

# The comparison of 50 grams glucose challenge test, HbA<sub>1c</sub> and fructosamine levels in diagnosis of gestational diabetes mellitus

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*Summary:* We evaluated the sensitivity, specificity, positive and negative predictive values of 50 grams glucose challenge test, serum fructosamine and HbA<sub>1c</sub> levels as screening tests for gestational diabetes mellitus. Forty-two pregnant patients between the 24th and 28th week of their pregnancies were included in the study. Blood fructosamine and HbA<sub>1c</sub> levels did not differ significantly from the 50 grams glucose challenge test and were concluded to be alternatives to this test. Any combination of these 3 tests gives better results than a single test, but no one of the combinations is superior to the others.

*Key words:* Gestational diabetes mellitus; Fructosamine; HbA<sub>1c</sub>, 50 grams glucose challenge test.

## INTRODUCTION

It has been recognized for many years that glucose intolerance in pregnancy can cause a high perinatal morbidity and mortality rate. Two to three percent of pregnancies are complicated by Gestational Diabetes Mellitus (GDM) and hence all pregnancies must be screened. Because of this high incidence, 50 grams glucose challenge test (50 GGCT) is advised by the National Diabetes Data Group as the most reliable screening test (<sup>1</sup>). The pur-

pose of this study was to examine the usefulness of glycosylated hemoglobin and fructosamine as a screening test for GDM, and to determine the predictive values, sensitivity and specificity of double screening tests (50 GGCT + HbA<sub>1c</sub>, Fructosamine + HbA<sub>1c</sub>, etc.).

## MATERIALS AND METHODS

Forty-two pregnant patients, followed in our antenatal outpatient clinic during last year were included in the study. The experimental protocol has been reviewed and approved by an ethics committee. Blood samples were obtained for HbA<sub>1c</sub> and fructosamine, and 50 GGCT was done between the 24th and 28th gestational weeks. The pregnancies beyond the 28th gestational week and previously diagnosed as diabetes mellitus were excluded from the study, and the test was done without interest as to whether the patient had eaten or was fasting. Venous blood was obtained 1 hour after ingestion of 50 gr glucose and the glucose level was measured in plasma by the glucose oxydase method.

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Blood fructosamine level was estimated by the colormatic method and the HbA<sub>1c</sub> level by colon chromatography using BIO Science Laboratory kits, and the cut off values were accepted as 2.85 mmol/l and 7.2%, respectively. A hundred grams oral glucose tolerance test (OGTT) was applied to all patients. The OGTT was done by the method defined by O'Sullivan and Mahan and was modified by Carpenter and Custon<sup>(2,3)</sup>. Patients were advised to take 150 gr of carbohydrate per day for 3 days prior to the test. Patients were administered 100 gr glucose orally in the morning.

Plasma glucose levels were determined in the fasting state and then hourly and the normal limits were 105 mg/dl, 190 mg/dl, 165 mg/dl, 145 mg/dl, respectively. The glucose tolerance test was considered abnormal when at least 2 values were equal to or higher than those values.

Statistical analyses were done by linear regression analysis and z-test among the proportions. The validity of the tests was evaluated in terms of sensitivity, specificity, (+) and (-) predictivities in a 2×2 table.

## RESULTS

The obstetrical characteristics of the patients were shown on Table 1. The mean age was  $27.05 \pm 4.33$ , mean gravidity was  $2.14 \pm 1.59$ , mean parity was  $0.69 \pm 1.24$ , mean gestational age was  $26.21 \pm 1.63$ .

The OGTT was abnormal in 11 of 24 (45.8%) patients who had 50 GGCT results equal to or higher than 140 mg/dl, and in only 3 of 18 patients (16.6%) who had 50 GGCT results below 140 mg/dl. Positive predictive and (-) predictive values, sensitivity and specificity of 50 GGCT were calculated as 45%, 84%, 75%, 53%, respectively, when the cut off value was accepted as 140 mg/dl, and 42%, 82%, 78% and 46% when the cut off value was accepted as 135 mg/dl.

OGTT was abnormal in 10 of 25 patients (40%) who had high fructosamine levels and in 4 of 17 patients (23%) who had normal fructosamine levels. According to these findings (+) and (-) predictive values, sensitivity and specificity were calculated as 40%, 76% and 71% and 46% respectively.

Table 1. - *Characteristics of the patients.*

	Mean $\pm$ SD
Age	$27.05 \pm 4.33$
Gravidity	$2.14 \pm 1.59$
Parity	$0.69 \pm 1.24$
Abortion	$0.38 \pm 0.62$
Gestational age (weeks)	$26.21 \pm 1.63$

HbA<sub>1c</sub> levels were high in 19 patients and 9 of them (47.4%) were diagnosed as GDM. On the other hand, in 23 patients, HbA<sub>1c</sub> levels were normal, and in only 5 of them (21.7%), OGTT was abnormal. Positive and (-) predictive values, sensitivity and specificity of HbA<sub>1c</sub> were calculated as 47%, 78%, 64% and 64% respectively.

When 50 GGCT and fructosamine were evaluated together, one of the tests was abnormal in 14 of the 34 patients (41.1%) who were diagnosed as GDM. However both tests were negative in 8 of them, and they were not accepted as GDM. Positive and (-) predictive values, sensitivity, specificity of this double screening test were estimated as 41%, 100%, 100% and 25%, respectively.

Both 50 GGCT and HbA<sub>1c</sub> levels were normal in 14 cases and one of them (7.1%) developed GDM. One of the tests was abnormal in 28 cases and in 13 of them (46.6%) OGTT was abnormal. Positive and (-) predictive values, sensitivity and specificity of this double screening test were 46%, 92%, 92% and 46%, respectively.

OGTT was abnormal in 13 of 32 patients (40.6%) who had an abnormal HbA<sub>1c</sub> and fructosamine level and only in 1 of 10 patients who had normal HbA<sub>1c</sub> and fructosamine levels. Positive and (-) predictive values, sensitivity and specificity of this double test were calculated as 40%, 90%, 93% and 32%, respectively. Triple test including 50 GGCT, HbA<sub>1c</sub> and fructosamine level was found to be highly sensitive. One of them

Table 2. - Statistical evaluation of the screening tests.

	Positive predictivity	Negative predictivity	Sensitivity	Specificity
50 GGCT > 140 mg/dl	45%	84%	78%	53%
50 GGCT > 135 mg/dl	42%	82%	78%	46%
Fructosamine > 2.85 mmol/l	40%	76%	71%	46%
HbA <sub>1c</sub> > 7.2%	47%	78%	64%	64%
50 GGCT > 140 mg/dl and Fructosamine > 2.85 mmol/l	41%	100%	100%	25%
50 GGCT > 140 mg/dl and HbA <sub>1c</sub> > 7.2%	46%	92%	92%	46%
Fructosamine > 2.85 mmol/l and HbA <sub>1c</sub> > 7.2%	40%	90%	92%	32%
50 GGCT > 140 mg/dl and Fructosamine > 2.85 mmol/l and HbA <sub>1c</sub> > 7.2%	41%	100%	100%	28%

was abnormal in 34 patients and 14 of them were GDM patients. Positive and (–) predictive values, sensitivity and specificity were calculated as 41%, 100%, 100% and 28%, respectively.

There was no statistically significant difference between these 7 methods for (+) predictive values. Although (–) predictive values and sensitivities of 50 GGCT, HbA<sub>1c</sub> and fructosamine were not significantly different, (–) predictive values and sensitivities of double screening tests were significantly higher than single screening test. These values were significantly higher in triple tests, than in single tests but there was no difference between the double and triple tests.

Linear regression analysis showed that there was good correlation between 50 GGCT and HbA<sub>1c</sub> level ( $r:0.3725$ ,  $p < 0.01$ ), between 50 GGCT and fructosamine level ( $r:0.31$ ,  $p < 0.05$ ), HbA<sub>1c</sub> and fructosamine levels ( $r:0.6160$ ,  $p < 0.00001$ ).

## DISCUSSION

The incidence of GDM is 1 - 2% and it can be diagnosed by convenient screening tests. The screening methods such as

random blood glucose level, glucose in urine, etc. had been used in the past but these methods were found to be unsatisfactory<sup>(4, 5)</sup>. The method that is advised by the National Diabetes Data Group (NDDG) and widely used today is 50 GGCT. This test is done between the 24th - 28th gestational weeks. OGTT was done if the plasma glucose level was equal to or above 140 mg/dl one hour after ingestion of 50 gr glucose. It was first done by O'Sullivan, and sensitivity and specificity were reported as 79% and 87% with a cut off value of 140 mg/dl<sup>(2)</sup>. In 1988 Carpenter reported the sensitivity and specificity of the test as 83% and 87%, respectively<sup>(3)</sup>. In the present study, we found the sensitivity and the specificity to be 78% and 53%. Although the specificity was lower than those in the literature, (–) predictive value and sensitivity were very high. These results showed that 50 GGCT can be used as a reliable screening test.

The most important and discussed point in this test is the cut off value. Some reports suggest that the sensitivity and the specificity of the test increase when the cut off value is accepted as 135 mg/dl instead of 140 mg/dl<sup>(6)</sup>. On the con-

trary, our study revealed no significant difference between the sensitivity, specificity, (+) and (−) predictive values when the cut off is 135 mg/dl. Therefore, we suggest that 140 mg/dl is a proper cut off value.

An ideal test should be sensitive, specific, convenient, innocuous and cost-effective. In 50 GGCT, the glucose load may produce nausea and vomiting. The test requires the cooperation of the patient and one hour of time. Patients may not tolerate glucose ingestion. Hence another suitable test should be sought.

Fructosamine was first defined by Johnson in 1982 (7). Glucose molecules are joined to protein molecules with a non-enzymatic mechanism, to form stable ketoamines or fructosamines. The serum fructosamine level increases depending on the abnormal high blood glucose concentration. Since the half-life of albumin is 14-20 days, the fructosamine level can provide useful information about blood glucose concentration over the past 2-3 weeks (8). There are few investigations about use of fructosamine as a screening test in GDM.

In a study performed by Alistair, a good correlation was found between the fructosamine level and 50 GGCT ( $r: 0.813$ ). Nine women had gestational diabetes diagnosed by the glucose tolerance test and eight of those had a high serum fructosamine level. They suggested that serum fructosamine may be a useful screening test for GDM (9). Four years later, the same author found the sensitivity, specificity, (+) and (−) predictive values of 50 GGCT and fructosamine to be 81%, 85%, 15%, 99% and 50%, 87%, 10%, 98%, respectively (10). In our study, we found a good correlation between 50 GGCT and fructosamine and there was no significant difference between their (+) and (−) predictive values, sensitivity and specificity. According to these results, we suggest that fructosamine can be used

as a screening test especially in pregnant patients who cannot tolerate glucose ingestion.

HbA<sub>1c</sub> is formed by the binding of glucose to valine amino acid in N terminal of Hb and reflects mean plasma glucose concentration, over 4-12 weeks prior to testing (11). Glycosylated hemoglobin as a screening test for carbohydrate intolerance in pregnancy had been studied by several authors. Cousins *et al.*, found that linear regression analyses of 50 GGCT and HbA<sub>1c</sub> demonstrated significant correlation. But, in comparison with HbA<sub>1c</sub>, 50 GGCT had greater sensitivity, specificity and (+) predictive value. They decided that 50 GGCT was better than HbA<sub>1c</sub> (12).

Artal showed that these 2 methods correlate well, but the high incidences of false negative and false positive results of HbA<sub>1c</sub> make this test inadequate as a screening test for GDM (13). In our study, linear analysis showed a good correlation and there was no difference between sensitivity, specificity, (+) and (−) predictive values. We suggest that HbA<sub>1c</sub> can also be used as a screening tool as well as fructosamine.

We could not find any investigation, which compares HbA<sub>1c</sub> and fructosamine as a screening method. In our study, we found a good correlation between these two tests.

Double screening test results were found more valuable than singles. Although there was no statistically significant difference between the single and double methods for (+) predictive values, (−) predictive values and sensitivities of double screening tests were significantly higher than those of singles. There was no significant difference between the double tests.

In conclusion, we may say that HbA<sub>1c</sub> and fructosamine levels are alternative and reliable methods to 50 GGCT as a screening test. Their (−) predictive va-

lues and sensitivities are similar, hence any of them could be chosen if we had to do only one test for the screening of GDM.

#### REFERENCES

- 1) Freinkel N., Gabbe S.G., Hadden: "Summary and recommendations of the Second International Workshop-Conference on GDM". *Diabetes*, 1985, 34, 123.
- 2) O'Sullivan J., Mahan C.M.: "Criteria for the oral glucose tolerance test in pregnancy". *Diabetes*, 1964, 13, 278.
- 3) Carpenter M.: "Testing for gestational diabetes in pregnancy". In: 'Principles and practice'. Reese E., Coustan D., eds. New York, Churchill Livingstone, 1988, 423.
- 4) Hatem M., Dennis J.: "A random plasma glucose method for screening for abnormal glucose tolerance in pregnancy". *Br. J. Obst. Gyn.*, 1987, 94, 213.
- 5) Lind T., McDougal A.N.: "Antenatal screening by random blood glucose sampling". *Br. J. Obst. Gyn.*, 1981, 88, 346.
- 6) Carpenter M.W., Coustan D.: "Criteria for screening tests for gestational diabetes". *Am. J. Obst. Gyn.*, 1982, 144, 768.
- 7) Johnson R.N., Metcalf P., Baker J.: "Fructosamine: a new approach to the estimation of serum glycoprotein. An index of diabetic control". *Clin. Chim. Acta*, 1982, 127, 87.
- 8) Armbruster D.A.: "Fructosamine: structure, analysis, and clinical usefulness". *Clin. Chem*, 1987, 33, 2153.
- 9) Alistair B.R., Baker J.R.: "Serum fructosamine: a screening test for diabetes in pregnancy". *Am. J. Obst. Gyn.*, 1986, 154, 1027.
- 10) Alistair B.R., Baker J.R., Metcalf P.: "Fructosamine compared with a glucose load as a screening test for Gestational Diabetes". *Obst. Gyn.*, 1990, 76, 773.
- 11) Madsen H.D.J., Hansen P., Hahnenmann N.: "Nemoglobine A<sub>1c</sub> determinations in diabetic pregnancy". *Diabetes Care*, 1981, 4, 541.
- 12) Cousins L., Dattel B.J., Hollingsworth D.R.: "Glycosylated hemoglobine as a screening test for carbohydrate intolerance in pregnancy". *Am. J. Obst. Gyn.*, 1984, 150, 455.
- 13) Artal R., Mosley G.M., Dorey F.J.: "Glycohemoglobine as a screening test for gestational diabetes". *Am. J. Obst. Gyn.*, 1984, 148, 412.

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