM). Venous blood samples from 32 pregnant women were analyzed for serum fructosamine and RBG. The actual fructosamine levels were corrected for serum protein (c-fructosamine) for more precise presentation. Subjects with RBG > 7.8 mmol L^{-1} were assigned to hyperglycemic group. The results showed a significant correlation between RBG and c-fructosamine (Pearson correlation = 0.53, $p<0.01$). Out of 32 subjects, 6 (18.75%) were found to be hyperglycemic (RBG >7.8 mmol L^{-1}). The levels of both RBG (9.916±0.82 versus 5.019±0.231 mmol L^{-1}, $p<0.0001$) and c-fructosamine (2.541±0.132 versus 2.251±0.057 mmol L^{-1}, $p<0.05$) were significantly higher in hyperglycemic subjects as compared to normal pregnant women. One patient with normal RBG showed above normal c-fructosamine (3.125 % false positive), whereas 3 patients with hyperglycemia had normal c-fructosamine (9.375% false negative). The findings of this preliminary study clearly indicate that the paired values of fructosamine and RBG could help in filtering high-risk individuals prior to OGTT, thereby avoiding cumbersome OGTT for identification of GDM in a large number of patients.

Key words: Diabetes mellitus, pregnancy, fructosamine, random blood glucose

Introduction

Gestational Diabetes Mellitus (GDM) is associated with adverse fetal and maternal outcomes that can be prevented by timely diagnosis and management of GDM (Kendrick, 2004; Gunton *et al*., 2002; Moses and Griffiths, 1995). Routine screening for GDM is therefore an important aspect of antenatal care in order to minimize its serious consequences (Griffith and Convay, 2004; Yogev *et al*., 2004). The measurement of Fasting Blood Glucose (FBG) (Laird *et al*., 1996; Miller and Steinhoff, 1982) and Random Blood Glucose (RBG) (Hatem and Dennis, 1987; Lind and Anderson, 1984) are the simplest and commonly used screening tests for GDM. Whereas, Oral Glucose Tolerance Test (OGTT) is recognized as a standard confirmatory tool for diabetes (McCance *et al*., 1997). Both FBG and RBG are instant tests and unable to predict the glycemic history whereas multiple OGTT (Gruendhammer *et al*., 2003), daily glucose profiles (Mello *et al*., 1997) or continuous glucose monitoring (Yogev *et al*., 2003) may be impractical for routine application due to their high cost, lengthy procedure and patients' noncompliance.

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On the other hand, measurement of glycated proteins including fructosamine (Baker *et al*., 1985; Austin *et al*., 1999) and glycated hemoglobin (HbA1c) (Paisey *et al*., 1980; Goldstein *et al*., 1986) has been employed for the assessment of short- (due to faster turnover of albumin than hemoglobin) and long-term glycemic control, respectively. Serum fructosamine is a simple, sensitive and precise method for the evaluation of glycemic control within a few weeks time (2-3 weeks) and is therefore more advantageous in timely detection of responses to diabetic treatment plan (Austin *et al*., 1999). The use of serum fructosamine for the screening of GDM has been widely reported (Hughes *et al*., 1995; Parfitt *et al*., 1993; Frandsen *et al*., 1988; Roberts and Baker, 1986; Roberts *et al*., 1983, 1988). Salemans *et al*. (1987) have noticed that fructosamine is more sensitive than HbA1c for the detection of abnormal glucose tolerance. Serum fructosamine has been correlated with FBG (Hom *et al*., 1998; Mula Abed and Al Naemi, 2003), OGTT (Roberts and Baker, 1986) and HbA1c (Parfitt *et al*., 1993; Rosic *et al*., 1993). In this study, an attempt has been made to examine a possible association between fructosamine and RBG and the usefulness of these two parameters for the screening of GDM.

Materials and Methods

Thirty-two Saudi pregnant women in their first trimester, attending the antenatal care clinics at the Armed Forces Hospital, Riyadh during the second half of the year 2004 were included in this study. Venous blood samples were collected from the non-fasted subjects for the analysis of RBG and serum fructosamine using Hitachi autoanalyzer. The actual fructosamine levels were corrected for serum protein (c-fructosamine) for more precise presentation (Hom *et al*., 1998; Kennedy *et al*., 1998; Gunter *et al*., 1995; Agarwal and Punnose, 2001). Subjects with the RBG concentrations>7.8 mmol L^{-1} were assigned to hyperglycemic group.

The data were evaluated by SPSS statistical package version 10. Pearson's correlation test was performed to analyze an association between RBG and c-fructosamine. Independent samples Student's t-test (2-tailed) was used to compare means between the normal and hyperglycemic groups. $p<0.05$ were considered as statistically significant.

Results

The mean value±standard deviation of RBG from 32 pregnant women was 5.937±2.353 (range, 2.30-12.40) mmol L^{-1} and the mean c-fructosamine was 2.306±0.316 (range, 1.84-3.07) mmol L^{-1}. A significant correlation was observed between RBG and c-fructosamine (Pearson correlation = 0.53, $p<0.01$) (Fig. 1).

Out of 32 subjects, 6 (18.75%) were found to be hyperglycemic on the basis of RBG cut-off as 7.8 mmol L^{-1}. The levels of RBG were significantly higher in hyperglycemic subjects (9.916±0.82 mmol L^{-1}) as compared to normal pregnant women (5.019±0.231 mmol L^{-1}) ($p<0.0001$, Fig. 2a). The concentration of c-fructosamine was also significantly higher in diabetic group (2.541±0.132 mmol L^{-1}) as compared to normal group (2.251±0.057 mmol L^{-1}) ($p<0.05$ and Fig. 2b).

Using the RBG cut-off of 7.8 mmol L^{-1} and c-fructosamine reference range of 1.8-2.5 mmol L^{-1}, 4 subjects showed incompatible paired values of RGB (c-fructosamine) as follows: 6.2 (3.07), 12.4 (2.46), 8.9 (2.31) and 7.9 (2.08) mmol L^{-1}. In other words, 1 patient with normal RBG showed above normal c-fructosamine (3.125% false positive), whereas 3 patients with hyperglycemia had normal c-fructosamine (9.375% false negative).

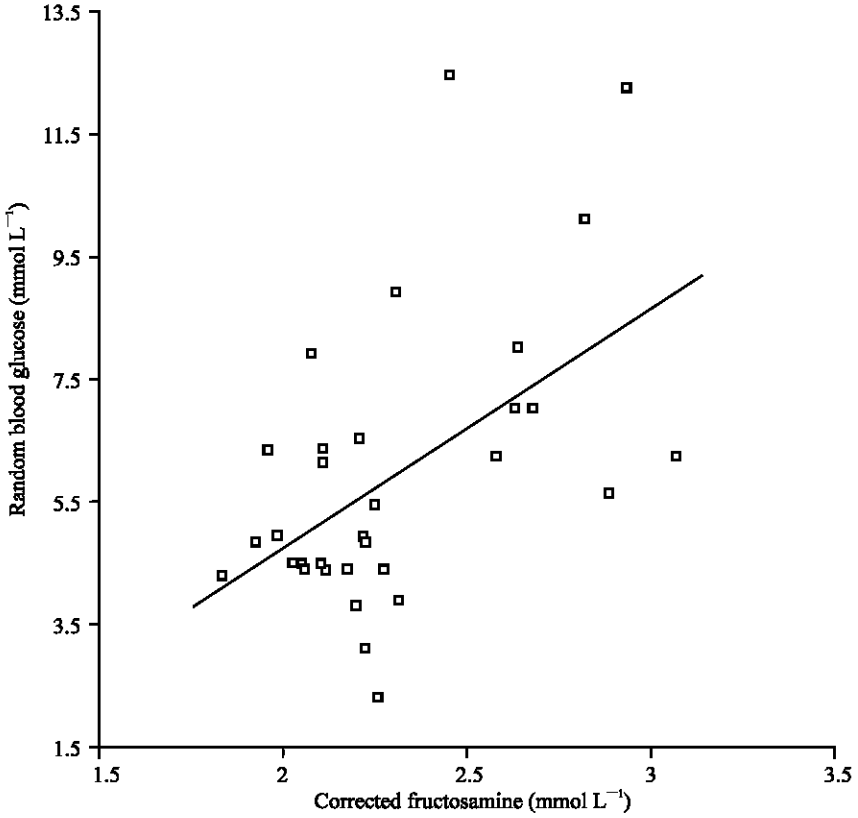

Fig. 1: Correlation between random blood glucose (RBG) and corrected fructosamine (c-fructosamine) levels in 32 pregnant women (R = 0.53, p<0.01, Pearson's test)

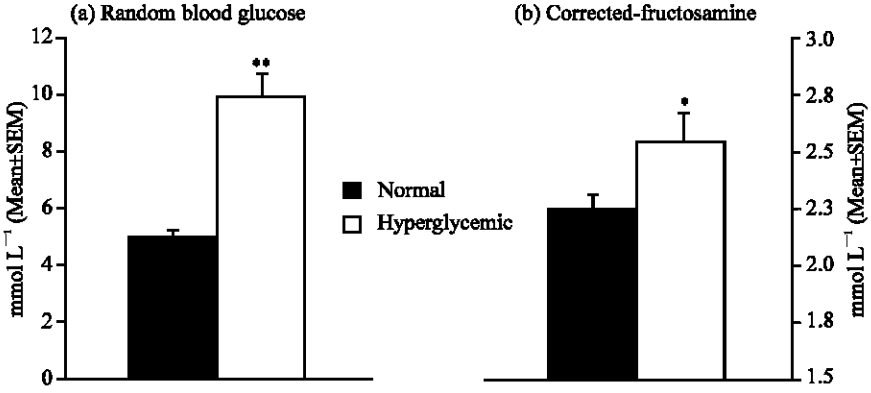

Fig. 2: Bar graphs showing (a) random blood glucose and (b) corrected-fructosamine levels in normal (N = 26) and hyperglycemic (N = 6) pregnant women. *p<0.05 and **p<0.001 versus normal group using 2-tailed Student's t-test

Discussion

The findings of this study showed a significant association between RBG and c-fructosamine. Significant correlations between serum fructosamine and preprandial (Frandsen *et al*., 1988) or postprandial (Kennedy *et al*., 1998) blood glucose levels have been reported earlier. Although both fructosamine and HbA1c are the reliable indicators of glycemic control, fructosamine has been regarded as the best predictor of blood glucose levels (Parfitt *et al*., 1993; Kennedy *et al*., 1998). In a series of 25 patients with type 2 diabetes, serum fructosamine was found to be better reflector of average blood glucose concentrations over the previous 3-6 weeks, whereas HbA1c being more useful for the previous 8-10 weeks (Chen *et al*., 2002). Moreover, a significant correlation between maternal and cord blood fructosamine has indicated the use of maternal fructosamine levels for indirect estimation of metabolic status of fetus (Czeszynska *et al*., 1998). It has been shown that maintaining the serum fructosamine levels <2.5 mmol L^{-1} can significantly reduce the neonatal complications (Roberts *et al*., 1988).

Although the usefulness of RBG for routine detection of GDM has been described (Hatem and Dennis, 1987; Lind and Anderson, 1984; Kirkpatrick *et al*., 1988; Maheshwari and Mataliya, 1989) many other studies have suggested that RBG alone cannot be considered as an efficient and reliable screening procedure for GDM (Jowett *et al*., 1987; Nasrat *et al*., 1988; Nielsen *et al*., 1988). Similarly the use of fructosamine alone for the screening of GDM may not be justified. In this study, serum fructosamine assay was associated with 3.125% false positivity and 9.375% false negativity on the basis of RBG values for the assessment of hyperglycemia. Earlier investigators have also reported 2.7% false positive and 32.6% false negative observations with a serum fructosamine cut-off value of 2.65 mmol L^{-1} (Mula Abed and Al Naemi, 2003). Hom *et al*. (1998) observed 23-26% error rates for fructosamine, c-fructosamine and HbA1c in a series of 450 diabetic patients. In another study, c-fructosamine test achieved 79.4% sensitivity and 77.3% specificity for the diagnosis of GDM (Hughes *et al*., 1995). Thus, the combined assessment of fructosamine and RBG would be more advantageous for the identification of GDM as compared to measuring only one of these parameters. Since fructosamine determines the average glucose over the past 2-3 weeks the test is not affected by the food eaten during the day. There was no significant difference between serum fructosamine levels measured fasting and 2 h after ingestion of 75 g glucose (Peiris, 2000). For this reason fructosamine can be measured at any time during the day and the same blood sample can be used for the analysis of both RBG and fructosamine. Thus, the paired values of RBG and fructosamine could be utilized in avoiding unnecessary OGTT in a large number of cases as suggested earlier (Agarwal *et al*., 2001; Ko *et al*., 1998).

In conclusion, the findings of this preliminary study point towards the usefulness of this simple and patient-friendly methodology for short-listing patients before referring them to standard OGTT for the confirmation of GDM.

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