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A comparative study of oxidant and anti-oxidant parameters in chronic renal failure, haemodialysis (pre & post) and controls

Dr. M. Madan Mohan Rao

Associate Professor in General Medicine at Rajiv Government Medical college, Kadapa, Andhra Pradesh, India

Dr. R. Salma Mahaboob

Associate Professor in Biochemistry at RSDKS Government Medical college and Hospital, Ambikapur, Chattisgarh. India

Dr. Obulesu Gundala

Associate Professor in Microbiology at RSDKS Government Medical college and Hospital, Ambikapur, Chattisgarh, India

*Corresponding author email: obulesu100@gmail.com

Abstract--Chronic kidney disease (CKD) is featured by a progressive decline of kidney function and is mainly caused by chronic diseases such as diabetes mellitus and hypertension. CKD is a complex disease due to cardiovascular complications and high morbidity; however, there is no single treatment to improve kidney function in CKD patients. Since biological markers representing oxidative stress are significantly elevated in CKD patients, oxidative stress is receiving attention as a contributing factor to CKD pathology. Aim of our study is comparison of oxidant and anti oxidant parameters in chronic renal failure, Hemodialysis (pre and post) and control subjects. Materials and Methods: The present study was conducted on a patient group comprising of 50 patients diagnosed with CRF, 50 were pre hemodialysis, 50 were post hemodialysis (MHD). This patient group was compared to a healthy group including 100 controls. All the study participants were admitted in the department of Medicine [Nephrology department] at “Rajiv Gandhi Institute Of Medical Sciences”, Kadapa. Andhra Pradesh. India. Study Period : July 2020 to December 2020 ,The obtained serum samples were used for biochemical analysis for estimating MDA, vitamin A and Glutathione Peroxidase (GPx). Conclusion: Our results reflects the primary mechanisms of oxidative stress and inflammation during hemodialysis which may cause of CVD development in hemodialysed patients.

Keywords---malondialdehyde MDA, reactive oxygen species (ROS), chronic kidney disease, oxidative stress.

Introduction

The worldwide increase in the incidence of ESRD is clear. Diabetes mellitus remains the most common cause of ESRD worldwide, with an increasing percentage of individuals entering ESRD with this diagnosis every year. this is true in the United States where the percentage of patients with ESRD due to diabetes is almost 44%.in India 56%,in Jalisco, Mexico it is almost 57%,in malaysia56%,in Japan 38%. The pima Indians of Arizona tend to develop ESRD at a younger age and at an accelerated rate compared with other populations (1). Kidney disease manifests in many ways. A patient may be completely asymptomatic or may be desperately ill with a life treating emergency. A greater appreciation for the prevalence of chronic kidney disease in the population has led to improvements in identification and diagnosis of chronic kidney disease leading to progressive renal failure and end stage renal disease(2).

Chronic Renal Failure (CRF) is a common health problem. patients with CRF most often present with nonspecific complications or are asymptomatic and are referred to a nephrologists because of abnormal blood or urine findings. the strongest factors associated with increased risk for CKD are diabetes mellitus and hypertension (3). other clinical factors are autoimmune disease, chronic system infections, CVD, cancer, drug exposure and urinary track infection.CKD is an independent risk factor for cardiovascular disease and all cause mortality.

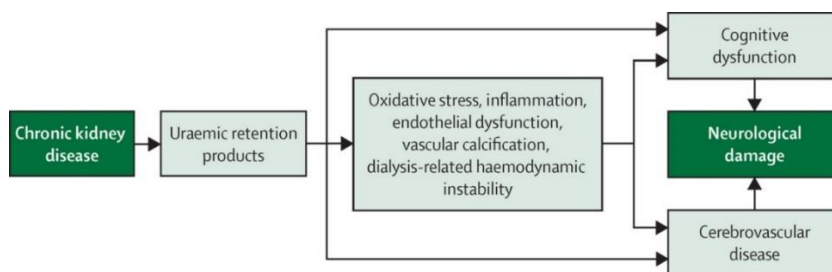


Figure 1. shows chronic renal failure causes neurological damage

The CRF patients who undergo to dialysis; are subjected to an oxidative stress, dialysis induced oxidative stress is one of the possible reason which creates atherosclerotic changes in hemodialysis patients. Over last few years, there has been increasing focus on the relationship of novel risk factors such as inflammation, oxidative stress, hyperhomocysteinemia, and high hs-CRP levels are associated with cardiovascular risk in CRF (3,4). Free radicals are highly reactive species characterized by an unpaired electron in their outer orbital. Free radical reactions, including lipid peroxidation, are considered to be important factors in the pathogenesis of a variety of diseases. Free radicals can damage proteins, lipids, carbohydrates and nucleic acids. Plasma membranes are critical targets of free radical reactions. Oxygen derived free radicals can easily produce injuries to cell membranes by initiation of polyunsaturated fatty acid

peroxidation, inactivation of membrane enzymes and receptors and protein cross linking and fragmentation(5).

Increased concentration of Malondialdehyde (MDA)- an intermediate product of oxidation of polyunsaturated fatty acid – have been reported in the plasma and erythrocytes as well as in platelets and in mononuclear cells, of haemodialyzed patients(6). It has been observed that chronic renal failure is a pro-oxidant state, characterized by increased levels of free radical oxidants relative to antioxidants(7). However, thus far it is not clear whether increased MDA level is caused by the dialysis procedure or by the kidney disease itself. To defend themselves against these free radicals' attack, cells have developed various antioxidant systems. Glutathione Peroxidase has four isoforms GSHPx-1 in red cells, GSHPx-2 in gastrointestinal mucosa, GSHPx-3 in blood plasma and the cell membrane located GSHPx-4(8).these enzymes use the reducing power of glutathione to remove an oxygen atom from hydrogen peroxide and lipid hydro peroxide. Vitamin A is fat soluble and among the tocopherols alpha tocopherol is biologically the most active. it is an antioxidant present in all cellular membranes and protects against lipid peroxidation. Alpha tocopherol can directly act on oxy radicals and thus serves as an important chain breaking antioxidant(9-10).

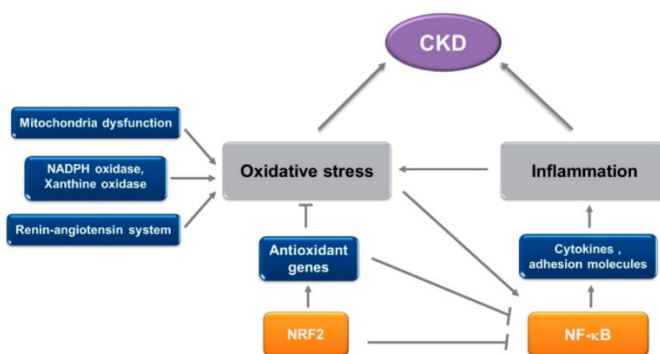


Figure 2. Factors involved in the progression of kidney dysfunction in CKD and the role of NRF2

Aim of our study is comparison of oxidant and anti oxidant parameters in chronic renal failure, hemodialysis(pre and post) and control subjects.

Material and Methods

All the Patients were admitted in the department of Medicine at Government medical college, Kadapa, Andhra Pradesh, India. Present study were divided into four groups. Study period July 2020 to December 2020

- Group-I: healthy controls - 100.
- Group-II –CRF Patients - 50.
- Group-III: CRF patients on haemodialysis (Pre HD) -50.
- Group-IV: CRF patients on haemodialysis (Post HD) - 50.

The exclusion criteria were patients with no clinical or laboratory evidence of diabetes mellitus, liver diseases, lupus nephritis, acute illness, respiratory diseases. None of the patients had history of antioxidant drugs supplementation. The study was conducted after obtaining Institutional Ethical Committee clearance and informed consent was obtained from the study participants. Five ml of whole blood samples were drawn into plain tubes to obtain serum samples after centrifugation at 4000rpm for 10 minutes. The obtained serum samples were used for biochemical analysis for estimating nitric oxide, oxi-LDL and Homocysteine levels.

Statistical analysis

All the values were expressed as mean and standard deviation (mean $\pm$ SD). The statistical analysis were done by using one way analysis of variance (ANOVA) using SPSS for windows version 11.5 (SPSS, Inc., Chicago). A p-value of <0.001 was considered to be statistically significant.

Results

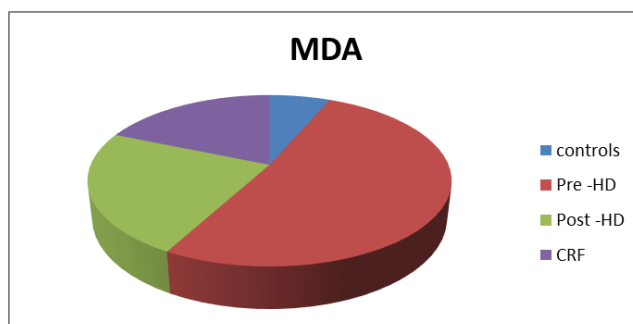
Laboratory data showed a significant change in the levels of biochemical parameters in CRF, pre and post hemodialysis groups in comparison to normal controls (Table I). All the data was presented as mean and standard deviation. P value of < 0.001 was considered statistically Significant. The Mean and standard deviation of plasma malondialdehyde showed significant difference between pre-dialysis and control group [$p < 0.001$]. It was significantly increased in the pre-dialysis group when compared with CRF, Post dialysis and control group [$p < 0.001$]. Pre Hemodialysis plasma MDA showed no significant rise when compared to post Haemodialysis level. And a significant rise when compared to control.

The Mean and standard deviation of erythrocyte glutathione peroxidase activity [GPx] was significantly reduced in the post dialysis group when compared with CRF, pre dialysis and control group [$p < 0.001$]. There was also a significant difference between pre dialysis and control group [$p < 0.001$]. The Mean and standard deviation of Vitamin A significantly reduced in the post dialysis group when compared with CRF, pre dialysis and control group [$p < 0.001$]. There was also a significant difference between CRF, pre dialysis and control group [$p < 0.001$]. Graph of all the investigations of this study were plotted by using the healthy controls - 100. CRF Patients -50. CRF patients on haemodialysis (Pre HD) -50. CRF patients on haemodialysis (Post HD) - 50. individual values of all investigations done in CRF Pre and Post HD and in control subjects.

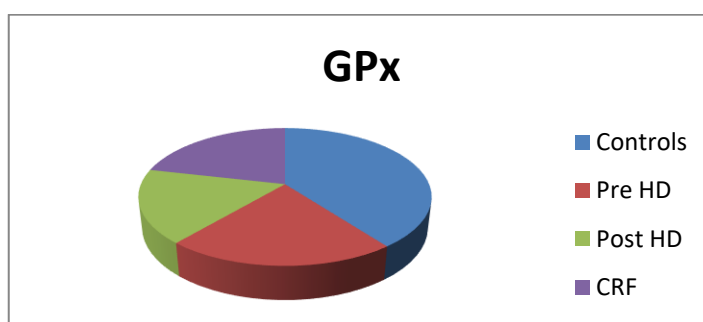
Table 1
Comparison of oxidant and anti-oxidant parameters in CRF, HD (pre and post) and controls (Mean + SD)

S.NO	Parameters	Controls	Pre HD	Post HD	CRF
1	MDA	0.70 + 0.01	5.62 + 0.90	2.54 + 0.32	2.03 + 0.64
2	GPx	24.85 + 2.24	13.49 +1.61	10.86 + 1.41	13.41 + 1.64

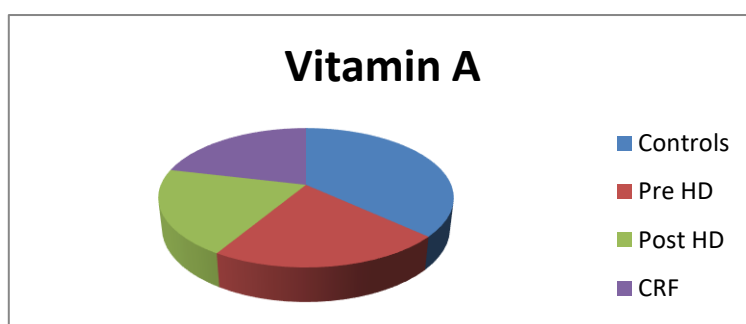
3	Vitamin A	60.91 4.84	+	36.18 3.14	+	33.18 +2.81	35.28 3.28	+
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Graph 1. Shows the values of MDA levels in CRF, Pre and Post HD and in control subjects



Graph 2. Shows the values of GPx levels in CRF, Pre and Post HD and in control subjects



Graph 3. Shows the values of Vitamin - A levels in CRF, Pre and Post HD and in control subjects

Discussion

In our present study the Mean and standard deviation of plasma malondialdehyde showed significant difference between pre-dialysis and control group [$p < 0.001$]. It was significantly increased in the pre-dialysis group when compared with CRF, Post dialysis and control group [$p < 0.001$]. Pre Hemodialysis plasma MDA showed no significant rise when compared to post Haemodialysis level. And a significant

rise when compared to control. The Mean and standard deviation of erythrocyte glutathione peroxidase activity [GPx] was significantly reduced in the post dialysis group when compared with CRF, pre dialysis and control group [$p < 0.001$]. The Mean and standard deviation of Vitamin A significantly reduced in the post dialysis group when compared with CRF, pre dialysis and control group [$p < 0.001$]. There was also a significant difference between CRF, pre dialysis and control group [$p < 0.001$]

Inflammation plays an important role in the development and progression of most chronic kidney disease. The kidney itself at end stage is characterized historically in virtually all cases by hallmark of chronic inflammation, including infiltration by white blood cells and fibrosis. Markers of inflammation including C- reactive protein, interleukin 1 and 6 and tumor necrosis factor, are elevated in plasma of patients with CKD(11-12). Oxidative stress and inflammation recently came in focus as nonconventional risk factors of cardiovascular morbidity and overall mortality in end stage renal disease. Oxidative stress occurring due to decreased antioxidant defenses and an increase in pro-oxidant factors is a well recognized phenomenon in hemodialysis patients(13). Hemodialysis is an effective treatment in most renal failure patients and forms an alternative to renal transplantation. Adequate dialytic treatment has prolonged the survival of patients with quality of life. Cardiovascular disease was found to be the most frequent cause of mortality in majority of patients on maintenance haemodialysis(14-15). Thus the results of our study shows that significant difference of antioxidant enzymes between pre and post dialysis group is thought to be related with the loss of antioxidant enzymes through the membrane and the decreased antioxidant enzymes may be related to increased of lipid peroxidation in hemodialysed patient.

Conclusion

Our results reflects the primary mechanisms of oxidative stress and inflammation during hemodialysis which may cause of CVD development in hemodialysed patients. Due to adverse effect of HD which is demonstrated by our results, the clinicians may plan to advice antioxidant therapy and use of antioxidant bounded membrane for HD will be new approach to over rule oxidative stress and inflammation during HD session.

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