Assessment of serum biomarkers of oxidative stress in patients with chronic renal failure

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Abstract: Chronic renal failure (CRF) is becoming a major health challenge among worldwide. Incidence of the disease is alarming, because an insufficient therapeutic methods. Based on the estimated glomerular filtration rate (eGFR), the CRF is being classified in to numerous phases. Recent guidelines classified the severity of CRF into 5 phases. First stage is being the mildest and fifth stage being a severe illness with less life expansion. The present study was designed to assess the link between CRF and oxidative stress markers, urea, creatinine and serum creatinine levels in Patients with chronic renal failure. A total fifty CRF patients and fifty healthy control subjects were considered, based on the eGFR values patients were assigned to five phases. The results indicating that serum lipid peroxidation was significantly increased in all the phases of CRF patients when compared to the controls. Serum superoxide dismutase mean values are not showing any variation in first phase but, in later phases values were gradually decreased as compared to control subjects. The study reinforce the possibility that antioxidant supplementation is helpful to CRF patients. It is extremely important to know oxidative stress in CRF patient right from the time of diagnosis is made. Efforts should be made to reduce oxidative stress by using antioxidant supplements and nutritional repletion.

Keywords: Chronic renal failure (CRF), Oxidative stress, Serum Nitric oxide, Urea, Creatinine, Estimated glomerular filtration rate (eGFR)

I. Introduction

Chronic renal failure is an irreversible deterioration in renal function, which classically develops over a period of years (1). Initially, CRF manifests only as biochemical abnormality. Thereafter, loss of excretory, metabolic and endocrine functions of kidney leads to the chronic renal failure. The diseases that bring about the alterations are many and include diabetes mellitus, hypertension, non-diabetic glomerular disease, polycystic kidney disease and tubule-interstitial disease (2). Chronic renal failure is associated with premature atherosclerosis and increased incidence of cardiovascular morbidity and mortality. Several factors contribute to atherogenesis and cardiovascular disease in patients with CRF. Notable among the CRF-induced risk factors are lipid disorders, oxidative stress, inflammation, physical inactivity, anaemia, hypertension, vascular calcification, endothelial dysfunction, and depressed nitric oxide availability (3, 4, 5).

Hence we thought it worthwhile to determine the extent of dyslipidaemia, the oxidant-antioxidant status and vascular inflammation in various stages of CRF. The present study aimed to assess the levels of serum Urea, Creatinine, superoxide dismutase, lipid peroxidation and Nitric Oxide levels in patients with chronic renal failure.

II. Material And Methods

The present study was carried out in the Department of Biochemistry, MNR Medical College and Hospital, Sangareddy. The study protocol was approved by Institutional Ethical Committee of MNR Medical College. The study contains fifty CRF patients and fifty age, sex matched control subjects. Depending on the estimated glomerular filtration rate (eGFR) and confirmed CRF patients were included. Patients who were not willing to participate, had undergone anti-microbial & anti-inflammatory therapy, used immunosuppressive drugs, with acute inflammatory illness were excluded from the study. According to the eGFR, all CRF patients were subdivided in to five phases and each phase includes 10 CRF patients. Phase I contains Complications in urine sample but healthy kidney function (eGFR >90), Phase II includes Mild renal functional alteration (eGFR 60-90), Phase III includes Moderate renal functional alteration (eGFR 30-60), Phase IV includes Severe renal functional alteration (eGFR 15-30), Phase V about to renal failure (eGFR <15).

After having deliberate consent from patient, clinical data was collected and 5 ml of venous blood was drawn aseptically and serum was separated. The following parameters were estimated various biochemical methods such as serum Urea by DAM method (6), serum Creatinine by Jaffe’s method (7), Superoxide Dismutase by the method of Marklund and Marklund (8, 9), Nitric oxide by the method of Najwa K. Cortas and Nabil W. Waked (10).
III. Results

The present study was conducted in Department of Biochemistry, MNR Medical College, Sangareddy during July 2016 to January 2017. The study contains fifty CRF patients and fifty age, sex matched control subjects.

Table 1. The mean values of Serum Urea in different phases of CRF patients and control subjects.

<table>
<thead>
<tr>
<th>Phases of CRF</th>
<th>Number</th>
<th>Serum Urea (mg/dL) Mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>10</td>
<td>61.42 ± 16.02</td>
</tr>
<tr>
<td>2</td>
<td>10</td>
<td>76.86 ± 23.71</td>
</tr>
<tr>
<td>3</td>
<td>10</td>
<td>97.92 ± 42.90</td>
</tr>
<tr>
<td>4</td>
<td>10</td>
<td>108.31 ± 40.27</td>
</tr>
<tr>
<td>5</td>
<td>10</td>
<td>127.98 ± 8.97</td>
</tr>
<tr>
<td>Control</td>
<td>50</td>
<td>24.82 ± 6.51</td>
</tr>
</tbody>
</table>

Fig 1. Mean values of serum creatinine in different phases of CRF patients and control subjects.

Table 2. The mean values of Serum Lipid peroxidation, Serum Superoxide Dismutase and Nitric Oxide at various phases of CRF Patients and control subjects.

<table>
<thead>
<tr>
<th>Phases of CRF</th>
<th>Number</th>
<th>Lipid Peroxidation (Mean ±SD) nmol/mL</th>
<th>Superoxide Dismutase (Mean ±SD) U/mL</th>
<th>Nitric oxide (Mean ±SD) µmol/L</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>10</td>
<td>3.14 ± 0.48</td>
<td>4.59 ± 1.02</td>
<td>56.27 ± 3.37</td>
</tr>
<tr>
<td>2</td>
<td>10</td>
<td>3.37 ± 0.42</td>
<td>3.98 ± 1.25</td>
<td>53.93 ± 3.72</td>
</tr>
<tr>
<td>3</td>
<td>10</td>
<td>5.29 ± 0.61</td>
<td>3.67 ± 0.91</td>
<td>51.68 ± 4.21</td>
</tr>
<tr>
<td>4</td>
<td>10</td>
<td>6.21 ± 0.71</td>
<td>2.12 ± 0.62</td>
<td>49.07 ± 3.62</td>
</tr>
<tr>
<td>5</td>
<td>10</td>
<td>7.57 ± 0.70</td>
<td>1.61 ± 0.59</td>
<td>47.04 ± 2.98</td>
</tr>
<tr>
<td>Control</td>
<td>50</td>
<td>2.59 ± 0.49</td>
<td>4.74 ± 1.11</td>
<td>55.58 ± 4.69</td>
</tr>
</tbody>
</table>

The results of above table (Table 2) indicating that serum lipid peroxidation was significantly increased in all the phases of CRF patients when compared to the controls. In related to Serum superoxide dismutase mean values are not showing variation in first phase of CRF and controls, later phases are values were gradual decline in CRF patients as compared to control subjects. Hence, significant increased values was observed in later phases of CRF patients.

IV. Discussion

Imbalance between production of reactive oxygen species (ROS) and antioxidant defense leads to oxidative stress, which may arise either from deficiencies of antioxidants or increased formation of ROS such as peroxynitrite, hypochlorous acid or superoxide anions (11).

High levels of oxidative stress markers such as F2-isoprostanes, advanced glycosylation endproducts, malondialdehyde and oxidized LDL have been demonstrated in patients with mild to moderate CRF patients (12). Oxidative modification of LDL is thought to be a key step in the initiation of atherosclerosis (13). Therefore, one may consider the oxidative stress hypothesis as a unifying concept of increased CVD risk in CRF patients (14). Superoxide dismutase (SOD) functions as an antioxidant by scavenging superoxide anion which is...
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derived from molecular oxygen by single electron transfer. SOD converts the highly reactive superoxide radical into less toxic hydrogen peroxide and decreases cell damage. The lower serum SOD levels point towards the deficient antioxidant mechanisms in chronic kidney disease (15).

In the present study the serum superoxide dismutase (SOD) was found to be lower in patients at all the phases of chronic renal failure. Nitin et al and Sasikala et al have been reported similar reduction in SOD levels in CKD patients (16, 17). In the present study, significant reduction of SOD levels at all phases correlating with the study by Nitin et al where SOD levels found to be highly significant in all stages of CRF patients (16).

Serum lipid peroxidation was significantly increased in all the phases of CRF patients when compared to the controls. Serum nitric acid levels were higher in first stage as compared to control subjects but significantly decreased in succeeding phases i.e. phase II to Phase V. Nitric oxide is a key factor in the anti-atherosclerotic effects of endothelium (18). Premature atherosclerosis is one of the primary cause of morbidity and mortality in patients with CRF (19). Hyperhomocysteinemia, oxidative stress and endothelial dysfunction may be interrelated, forming a cascade of athero-thrombotic processes in CRF.

V. Conclusion

Chronic renal failure is a progressive loss in renal function over a period of time. This study aimed to assess the oxidative stress, serum nitric acid, Urea, creatinine and nitric oxide levels in CRF patients. The results concluding that oxidative stress markers are increasing, while superoxide dismutase levels were decreased, which presides into endothelial dysfunctional along with nitric oxide levels reduction. It is extremely important to know oxidative stress in CRF patient's right from the time of diagnosis is made. Efforts should be made to reduce oxidative stress by using antioxidant supplements and nutritional repletion.

Acknowledgements: No

References