Original Article

Relationships of Serum Level of High-Sensitivity C-Reactive Protein (hs-CRP) and White Blood Cell (WBC) Count with Gamma-Glutamyltransferase among Iranian Healthy Adults

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ABSTRACT

Background & Objective: There are many common infections and inflammations among people over the world. This demands an affordable and reliable test with high sensitivity/specificity to predict or confirm the diagnosis of such cases in routinely clinical practice. In the present study, we aimed to find any potential correlation between serum levels of GGT and CRP-Q and/or hs-CRP and WBC count as the well-known markers of inflammation in human body.

Materials and Methods: Through a cross-sectional study, serum levels of CRP-Q, hs-CRP, and GGT, in addition to WBC count were measured in 1,500 healthy people, referred to Blood Transfusion Organization from across the country. Data were analyzed after the patients were checked by physical examination for ruling out the presence of any inflammation or other illness. Serum levels of GGT, CRP-Q, hs-CRP, and WBC count were analyzed by SPSS for windows version 16.

Results: Analysis showed a positive linear correlation between CRP-Q and hs-CRP with GGT also confirmed by non-parametric tests.

Conclusion: Serum GGT may be an inflammatory index and a useful marker in approaching to inflammatory diseases.

Key words: Gamma Glutamyltransferase, C-Reactive Protein, White Blood Cell Count

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**Introduction**

C-reactive protein (CRP), as an acute phase reactant, is a reliable marker of inflammation employed in three types: qualitative, quantitative (CRP-Q) and highly sensitive (hs-CRP) CRP. Serum concentration of CRP increases due to a wide spectrum of inflammations and infections. In acute infections, its serum level would be 50-100 mg/L, but usually not more than 10 mg/L in case of chronic inflammatory conditions like atherosclerosis (1). The specific diagnostic and predictive role of CRP in many conditions such as cardiovascular diseases, atherosclerosis, diabetes mellitus, trauma, malignancies, etc. is truly disclosed (1). Nevertheless, the most challengeable aspects of hs-CRP testing are its availability and cost. This could lead to seeking a substitute test with lower laboratory price and easier accessibility to cover its role, having acceptable sensitivity and specificity (2), and costing more reasonably.

Gamma-glutamyltransferase (γ-GT or GGT) is a known liver enzyme with a main role in catalyzing some reactions in the body. It could also have a relatively prominent role in anti-oxidant processes. For instance, it cleaves extracellular glutathione to procure and present the precursor amino acids to cells in charge of intracellular re-synthesis of the same substance (2-4). It means that GGT is involved in the transfer of amino acids across the cellular membrane (3, 4). GGT is also a part of intracellular homeostasis system of oxidative stress (3-6) and leukotriene metabolism (7). GGT would be found on the surface of all cells, with higher concentration in the liver, bile ducts, and kidney.

The simplest usage of elevated serum level of GGT might be the identification of alcohol abuse even in a period of 3-4 weeks prior to the test (5, 6). Furthermore, it is a valuable marker of liver damages, congestive heart failure, coronary heart diseases (5, 8), as well as consumption of many drugs such as non-steroidal anti-inflammatory drugs (NSAIDs) (9,10). There are many common infections and inflammations among people over the world. This entails an affordable and reliable test with high sensitivity/specificity to predict or confirm the diagnosis of such cases in routinely clinical practice. The aforementioned test would be more acceptable than hs-CRP test which is out of access in many cases and expensive.

The predictive role of GGT for some conditions has been expressed by some authors including diabetes type 2, hypothyroidism, stroke, dyslipidemia, chronic kidney disease, and cancer in addition to obesity, smoking, high meat consumption, and a non-healthy lifestyle (5, 6, 9-19). Besides, age, race, and gender could affect on the serum level of GGT (9).

In the present study, we aimed to find any potential correlation between serum levels of GGT and CRP-Q and/or hs-CRP and WBC count as the well-known markers of inflammation in human body.

**Materials and Methods**

One thousand and five hundred healthy people attending the Blood Transfusion Organization (BTO) from across the country of Iran entered our cross-sectional study between January 2010 and February 2011. Participants were included in the study by census after they were examination by the resident practitioners in BTO in order to rule out the presence of any inflammation and other illnesses.

Informed consent was obtained from the participants before starting the investigation. The study was carried out according to the principles of declaration of Helsinki and the local Ethics Committee of Tehran University of Medical Science approved the whole protocol.

Serum levels of CRP and GGT was measured...
CRP was tested by two sets of techniques: quantitative (CRP-Q) and highly sensitivity (hs-CRP) methods. CRP-Q was tested conventionally in the laboratory using the routine kits, while hs-CRP was measured using a recently introduced kit by “BioSystems, Spain” company. The latter method is based on the agglutination of the latex particles coated with anti-human CRP by serum CRP.

Gamma-GT was measured by “Szasz” method through which human’s plasma would be mixed with heparin or EDTA and evaluated in 37 °C. Normal serum level of GGT in this method was considered 32 IU/L for women and 49 IU/L for men.

White blood cells count was calculated conventionally during the study and reported as a single number.

Serum levels of GGT, CRP-Q, hs-CRP, and WBC count were analyzed by SPSS for windows version 16. Correlations especially between GGT and the two other inflammatory markers were desired to detect. Non-parametric tests of “Kendall” and “Spearman” were applied due to the non-normal distribution of variables in the study and the results were deemed significant at $P$ value < 0.05.

**Results**

The participants consisted of 1,265 men and 235 women, aging 22 to 61; the mean age was 42.98 ± 9.96. There was a positive linear correlation between CRP-Q and hs-CRP and GGT (Fig. 1) confirmed by non-parametric tests ($P$ < 0.001).

The regression line formula was defined as:

$$hs\text{-}CRP = 0.733 + 1.11 \text{CRP-Q}$$

There was also a correlation observed between GGT and CRP-Q, hs-CRP, and WBC ($P$: 0.003, 0.003, and 0.001, respectively).

No confounding factor was identified for age in this regard.

**Discussion**

The role of GGT in protecting cellular integrity from oxidative stress is of no doubt and it is clear now that the elevation of this biomarker could be representative of the anti oxidative challenge it is dealing with in the body. Elevated levels of GGT due to inflammation and oxidative stress had been shown in alcoholism earlier; however, certain role of this marker in subjects otherwise healthy was not evidenced until recent years (20-26).

The majority of blood donors in our population were male with women showing meager interest. This was due to the selection of our samples from one center of blood transfusion organization.

Our initial conception that GGT would be correlated with the studied inflammatory markers namely CRP-Q, hs-CRP, and WBC counts did not receive statistically significant difference. Many studies had found a positive relationship between GGT and at least other inflammatory markers or risk of diseases. Among these, Strasak and colleagues investigated the association of serum GGT with CAD related mortality and found the correlation between them in men (27). Lee et al. showed that inflammation is the main mechanism connecting CAD to GGT; they evaluated serum GGT and CRP along with the whole WBC count among 4562 Korean adults and finally reported
higher odds ratio for CRP serum level and WBC count in higher concentrations of GGT related cardiovascular mortality (28). Furthermore, higher risk of malignancies was obviously associated with elevated level of GGT having a clear dose-response relationship observed in a study by Strasak in Austria (13). Kim et al. used serum ferritin level as a marker of oxidative stress to point out the role of serum GGT in this regard and succeeded to show a significant relationship for GGT on one side and BMI, ferritin, triglyceride, cholesterol, fasting blood glucose, AST, and ALT on the other (4).

GGT and its role in metabolic syndrome (MS) were perfectly pointed out earlier (29). The authors disclosed that MS prevalence was significantly higher in the highest quartile of GGT level. The cut-off point for GGT in diagnosing MS was defined 42 IU/ L for men and 21 IU/ L for women. Previously, elevated serum level of GGT was reported to be as an index of the MS onset (30). Although we could not achieve the main idea of the research we initially aimed to, it would be of high importance to perform multicentral studies to get reliable results in case of any correlation between serum level of GGT and other inflammatory markers. In such way, we would be able to replace the latter tests for these markers in case of cost-ineffectiveness or inaccessibility by GGT. Availability and simplicity of GGT measurement test could pose it as a valuable surrogate for these mentioned inflammatory markers. However, there is still ways to go to reach to that target.

**Conclusion**

Our findings suggest that serum GGT might be an inflammatory index and a useful marker in approaching to inflammatory diseases.

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