A study of trace elements and IL-6 in coronary heart disease patients

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Abstract

Coronary Heart Disease is a disease of attention as it is increasing in elderly as well as involving young population. Trace elements are important in many biochemical reactions and their concentration in blood may be related to CHD. Elevated levels of serum IL-6 are a powerful predictor of cardiovascular mortality and mortality from all causes. A cross sectional analytical study was done. Total 200 cases and 200 controls were engaged in study after applying inclusion and exclusion criterion. Serum level of copper, zinc and Il-6 was recorded. Most common group was 50-59 year age group. Serum level of copper and zinc was significantly low in cases than controls. Level of Il-6 was found significantly high. In conclusion copper Deficiency and deficiency of zinc have significant relationship with CHD. Level of Il-6 very much increased in patients of CHD.

Keywords: Coronary heart disease, copper, zinc, IL-6

Introduction

Cardiovascular diseases is one of the major cause of morbidity and mortality in India and worldwide. It is responsible for more than one third of total deaths [1]. Coronary artery disease (CAD) leading the tally and regarded as most prevalent [2]. Indeed, CAD is acknowledged as an important threat to sustainable development in the 21st century [3]. The primary pathological process that leads to CAD is atherosclerosis, an inflammatory disease of the arteries associated with lipid deposition and metabolic alterations due to multiple risk factors. More than 70% of at risk individuals have

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multiple risk factors for CAD and only 2-7% of the general population have no risk factors [4].

Traditional risk factors such as lipid profile, blood pressure and smoking account for not more than 50% of CAD mortality [5]. Role of free redicals in developing degenerative diseases is well known [6]. Trace elements, inflammatory markers and vitamins have role in formation atherosclerotic plaque. Zinc is an important component of copper zinc superoxide dismutase (Cu Zn SOD), which plays an emergent role in CHD. Zn deficiency can cause an increase in tissue oxidation damage. Imbalances between Cu and Zn may have role in atherosclerotic process [7]. IL-6 raises not only the levels of CRP that are produced, but also the viscosity of the blood, the number of platelets and the activity of those platelets. There is a correlation between elevated levels of circulating IL-6 and insulin resistance, hypertension and central obesity, all of which are risk factors for the development of cardiovascular disease [8].

Material and Methods

A cross sectional analytic study was done at Pacific Medical College and Hospital. Total 200 cases and 200 controls of age between 40 to 70 years were engaged in study who visited in cardiac department in hospital and diagnosed as CHD. In these patients IL-6 was estimated using Competitive electro-chemiluminescence protein binding assay on cobas e411. Serum Copper and Serum Zinc were analyzed in semi auto analyzer. Data thus collected was entered in Microsoft Excel sheet and was analyzed by using standard statistical software (SPSS version 20). Student T-test (unpaired t-test) was used for testing difference of Mean ±SD between two groups. P-Value< 0.05 was considered statistically significant.

Results

The mean age of cases was 58.71 ± 6.50 and control was 58.58 ± 6.41. most (30.5%) of the participants belonged to age group of 56-60 years, followed by 51-55 years (23%). A very few individuals belonged to 41-45years of age (1.75%). The mean Serum IL-6 of cases is 65.47 with SD 26.83 and while in control mean Serum IL-6 is 15.86 with SD 6.19.The difference is statistically significant. Average Serum copper of cases is 85.11with SD35.03 and control is 113.49 with SD 25.82 the difference is statistically significant. Average Serum zinc level of cases is 58.17 with SD 19.08 and control is 81.25 with 18.83. The difference is statistically significant.

Table 1

Parameter in ng/ml	Case (n-200)	Control (n-200)	p-value
IL-6	65.47±26.83	15.86±6.19	<0.001

Table 2

Parameter in ng/ml	Case (n-200)	Control (n-200)	p-value
S. copper	85.11±35.03	113.49±25.82	<0.001

S. zinc	58.17±19.08	81.25±18.83	<0.001

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Discussion

Present study is conducted in a tertiary care hospital of southern Rajasthan. Patients were of mostly 56-60 age group but disease was also present in 41-45yrs category which may be representative of early shift of epidemic of CAD. Early shift of epidemic was also mentioned by other studies done recently [9]

In present study mean Serum IL-6 values of serum in cases was found statistically significantly high. (p value<0.001). Results of our study are in parallel with the study done by Tentolouris *et al*. [10], in which levels of IL-6 were higher in patients having ischemic cardiomyopathy. Another study done by St-Pierre, *et al*. [11] also support our study results and they found IL-6 as a individual risk factor for cardiac ischemic heart disease, Study also mentioned that raised levels of plasma IL-6 were having nearly a 70% bigger risk of IHD which further supports the findings of our study.

One more study done by Tousoulis, *et al*. [12] and Assier *et al*. [13] also states the similar results that IL-6 acts as inflammatory cytokine, and there is a defined role in regulating the acute phase response, which is mostly related to early response. Martin josephs sto *et al*. [14] in their recent study shows very significantly high levels of IL-6 in cases of Coronary Heart Disease than non-cardiac patients. Their study also states that raised levels of IL-6 increases the probability of CHD by 25% in comparison to normal levels of IL-6 patients. Further there are other studies which are consistent to our results and showed a positive association between mortality from CAD and serum IL-6 concentration [15-18]. However, the causal role of elevated serum IL-6 in CAD mortality remains unclear. A recent study [19] reported a possible causal role of IL-6 in the development of coronary heart disease as interleukin6 receptor (IL-6R) blockade may be responsible for reduced systemic and articular inflammation. Furthermore, a collaborative meta-analysis [20] also supports this causal association between IL-6 Receptor related pathways and coronary heart disease strongly.

In our study Serum copper levels in cases were statistically significantly low in comparison to control. A study done by Aysegul Cebi *et al*. [21] in turkey revealed there is no significant difference in Serum levels of copper between CHD patients and normal individuals. Reunanen *et al*. [22] and Lukaski *et al*. [23] in contrast reported increased levels of serum Cu and a signficant increase in urine Cu levels in patients suffering from myocardial infarction. Serum Zinc levels were significantly low on our study. Low serum Zn levels have been associated with increased cardiovascular mortality [24]. Results of many studies are consistent to our study [24-26].

Conclusion

In this study we found significant difference in levels of IL-6 between cases and controls. Serum zinc found significantly low. Serum copper levels are low and difference was significant. Our study provides evidence in favour of role of IL-6 in inflammation and atherosclerosis and also shows significant difference in levels of copper and zinc.

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References

1. Heart disease and stroke statistics 2016 update. A report from the American Heart Association. Mozaffarian D, Benjamin E, Go A, *et al*. Circulation, 2016, 133.

2. Global, regional and national burden of cardiovascular diseases for 10 causes, 1990 to 2015. Roth GA, Johnson C, Abajobir A, *et al*. J Am Coll. Cardiol. 2017;70:1-25.

3. The changing patterns of cardiovascular diseases and their risk factors in the states of India: The Global Burden of Disease Study 1990 2016. Prabhakaran D, Jeemon P, Sharma M, *et al*. Lancet Glob Health. 2018;6:1339-1351.

4. Frequent use of social networking sites is associated with poor psychological functioning among children and adolescents. Sampasa Kanyinga H, Lewis RF. Cyberpsychology Behav Soc Netw. 2015;18:380-385.

5. Gey KF, Puska J, Jordon P. *et al*. Inverse correlation between plasma vitamin E and mortality from ischemic heart disease in cross cultural epidemiology. Am J Clin Nutr. 1991;53:326-334.

6. Ames BN, Shigenaga MK, Hagen TM. Oxidants, antioxidants and the degenerative diseases of aging. Proc Natl Acad. Sci. 1993;90:7915-7922.

7. Zatta P, Lucchini R, Van Rensburg SJ, Taylor A. The role of metals in neurodegenerative processes: aluminum, manganese and zinc. Brain Res Bull. 2003 Nov;62(1):15-28. Doi: 10.1016/s0361-9230(03)00182-5. PMID: 14596888.

8. Yudkin JS, Kumari M, Humphries SE, Mohamed Ali V. Inflammation, Obesity, stress and coronary heart disease: is interleukin 6 the link? Atherosclerosis. 2000;148:209-14.

9. Ullewar MP, Ingale SV, Ingale VC, Upadhye JJ. Lipid prole in patients with coronary heart disease. Int J Sci Rep. 2017;3(10):259-64.

10. Tentolouris C, Tousoulis D, Antoniades C, Bosinakou E, Kotsopoulou M, Trikas A, *et al*. Endothelial Function and Pro inflammatory Cytokines in Patients with Ischemic Heart Disease and Dilated Cardiomyopathy. International Journal of Cardiology. 2004;94(2-3):301-5.

11. St-Pierre A, Pirro M, Cantin B, Bergeron J, Dagenais G, Despres JP, *et al*. Inflammatory markers and long-term risk of ischemic heart disease in men, a 13-year follow-up of the Quebec Cardiovascular Study. Atherosclerosis. 2005;182:315-21.

12. Tousoulis D, Charakida M, Stefanadis C. Endothelial function and inflammation in coronary artery disease. Heart. 2006;92(4):441-44.

13. Assier E, Boissiera MC, Dayer JM. Interleukin-6: From identification of the cytokine to development of targeted treatments. Joint Bone Spine, 2010, 532-536.

14. Martin Joseph Sto. Tomas, Patricia Megan Baluyot, Ana Loraine Delos Santos, Jenelle Faustino, Eunice Licudine, Ella Marie Mendoza, *et al*. Jennifer Tiburcio Interleukin 6 as a Biomarker of Ischemic Heart Disease. International Journal of Scientific and Research Publications, 2015, 5(7). ISSN 2250-3153.

15. Luc G, Bard JM, Juhan-Vague I, *et al*. C-reactive protein, interleukin-6 and fibrinogen as predictors of coronary heart disease: the PRIME study. Arteriosclerosis, Thrombosis, and Vascular Biology. 2003;23(7):1255-1261.

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16. Baune BT, Rothermundt M, Ladwig KH, Meisinger C, Berger K. Systemic inflammation (interleukin 6) predicts all-cause mortality in men: results from a 9-year follow-up of the MEMO study. Age. 2011;33(2):209-217.

17. Jaremo P, Nilsson O. Interleukin-6 forecasts long-term mortality after acute myocardial infarctions, Bologna, Italy, Medimond S R L, 2007.

18. Fisman EZ, Benderly M, Esper RJ, *et al*. Interleukin-6 and the risk of future cardiovascular events in patients with angina pectoris and/or healed myocardial infarction. American Journal of Cardiology. 2006;98(1):14-18.

19. Alley DE, Crimmins E, Bandeen-Roche K, Guralnik J, Ferrucci L. Three-year change in inflammatory markers in elderly people and mortality: the Invecchiare in Chianti study. Journal of the American Geriatrics Society. 2007;55(11):1801-1807.

20. Sarwar N, Butterworth AS, Freitag DF, *et al*. Collaboration IRGCERF: interleukin-6 receptor pathways in coronary heart disease: a collaborative meta-analysis of 82 studies. The Lancet. 2012;379:1205-13.

21. Cebi A, Kaya Y, Gungor H, Demir H, Yoruk IH, Soylemez N, *et al*. Trace Elements, Heavy Metals and Vitamin Levels in Patients with Coronary Artery Disease. Int J Med Sci. 2011;8(6):456-460. Doi: 10.7150/ijms.8.456. Reunanen A https://www.medsci.org/v08p0456.htm

22. Reunanen A, Knekt P, Marniemi J. *et al*. Serum calcium, magnesium, copper and zinc and risk of cardiovascular death. Eur J Clin Nutr. 1996;50:431-7.

23. Lukaski HC, Klevay LM, Milne DB. Effects of dietary copper on human autonomic cardiovascular function. Eur J Appl Physiol. 1988;58:74-80.

24. Dasti MA, Hashmi SFA, Baloch GH, Shas SZA. Acute myocardial infarction serum zinc level in patients. Professional Med J. 2013;(4):556-61.

25. Nazir S, Ullah E, Hussain S, Bukhari SA Study of Serum zinc levels among patients of coronary artery disease conducted in a Tertiary Care Hospital. Bio-medica 29, 2013.

26. Little PJ, Bhattacharya R, Moreyra AE, Korichneva IL. Zinc and cardiovascular disease. Nutrition. 2010;26(11-12):1050-57.

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