Evaluation of serum trace elements levels in patients with chronic kidney disease

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INTRODUCTION

Chronic kidney disease (CKD) is a major health problem due to increasing incidence and prevalence, high cost and poor outcomes. Globally, CKD is the 12th cause of death and the 17th cause of disability, respectively (Grassmann A et al 2005). Its prevalence is estimated to be 8-16% globally (Jha V et al 2013). In India, it has been recently estimated that the age-adjusted incidence rate of ESRD to be 229 per million population (pmp).

The Kidney Disease Outcomes Quality Initiative defines chronic kidney disease as either kidney damage or a decreased kidney Glomerular Filtration Rate (GFR) of less than 60 ml/min/1.73m² for 3 or more months (Levey AS et al 2005). It is a pathophysiological process with multiple etiologies resulting in the inevitable attrition of functional nephrons and frequently leading to End Stage Renal Disease (ESRD).

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Minerals are essential to life. Serum trace element levels in CKD patients had a great impact on patient's general condition and might lead to cardiovascular diseases, carotid atherosclerosis, cancers, decline of renal function, renal osteodystrophy, insulin resistant and anemia. Oxidative stress is related to several diseases, including chronic renal disease. The result illustrated that serum Zn (Zinc) was significantly deceased in CKD patients while no significant change was found in the serum Cu (Copper) level, however, Cu/Zn ratio and serum Mg (Magnesium) level were significantly increased in CKD patients compare to controls. Our results revealed that there is an altered Zn, Mg and Cu/Zn ratio status in CKD patients. Close and careful nutritional support of patients with CKD, particularly in the early stages of the disease, is necessary.

Key words: Chronic Kidney Disease, Trace elements, cardiovascular disease.
components of biologic enzymes which have a key role in decreasing reactive oxygen.

The status of trace elements in CKD patients has not been fully characterized. The incidence of abnormal trace element status in dialysis patients has not been comprehensively studied. It has been mentioned that during dialysis some trace elements can accumulate while other may be removed from blood, leading to deficiency of some trace elements. Abnormality of trace elements is primarily a result of uremia. To prevent complications in CKD patients, it is very important to know and regulate the level of trace elements (Utas C et al 1993). The status of trace elements in CKD, is often unexplored. The purpose of this study was to assess the levels of serum copper, zinc and magnesium in patients with CKD.

MATERIAL AND METHODS

The study comprised of a total of 50 patients with evidence of CKD. The patients were admitted into Nephrology unit of IKD hospital, Ahmedabad. They were included in the study on the basis of clinical signs and symptoms of kidney disease along with an elevated serum urea and serum creatinine level and a lowered eGFR (estimated Glomerular Filtration Rate). Patients with eGFR values of less than 15 ml/min were included under stage V (ESRD) and rest of the others whose eGFR ranged from 90 ml/min to 15 ml/min were grouped under stages I to IV. The patients suffering from other diseases, such as diabetes, inflammatory diseases, hepatic or respiratory diseases as well as smokers and alcoholics were excluded from study. The control group comprised of 50, age and sex matched healthy subjects who were free of features of kidney disease and having a normal serum urea and serum creatinine level. Informed and written consent was taken from the patients and subjects who participated in the present study. Only those individuals, who volunteered to participate in the study, were selected and the data was kept confidential. In all these group serum urea, creatinine and trace elements were estimated. The serum urea was estimated by GLDH–Urease method, serum creatinine was estimated by Jaffe’s method. The serum copper and zinc were analyzed using colorimetric method, magnesium assessment was carried out by calmagite method. The eGFR was computed by MDRD formula. All the data are expressed in mean and standard deviation. For the statistical significance, student ‘t’ test was performed using Graphpad software. The probability less than 0.05 were considered significant.

RESULT AND DISCUSSION

CKD is associated with significant morbidity and mortality due to accelerated cardiovascular disease and infection (Zima et al., 1999). An increase in serum urea and serum creatinine levels in patients with CKD when compared to those of controls was observed and this was due to the declining of glomerular filtration in patients with CKD. Though trace elements occur in very low concentrations in the body, their role in the maintenance of undisturbed biological functions is nonetheless highly important. CKD patients are at theoretical risk for both deficiency and accumulation of trace elements, depending on dietary intake, removal by dialysis, the composition of the source water used for hemodialysis and residual kidney function. Or due to dialysate contamination / depletion may also disturb trace element concentration in dialysis patients (D’Haese and de Broe, 1996).

Average blood levels of biologically important trace elements were considerably different in CKD patient, trace element status influences the risk of adverse clinical outcomes, in order to prevent some complications in CKD patients, it is very important to regulate levels of trace elements.

Copper (Cu) is an essential trace element that is required for a number of enzymes. Cu has vital roles in hemoglobin synthesis and immune function. Excess blood Cu, particularly the free fraction, may lead to tissue injury apparently due to its pro-oxidant effects and the depletion of anti-oxidant reserves (Maggini et al. 2007).

In the present study, serum copper is not altered in CKD patients when compared with control group. In some studies, serum
Cu levels were higher in CKD patients (Lin TH et al 1996), on the other hand, Anees et al. (2011) reported that Cu was significantly deficient in CKD patients, while in others the serum Cu levels in patients with CKD were within normal ranges (Paydas S et al 1989, Shouman et al. 2009). The results of the present study do agree with the latter. Further studies are required to clarify the status of serum copper levels in CKD.

Zinc (Zn) is a dietary metal required for the healthy functioning of the body. It is one of the most important trace elements in the body and it is essential as a catalytic, structural and regulatory ion. It is involved in homeostasis, in immune responses, in oxidative stress, in apoptosis and in ageing (Salwen 2011). Zinc deficiency is linked to decreased immunity leading to increased infection susceptibility frequently encountered in uremic patients (Hirano et al. 2008).

In the present study the mean serum zinc was significantly decreased in CKD patients when compared with control (p<0.0001; Table 1). This observation is in agreement with Ghoreshi Z et al (2001). Dietary protein is a major source of zinc and limited protein intake due to low-protein diets may contribute to a low zinc level (Gilmour ER et al 1998). It is possible that the observed hypozincemia may be due to the increased urinary zinc excretion and the decreased intestinal zinc absorption (Vanholder R et al 2002).

Copper to zinc ratio is a more variable indicator in CKD patients. Cu/Zn ratio was significantly increased in CKD patients in the present study. The result of Cu/Zn ratio may indicate the utility of using this ratio more efficiently in the assessment of serum levels of these two highly correlated trace elements, than using each one alone. Torre MLR et al (2014) found the Cu/Zn ratios higher in CKD patients than in controls, this finding is consistent with our study. The present study added the facts of aggravated Cu/Zn ratios in CKD patients, implying an increased risk of diseases associated with elevated oxidative stress, inflammation and depressed immune function, such as cardiovascular diseases.

Magnesium (Mg) is another trace element which is essential for maintaining proper body functions. It is vital for body’s immune system, cardiovascular and musculoskeletal systems. Deficiency of this element will lead to hypertension, diabetes, kidney disease and cardiovascular diseases. Hypermagnesemia in CKD may be due to the limited ability of the kidneys to excrete excess magnesium.

Serum magnesium concentration is a significant predictor of mortality in maintenance CKD patients. Hypomagnesemia is significantly associated with the presence of vascular calcification of the arteries. These results suggest that higher serum magnesium concentrations may play an important protective role in the development of vascular calcification in CKD patients. As far as serum Mg levels are concerned, the results of our study agree with that of Najem SN 2005. Our results shown significantly higher level of magnesium in CKD patients and this fortunately is helpful to our patients since patients with mildly elevated serum magnesium levels could have a survival advantage over those with lower magnesium levels (Massy and Drueke 2012). Low serum magnesium may be an independent risk factor for premature death in CKD patients.

**Table: 1 Comparative study of Trace elements in control and CKD Patients.**

<table>
<thead>
<tr>
<th>Trace elements</th>
<th>Control (Mean±SD)</th>
<th>CKD Patients (Mean±SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Copper (µg/dl)</td>
<td>109.3±5.83</td>
<td>111.72±6.91</td>
</tr>
<tr>
<td>Zinc (µg/dl)</td>
<td>97.56±6.97</td>
<td>58.82±4.36*</td>
</tr>
<tr>
<td>Cu / Zn Ratio</td>
<td>1.13±0.09</td>
<td>1.91±0.20</td>
</tr>
<tr>
<td>Magnesium (mg/dl)</td>
<td>2.41±0.21</td>
<td>3.66±0.25*</td>
</tr>
</tbody>
</table>

*P<0.0001

**CONCLUSION**

Alteration in trace elements may occur in CKD. This aspect requires attention and rectification where necessary. A continuous evaluation of trace elements is important in CKD patients. These alterations in serum trace elements in CKD enhance the risk of atherosclerosis and favours higher incidence of cardiovascular complications.

On the basis of the findings of the present study, it is suggested all CKD patients...
should be evaluated for trace elements to decrease the risk of complications in CKD patients. Patients with CKD should be considered a “very high risk” category and aggressive therapeutic intervention initiated to reduce the risk of associated complications. A close and careful nutritional support of patients with CKD, particularly in the early stages of the disease, is necessary. To prevent complications in CKD patients, it is important to regulate levels of trace elements. Otherwise, ongoing oxidative stress presents in the CKD patients play a pathophysiological role in the development of cardiovascular disease. The regular monitoring of serum trace elements levels in patients with CKD who are following a protein-restricted diet is recommended. Planning for the preventive health policies and allocation of more resources for the treatment of CKD patients are essential in India.

REFERENCES
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