Fasting Plasma Glucose and Glycated Hemoglobin in the Prediction of Diabetic Retinopathy in a Rural Population


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ABSTRACT

The presence of Diabetic Retinopathy is the best criterion from which to compare glycemic measures because it is a specific and early clinical complication of diabetes. The aim of this study was to assess the significance of fasting plasma glucose and HbA1c values in predicting retinopathy among Type 2 diabetics. 200 Type 2 diabetic patients were examined for presence of diabetic retinopathy. Out of these patients, 135 were negative for retinopathy (controls) and 65 were positive for retinopathy (cases). The study participants, 83% belonged to age group 41-70 years. 55% of cases and 43% of controls were females. Diabetic Retinopathy was significantly associated with HbA1c values with a cut off of 7.0% between the cases and controls, with a higher HbA1c in cases than controls (chi square value = 14.35, df = 1, p=.000, Odds Ratio=4.46, 95% Confidence interval=1.97-10.106). Fasting plasma glucose (FPG) values with a cut off of 126 mg/dl (7mmol/l) did not show any significant difference in values among the cases and controls.

Key words: Diabetic Retinopathy, fasting plasma glucose, HbA1c

INTRODUCTION

Diabetes Mellitus (DM) is a major health problem with long term micro and macro vascular complications.1 Diabetic retinopathy is one of the leading causes of blindness in the world that increases the chance of losing the sight about 25 times higher compared to normal individuals.2 The presence of diabetic retinopathy is the best criterion from which to compare glycemic measures because it is a specific and early clinical complication of diabetes.3 Both the World Health Organization (WHO)4 and the American Diabetes Association (ADA)5 use fasting plasma glucose (FPG) values of ≥7.0mmol/l (≥126mg/dl), to define diabetes. This criterion is based on an underlying assumption that there exists a clear glycemic threshold that separates persons at high and low risk of diabetic micro vascular complications.6 Approximately two decades ago, three pivotal epidemiological studies among Pima Indians,7 Egyptians,8 and the NHANES III9 showed that retinopathy signs were rare below a FPG threshold of 7.0 mmol/l, but their prevalence increased dramatically above it.9 A key observation was that the FPG cut-off of 7.0mmol/l had high sensitivity and specificity for identifying persons with and without retinopathy. This cut-off was therefore used by the World Health Organization (WHO) and American Diabetes Association (ADA) to diagnose diabetes.9, 10 Glycated hemoglobin (HbA1c) is a routinely used marker for long-term glycemic control. In accordance with its function as an indicator for the mean blood glucose level, HbA1c predicts the risk for the development of diabetic complications in diabetic patients.11 The amount of glycated hemoglobin (HbA1c) reflects the glycaemic control of a patient during the 6 – 8 weeks period before the blood sample was obtained. The amount of HbA1c correlates well with fasting and postprandial blood glucose levels. At present HbA1c is the best surrogate marker we have for setting goals of treatment.12 The level of HbA1c value 7.0% was said to be appropriate for reducing the risk of cardiovascular complications.13 HbA1c levels are being considered as an alternative diagnostic tool for diabetic diagnosis.14 Unlike FPG, HbA1c does not require an overnight fast, is not affected by short-term lifestyle changes, and has less variability within individuals than FPG.15, 16, 17 Nevertheless, few studies have examined the prevalence of retinopathy across the spectrum of HbA1c levels, which could assist in the designation of ideal HbA1c diagnostic cut points.7,8 The Diabetes Complications and Control Trial (DCCT) established glycated hemoglobin (HbA1c) as the gold standard for measuring treatment success in long term glycemic control in both type 1 and type 2 diabetes.18

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standard of glycemic control, with levels ≤7.0% deemed appropriate for reducing the risk of vascular complications. Australian Diabetes Society, has reported that the patients with DR had significantly higher HbA1c levels.

**AIM OF THE STUDY**
To assess the significance of fasting plasma glucose and HbA1c values in predicting retinopathy among Type 2 diabetics. Few studies have been done in India on this issue. Hence this study becomes imperative to know the trends in Indian population.

**MATERIALS AND METHODS**
200 Type 2 Diabetic patients who attended the ophthalmic outpatient services of S.R.M. Medical College Hospital and Research Centre for retinopathy screening from June 2012 to September 2012 were included in the study. An informed written consent was obtained from all the participants. The study was approved by the Institutional Ethical Committee. Patients with hypertension, ischemic heart disease, gestational diabetes mellitus, media opacity and previous history of cataract surgery were excluded from the study.

All subjects underwent detailed eye examination with slit lamp and fundus examination with +90D lens and Indirect Ophthalmoscopy. Based on the International Clinical Diabetic Retinopathy Severity Scale adopted by the American Academy of Ophthalmology (AAO) and the International Council of Ophthalmology (ICO), the patients were classified into two groups. (1)Group A- diabetic retinopathy positive (2)Group B- diabetic retinopathy negative.

5 ml of venous blood was collected from them after an overnight 12 hour fast and analysis of fasting plasma glucose and HbA1c were carried out using standard kits in auto analyzer on the same day of sample collection. Based on fasting plasma glucose, the respondents were classified into two groups. (1)Group A- <126mg/dl (<7mmol/l) (2)Group B- ≥126mg/dl (≥7mmol/l)

Based on HbA1c, the respondents were classified into two groups. (1)Group A-Good Glycemic Control ≤7.0% (2)Group B- Poor Glycemic Control >7.0% .

**STATISTICAL ANALYSIS**
All data were analyzed using SPSS 16.0. The mean, standard deviation and the statistical significance of biochemical parameters for the subjects were analyzed by using unpaired student’s t-test and p<0.05 was accepted as statistically significant.

**RESULTS**
Among the 200 participants of the study, 65 patients (cases) had Diabetic Retinopathy (DR) and 135 patients (controls) were without Diabetic Retinopathy. 32% were in the age group 51-60 years, 28% in the age group 41-50 years and 23% in the age group 61-70 years.

The mean age of the cases was 51.43 years (SD ± 10.97) and controls was 55.62 years (SD ± 11.22). With regard to sex distribution of the participants, 102 (51%) were females and 98 (49%) were males. 74 (55%) among the 135 controls and 28 (43%) among the 65 cases were females.

The mean value of HbA1c was 8.76% while SD was ±2.25 among all the respondents. Among the participants with HbA1c values of ≤7.0%, there were 52 (86.7%) controls with no DR and 8 (13.3%) cases with DR, whereas in the group with HbA1c values of >7.0%, there...
Table 2. Showing statistical values of HbA1c and FPG among cases and controls

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Value</th>
<th>Diabetic retinopathy</th>
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<tbody>
<tr>
<td></td>
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<td>Status</td>
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<tr>
<td>HbA1c (%)</td>
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</tr>
<tr>
<td></td>
<td>&gt;7</td>
<td>83</td>
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<td>Fasting plasma glucose (mg/dl)</td>
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<tr>
<td></td>
<td>≥126</td>
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were 83 (59.3%) controls with no DR and 57 (40.7%) cases with DR. The mean HbA1c values among the cases with DR and the controls without DR were 9.18% and 8.56% respectively. In our study, HbA1c values with a cut off of 7.0% showed significant difference between the cases and controls with a higher HbA1c in cases than controls (chi square value = 14.35, df = 1, p=0.000, OR=4.46, 95% CI=1.97-10.106).

The mean value of fasting plasma glucose was 170.8 mg/dl while SD was ±79.3 among all the respondents. In the FPG group with values of <126 mg/dl (<7mmol/L), there were 47 (63.5%) controls with no DR and 27 (36.5%) cases with DR in comparison to the group ≥126mg/dl (≥7mmol/L), there were 88 (69.8%) controls with no DR and 38 (30.2%) cases with DR. The mean FPG values of the group with DR and the group without DR were 168.9mg/dl and 172.03mg/dl respectively. FPG values with a cut off of 126 mg/dl did not show any significant difference in values among the cases and controls.

In this study, out of 140 patients with HbA1c value >7.0%, 57 (41%) were positive for diabetic retinopathy. Among 60 patients with HbA1c ≤7.0%, only 8 (13%) were positive for retinopathy.

Patients with HbA1c >7.0% were at a higher risk of developing diabetic retinopathy compared to the group with HbA1c ≤7.0% with odds ratio being 4.46 and 95% CI=1.97-10.106.(Table 2.)

FPG values with a cut off of 126 mg/dl did not show any significant difference in values among the cases and controls with the odds ratio being 0.751 and 95% CI=0.409-1.379.

**DISCUSSION**

As a glycemic indicator, higher levels of glycated hemoglobin, (HbA1c) was found to be related to higher frequency of retinopathy. Hyperglycemia, as measured by HbA1c, is considered an important risk factor associated with DR and it was significantly associated with retinopathy in our study. In our study, HbA1c values with a cut off of 7.0% showed significant difference between cases and controls with a higher HbA1c in cases than controls (chi square value = 14.35, df = 1, p=0.000, OR=4.46, 95% CI=1.97-10.106). This is consistent with other studies.

Many clinical trial results from the Diabetes Control and Complications Trial (DCCT) and the epidemiological data from the Wisconsin Epidemiological Study of Diabetic Retinopathy (WESDR) have emphasized the strong relationship of glycemic control with the development and progression of DR.

Many studies have clearly demonstrated the benefits of improving glycemic control, by reducing HbA1c concentration, in decreasing the complication rate. The United Kingdom Prospective Diabetes Study Group (UKPDS) reported that patients with intensive glucose control had reduction in retinopathy, a 25 percent drop in the overall micro vascular complications and for every 1 percent decrease in HbA1c, a 35 percent reduction in risk for micro vascular complications was observed. The authors concluded that slowing the progression of retinopathy with intensive control resulted in preservation of sight, decreased morbidity and fewer interventions.

In a study done by Wong TY et al (2008), the authors found that FPG values with a cut off of 126 mg/dl did not show any significant difference in values among the cases and controls. A recent meta-analysis across three different populations found no consistent FPG threshold for retinopathy with the data instead of suggesting a continuous linear relationship and poor performance of the 7.0 mmol/l FPG cut-off point in discriminating the presence of retinopathy. Such findings raise doubts about the underlying premise of a uniform glucose threshold for retinopathy.

Randomized controlled trials and observational studies have shown that glycated haemoglobin or HbA1c is also a good predictor of micro vascular complications and is highly correlated with FPG and does not require measurement in the fasting state.

Good control of hyperglycemia which is indicated by glycated hemoglobin level of <7.0% will help in preventing diabetic retinopathy, a micro vascular complication of diabetes.

**CONCLUSION**

The findings of this study show that glycemic control as indicated by HbA1c level is a good predictor of diabetic retinopathy in diabetic patients. Good glycemic control of diabetes with target HbA1c of 7.0% and regular
Ophthalmic screening for diabetic retinopathy changes will reduce morbidity due to diabetic retinopathy.

REFERENCES
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