Relation of Hypertension, Elevated Alanine Aminotransferase and Fatty Liver in Dyslipidaemic Impaired Glucose Tolerance Patients

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Impaired Glucose Tolerance (IGT) is often associated with a cluster of inter-related cardiovascular risk factors known as the Metabolic Syndrome, Insulin Resistance Syndrome or Syndrome X. These are: High blood pressure (hypertension), Fatty Liver and Elevated Alanine Aminotransferase. This is a cross-sectional study, carried out in Rangpur Medical College Hospital, and Hypertension & Research center, Rangpur from July 2011 to June 2012. Patients fulfill the criteria of Impaired Glucose Tolerance were included for the study. During the study period a total of 116 patients were studied. 73.27% (85) patients had dyslipidemia and 26.73%(31) patients are with normal lipid profile. The study population was divided into group I and group II. Group I: IGT subjects with dyslipidemia attending at the above mentioned places were included as case. Group II: IGT subjects with normal lipid profile. Normotensive patients were found 22(25.9%) in group I and 13(41.9%) in group II. Hypertensive patients was found 63(74.1%) and 18(58.1%) in group I and group II respectively. ALT >45 patients were found 28(32.9%) in group I and 1 (3.2%) in group II. ALT <45 patients were found 57(67.1%) and 30(96.8%) in group I and group II respectively. Fatty liver patients were found in 46(54.1%) in group I and 3 (9.7%) in group II. The difference was statistically significant (P<0.05) between two groups in chi square test. Among dyslipidemic impaired Glucose tolerance group, Hypertension, elevated Alanine aminotransferase and fatty liver is more common. So, dyslipidemic impaired Glucose tolerance patients should be screened for hypertension, elevated Alanine aminotransferase and fatty liver.

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**Key Words:** Hypertension, Alanine aminotransferase, Fatty Liver, Impaired Glucose Tolerance, Dyslipidaemia

**Introduction**

Cardiovascular complications such as increased atherosclerosis associated with type 2 diabetes begin to develop well before type 2 diabetes is diagnosed. By that time, macrovascular damage may already be well advanced.1 Impaired glucose tolerance (IGT) is a pre-diabetic state of dysglycemia that is associated with insulin resistance and increased risk of cardiovascular pathology. IGT may precede type 2 diabetes mellitus by many years. IGT is also a risk factor for mortality.2 Epidemiologic research indicates that glucose intolerance and hypertension are interrelated phenomena, each powerfully predisposing to atherosclerotic

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cardiovascular disease. Both diabetic and hypertensive patients have greater amounts of atherogenic risk factors, including dyslipidemia, hyperuricemia, elevated fibrinogen, and left ventricular hypertrophy. Diabetic persons have an increased prevalence of hypertension (50%), and glucose intolerance is more common in hypertension (15% to 18%). Both share a strong relationship to excess weight, but the excess of hypertension in diabetic persons occurs in both lean and obese subjects. Diabetes doubles the risk of hypertension associated with overweight. The risk of coronary disease, stroke, and peripheral arterial disease increases with increasing blood pressure to the same degree in diabetic persons as in nondiabetic persons, but at any level of blood pressure, diabetic persons have a doubled risk of these outcomes. Both diabetic and hypertensive patients are particularly prone to silent or unrecognized myocardial infarctions.4

Metabolic insulin resistance syndrome is a critical factor in the pathogenesis of atherosclerosis and coronary heart disease in Indians reported by Misra et al. (1999). In a preliminary case-control study, 44 young patients (age<40 years) with coronary heart disease (angina, myocardial infarction), not previously diagnosed to have diabetes mellitus, were recruited seven days to six weeks after the cardiac event (group I), and compared to 20 healthy subjects (group II). After recording history and anthropometric data, they were subjected to oral glucose tolerance test. Each group was divided into A and B subgroups according to the magnitude of impaired glucose tolerance. Hypertension was recorded in 11 (25%) patients in group I, while all the subjects in group II were normotensive (p < 0.05). The study demonstrates significantly high prevalence of hypertension, obesity, impaired glucose tolerance, hyperinsulinemia and dyslipidemia, suggesting fully developed metabolic insulin resistance syndrome in young north Indian patients with manifest coronary heart disease.4 Proportions of an elevated ALT (>50 IU/l) in men with normal glucose tolerance, IFG, IGT, and newly diagnosed diabetes mellitus were 3.5%, 9.5%, 7.7%, and 18.0%, respectively5. AST and ALT independently predict type 2 diabetes. Baseline elevations of these markers may reflect NAFLD or related pathologies6. In Obese children and adolescents, 4 % have increase ALT and 7 % have increase IGT7. In severely Obese patients ALT increase in 26.4 % persons8. Liver pathology among diabetics is similar to that of alcoholic liver disease, including fatty liver (steatosis), steatohepatitis, fibrosis, and cirrhosis. Elevated ALT was more common among diabetics of both sexes, but significantly among men. Both men and women with impaired glucose tolerance had a prevalence of elevated ALT higher than persons with normal glucose tolerance but lower than diabetics.9

Elevated ALT levels were highly prevalent and associated with the metabolic syndrome, insulin resistance, high triglycerides, and low HDL-cholesterol. In an obese multiethnic pediatric population, elevated ALT, suggestive of the presence of NAFLD, was highly prevalent and associated with (components of) the metabolic syndrome and insulin resistance.10

The prevalence of elevated alanine aminotransferase (ALT) level increased with the accumulation of components of metabolic syndrome. Transaminitis with NAFLD is increasingly being recognized as an association with obesity and the metabolic syndrome.11

Elevated ALT was independently associated with insulin resistance when included in
models with waist circumference, National Cholesterol Education Program criteria for metabolic syndrome, hypertriglyceridemic waist, elevated triglyceride-to-HDL ratio, or homeostasis model assessment of insulin resistance (HOMA-IR) (all \( P < 0.01 \)). Finally, the addition of elevated ALT improved classification of insulin resistance by area under the receiver operating characteristic curve criteria for all models except HOMA-IR. ALT was associated with insulin resistance independently of conventional and more detailed metabolic measures. These findings suggest that the addition of ALT to existing clinically based metabolic risk definitions is an inexpensive way to improve the identification of subjects with insulin resistance.\(^\text{12}\) The association of nonalcoholic fatty liver disease (NAFLD) with insulin resistance and metabolic syndrome has been documented for obese men and middle-aged men. According to the OGTT results in NAFLD (75 patients), 24 (32\%) patients were diagnosed as having IGT and 12 (16\%) patients were diagnosed as having diabetes and rest of the patients were having normal blood glucose.\(^\text{13}\)

Non-alcoholic fatty liver disease (NAFLD) is frequently associated with type 2 diabetes mellitus, obesity, and dyslipidemia. Performing OGTT in cases with nonalcoholic fatty liver disease may be useful for early screening of diabetes mellitus.\(^\text{14}\) Non-alcoholic steatohepatitis (NASH) is increasingly recognized as an important cause of chronic liver disease. In NASH 47\% have DM. In non DM pts 30\% have IGT and 2\% have IFG by OGTT test.\(^\text{15}\) The prevalence of non-alcoholic fatty liver disease is estimated to be 20-30\% in Western populations. Of the patients with the disease who have raised aminotransferase levels, 43-55\% have histological steatohepatitis.\(^\text{16}\) In NAFLD patients: 37\% have Increase ALT, 26\% have IGT and 30\% obese BMI >30\(^\text{17}\). In a study, 88 patients with fatty liver and impaired glucose tolerance undergone liver biopsy. Among these patients, 59 (71\%) had the metabolic syndrome, 41 (49\%) had NASH and 36 (43\%) had fibrosis. Abnormal glucose tolerance (T2DM or impaired glucose tolerance) was the only independent risk factor for NASH (OR: 3.14; 95\% CI: 1.20–8.23). The probability of these potentially progressive stages of NAFLD increases with the presence of abnormal glucose tolerance.\(^\text{18}\) The prevalence of NAFL is higher in type-2 diabetic patients. Obesity, dysglycemia, dyslipidemia and elevated liver enzymes are seen more frequently in fatty liver than non-fatty liver type-2 diabetic patients.\(^\text{19}\) This study also shows whether elevated ALT in IGT group of patients causes early hepatic damage. ALT is also a predictor of Metabolic Syndrome.

**Methods**

This is a descriptive cross-sectional study, carried out in Rangpur Medical College Hospital, and Hypertension & Research center, Rangpur from July 2011 to June 2012. Patients fulfill the criteria of IGT were included for the study. Systemic randomized sampling method was followed as per inclusion and exclusion criteria and sample size was 116. The data were analyzed by using the computer software SPSS program.

**Results**

A total of 116 patients were included in the study. The study population was divided into group I and group II. Group I: IGT subjects with dyslipidemia and Group II: IGT subjects with normal lipid profile.

Table I shows the hypertensive and normotensive of the study patients. Normotensive patients were found 22(25.9\%) in group I and 13(41.9\%) in group II. Hypertensive patients were found 63(74.1\%)
and 18(58.1%) in group I and group II respectively. The difference was not statistically significant (P>0.05) between two groups in chi square test.

Table I: Distribution of the study patients according to hypertensive and normotensive (n=116)

<table>
<thead>
<tr>
<th>Hypertension</th>
<th>Group I (n=85)</th>
<th>Group II (n=31)</th>
<th>n</th>
<th>%</th>
<th>n</th>
<th>%</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normotensive</td>
<td>22</td>
<td>25.9</td>
<td>13</td>
<td>41.9</td>
<td></td>
<td></td>
<td>ns</td>
</tr>
<tr>
<td>Hypertensive</td>
<td>63</td>
<td>74.1</td>
<td>18</td>
<td>58.1</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

ns= not significant  
P value reached from chi-square test

ALT >45 patients were found 28(32.9%) in group I and 1 (3.2%) in group II. ALT <45 patients were found 57(67.1%) and 30(96.8%) in group I and group II respectively. The difference was statistically significant (P<0.05) between two groups in chi square test.

Table II: Distribution of the study patients according to ALT (n=116)

<table>
<thead>
<tr>
<th>ALT (U/L)</th>
<th>Group I (n=85)</th>
<th>Group II (n=31)</th>
<th>n</th>
<th>%</th>
<th>n</th>
<th>%</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥45</td>
<td>28</td>
<td>32.9</td>
<td>1</td>
<td>3.2</td>
<td></td>
<td></td>
<td>0.001*</td>
</tr>
<tr>
<td>&lt;45</td>
<td>57</td>
<td>67.1</td>
<td>30</td>
<td>96.8</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

s= significant  
P value reached from chi-square test

Discussion
This descriptive study was carried out with an aim to find out the Relation of Hypertension, elevated Alanine aminotransferase and Fatty Liver in Dyslipidaemic Impaired Glucose Tolerance patients. A total number of 116 consecutive patients with impaired glucose tolerance (IGT), out of which 85 patients having dyslipidemia was considered as group I and rest 31 had normal lipid profile was considered as group II, who came in Hypertension & Research Centre, Rangpur and Rangpur Medical College Hospital (RPMCH), Rangpur, during July 2011 to June 2012 were enrolled in this study.

In this study, it was observed that the mean systolic blood pressure was found 140.65±21.17 mmHg and 135.58±20.07 mmHg in group I and group II respectively. Similarly, the mean diastolic BP was found 89.65±11.52 mmHg in group I and 85.65±11.01 in group II. The mean systolic and diastolic BP were not statistically significant (P>0.05) between two groups.

In this series, it was observed that the mean ALT was found 39.03±16.4 mg/dl in group I and 26.68±8.62 mg/dl in group II, which was significantly (P<0.05) higher in group I. Park et al. (2005) reported in their study that the metabolic syndrome strongly associated with elevated ALT concentrations and the odds ratio for having an elevated ALT among those with metabolic syndrome versus those not
having the syndrome was 6.2 (95% CI 2.3 to 16.8). The risk was graded and increased with the number of components of the syndrome; the odds ratios for elevated ALT were 1.5 (95% CI 0.7 to 3.1), 2.6 (95% CI 1.1 to 6.2), and 6.2 (95% CI 2.3 to 16.8) in the adolescents with 1, 2, and 3 or more risk factors, respectively.\textsuperscript{20}

In this present study it was observed that almost three fourth (74.1%) patients were hypertensive in group I and 58.1% in group II. Hypertensive patients were higher in group I, but not significant (p>0.05). In a study, Bartnik et al. (2004) showed hypertensive patients were significantly (P=0.028) higher in group I, where the investigators found 32.0% and 18.0% patients were hypertensive patients in group I and group II respectively, which is comparable with the current study.\textsuperscript{21}

In this current series, it was observed that 32.9% patients had ALT >45 U/L in group I and 3.2% in group II. ALT >45 U/L was significantly (P<0.05) higher in group I. Lopez-Capape et al. (2009) found 8.0% and 4.0% had elevated ALT levels respectively.\textsuperscript{22}

In this study, it was observed that fatty liver patients were found 54.1% in group I and 9.7% in group II. Fatty liver was significantly (p<0.05) higher in group I. Lopez-Capape et al. (2009) showed 18% patients having impaired glucose tolerance (IGT) had fatty liver.\textsuperscript{22}

Conclusion
This study provided some important information of the Relation of Hypertension, elevated Alanine aminotransferase and Fatty Liver in Dyslipidaemic Impaired Glucose Tolerance patients. This cross sectional study showed elevated alanine aminotransferase and fatty liver were significantly (P<0.05) higher and hypertension also more(not significant) in patients having dyslipidemia. So every IGT patients with dyslipidemia should be screened for the presence of hypertension, alanine aminotransferase and fatty liver.

References
13. Jung Won Yun, Yong Kyun Cho, et al. Department of Internal Medicine, Division of Gastroenterology, Kangbuk
Samsung Hospital, Sungkyunkwan University School of Medicine, 108, Pyung-Dong, Jongro-ku, Seoul 110-746. (Epub Korea. October 9, 2008).


19. Shobha Luxmi, Rukhsana Abdul Sattar and Jamal Ara; Association of Non Alcoholic Fatty Liver with type 2 Diabetes Mellitus; JLUMHS Sep – Dec 2008.

