Alternations of selenium and malondialdehyde status in chronic kidney disease

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ABSTRACT

Chronic kidney disease (CKD) is a major public health burden worldwide. CKD patients have cardiovascular risk factors such as diabetic mellitus and hypertension. These factors are associated with oxidative stress which accelerates renal injury in CKD patients. This study aimed to determine selenium (antioxidant trace element) and malondialdehyde (MDA, oxidative stress marker) in patients with CKD. Serum selenium and MDA levels are analyzed in CKD patients (n=20) compared with values observed in control (n=20). Serum urea, creatinine and MDA levels were determined with spectrophotometric methods and serum selenium level was measured by atomic absorption spectrophotometry. Serum selenium and MDA in CKD patients showed significant differences in comparison with control – MDA 2.42 ± 0.57 vs. 0.98 ± 0.09 µmol/L (p<0.001) and selenium 81.52 ± 10.24 vs. 105.46 ± 10.53 µg/L (p<0.001). A significant negative correlation was observed between serum selenium and MDA in CKD patients (r = -0.88, p < 0.0001), while there was a significant positive correlation of selenium level with creatinine clearance in CKD (r = 0.714, p <0.001). There is imbalance between oxidative stress and antioxidant status in CKD. We suggest MDA could be used as oxidative marker for progressive kidney diseases.

Key words: Antioxidant; Chronic kidney disease; Malondialdehyde; Oxidative stress; Selenium

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Introduction

Chronic kidney disease is a progressive decline in renal function particularly associated with diabetes mellitus, hypertension, obesity and intrinsic renal diseases (Gansevoort et al. 2013). It is defined by the marker of renal damage – glomerular filtration rate (GFR) estimated from serum creatinine level (KDOQI, 2002). The global prevalence of CKD is high estimating to11-13% in 2016 (Hill et al. 2016). CKD is regarded as a pro-oxidant state because the markers of oxidation are higher in CKD compared with control. The link between oxidative stress and inflammatory process remains unrevealed (Massyet et al. 2009). Glutathione peroxidase, which neutralize harmful peroxides, requires selenium for optimal function. Selenium deficiency is commonly encountered in renal patients (Iglesias et al. 2013). In addition, selenium supplementation reduces the oxidative stress in renal patients, yet its association with renal function and oxidative stress is still left to be determined (Iglesias et al. 2013).

Selenium plays an important role in many diseases including kidney diseases and cardiovascular diseases (Rayman, 2000). The kidneys maintain the homeostasis of small
molecules including selenium and other trace elements (Wasowicz, 1987; Schweizer et al. 2005). Although decreases in plasma selenium concentration have been found to be directly proportional to chronic kidney disease progression, the underlying mechanism remains unclear (Zachara et al. 2004). The present study aims to determine serum selenium and malondialdehyde (MDA) levels and correlate serum selenium with oxidative stress and renal function in patients with CKD compared with control.

**Materials and Methods**

The study was conducted after the approval of the Academic Board of Postgraduate Study, the University of Medicine (2), Yangon. Twenty patients with CKD were recruited from North Okkalapa General Hospital and Defense Services General Hospital, Yangon, Myanmar. The KDIGO criteria for CKD were used to find out the CKD patients. Twenty healthy control were selected from volunteer staff working in the University of Medicine (2), Yangon.

After detailed explanation about the research, written informed consent were obtained. Ten milliliters of venous blood were collected from antecubital vein of the participants. Blood sample to determine urea and creatinine levels were collected in EDTA tubes. For other biochemical estimations, metal-free test tubes were used to collect blood and serum preparation. Biochemical measurements were undertaken on the day of sample collection, except selenium determination for which the samples were stored at -20°C, and 24-hour urine samples were collected in clear dry urine bottles with toluene preservation.

Regarding biochemical methods, diacetyl monoxime method (Marsh et al. 1965) for plasma urea, Jaffe reaction (Hawket al. 1957) for plasma and urinary creatinine, thiobarbituric acid reaction for MDA (Esterbauer and Cheeseman 1990) and atomic absorption spectrophotometry (Oster and Prellwitz 1982) for serum selenium were used.

The statistical analysis was done by using STATA software. Unpaired t-test was used to compare biochemical parameters between two groups and Pearson’s correlation was determined for possible associations. P value less than 0.05 was considered statistically significant.

**Results**

The biochemical parameters of the patients with CKD and control have been estimate for this study (Table 1). Plasma urea and creatinine levels were significantly higher and creatinine clearance was significantly decreased in patients with CKD as compared with control. Regarding oxidative stress and antioxidant status, serum MDA was significantly raised and serum selenium level was significantly low in CKD patients when compared with those in healthy individuals.

<table>
<thead>
<tr>
<th>Table 1: Biochemical Parameters of CKD Patients and Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parameter</td>
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<tr>
<td>-------------------</td>
</tr>
<tr>
<td>Plasma urea</td>
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<tr>
<td>Plasma creatinine</td>
</tr>
<tr>
<td>Creatinine clearance</td>
</tr>
</tbody>
</table>

In the present study, serum selenium concentration with creatinine clearance in CKD patients have been shown contrary finding in terms of their correlation (Table 3). A direct correlation of serum selenium concentration with creatinine clearance in patients with renal diseases. Yet, selenium level was not correlated with creatinine clearance in control.

**Discussion**

The present investigation drew the major evidence that serum selenium was low and MDA was high in CKD patients, suggesting the alterations of antioxidant status and oxidative stress in the pathophysiology of CKD. The pathogenesis of CKD is complex, yet, it is partly due to oxidative-induced stress (Reddi and Bollineni 2001).
Table 1: Biochemical parameters of patients with CKD and control

<table>
<thead>
<tr>
<th>Biochemical parameters</th>
<th>CKD (n=20)</th>
<th>Control (n=20)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plasma urea (mg/dL)</td>
<td>51.47 ± 4.34</td>
<td>20.19 ± 5.49</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Plasma creatinine (mg/dL)</td>
<td>2.28 ± 0.37</td>
<td>0.93 ± 0.11</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Creatinine clearance (ml/min/1.73m²)</td>
<td>55.18 ± 12.3</td>
<td>97.46 ± 7.55</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Serum MDA (µmol/L)</td>
<td>2.42 ± 0.57</td>
<td>0.98 ± 0.09</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Serum selenium (µg/L)</td>
<td>81.52 ± 10.24</td>
<td>105.46 ± 0.53</td>
<td>&lt;0.001*</td>
</tr>
</tbody>
</table>

*statistically significant

Table 2: Correlation between serum selenium and MDA levels in patients with CKD and control

<table>
<thead>
<tr>
<th>Selenium (µg/L)</th>
<th>MDA (µmol/L)</th>
<th>r</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>CKD (n=20)</td>
<td>81.52 ± 10.24</td>
<td>-0.88</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Control (n=20)</td>
<td>105.46 ± 10.53</td>
<td>-0.07</td>
<td>0.7693</td>
</tr>
</tbody>
</table>

*statistically significant

Table 3: Correlation between serum selenium and creatinine clearance in patients with CKD and control

<table>
<thead>
<tr>
<th>Selenium (µg/L)</th>
<th>Creatinine clearance (µmol/L)</th>
<th>r</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>CKD (n=20)</td>
<td>81.52 ± 10.24</td>
<td>0.714</td>
<td>&lt;0.0001*</td>
</tr>
<tr>
<td>Control (n=20)</td>
<td>105.46 ± 10.53</td>
<td>0.349</td>
<td>0.13151</td>
</tr>
</tbody>
</table>

*statistically significant

Selenium excretion depends on the glomerular filtration of the kidneys and selenium excretion per day was found to be positively correlated with 24-hour excretions of creatinine and urea (Oster and Prellwitz 1990). Low selenium levels in chronic renal disease was not improved with erythropoietin treatment (Kaminska-Galwas et al. 1993). Thus, selenium does not reflect hormonal derangement in CKD. Low serum selenium implies reduced antioxidant status in renal diseases.

Many studies have focused on the role of oxidative stress in the development and progression of CKD (Zachara et al. 2004). In this study, serum MDA level was significantly raised in CKD patients. Similarly, CKD is also associated with accelerated carbonyl stress, another oxidative marker (Miyata et al. 2000). In addition, present study demonstrated that serum selenium level was positively correlated with MDA level in CKD patients. This finding was consistent with that of Morena and coworkers (Morena et al. 2002). As a result, it is suggested that serum MDA may be used as a marker of oxidative stress in renal diseases.

Selenium is a known cofactor for glutathione peroxidase which neutralizes the harmful peroxides. Ceballos and colleagues reported creatinine clearance was directly correlated with plasma glutathione peroxidase activity and selenium level in renal patients (r=0.65, p<0.001; and r=0.47, p<0.001 respectively) (Ceballos-Picot et al. 1996). In this study, selenium level was positively associated with creatinine clearance in patients with CKD. In addition, dietary selenium deficiency might contribute renal insufficiency. The mechanism of renal injury induced by selenium deficiency seems to be enhancement of glomerular sclerosis (Reddi and Bollineni 2001). In an experimental study, dietary deficiency of selenium injured the rat kidneys, but this was overwhelmed by supplementing selenium for 9 weeks (Nath and Salahudcen 1990). Thus, low selenium level either indicate oxidative stress in renal injury or dietary deficiency accelerating renal injury.
Conclusion

The analytical results of the study revealed that oxidative stress turn out to be higher in CKD as indicated by raised MDA level. Thus, we suggest serum MDA might be used as a marker of progressive renal injury. On the other hand, antioxidant trace element- selenium reflects creatinine clearance in patients with CKD. Hence, this study confirmed the previously known oxidative stress-induced renal injury in CKD.

Conflict of interest

There is no conflict of interest.

Acknowledgements

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References


