



ROLE OF CARDIAC MARKERS IN CHRONIC RENAL FAILURE PATIENTS.

Biochemistry

Ramesh Chand Thanna

Amaltas Institute Of Medical Sciences.

Dr. B K Agarwal

Index Medical College Hospital Research Centre, Indore, M.P., India.

Rakesh Romdey

Amaltas Institute Of Medical Sciences.

Dr. Neha Sharma*

Associate professor, Biochemistry, Geetanjali medical college and Hospital Udaipur, Rajasthan, India. *Corresponding Author

ABSTRACT

Introduction: Cardiovascular diseases (CVD) are known as important reasons of the increased morbidity and mortality observed in patients with chronic renal failure (CRF). The association of serum Interlukin-6, homocysteine as well as other cardiovascular risk factors in relation to existence and cause of CVD were investigated.

Method: In this study 200 CRF patients were recruited and further stratified into group with Male and Female as case groups. Those without renal failure were assigned as control group (n=200).

Results: The patients with CRF showed a significant increase in plasma levels of Cpk-MB, homocysteine and C-reactive protein (CRP) compared to control. The positive association were observed between homocysteine, Urea and Hs-CRP, IL-6. It shows a significant Association of parameters in CRF.

Conclusion: The results demonstrated elevation in plasma values IL-6, homocysteine and HS-CRP in patients with CRF. However, these modifications may lead to atherosclerosis and consequence CVD event. These parameters may be important with respect to the high morbidity and mortality of CVD found in patients with CRF.

KEYWORDS

Chronic Renal Failure (CRF), CVD, homocysteine, CPK-MB, HS-CRP.

INTRODUCTION:

Chronic kidney disease (CKD) is common, and is associated with a high burden of cardiovascular disease. This cardiovascular risk is incompletely explained by traditional risk factors, calling attention to a need to better understand the pathways in CKD contributing to adverse cardiovascular outcomes. (1) Elements of the pathophysiology of CKD itself potentiate progression of CVD and adverse outcomes. Beyond traditional CVD risk factors, the consequences of progressive renal dysfunction, including disorder of sodium and water homeostasis, RAA and sympathetic nervous system activation, anemia, disorder of bone and mineral metabolism, disorder of potassium homeostasis, uremia, and toxins, may contribute directly to CVD. Understanding the relationship between these disturbances and CVD progression may inform novel approaches to therapy in patients with established CKD, and more importantly, may inspire increased emphasis(2).

Hyperhomocysteinemia and lipid abnormalities are commonly found in patients with CRF; both are recognized as risk factors for atherosclerosis (3). Inflammation plays a central role in the pathogenesis of atherosclerosis in CRF patients. C-reactive protein (CRP) level was found to be elevated in kidney failure and may be related to cardiovascular complications (4,5). Due to the high mortality and morbidity rate in CRF patients caused by CVD, it is vital to find way which could reduce the death toll in these patients.(6)

The current study was conducted to determine the role of non-traditional risk factors in the development of cardiovascular disease in CRF patients. In this regard, biomarker of CPK-MB, homocysteine, HS-CRP were measured.

MATERIAL AND METHODS:

Unique ID number was given to each participant of the study and same ID was given on sample container. After obtaining informed consent from all patients and healthy control, 5 ml of venous blood was collected in a sterile plain bulb under all aseptic precautions. Blood was drawn from antecubital vein in plain vial. After samples collection, samples were centrifuged in REMI centrifuge at 3000 RPM for a period of 15 minutes at central laboratory of Amaltas Hospital. Serum was separated after centrifugation. Serum was kept frozen at -20°C (for IL-6) until assayed. While analyzed for the following parameters:- CPK-MB, IL-6 and HS-CRP, Homocysteine. Machine used Chem-7 semi automated and EM-360 fully automated, Alere Elisa Reader and washer by colorimetric, spectrophotometric and

Elisa method.

Statically Analysis:

Calculated mean Sd and student t-test, Correlations with the help of Ms-Excel 2010.

RESULTS:-

The results demonstrated elevation in plasma values IL-6, homocysteine and HS-CRP in patients with CRF.

One way Anova-

Parameters	Subjects		Control		F test	p-value
	Male	Female	Male	Female		
Cpk-MB	45.28 ±17.7	37.78 ± 14.62	14.38 ±6.0	13.64 ±4.7	181.597	0.0001 S
IL-6	21.89 ± 13.88	29.67 ±28.36	1.11 ±0.54	1.01 ±0.53	88.662	0.0001 S
Hs-CRP	6.41 ± 8.67	7.07 ±9.38	0.45 ±0.26	0.41 ± 0.21	32.63	0.001 S
Homocystine	20.74 ±9.16	22.45 ±11.1	9.51 ±2.80	8.40 ±2.90	97.94	0.000 S
Urea	140.32 ± 49	175.53 ± 20.52	27.46 ±6.91	27.76 ± 7.3	731.42	0.000 S

Table Shows A Significant Change In Level Of Urea, cpk-MB, Homocysteinine And Hs-crp, il-6 In Subjects In Comparisons To Control.

DISCUSSION:

The results of the present study indicated that CRF patients had significantly increased levels of homocysteine, HS-CRP and CPK-MB, IL-6 as non-traditional risk factors compared to control subjects which are in agreement with other reports.(7)

The pathologic mechanisms involved in atherosclerosis remain unclear but experimental data support a range of possibilities, including hyperhomocysteinemia, endothelial cell injury (8), enhanced LDL oxidation (9) increased thromboxane-mediated platelet aggregation (Mackman, 2008) and inhibition of the anticoagulant protein C and promotion of smooth muscle cell proliferation. Homocysteine interferes with the coagulation system and lead to prothrombotic effects. It is recognized 30-50% of pre-dialysis and dialysis patients have activated inflammatory response (10).

In this regard, our study showed positive correlation between homocysteine, Urea. Hyperhomocysteinemia, oxidative stress and endothelial dysfunction may be organized, forming a flow of atherothrombotic processes in CRF patients (11) Our results showed that, CRF patients had significant high concentration of HS- CRP compared with control groups. Our study showed significant relationship between HS- CRP and increase risk of CVD in CRF patients. The mechanisms involved in HS- CRP seems to be a direct mediator of endothelial dysfunction and inflammatory cell employment via the up-regulation of expression of endothelial cell adhesion molecules, by rising the release of monocyte chemotactic protein (MCP-1)(12) and/ or endothelial derived contracting factors and by inhibiting the nitric oxide production (13).

The results presented in this study were in agreement with numerous evident that patients with CRF have a substantially increased risk of CVD (14). The non traditional risk factors in this study such as hyperhomocysteinemia, HS- CRP marker had strong association with the status of the CRF patients in our hospital which attribute the severity of the chronic renal failure of the patients. This finding may have important clinical consequences (15).

CONCLUSION:

The results demonstrated elevation in plasma values IL-6 , homocysteine and HS-CRP in patients with CRF . However, these modifications may be lead to atherosclerosis and consequence CVD event. These parameters may be important with respect to the high morbidity and mortality of CVD found in patients with CRF.

REFERENCES:

- Mason NA, Baille GR, Satayathum S, et al. HMG-coenzyme A reductase inhibitor use is associated with mortality reduction in hemodialysis patients. *Am J Kidney Dis.* 2005;45:119e26.
- Wilson PWF, D'Agostino RB, Levy D, et al. Prediction of coronary heart disease using risk factor categories. *Circulation.* 1998;97:1837e47.
- Rattazzi M, Puato M, Faggini E, Bertipaglia B, Grego F & Paultetto P. (2003). New markers of accelerated atherosclerosis in end-stage renal disease. *Journal of Nephrology*, 16, 11-20.
- Mallamaci F, Zoccali C, Tripepi G, Fermo I, Benedetto FA, Cataliotti A, Malatino LS, Bellanuova I & Solderini A. (2002). Hyperhomocysteinemia predicts cardiovascular outcomes in hemodialysis patients. *Kidney Int*, 61, 609-614.
- Kronenberg F, Neyer U, Lhotta K, Trenkwalder E, Auinger M, Pribasnik A, Meisl T, Konig P & Dieplinger H. (1999). The low molecular weight apo(a) phenotype is an independent predictor for coronary artery disease in haemodialysis patients: a prospective follow-up. *J Am Soc Nephrol*, 10, 1027-1036.
- Levey AS & Coresh J. (2002). K/DOQI clinical practice guidelines for chronic kidney disease evaluation, classification, and stratification. *Kidney Disease Outcome Quality Initiative. Am J Kidney Dis*, 39(suppl), S1-S246.
- Pawlak K & Pawlak D, Michael. (2006). Inflammation but not oxidative stress is associated with β -chemokine levels and prevalence of cardiovascular disease in uraemic patients. *Cytokine*, 35, 258-262.
- Stenvinkel P. (2002). Inflammation in end-stage renal disease: could it be treated. *Nephrology Dialysis Transplantation*, 17 (8), 33-38.
- Wong LY, Leung RY, Ong KL & Cheung BM. (2007). Plasma levels of fibrinogen and C-reactive protein are regulated to interleukin-6 gene-572C > G polymorphism in subjects with and without hypertension. *J Hum Hypertens*, 21, 875-882.
- Ortega O, Rodriguez L, Gallar P, Carreno A, Ortiz M & Espejo B. (2002). Significance of high C-reactive protein levels in predialysis patients. *Nephrology Dialysis Transplant*, 17, 1105-1109.
- Querfeld U. (2001). Under treatment of Cardiac risk factors in adolescents with renal failure. *Peritoneal Dialysis International*, Vol. 21: Supplement 3.
- Jialal I, Devaraj S & Uma, Singh. (2006). C - reactive protein and the Vascular Endothelium Implications for Plaque Instability. *Journal of the American College of Cardiology*, 47(7), 1379-1381.
- Nagane NS. (2009). Oxidative stress, serum homocysteine and serum nitric oxide in different stages of chronic renal failure, *Ind Medica*, 20(1)(2009-01 - 2009-04).
- Devaraj S., Papanicolaou R., Kumaresan & Jialal I. (2004). Effect of C-reactive protein on chemokine expression in human aortic endothelial cells. *Journal of Molecular and Cellular Cardiology*, 36, 405-410.
- Lim, PS., Hung, WR., Wei, YH. (2001). Polymorphism in methyl tetra hydrofolate reductase gene its impact of plasma homocysteine levels and carotid atherosclerosis in ESRD patients receiving haemodialysis. *Nephron*, 87 249-56.