Original article:

Evaluation of association between serum gamma glutamyltransferase activity and carotid intima media thickness

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Abstract:

Introduction: Gamma-glutamyltransferase (GGT) is a plasma membrane enzyme that plays a central role in oxidative metabolism. It regulates extracellular catabolism of glutathione. Gamma-glutamyltransferase is usually known as diagnostic marker for hepatobiliary disease and excessive alcohol consumption. Timely assessment of common carotid artery IMT and serum gamma-glutamyl transferase can be used to assess the consequences. Therefore, I investigated the association between serum GGT activity and carotid IMT in this study.

Materials and methods: Sixty patient admitted in medicine wards are included in this study over a period from July 2012 to September 2014 are included in this study. “Institute Ethics Committee Clearance was obtained before start of Study”. Measurement of gamma-glutamyltransferase activity: Serum GGT activity was measured by an enzymatic colorimetric test at 37_C, using a Roche/Hitachi analyzer (Mannheim, Germany). The reference range of GGT activity in our laboratory is 8-61 U/L.

Observations and results: Above table and below graph shows correlation between CIMT and serum GGT value. It showed positive relation sheep. P value significant (<0.001) and r value (0.783) is positive indicating that CIMT and Serum GGT has significant positive correlation. CIMT increases as Serum GGT level increases.

Conclusion: In present study serum GGT activities within the reference range were associated with carotid IMT and serum GGT activities were increased in patients with carotid artery intimal hyperplasia. Carotid IMT is a widely used surrogate marker for atherosclerotic disease. Therefore, the association between carotid IMT and serum GGT activity suggests that serum GGT activity is a marker for atherosclerotic disease.

Keywords: Gamma-glutamyltransferase, carotid intima media thickness

Introduction

Gamma-glutamyltransferase (GGT) is a plasma membrane enzyme that plays a central role in oxidative metabolism. It regulates extracellular catabolism of glutathione. Gamma-glutamyltransferase is usually known as diagnostic marker for hepatobiliary disease and excessive alcohol consumption. Recently, serum GGT activity was found to be associated with cardiovascular diseases (CVD), other vascular risk factors, and prognosis of acute coronary syndrome. GGT has also been identified in atherosclerotic plaques. Timely assessment of common carotid artery IMT and serum gamma-glutamyl transferase can be used to assess the consequences. Therefore, I investigated the association between serum GGT activity and carotid IMT in this study.

Materials and methods

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**Inclusion criteria**
Sixty patients who had normal liver function test (aspartate aminotransferase, alanineaminotransferase and alkaline phosphatase) were consecutively enrolled in this study. Patient between the age group of 45-70 years randomly selected irrespective of sex, duration, glycemic control with or without hypertension and with or without diabetic macrovascular complication with normal liver function tests.

**Exclusion criteria**
1. Age>70years.
2. Chronic alcoholic (>30g/day).
3. Pregnant women.
4. Active or chronic Renal/liver disease.
5. Patient on ocp and long term steroids or any hepatotoxic drug.

Documented coronary or peripheral artery disease

**Measurement of gamma- glutamyltransferase activity**: Serum GGT activity was measured by an enzymatic colorimetric test at 37°C, using a Roche/Hitachi analyzer (Mannheim, Germany). The reference range of GGT activity in our laboratory is 8-61 U/L.

**Evaluation of Intimal Media Thickness**: All patients were examined in supine position with neck extended with a pillow under the shoulder. Ultrasonography of the common carotid artery, carotid bifurcation, and internal carotid artery of the left and right carotid arteries was performed with a 7.5-MHz linear-array transducer (Siemens Acuson x300).

On a longitudinal, two-dimensional ultrasound image of the carotid artery, the anterior (near) and posterior (far) walls of the carotid artery are displayed as two bright white lines separated by a hypoechoic space. The distance between the leading edge of the first bright line of the far wall (lumen-intima interface) and the leading edge of the second bright line (media-adventitia interface) indicates the intima-media thickness. For the near wall, the distance between the trailing edge of the first bright line and the trailing edge of the second bright line at the near wall provides the best estimate of the near-wall intima-media thickness.

Left carotid was examined first and then the right. Three sites were selected in each carotid artery. The carotid artery bulb was traced and the first reading is taken 1 cm proximal to the carotid bulb. The second reading is taken within the bulb and the site with maximum diameter recorded. The third reading is taken 1 cm distal to the carotid bulb along the internal carotid artery. For all three sites both near wall and far wall measurements are taken. The recordings are taken up to 2 decimal points. An average of each artery is computed taking into account all six readings.

At the time, a note was made of presence of any plaque or calcification and duly recorded.

**Statistical Analysis**
Statistical analyses were performed with SPSS software (Statistical Package for the Social Sciences, version 10.0, SSPS Inc., and Chicago, Illinois).
Observations and results:

Table 1: Correlation between CIMT and Serum GGT level (n=60)

<table>
<thead>
<tr>
<th></th>
<th>Mean</th>
<th>Std. Deviation</th>
<th>Pearson Correlation (r value)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carotid intima media thickness (mm)</td>
<td>0.54</td>
<td>0.256</td>
<td>0.783</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Serum GGT level (U/L)</td>
<td>28.53</td>
<td>12.461</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Above table and below graph shows correlation between CIMT and serum GGT value. It showed positive relation sheep. P value significant (<0.001) and r value (0.783) is positive indicating that CIMT and Serum GGT has significant positive correlation. CIMT increases as Serum GGT level increases.

Discussion:

The present study showed that serum GGT activities within the reference range were associated with carotid IMT and serum GGT activities were increased in patients with carotid artery intimal hyperplasia. Serum GGT level was higher in hyperplasia group (mean 35.46u/L) in comparison to non-hyperplasia group where mean serum GGT level was 26.62 u/L and this difference was statistically significant. P value significant (<0.001) and r value (0.783) is positive indicating that CIMT and Serum GGT has significant positive correlation. CIMT increases as Serum GGT level increases. Carotid IMT is a widely used surrogate marker for atherosclerotic disease.

Recent studies suggest an independent role of GGT in the pathogenesis of CVD. Gamma-glutamyltransferase has been identified in atherosclerotic plaques in the carotid, cerebral, and coronary artery, and histochemical evidence of GGT activity was detected in human atherosclerotic plaques. Gamma-glutamyltransferase was expressed in CD68 macrophage-derived foam cells, and GGT positive foam cells were localized with immunoreactive oxidized LDL in the arterial wall. Furthermore, glutathione hydrolysis by GGT can trigger iron-catalyzed LDL oxidation, as well as production of reactive oxygen species, likely promoting plaque complications. Previous findings suggest that serum GGT contributes to the accumulation of GGT within atherosclerotic plaques. Therefore, serum GGT activities could reflect GGT activity in atherosclerotic plaques. The reverse is also possible.

In present study proportion of hyperplasia was not significantly differ in male and female. The p value for the same was more than 0.05. Similar results were
also found by Nuti M et al (12) where he concluded that age-adjusted CIMT values did not differ by GGT levels in males or females.

The present study showed that hyperplasia was higher in elderly compare to lower aged patients and it was statistically significant. (p<0.001)

Results of different studies are inconsistent with the active contribution of GGT in the initiation and progression of atherosclerotic vascular disease, at least to the extent reflected by carotid imaging. This issue has been addressed by a few studies biased by low statistical strength of the reported correlations, limited sample size, and unbalanced male-to-female ratios and, most importantly, missing adjustment for sex and age. (13) This latter limitation is of particular relevance when considering the confounding effect of demographic variables on CIMT in this study. This is in agreement with Volzke et al’s study on a large sample of patients with non-alcoholic fatty liver disease (14) in which anatomic alterations ranging from mere liver steatosis to steatohepatitis coexisted with elevated GGT and related metabolic abnormalities. (15)

This conclusions are further supported by negative results reported in several series of patients with non-alcoholic fatty liver disease, (16) a condition that affected also an undefined but large portion of our patients, particularly those with higher ALT, a measure of hepatic fat accumulation. (17) It must be recognized, however, that the issue of the non-alcoholic fatty liver disease as a marker of more advanced carotid atherosclerosis is controversial (17)

**Conclusion**

In present study serum GGT activities within the reference range were associated with carotid IMT and serum GGT activities were increased in patients with carotid artery intimal hyperplasia. Carotid IMT is a widely used surrogate marker for atherosclerotic disease. Therefore, the association between carotid IMT and serum GGT activity suggests that serum GGT activity is a marker for atherosclerotic disease.

**References:**


