TG/HDL-C Ratio: A Surrogate Marker of Insulin Resistance in Patients with Metabolic Syndrome

Parineeta Samant, Padma Chavan, Sandeep Rai

ABSTRACT

Insulin resistance (IR) is hallmark of metabolic syndrome. It is important to identify IR as it is the early stage before development of diabetes mellitus. The standard method to measure insulin resistance is the euglycemic clamp technique, which is laborious. Hence, a number of surrogate measures like homeostasis model assessment of insulin resistance (HOMA-IR), quantitative insulin sensitivity check index (QUICKI) and triglyceride/high density lipoprotein cholesterol (TG/HDL-C) ratio have been developed. Both of the former involve calculations, while TG/HDL ratio may be readily available for clinicians. Therefore, this study was undertaken to assess whether TG/HDL-C ratio serves as a better predictive marker of IR.

Objectives: The aim of the present study was to evaluate the triglyceride/HDL-C ratio as a surrogate marker of IR in metabolic syndrome patients.

Materials and methods: Total 110 patients were recruited in the study after obtaining informed written consent. They were divided into two groups. Group I included healthy controls (n = 50) and subjects with metabolic syndrome (MS) (n = 60) as per NCEP ATP III criteria were included in group II. Anthropometric measurements and biochemical analysis was performed in all subjects.

Results: There was statistically significant difference in anthropometric, glycermic and lipid parameters in control and study group (p < 0.0001). The regression model between HOMA-IR and TG/HDL-C ratio showed positive correlation (r = 0.29, p = 0.01) while between QUICKI and TG/HDL-C ratio showed negative correlation (r = -0.37, p = 0.002).

Conclusion: We report in our study that TG/HDL-C can be adopted in routine laboratory practice as a surrogate marker for prediction of insulin resistance. So that patients with metabolic syndrome may be beneficial at an early stage.

Keywords: Insulin resistance, Triglycerides, High density lipoprotein, Metabolic syndrome, HOMA-IR, QUICKI.


Source of support: Nil

Conflict of interest: None

INTRODUCTION

Insulin resistance (IR) is a major finding in metabolic syndrome (MS) and a contributing factor for risk of development of type 2 diabetes and cardiovascular diseases (CVD). Therefore, a reliable measure of insulin resistance is important for investigating its link with metabolic syndrome (MS). For this, the homeostasis model assessment of insulin resistance (HOMA-IR), is widely accepted method as an alternative to the glucose clamp which is laborious. HOMA-IR is comparable to the glucose clamp technique in terms of precision but not accuracy and, hence, it is possible to study large number of subjects using a single measurement of glucose and insulin in fasting state. In addition to HOMA-IR, the quantitative insulin sensitivity check index (QUICKI) derived from logarithmically transformed fasting plasma glucose (FPG) and insulin levels has also proven to be a first-rate index of insulin resistance in comparison with clamp-IR.

QUICKI provides a consistent and precise index of insulin sensitivity with better positive predictive power. It is simply a variation of HOMA equations, as it transforms the data by taking both the logarithm and the reciprocal of the glucose-insulin product, thus slightly skewing the distribution of fasting insulin values. QUICKI has been seen to have a significantly better linear correlation with glucose clamp determinations of insulin sensitivity than minimal-model estimates, especially in obese and diabetic subjects. QUICKI should not be considered, as a new model rather simply logs as HOMA-IR, which explains the near perfect correlation with HOMA.

Another alternative proposed for the identification of IR is determination of fasting triglycerides (TG) to HDL-C ratio and glucose. Since elevated triglyceride is one of the NCEP ATP III criteria for MS, hypertriglyceridemic state which may accompany either normal or impaired fasting glucose should promote screening for IR.

Plasma TG and HDL-C concentrations are independently associated with insulin sensitivity and a ratio of TG/HDL-C concentration is significantly related to a direct measure of insulin-mediated glucose disposal. Recently, it is proposed that triglycerides/high density lipoproteins (HDL) cholesterol ratio is one of the indices to evaluate the atherogenic state due to the association between dyslipidemia and IR. IR significantly impacts lipoprotein
metabolism and is associated with increased in TG levels and depressed HDL levels.16,17

The purpose of this study was to compare the existing model of HOMA-IR and QUICKI with TG/HDL-C ratio for assessment of insulin resistance in MS patients.

MATERIALS AND METHODS

This was an observational prospective study approved by Institutional Ethics Review Committee. A total of 110 subjects between age group of 35 and 65 years were recruited for the study after obtaining their informed consent. As occurrence of the disease (MS and DM) is common, the selected sample size will be representative of population and sample size was approved by institutional biostatistician. The subjects were divided into two groups. Group I included healthy controls and Group II included subjects with metabolic syndrome. All the subjects were matched for age, gender and were excluded for chronic diseases of kidney and liver as well as for cancer and diabetes mellitus. The diagnosis of metabolic syndrome was based on NCEP ATP III criteria. Measurements of height and weight were done with the subjects standing, without shoes and with light clothing. Body mass index (BMI) was calculated as weight in kg divided by height in meter squared. WC was measured at the level of the umbilicus with a tape in centimeter scale.

Venous blood samples were obtained from the antecubital vein under conditions of 12 hours of fasting. Fasting plasma glucose, TG, total and HDL cholesterol levels were measured by enzymatic techniques on fully automated analyzer. LDL and VLDL values were obtained by using Friedewald’s formula.18 Fasting plasma insulin was measured by ELISA technique. Insulin resistance was determined by means of HOMA-IR using the following formula:

\[
\text{HOMA-IR} = \frac{\text{fasting insulin (μIU/mL)} \times \text{fasting glucose (mg/dl)}}{405}
\]

QUICKI was determined using the formula:

\[
\text{QUICKI} = \frac{1}{[\log (\text{insulin μU/mL}) + \log (\text{glucose mg/dl})]}
\]

The TG/HDL-C ratio was calculated using the formula:

\[
\text{fasting TG (mg/dl)/HDL-cholesterol (mg/dl)}
\]

STATISTICAL ANALYSIS

Data are presented as means ± SD, student t-test was used to compare age, BMI, W/H ratio, SBP, DBP, FPG, FPI and lipid profile levels between patients and controls. The correlation of TG/HDL-C ratio with both HOMA-IR and QUICKI was determined by Pearson correlation coefficient and simple regression model was used. Statistical Package for Social Sciences (SPSS, version 17.0) was used. p-values <0.05 were considered statistically significant.

RESULTS

Table 1 shows anthropometric and clinical characteristics of control and study group. There were significant differences in the values of BMI, waist circumference, systolic blood pressure, diastolic blood pressure in control and study group (p < 0.0001). The difference in fasting plasma glucose and LDL cholesterol was also statistically significant in control and study group (p < 0.0001). The HOMA-IR was elevated and QUICKI was decreased in metabolic syndrome group compared to controls. The regression model between HOMA-IR and TG/HDL-C ratio showed was positive correlation (r = 0.29, p = 0.01) while between QUICKI and TG/HDL-C ratio showed negative correlation (r = –0.37, p = 0.002), refer to Graphs 1 and 2 respectively. The mean high density lipoprotein-cholesterol (HDL-C) level was significantly lower in group II (p < 0.0001).
DISCUSSION

In our study, we have used HOMA-IR and QUICKI, the widely accepted model for assessment of IR and compared with TG/HDL-C as marker of IR.

The TG/HDL-C ratio was calculated in metabolic syndrome patients and control group and we found that TG/HDL-C ratio was higher in the study group. There was significant positive correlation between HOMA-IR and TG/HDL-C ratio ($r = 0.29; p < 0.05$) in the study group. The regression model showed $R^2$ value of 0.09, indicating 9.0% variation in the HOMA-IR due to TG/HDL-C ratio, refer to Graph 1.

Our results are in accordance with Salazar et al,$^{20}$ Morato et al,$^{21}$ and Brehm et al,$^{22}$ who demonstrated positive correlation between TG/HDL-C ratio and insulin resistance, confirming that TG/HDL-C ratio predicts insulin resistance in metabolic syndrome. But, an independent study by Knight et al,$^{23}$ stated that triglyceride/high-density lipoprotein cholesterol ratio fails to predict insulin resistance in African-American women.

The regression model of TG/HDL-C and QUICKI showed strong negative correlation ($r = -0.37; p < 0.005$). The $R^2$ value showed by regression model is 0.14 showing 14% variation in QUICKI due to TG/HDL-C ratio, refer to Graph 2. These finding are similar to the finding of Brehm et al who found that QUICKI indicated severe insulin resistance in individuals with impaired glucose tolerance.$^{22}$

Thus, the regression model indicates that TG/HDL-C ratio is a significant variable of insulin resistance in metabolic syndrome patients. Most of the studies have compared HOMA-IR with either TG alone or with TG/HDL-C ratio.$^{21,24}$ But, combined model of TG/HDL-C with HOMA-IR and QUICKI has been reported in very few studies. TG/HDL-C ratio is an economic and it is easy to calculate$^{25}$ and a good predictor of LDL size. This ratio offers the most practical approach to identify insulin resistance. Moreover, it is associated with a higher risk for cardiovascular diseases than just serum TG concentrations in a population including 8 to 14% diabetic patients.$^{26}$ These data suggest that the TG/HDL-C ratio may serve as a surrogate marker of IR. It is easy to determine and links insulin resistance and cardiovascular risk in nondiabetic individuals.

This study is limited by the fact that HOMA-IR index and QUICKI was not correlated with insulin sensitivity by the gold standard method, such as euglycemic clamp.$^{14}$

CONCLUSION

This study demonstrates that TG/HDL-C ratio positively correlates with insulin resistance in metabolic syndrome patients. Therefore, we propose that TG/HDL-C ratio serves as an easily available and economic laboratory marker for the busy clinicians to identifying insulin resistance in metabolic syndrome patients.

ACKNOWLEDGMENT

This work was supported by MGM Medical College and Hospital, Kamothe, Navi Mumbai, Maharashtra, India. We acknowledge Mr Pandurang Thatkar, Statistician, for helping with data analysis.

### Table 1: Descriptive and comparative statistics for different groups by student t-test

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Group I (control)</th>
<th>Group II (metabolic syndrome)</th>
<th>*p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>BP (systolic) mm/Hg</td>
<td>115 ± 6.98</td>
<td>134 ± 2.86</td>
<td>0.0001</td>
</tr>
<tr>
<td>BP (diastolic) mm/Hg</td>
<td>76.7 ± 4.98</td>
<td>96 ± 0.60</td>
<td>0.0001</td>
</tr>
<tr>
<td>BMI in kg/m²</td>
<td>23.3 ± 1.39</td>
<td>29.6 ± 0.53</td>
<td>0.0001</td>
</tr>
<tr>
<td>W/H ratio</td>
<td>0.802 ± 0.03</td>
<td>0.99 ± 0.01</td>
<td>0.0001</td>
</tr>
<tr>
<td>Fasting plasma glucose mg/dl</td>
<td>88.1 ± 5.06</td>
<td>113.3 ± 1.19</td>
<td>0.0001</td>
</tr>
<tr>
<td>Fasting plasma insulin μIU/ml</td>
<td>10.2 ± 3.2</td>
<td>22 ± 0.11</td>
<td>0.0001</td>
</tr>
<tr>
<td>HOMA-IR</td>
<td>2.23 ± 0.69</td>
<td>6.14 ± 0.09</td>
<td>0.0001</td>
</tr>
<tr>
<td>QUICKI</td>
<td>0.34 ± 0.03</td>
<td>0.29 ± 0.02</td>
<td>0.0001</td>
</tr>
<tr>
<td>Cholesterol mg/dl</td>
<td>146.3 ± 10.59</td>
<td>174 ± 15</td>
<td>0.0001</td>
</tr>
<tr>
<td>Triglycerides (TG) mg/dl</td>
<td>110 ± 17.2</td>
<td>189 ± 7.5</td>
<td>0.0001</td>
</tr>
<tr>
<td>High density lipoprotein cholesterol (HDL-C) mg/dl</td>
<td>44.5 ± 3.58</td>
<td>40 ± 0.6</td>
<td>0.0001</td>
</tr>
<tr>
<td>Very low density lipoproteins mg/dl</td>
<td>21.59 ± 2.72</td>
<td>36 ± 2.1</td>
<td>0.0001</td>
</tr>
<tr>
<td>Low density lipoproteins mg/dl</td>
<td>83.92 ± 14.2</td>
<td>103 ± 22.2</td>
<td>0.0001</td>
</tr>
<tr>
<td>TG/HDL-C ratio</td>
<td>2.4653 ± 0.2094</td>
<td>4.554 ± 0.152</td>
<td>0.0001</td>
</tr>
</tbody>
</table>

Data are expressed as mean ± SD. *Student’s t-test for independent samples
AUTHORS’ CONTRIBUTIONS

Ms Parineeta Samant performed the biochemical assays and assisted in writing the paper. Dr Padma Chavan analyzed the results critically and wrote the paper. Dr Sandeep Rai gave valuable inputs in the manuscript. All authors read and approved the final manuscript.

REFERENCES