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ANTIOXIDANTS STATUS OF PATIENTS WITH CHRONIC KIDNEY DISEASE ON HEMODIALYSIS AND CONSERVATIVE THERAPY - A COMPARATIVE STUDY

Nutritional Science

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ABSTRACT

Background: There is growing evidence from experimental and clinical studies that oxidative stress is a potentially important source of morbidity and mortality in patients with chronic kidney disease (CKD). This study was carried out to determine the selected antioxidant status of patients with CKD involving forty-five (45) subjects consisting of 15 patients on conservative therapy and another 15 patients on haemodialysis (experimental groups) and also 15 apparently healthy volunteers as control. **Methodology:** Ten (10) mls of blood samples were obtained from the subjects into heparinized bottles for determination of selected antioxidants such as serum retinol, α-tocopherol and lycopene using high performance liquid chromatography (HPLC) method and ascorbic acid and selenium using atomic absorption spectrophotometry method. **Results:** The serum retinol, (57.31±5.97 µg/dl and 59.19±7.71 µg/dl), serum ascorbic acid, (34.62±7.06 mmol/l and 37.16±7.26 mmol/l), serum α-tocopherol, (1.05±0.23 mg/dl and 1.11±0.31 mg/dl) and lycopene, (36.34±7.67 µg/dl and 37.48±6.76 µg/dl) of the patients on conservative therapy and haemodialysis respectively were significantly higher than the values 44.62±7.38 µg/dl, 29.41±7.41 mmol/l, 0.63±0.13 mg/dl and 23.09±4.24 µg/dl observed in the control respectively ($p<0.05$). The serum selenium of the patients with CKD was not significantly different from the control ($p>0.05$). **Conclusion:** The diet of patients with CKD should be planned individually and tailored towards their biochemical information to maintain nutritional status and avoid nutrient toxicity.

KEYWORDS

Antioxidant status, chronic kidney disease, haemodialysis.

Background

The magnitude of the problem of chronic kidney disease (CKD) is enormous, and the prevalence of kidney failure is rising1. Globally, in 2017, 1·2 million (95% uncertainty interval [UI] 1·2 to 1·3) people died from CKD. The global all-age mortality rate from CKD increased 41·5% (95% UI 35·2 to 46·5) between 1990 and 2017—2. Oxidative stress has been described to play an important role in disease progression and development of cardio-vascular complications in chronic kidney disease (CKD) patients——3. Assessment of nutritional status is *an integral part of care for* patients with chronic kidney disease, with nutritional deficiencies negatively impacting quality of life4. In addition, understanding the risk factors such diabetes, hypertension and other non-communicable diseases and implementing screening of at risk populations will increase early detection, initiate treatment of modifiable risk factors for ESRD, along with appropriate treatment for CKD–[r57].

Much attention has been focused on providing adequate protein and calories (macronutrients) to patients with CKD in an effort to prevent development of malnutrition'—8. Comparatively less attention has been paid in recent years to the possibility that micronutrient deficiencies can also contribute to poor outcomes in patients with CKD. Yet micronutrients and a variety of water- and fat-soluble vitamins, are essential cofactors that provide the necessary cellular machinery for energy transfer and the maintenance of physiological energy homeostasis9. For some time, past various therapeutic interventions have been attempted in order to reduce oxidative stress in chronic kidney disease in the hope to improve patient outcome. Also of great importance in renal failure are the dietary restrictions of fruits and vegetables which are good sources of antioxidants such as ascorbic acid, α-tocopherol and carotenoids. Deficiencies of these antioxidants may be a problem in these patients—10.

Reports on the antioxidant status of Nigerian patients with chronic kidney disease are limited. Thus, this study is designed to determine selected antioxidant status of Nigerian patients with severe chronic kidney disease. The result of these findings will help to develop clinical interventions aimed at preventing antioxidant deficiencies in patients with chronic kidney disease in Nigeria.

MATERIALS AND METHODS.

Study design:

This study was a descriptive and analytical study.

Study population and sample size:

The study population included fifteen (15) male and female adult patients with chronic kidney disease (CKD) either admitted into the male and female medical wards of UCH or out-patients who have not yet undergone haemodialysis (patients on conservative therapy), another fifteen (15) patients with CKD presently undergoing haemodialysis (haemodialysis therapy) and fifteen (15) apparently healthy non-smoking adult individuals (control), who give their consent to participate in the study. The patients with CKD were confirmed by the nephrologists to have CKD. The study subjects were matched for age and sex and the overall study population was forty-five (45). The patients with CKD (conservative therapy and haemodialysis therapy) served as the experimental groups while the healthy volunteers served as the control.

Any subject who refused to give their consent was excluded from the study.

Sampling method:

Subjects with CKD admitted into the male and female medical wards of UCH and the healthy volunteers, who gave their consent to participate in the study, were purposively selected for the study.

Data collection procedure:

10ml of blood samples was drawn by medical doctors in the ward. Specimens were taken into heparinized bottles protected from light and transported immediately to the Chemical Pathology Department of the University College Hospital (UCH), Ibadan.

The blood sample was centrifuged at 2,500rpm at 4°C for 10 minutes to obtain serum. Hemolysed samples were excluded. The serum was stored at 20°C until analysed. The determination of retinol, lycopene and α-tocopherols was performed using a reversed-phase high-performance liquid chromatography (HPLC), determination of serum ascorbate was performed using spectrophotometric method while determination of selenium was performed using atomic absorption spectrophotometry (AAS) method.

Method of data analysis

Analyses were done using SPSS version 16 and Total Dietary Assessment software 2001 (to calculate dietary intake). Data cleaning was done by running frequencies of all relevant variables to identify inaccurate entries and missing values. Descriptive statistics, t-test, Analysis of Variance (ANOVA) and chi-square test were performed on data obtained at 5% level of significance.

T-test and ANOVA were used to evaluate differences in mean values between groups. The regression analysis was used to determine the relationship between dependent variable and independent variables. Correlation was performed at 99% level of significance.

Ethical considerations

Ethical approval was obtained from the department of human nutrition, UI and also UI/UCH ethical review committee. Permission to conduct the study was also obtained from the nephrologists of the renal unit, department of medicine, UCH.

RESULTS:

The serum antioxidant status of the experimental groups and control are presented in table 1.

The subjects on haemodialysis had higher level of serum retinol (59.19±7.71 µg/dl) than the subjects on conservative therapy (57.31±5.97 µg/dl) or control (44.62±7.38 µg/dl). The serum retinol of the subjects on conservative therapy and heamodialysis were significantly greater when compared with the control ($p<0.05$).

Similarly, the serum ascorbic acid of the subjects on haemodialysis therapy (37.16±7.26 mmol/l) was greater than the level observed (34.62±7.06 mmol/l) in subjects on conservative therapy and the controls (29.41±7.41 mmol/l). The control had significantly less ascorbic acid than the experimental group ($p<0.05$).

Similarly, the control group had significantly lower level of α-tocopherol (0.63±0.13 mg/dl) when compared with level of α-tocopherol on subjects on haemodialysis (1.11±0.31 mg/dl) and conservative therapy (1.05±0.23 mg/dl) ($p<0.05$).

Also, the lycopene of the control group (23.09±4.24 µg/dl) was significantly lower than the subjects on haemodialysis therapy (37.48±6.76 µg/dl) and conservative therapy (36.34±7.67 µg/dl).

In summary, the control had significantly less serum retinol, ascorbic acid, α-tocopherol and lycopene than the experimental groups ($p<0.05$) while subjects on haemodialysis had higher levels of serum retinol, ascorbic acid, α-tocopherol and lycopene than subjects on conservative therapy or the control. The serum selenium of the experimental groups and the control were not significant. It was also observed that there was no significant difference observed between experimental groups (conservative and haemodialysis therapy).

Table 1: The mean Antioxidant status of all the subjects (experimental groups and control).

	Conservative therapy		Haemodialysis therapy			Control		
	Range	mean ±SD	Range	mean± SD	P -value+	Range	mean ±SD	P -value++
Retinol (µg/dl)	48.22 - 70.01	57.31 ±5.97	41.61- 72.01	59.19± 7.71	0.46 1	33.22 – 56.22	44.62 ±7.38	0.000 *
Ascorbic (mmol/l)	21.15 - 44.18	34.62 ±7.06	26.40 – 47.19	37.16± 7.26	0.33 9	18.20 – 41.51	29.41 ±7.41	0.017 *
α-tocopherol (mg/dl)	.68 - 1.53	1.05± 0.23	0.73 – 1.68	1.11±0 .31	0.55 4	0.41 – 0.87	0.63± 0.13	0.000 *
Lycopene (µg/dl)	23.11 - 47.12	36.34 ±7.67	22.19 – 46.14	37.48± 6.76	0.66 7	17.01 – 30.22	23.09 ±4.24	0.000 *
Selenium (µg/dl)	19.75 - 41.25	27.21 ±5.73	18.97 – 31.19	23.86± 4.37	0.08 2	19.56 – 41.01	27.35 ±5.52	0.147

*P<0.05

+T-test for equality of means between the conservative therapy and haemodialysis therapy.

++ANOVA (test of significance between the 3 groups at 5% sig. level)

DISCUSSION.

Antioxidants.

Serum retinol.

The serum retinol of the patients on conservative therapy was quite lower than the level observed in patients on haemodialysis (57.31±5.97µg/dl and 59.17±7.71µg/dl). The values were quite higher than the serum level observed in the control.

The higher serum level of vitamin A observed in the two groups of patients was similar to those of several reports[10,11]. The high level of serum retinol in patients with CKD was suggested to be due to the failing of the kidneys to metabolize retinol to retinoic acid, leading to decreased excretion through bile and urine, or a defect in retinal binding protein catabolism (vitamin A carrier) by the diseased kidneys[12]. Vitamin A can lead to hypervitaminosis in patients with CKD, most especially in haemodialysis patients, which has been reported to be tolerated due to extra carrying capacity for vitamin A[11]. High serum vitamin A concentration that occurs in patients with chronic kidney disease has toxic effects. Reports indicate the hypercalcaemia probably occurs as a consequence of the effect of elevated vitamin A on bone mass[12]. In established renal failure, retinol binding protein is retained in plasma and retinol concentration increases. In this study, an increase in serum vitamin A levels was observed in patients with CKD and the rise was statistically significant. This finding is also in agreement with those of Peuchant et al[14].

Ascorbic acid

Vitamin C is one of the most important hydrosoluble antioxidants; it exerts its beneficial effects by inhibition of lipid peroxidation and directly scavenges O_2 and OH^- [15,16]. The serum ascorbic acid of the patients on haemodialysis (37.16±7.26 mmol/l) in this study was higher than patients on conservative therapy (34.62±7.06 mmol/l) and the control who had the lowest serum ascorbic acid (29.41±7.41).

This result was however contrary to some other studies which reported a lower-than-normal plasma concentration of ascorbic acid in patients with chronic kidney disease[12,17] and it was attributable to the loss of the vitamin through the dialysis membrane because of its hydrosolubility and/or the dietary restriction of fruits and vegetables for patients with CKD. The reason for this higher value in patients on haemodialysis could be attributable to the fact that most patients on haemodialysis in UCH do receive vitamin C supplements of about 600mg/day (especially the in-patients). Also, it was observed that the dietary intake of vitamin C was highest in haemodialysis patients. This could also be a contributing factor as most of the haemodialysis patients reported not to be on any dietary restriction. Washio et al in a study have confirmed that in maintenance haemodialysis patients, vitamin C administration resulted in a significant increase in the postdialysis level of the oxidized form of vitamin C, which suggested an increase in antioxidant effect[18].

α-tocopherol

Vitamin E is the most important lipophilic antioxidant in the biological system and protects cell membranes from oxidation by the formation of low-reactivity tocopheroxyl radicals[11,15,19]. In this present study, serum levels were within the normal range in all the patients with CKD, in accordance with earlier studies[20,21]. This was probably because of either complete and adequate absorption or storage of the fat-soluble vitamins[15,22]. Another possibility is that serum levels are not dependent on or are only weakly related to the intake amount of the vitamin, unless liver reserves are severely depleted[22].

Serum α-tocopherol concentrations were observed to be higher in haemodialysis patients (1.11±0.31 mg/dl) compared to patients on conservative therapy (1.05±0.23 mg/dl) and the control (0.63±0.13 mg/dl). This observation is in agreement with previous reports which also showed a higher level of α-tocopherol in haemodialysis patients[23,24].

The reports regarding plasma vitamin E level in haemodialysis patients are however conflicting. For example, Peuchant et al reported a decrease in plasma vitamin E levels in haemodialysed patients[14]. Paul et al did not find any change in the plasma levels of the vitamin E as such but found a decrease when the levels were corrected for cholesterol[25]. Ha et al, as well as Dakshinamurty et al, did not find any difference in the vitamin E status as such[10,26]. On the contrary to the above reports, in this study, a significant difference was observed between serum α-tocopherol of the 3 groups of subjects. Regardless of high serum α-tocopherol concentrations, supplementation with vitamin E leads to a decrease in lipid peroxidation in haemodialysis patients[24] and the increase in α-tocopherol concentrations have also been attributed to decreased renal clearance[27].

Lycopene

Serum lycopene of haemodialysis patients (37.48±6.76 µg/dl) in this study was however higher than the patients on conservative therapy (36.34±7.67 µg/dl) and control (23.09±4.24 µg/dl). This is however

not similar with other results which reported a lower level of lycopene in haemodialysis patients[10]. Low lycopene levels have been found to be associated with risk of chronic kidney disease[28].

Selenium

Selenium has also been found to be responsible for the antioxidase protection of cells against destruction by hydrogen peroxide and free radicals[29]. In this study, the selenium level of the patients on haemodialysis (23.86±4.37 µg/dl) was found to be lower that the patients on conservative therapy (27.21±5.73 µg/dl)[18]. This was similar to a previous study which showed selenium concentrations to significantly decline as the CKD stage increased[30].

CONCLUSION

Renal failure is accompanied by oxidative stress which results in excessive generation of reactive oxygen species and impaired efficiency of antioxidant defense mechanisms causing damage of biological structures[31].

It has been reported that humans require external sources of vitamins E and C and beta-carotene because they are not produced by the body; they must be obtained from the diet[32]. These antioxidant compounds are found naturally in a wide variety of food and plants, including many fruits and vegetables, nuts, seeds, oils and fats[11,33]. Since haemodialysis patients live under pro-oxidative conditions, they may require an increase level of antioxidant protection[15].

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