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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

for each patients. 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- CRP = 0.733 + 1.11 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.

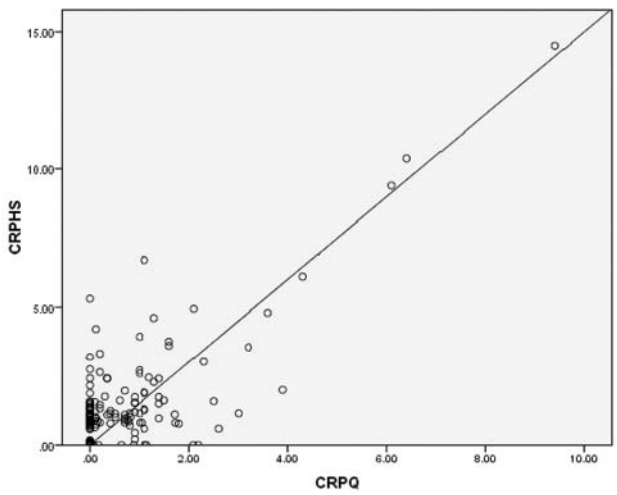

Fig. 1- The correlation between CRP-Q and CRP-hs among the studied healthy population

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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References

1. Eiji Oda E, Kawai R, Watanabe K, Sukumaran V. Prevalence of Metabolic Syndrome Increases with the Increase in Blood Levels of Gamma Glutamyltransferase and Alanine Aminotransferase in Japanese Men and Women. Inter Med 2009; 48: 1343-1350.

2. Lee DS, Evans JC, Robins SJ, Wilson PW, Albano I, Fox CS, *et al*. Gamma glutamyl transferase and metabolic syndrome, cardiovascular disease, and mortality risk: the Framingham Heart Study. Arterioscler Thromb Vasc Biol 2007; 27: 127-133.

3. Misra A. C- Reactive Protein in Young Individuals: Problems and Implications for Asian Indians. Nutrition 2004;20:478–81.

4. Kim JH, Lee HR, Han AR, Im JA, Lee DC. Relationship between Serum gamma-glutamyltransferase Level and Serum Ferritin Level in Healthy Adults. J Korean Acad Fam Med 2006;27(8):645-51.

5.Schulman JD, Goodman SI, Mace JW, Patrick AD, Tietze F, Butler EJ. Glutathionuria: inborn error of metabolism due to tissue deficiency of gamma-glutamyl transpeptidase. Biochem. Biophys Res Commun 1975;65(1):68–74.

6. Yokoyama H. Gamma glutamyl transpeptidase (gammaGTP) in the era of metabolic syndrome in Japanese. Nihon Arukoru Yakubutsu Igakkai Zasshi 2007;42 (3):110–24.

7. Fraser A,Thinggaard M, Christensen K,Lawlor DA. Alanine aminotransferase, gamma-glutamyltransferase (GGT) and all-cause mortality: results from a population-based Danish twins study alanine aminotransferase, GGT and mortality in elderly twins. Liver Int 2009;29(10):1494-9.

8. Lee DH, Blomhoff R, Jacobs DR JR. Is serum gamma glutamyltransferase a marker of oxidative stress? Free Radic Res 2004;38: 535–9.

9. Raulf M, Stüning M, König W. Metabolism of leukotrienes by L-gamma-glutamyl-transpeptidase and dipep-

tidase from human polymorphonuclear granulocytes. Immunology 1985;55(1):135–47.

10. Fraser A, Harris R, Sattar N, Ebrahim S, Smith GD, Lawlor DA.Gamma-glutamyltransferase is associated with incident vascular events independently of alcohol intake: analysis of the British women's heart and health study and meta-analysis. Arterioscler Thromb Vasc Biol 2007;27:2729–35.

11. Lee DH, Jacobs DR JR.Serum gamma-glutamyltransferase: new insights about an old enzyme. J Epidemiol Community Health 2009;63(11):884-6.

12. Targher G, Kendrick J, Smits G, Chonchol M. Relationship between serum gamma-glutamyltransferase and chronic kidney disease in the United States adult population. Findings from the National Health and Nutrition Examination Survey 2001-2006. Nutr Metab Cardiovasc Dis 2010;20(8):583-90.

13. Strasak AM, Rapp K, Brant LJ, Hilbe W, Gregory M, Oberaigner W, *et al*. Association of gamma- glutamyltransferase and risk of cancer incidence in men: a prospective study. Cancer Res 2008;68:3970–7.

14. Lee DH, Silventoinen K, Hu G, Jacobs DR, Jousilahti P, Sundvall J, *et al*. Serum gamma glutamyltransferase predicts nonfatal myocardial infarction and fatal coronary heart disease among 28,838 middleaged men and women. Eur Heart J 2006;27:2170–6.

15. Ryu S, Chang Y, Kim DI, Kim WS, Suh BS. gamma-Glutamyltransferase as a predictor of chronic kidney disease in nonhypertensive and nondiabetic Korean men. Clin Chem 2007;53:71–7.

16. Lee DH, Jacobs DR Jr, Gross M, Steffes M. Gamma glutamyltransferase is a predictor of incident diabetes and hypertension: the Coronary Artery Risk Development in Young Adults (CARDIA) Study. Clin Chem 2003;49:1358–66.

17. Lee DH, Steffen LM, Jacobs DR Jr. Association between serum gamma glutamyltransferase and dietary factors: the Coronary Artery Risk Development in Young Adults (CARDIA) Study. Am J Clin Nutr 2004;79:600–5.

18. Westerbacka J, Corner A, Tiikkainen M, Tamminen M, Vehkavaara S, Häkkinen AM, *et al*. Women and men have similar amounts of liver and intra-abdominal fat, despite more subcutaneous fat in women: implications for sex differences in markers of cardiovascular risk. Diabetologia 2004;47:1360–9.

19. Lee DH, Steffes M, Jacobs D. Can persistent organic pollutants explain the association between serum gamma-glutamyltransferase and type 2 diabetes? Diabetologia 2008;51: 402–7.

20. Miyatake N, Matsumoto S, MakinoH, Numata T. Comparison of hepatic enzymes between Japanese men with and without metabolic syndrome. Acta Med Okayama 2007; 61:31–4.

21. Fraser A, Harris R, Sattar N, Ebrahim S, Davey Smith G, Lawlor DA. Alanine aminotransferase, gamma glutamyltransferase and incident diabetes: the British Women's Heart and Health Study and meta-analysis. Diabetes Care 2009;32:741–50.

22.Whitfield JB. Gamma glutamyl transferase. Crit Rev Clin Lab Sci 2001;38:263–355.

23. Emdin M, Pompella A, Paolicchi A. Gamma- glutamyltransferase, atherosclerosis, and cardiovascular disease: Triggering oxidative stress within the plaque. Circulation 2005;112:2078–80.

24. Paolicchi A, Emdin M, Ghliozeni E, Ciancia E, Passino C, Popoff G, *et al*. Atherosclerotic plaques contain gamma-glutamyl transpeptidase activity. Circulation 2004;109:1140.

25. Bo S, Gambino R, Durazzo M, Guidi S, Tiozzo E, Ghione F, *et al*. Associations between gamma-glutamyl transferase,metabolic abnormalities and inflammation in healthy subjects from a population-based cohort: A possible implication for oxidative stress. World J Gastroenterol 2005;11:7109–17.

26. Ulus T, Yildirir A, Demirtas S, Demir O, Sade LE, Bozbas H, *et al*. Serum gamma-glutamyl transferase activity: A new marker for stent restenosis? Atherosclerosis 2007;195:348–53.

27. Strasak AM, Kelleher CC, Klenk J, Brant LJ, Ruttmann E, Rapp K, *et al*. Longitudinal change in serum gamma-glutamyltransferase and cardiovascular disease mortality: a prospective population-based study in 76,113 Austrian adults. Arterioscler Thromb Vasc Biol

2008;28(10):1857-65.

28. Lee YJ, Kim JK, Lee JH, Lee HR, Kang DR, Shim JY. Association of serum gamma-glutamyltransferase with C-reactive protein levels and white blood cell count in Korean adults. Clin Chem Lab Med 2008; 46(10):1410-5.

29. Oda E, Kawai R. Comparison between high-sensitivity C- reactive protein (hs- CRP) and whit e blood cell count (WBC) as an inflammatory component of metabolic syndrome in Japanese. Intern Med 2010;49(2):117-24.

30. Lee MY, Koh SB, Koh JH, Nam SM, Shin JY, Shin YG, *et al*. Relationship between gamma- glutamyltransferase and metabolic syndrome in a Korean population. Diabet Med 2008;25(4):469-75.