
N Baral, B C Koner, P Karki, C Ramaprasad, M Lamsal and S Koirala

ABSTRACT

Aim of the study: The present study was designed to (a) evaluate the implications of revised WHO diagnostic criteria on prevalence of abnormal glucose tolerance, (b) compare glycated hemoglobin level amongst healthy, impaired glucose tolerance (IGT), impaired fasting glucose (IFG) and diabetic subjects and (c) evaluate the assay of glycated hemoglobin in screening IGT, IFG from normal subjects.

Methodology: Hospital based, cross-sectional study. Plasma glucose and glycated hemoglobin (gHb) were estimated by glucose oxidase and affinity chromatography method respectively.

Results: The crude prevalence of IFG, IGT and diabetes were 9%, 18% and 5.29% respectively with no significant difference between Mongol and non-Mongol population. Newly introduced IFG group falsely incorporate 12% diabetic subjects and fails to detect 83% IGT subjects as impaired glucose metabolism. The gHb level is raised in IGT and diabetic group but not in IFG group.

Conclusion: The assay of gHb may be used to screen abnormal glucose tolerance but paired estimation of fasting glucose increases the reliability of diagnosis. The level of gHb in mild carbohydrate intolerance mostly depend on the level of rise in post prandial glucose (where the variation is wide, as in IGT) but not on the narrow variance in fasting plasma glucose level as found in IFG.

Keywords: Glycated hemoglobin (gHb), Impaired fasting glucose (IFG), Diabetes mellitus, Impaired glucose tolerance (IGT)

INTRODUCTION:

Diabetes mellitus affects millions of people throughout the world, which is widely prevalent chronic debilitating disease to cause short term and long term complications. Diagnosis of diabetes is done by measuring blood/plasma glucose level. Besides diabetes mellitus, in 1985, WHO introduced impaired glucose tolerance (IGT) as a new category of abnormal response following oral glucose tolerance test (OGTT). A fasting plasma glucose level less than 140mg % and 2 hours after load plasma glucose value in between 140-199mg % were the criteria for diagnosis of IGT(1). Recently proposed WHO criteria (1998) and American Diabetes Association criteria (1997) have redefined diabetes and IGT. The major modification is that for diagnosis of diabetes mellitus, the diagnostic threshold for fasting glucose has been lowered from 140 to 126mg %. IGT is changed to allow for new fasting level(2,3). The recent introduction of new intermediate category, the impaired fasting glucose (IFG) is defined as fasting glucose concentration of 110 - 126mg %. The implication of these intermediary glucose tolerance on morbidity risk (coronary artery disease, atherosclerotic disease, hypertension, obesity etc.) has been claimed(1,4).

The glycation of hemoglobin occurs due to non-enzymatic process and is considered a good index of long term diabetes control. Because of certain pitfalls of oral glucose tolerance test (OGTT) and measure of glycated hemoglobin (gHb) being a better measure of real life week/month long blood glucose concentration, the gHb might be a better index of long term glucose dynamics in body(5). The screening, diagnostic and prognostic value of glycated hemoglobin has been evaluated by many investigators(6).

In view of above the present study was designed to (a) evaluate the implication of revised diagnostic criteria on prevalence of abnormal glucose tolerance, (b) compare glycated hemoglobin amongst normal, IGT, IFG and diabetic subjects and (c) evaluate the assay of glycated hemoglobin in screening subjects with IGT and IFG.
MATERIALS AND METHODS

Study was conducted in subjects (n=920) of age group 30-65 years, non-pregnant who were referred to laboratory for OGTT. Plasma glucose was estimated by glucose oxidase (Glucose GOD/POD kit, E. M erck India Ltd., Mumbai, India) method following standard norms. Glycated hemoglobin (HbA1) was estimated by affinity chromatography (Glyc - H b K it, E. M erck India Ltd.). Subjects were classified according to WHO criteria (1998) into control, IFG, IGT, and diabetic groups.

RESULTS

The Crude prevalence of IFG, IGT and diabetes was found to be 9%, 18% and 5.29% respectively in the present study (Table I). There was no significant difference in the crude prevalence of the above among Mongol and non-Mongol people incorporated in the study. Out of 83 subjects who were found to have IFG, 10 subjects were detected as diabetic and 28 as IGT on the basis of their 2 hour post load plasma glucose value (Fig. 1). The within run, day to day and total variance component (CV) for low values (normal subjects) of glycated hemoglobin was estimated by ANOVA one stage nested design(10).

Table I. Age and race distribution and crude prevalence of IFG, IGT and diabetic in the study population (n=920).

<table>
<thead>
<tr>
<th>Age</th>
<th>Control</th>
<th>IFG</th>
<th>IGT</th>
<th>Diabetic</th>
</tr>
</thead>
<tbody>
<tr>
<td>31-40</td>
<td>319</td>
<td>17</td>
<td>23</td>
<td>4</td>
</tr>
<tr>
<td>41-50</td>
<td>207</td>
<td>30</td>
<td>52</td>
<td>8</td>
</tr>
<tr>
<td>51-60</td>
<td>80</td>
<td>27</td>
<td>62</td>
<td>22</td>
</tr>
<tr>
<td>61+</td>
<td>63</td>
<td>9</td>
<td>29</td>
<td>15</td>
</tr>
<tr>
<td>Total</td>
<td>669</td>
<td>83</td>
<td>166</td>
<td>49</td>
</tr>
</tbody>
</table>

Crude prevalence (72.7%) (9%) (18%) (5.29%)

Table II. Distribution of mild, moderate and severe degree of glycation of hemoglobin in group with different glycemic status.

<table>
<thead>
<tr>
<th>Groups</th>
<th>Normal (&lt;6%)</th>
<th>Mild (6-8%)</th>
<th>Moderate (8-10%)</th>
<th>Severe (&gt;10%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>96</td>
<td>4</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>IFG</td>
<td>53</td>
<td>43.4</td>
<td>3.6</td>
<td>-</td>
</tr>
<tr>
<td>IGT</td>
<td>15.7</td>
<td>50</td>
<td>30.12</td>
<td>4.2</td>
</tr>
<tr>
<td>DM</td>
<td>-</td>
<td>-</td>
<td>8.16</td>
<td>91.8</td>
</tr>
</tbody>
</table>

Fig. 1 Distribution of normal, IGT, diabetic types of PP Glucose level among the IGT subjects.

Fig. 2 Mean and SD of gHb in IFG, IGT and DM.
There was significant positive correlation between PP glucose and gHb levels in IGT and diabetes groups. Fasting glucose level had a significant positive correlation with gHb in the case of diabetes but not in other groups (Table III).

**DISCUSSION**

There is no difference in crude prevalence of diabetes, IFG and IGT in non-mongol and mongol population in Nepal. No data regarding prevalence of diabetes in Nepal is available in indexed literature. However, the prevalence shown in the present study may not be true reflection of the prevalence of diabetes in Nepal. Because it was conducted in a hospital, situated in eastern part of Nepal, (a hospital based study) and selection criteria only incorporated the subjects referred to Biochemistry lab for an OGTT.

A merican diabetic association (ADA) in their final report has given more emphasis in estimation of glucose for diagnosis of diabetes with an intention that the new definition of diabetes with fasting glycemia value \( \geq 126 \text{mg} \% \) will allow to do diagnosis without OGTT. This is an attempt to better correlate fasting glycemia with 2 hour post load value during OGTT\(^{16}\). However the criteria of IFG missed 83% (15% of total study population) of IGT subjects to detect their impaired glucose metabolism and diagnose an additional 4.8% of the subjects in the study group as having mild impairment of glucose metabolism (but they do not belong to IGT group). If we consider PP glucose \( \geq 200 \text{mg} \% \) as gold standard for diagnosis of diabetes, 11% IFG subjects were found to be diabetic. The similar pitfall of using PP glucose for the diagnosis of diabetes was found in other studies also\(^{12,13,14,15}\). The difference in percentage distribution of the different studies including the present one may be due to various factors, e.g. the difference in the study design, population and race included etc.

Glycated Hemoglobin in IGT group was significantly higher in comparison to control and lower in comparison to diabetic groups in the present study. The finding is in consistence with the previous reports\(^{8,9,10}\). There was no significant difference in gHb level between control and IFG groups. But only 53% IFG subjects were found to have normal glycated hemoglobin level, which is much less than found by Davidson MB et al, 1999\(^{16}\). This variation might be due to difference in grading system of gHb and cut off limit between normal and abnormal gHb level used by them. Secondly, we estimated HbA1 where as D avidson MB et. al. group has measured HbA1c. All the diabetics in the present study had moderate to severe rise in gHb level, whereas the previous study group has reported normal gHb in 60.9% cases with diabetes. This reflects poor management of diabetic patients in this region because of ignorance, poverty, poor health education etc. A weak correlation between fasting glucose and gHb in control, IFG and IGT group and a significant positive correlation between PP glucose and gHb in IGT reveals that the gHb in mild glucose intolerance mostly depend on the level of rise in post load glucose (where the variation is wide, as in IGT) but not on the narrow variance in fasting plasma glucose level as found in IFG. The variation in fasting glucose in diabetics is more. Hence, a significant positive correlation between fasting glucose and gHb was obtained in this group. The above evidences further substantiate that a paired value of fasting plasma glucose and gHb could be better predictor of mild carbohydrate intolerance\(^{14}\).

**ACKNOWLEDGMENT**

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**REFERENCES**