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RESEARCH ARTICLE

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OXIDATIVE STRESS AND ITS ASSOCIATION WITH CARDIO VASCULAR RISK IN ACUTE RENAL FAILURE

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ABSTRACT

Acute renal failure (ARF) is a clinical syndrome in which there is a rapid decrease in the kidney function. Underlying renal disease itself leads to elevated formation of reactive oxygen species which is shown to have an active role in pathogenesis of renal disease. Oxidative stress reduces Total antioxidant status and is implicated in atherogenesis. Patients with Acute renal failure are often prone for cardiovascular disease. Oxidative stress and a subclinical inflammation are crucial factors in its development. The aim of the present study is focused on the association of oxidative stress and atherogenic index in acute renal failure. This study includes 62 patients with ARF and 50 healthy individuals as controls. The levels of Blood urea, Serum creatinine, serum Triglycerides, Total cholesterol, LDL cholesterol, VLDL cholesterol, MDA and Total antioxidant capacity were analyzed with fasting blood sample using standard methods in patients with ARF and controls. TC/HDL, LDL/HDL ratio, atherogenic index of plasma, MDA/TAC ratio were calculated. A significant decrease in TAC and increase in MDA were found in patients with ARF compared to controls. Serum creatinine showed significant correlation with HDL- cholesterol, atherogenic index of plasma and MDA/TAC ratio. Hence the study may be useful in designing clinical studies that target utilizing antioxidant systems to provide protective pathways on the pathogenesis of renal failure.

KEY WORDS

Acute renal failure; atherogenic index of plasma; MDA/TAC ratio; Total antioxidant capacity.

INTRODUCTION

Acute Renal Failure (ARF) is defined as an abrupt deterioration of renal function sufficient to result in failure of urinary elimination of nitrogenous waste products[1].The common etiological factors for ARF are ischemic renal failure, acute gastroenteritis, sepsis and hemolytic uremic syndrome[2]. Metabolic derangements like renal toxicity, dysregulated inflammation, ischemia and altered metabolism may increase oxidative stress in ARF patients [3]. An enhanced oxidative stress due to increased pro oxidant activity results in reduced antioxidant systems [4]. Renal failure itself is recognized as stimulus for increased oxidative stress[5]. Furthermore an increase in oxidative stress is considered an important pathogenic mechanism in the development of various complications like cardio vascular, cerebrovascular and peripheral vascular disease[6]. During this process poly unsaturated fatty acid present in cell membrane are oxidized in vivo to form Malondialdehyde. This lipid peroxidation product can structurally alter major biomolecules[7].Lipid abnormalities and enhanced oxidative stress in ARF patients accelerates the process of atherosclerosis resulting in cardiovascular complications[8]. Hence this study was undertaken to study the association of oxidative stress and atherogenic index to assess the cardiovascular risk in acute renal failure.

MATERIALS AND METHODS

Sixty two patients of both sexes, in the age group of 30-60 admitted with clinically diagnosed acute renal failure in Vinayaka Mission's Medical College & Hospitals, Salem were taken for the study. We excluded cases with Diabetes mellitus, chronic renal failure, kidney transplanted patients, patients on antioxidant and hypolipidemic drugs. A group of 50 healthy subjects were used for comparison of oxidative stress and cardiovascular status. The study was approved by the Institutional Review Board, and informed consent was obtained from all study participants.

About 5ml of venous blood was drawn under aseptic precautions in a sterile tube from selected subjects after a period of overnight fasting of 12 hr, and serum was separated by centrifugation and stored at -20C. Serum urea, creatinine, Lipid profile parameters were measured by enzymatic method in auto analyzer and LDL was calculated by Friedwald formula. Total antioxidant capacity was measured by FRAP method[9],lipid peroxidation was estimated by Satoh method[10]. Atherogenic index was calculated by logTg/HDL[11] and MDA/TAC ratio was calculated as an index of oxidative stress[12].

Values were expressed as mean ± SD. Student t test was used to find out the significance level and the Pearson correlation study was used to find the association between the biochemical parameters.

TABLE: 1
Comparison of demographic data's between control and acute renal failure patients

Particulars	controls(n=50)	ARF Patients (n=62)
Age	45.38±14.34	48.36 ± 13.31
SBP (mm/Hg)	119 ± 13.37	128.71 ± 20.614
DBP (mm/Hg)	82.5 ± 5.89	90.323 ± 10.796*

Data's are expressed as (mean + S.D).*p<0.05

There were no significant changes in age, and SBP between control and acute renal failure patients but significant increase in DBP was observed in acute renal patients as compared to control.

TABLE 2
Biochemical parameters of control and acute renal failure patients.

Particulars	Controls (n=50)	ARF Patients (n=62)
Fasting Blood sugar (mg/dl)	86.3 ± 13.4	85.90 ± 11.7
Urea (mg/dl)	31.6±6.415	93.6 ± 31.76*
Creatinine(mg/dl)	0.92±0.132	3.09 ± 0.9163*
eGFR	82.5±21.2	23.065±7.677*
Urine Volume/day (ml/L)	1377 ± 120.19	821.94 ± 475.22*
Sodium (mEq/L)	138.1± 4.28	136.16 + 6.79
Potassium (mEq/L)	3.79 ± 0.277	4.85 + 0.98*
Total Protein (g/dl)	6.22 ± 0.311	6.31+ 0.484
Albumin (g/dl)	3.48± 0.293	3.19 ± 0.399*

Data's are expressed as (mean + S.D).*p<0.05

When compared to control, ARF patients showed significant increase in the level of Blood urea, serum creatinine and potassium and a decrease in Urinary volume and eGFR.

TABLE 3
Parameters for oxidative stress

Particulars	Control (n=50)	ARF Patients (n=62)
Total Antioxidant capacity(µmol/L)	822.1 ± 60.42	603.32 ± 131. 3*
MDA (nmol/ml)	1.56 ± 0.54	4.03 ± 1.1397*
MDA/TAC ratio	0.0019 ± 0.0007	0.007 ± 0.0026*

Data's are expressed as (mean + S.D).*p<0.05

Table 3 shows the comparative analysis of serum Total antioxidant capacity, MDA and MDA/TAC ratio between control and ARF patients. When compared to control, ARF patients showed significant increase in the MDA & MDA/TAC ratio.

TABLE 4
Comparison of serum lipid profile between Controls and Acute renal failure patients

Particulars	Controls (n=50)	ARF Patients (n=62)	comparison
Total Cholesterol (mg/dl)	159.5± 17.07	171.42 ± 26.927	0.975 NS
Triglycerides (mg/dl)	128±24.6	189.39±48.91	0.0006***
HDL (mg/dl)	45.7±4.21	38.969±5.199	0.0005***
LDL (mg/dl)	89.1±17.46	94.0±29.126	0.6191 NS
VLDL (mg/dl)	24.7±5.93	37.871±9.72	0.0001***
TC/HDL ratio	3.52±0.55	4.42±0.9776	0.0088**
LDL/HDL ratio	1.98±0.51	2.387±0.9892	0.2248 NS
Atherogenic index ratio (logTg/HDL)	0.1±0.06	0.3071±0.1451	0.0001***

Data are expressed as (mean + S.D) **p <0.01 ,P<0.001***

Table 4 displays the comparative analysis of serum lipoprotein between ARF patients and controls. When compared to control the mean values of TC, TG, LDL cholesterol, VLDL Cholesterol were increased, whereas serum HDL cholesterol level was significantly lower in acute renal failure compared to control. The AIP and LDL C /HDL C ratio were increased in acute renal failure patients when compared to controls.

TABLE 5
Correlation between Parameters in ARF patients

Correlation between parameters	r value	P value
Serum Creatinine and eGFR	-0.4711	0.0075**
Serum creatinine and HDL	-0.4241	0.0174***
Serum creatinine and MDA/TAC ratio	0.3956	0.0276*
Creatinine and Atherogenic index of plasma	0.3799	0.0351 *

p <0.05, **p <0.01 ,*P<0.001*

DISCUSSION

Imbalance between generation of free radicals and antioxidant defense system and disorders of lipoprotein metabolism during uremia is an important mechanism of atherogenesis in ARF. Traditional risk factors such as DM, Obesity, and metabolic syndrome as well as nontraditional risk factors can damage kidney directly by promoting atherogenesis. Evidence indicates that increased oxidative stress may mediate most of the risk factor on the kidney. The primary event leading to the renal failure is a free radical mediated injury [13]. Once free radical attacks the kidney progressive development of disease occurs, which leads to the increase in the level of lipid peroxidation because the cell membrane contains excess amount of poly unsaturated fatty acids which reacts with the ROS to form peroxide derivative [14, 15]. Evidence indicates that increased oxidative stress and inflammation may mediate most of the risk factor on the kidney. Oxidative injury alters

the structure and functions of glomerulus, because of the effect of ROS on mesengial and endothelial cells. Our study reports an increase in oxidative stress as depicted by increase in MDA with the concomitant decrease in TAC as compared to controls. MDA concentration increases with the severity of kidney function. Total antioxidant capacity summarizes the overall activity of antioxidants and antioxidant enzymes [16].The co operation between different antioxidant pathways provides greater protection against attack by ROS, compared to any single compound. Thus the overall antioxidant capacity may give more relevant biological information compared to that obtained by the measurement of individual biomarkers [17]. A depression of antioxidative system in acute renal failure was earlier studied by PH .G.H.Metnitz et al[18]. A positive correlation was seen between serum creatinine and MDA/TAC ratio. This shows that increase in creatinine level causes increase in the oxidative stress. MDA/TAC ratio was identified as an ideal marker to assess the oxidative stress [12].

Striking alterations in serum lipid levels of ARF includes hyper Triglyceridemia and markedly decreased levels of HDL cholesterol. Increase in Triglyceride and VLDL and decrease in HDL cholesterol level shows the deregulation of HDL cholesterol and Triglyceride metabolism. This may be due to the alterations in the composition and anti oxidant and anti inflammatory functions of HDL cholesterol and clearance of triglyceride rich lipoprotein and their atherogenic remnants[19]. A negative correlation was seen between serum creatinine and HDL cholesterol in ARF patients. The mean value of triglyceride is significantly increased in patients when compared to control. This is in accordance with the study of Ogara et al and Drum W et.al.[20,21] Patients who subsequently developed ARF also had higher baseline Diastolic BP , serum creatinine, triglyceride level and Atherogenic index but Lower HDL. A significant increase of atherogenic index was observed, primarily due to the decreased serum HDL C levels, suggesting these patients are possibly exposed to higher risk of atherosclerosis. All these were associated with higher risk for development of CVD in ARF.[22] Sutton et al demonstrated in an animal model that renal micro vascular injury in endothelial cells occurs after ischemia and that it leads to increased micro vascular permeability and interstial edema. It is possible that previous vascular injury in the kidney may enhance the risk for further micro vascular damage and diminution in renal function. A positive correlation was seen between creatinine and MDA/TAC ratio and creatinine and atherogenic index of plasma. The severity of ARF complications is highly correlated with the oxidative stress status of the patients, which may leads to the pathogenesis of CVD in patients with ARF.

CONCLUSION

Enhanced oxidative stress with increased atherogenic index in the patients with acute renal failure may accelerate the process of atherosclerosis resulting in cardio vascular complications. Hence attention should be paid not only to already accelerated atherogenicity in acute renal failure but also to the supplementation of antioxidants.

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