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# ORIGINAL ARTICLE

## Oxidative Stress among Ghanaian Patients presenting with Chronic Kidney Disease

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**Dyslipidaemia and lipid peroxidation are known risk factors for chronic kidney disease (CKD). This study assessed the lipid profile and oxidative stress/lipid peroxidation in CKD patient, using the oxidative stress marker, Malondialdehyde (MDA) and antioxidants; Vitamins A and C, Catalase and Uric Acid. The study population included 146 individuals with mean age 50.18 ± 1.14 with various CKD, s and who were undialysed. Another 80 healthy subjects without kidney pathology but of similar age and sex distribution were used as controls. With the exception of HDL-C, which showed no significant difference when CKD patients were compared with controls (1.35±0.0 5 vs 1.61±0.20, p= 0.2114, total cholesterol (TC) (4.54±0.13 vs 5.63±0.13, p=0.0274), low density lipoprotein cholesterol (LDL-C) (106.30 ± 4.00 vs 126.30± 5.57, p=0.0134), and triglycerides (TG) (1.52± 0.08 vs 1.84±0.09, p=0.0086) increased significantly in the CKD patients. Serum MDA increased significantly (1.22 ± 0.10 vs 2.66 ± 0.07, p=0.0001) in the CKD patients as compared to the controls and increased with the severity of the condition. Vitamin A (9.76±3.03 vs 16.1±5.21, p=0.0012), Catalase (57.49±1.18 vs 71.98±2.91, p=0.0001) and Uric Acid (266.68±11.00 vs 333.90±10.02, p=<0.0001) increased significantly in the CKD subjects compared to controls, whilst vitamin C (0.54±0.02 vs. 0.34±0.05, p=0.0001) decreased significantly among the CKD subjects. Dyslipidaemia and increased oxidative stress with abnormal antioxidant levels are common in CKD patients. Therapeutic regimens aimed at strengthening the antioxidant defenses besides normalizing lipid concentrations would protect CKD patients against oxidative stress and any related complications.**
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**Keywords***:* Chronic kidney disease; dyslipidaemia; lipid peroxidation; MDA; catalase

### INTRODUCTION

The prevalence of chronic kidney disease (CKD) has reached epidemic proportions globally. (Coresh *et al.*, 2007; Di Angelantonio *et al.*, 2007; Flessner *et al.*, 2009). Nationally representative samples from USA and Taiwan report a prevalence of 12-13%, (Wen *et al.*, 2008) though most of these individuals may not be aware of their condition. In Ghana, data on the prevalence of CKD has been varied over the years. Bamgboye in 2006 put the prevalence at 1.6% per million people (Bamgboye, 2006). However, Addo *et al.,* (2009) put the prevalence among Ghanaian hypertensives at 4%. In a recent publication, Osafo et al., (2011) put the prevalence at 46.9% among hypertensives in Ghana.

The most severe forms of CKD are characterized by kidney failure and patients need renal replacement therapy (haemodialysis, peritoneal dialysis or renal transplantation); however more patients may be affected by less severe forms of CKD. Together with obesity or smok-

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ing, CKD contributes to around a tenth of all deaths in Taiwan (Wen *et al*., 2008) than any other cause in the general population.

CKD leads to numerous complications as the condition progresses. Notable among them are cardiovascular, cerebrovascular and peripheral vascular diseases. Cardiovascular complications are the main cause of death and are about 20 folds higher in CKD patients than any other cause in general population (Oda and Keane, 1998). These complications are down to several metabolic and endocrinal disturbances among which dyslipidaemia is a regular feature. Abnormalities in lipid profiles are noticed immediately renal function begins to decline (GFR≤60ml/min/1.73m) though the type and severity vary among patients (Oda and Keane, 1998; Wanner, 2000). Similarly, CKD patients are also at risk of increased oxidative stress characterized by low antioxidant systems and an upsurge in prooxidant activity (Locatelli *et al*., 2003). In the course of the process, polyunsaturated fatty acids (PUFA), located in cell membrane are oxidized in vivo to produce aldehydes of different chain length like malondialdehyde (MDA). This product of lipid peroxidation can structurally change DNA, RNA, body protein and other biomolecules (Daschner *et al*., 1996). Lipid abnormalities and enhanced oxidative stress in CKD patients are involved in disease progression and accelerates the process of atherosclerosis resulting in cardiovascular complications. This study, sought to assess the lipid profile and oxidative stress/lipid peroxidation in patients presenting with CKD by determining relevant oxidative stress markers (MDA) and antioxidant levels (vitamins A and C, catalase and uric acid).

## MATERIALS AND METHODS

### Study area and subjects

This study was carried out at the Komfo Anokye Teaching Hospital (KATH), Kumasi and Tamale Teaching Hospital (TTH) between August 2007 and September 2009. One hundred and forty six (146) patients comprising of eighty (80) females and sixty-six (66) males within age range 14-80 years were signed on as cases. Patients with clinically diagnosed CKD including those yet to start dialysis were randomly selected for the study. Patients on any form of dialysis were excluded from the study. The aetiology of the CKD ranged from diabetic nephropathy, 90(61.6%) patients; chronic glomerulonephritis, 12(8.2%) patients; adult polycystic kidney disease, 1(0.7%) patient; hypertensive nephropathy, 10(6.8%) patients and chronic kidney disease of unknown aetiology, 33(22.6%) patients. Eighty (80) healthy volunteers of similar age and sex distribution were studied as controls. The participation of the respondents who are all indigenes of Ghana was voluntary and informed consent was obtained from each of them. The study was approved by the School of Medical Sciences and KATH Committee on Human Research, Publication and Ethics (CHRPE).

### Sample Collection

Venous blood samples were collected after an overnight fast (12 – 14 hours). About 5 ml of venous blood was collected and dispensed into vacutainer® plain tubes. After centrifugation at 500 g for 15 min, the serum was stored at - 80°C until assayed.

### Biochemical assays

Serum biochemistry was performed with ATAC® 8000 Random Access Chemistry System (Elan Diagnostics, Smithfield, RI, USA). Parameters that were determined include; blood urea nitrogen (BUN), creatinine (CRT), total cholesterol (TC), triglycerides (TG), high density lipoprotein cholesterol (HDL-C) and low density lipoprotein cholesterol (LDL-C) which was calculated using the Friedwalds formula (Friedewald *et al*., 1972).

The methods adopted by the automated instrument for the determination of the above parameters were predetermined by the reagent manufacturer - JAS™ diagnostics, Inc. (JAS Diagnostics, Inc. Miami Florida, USA). Total cholesterol and HDL-C determination was according to the method described by Trinder (Trinder, 1969). Triglycerides determination employed a modified Trinder method (Trinder, 1969; Barham and Trinder, 1972). Low density lipoprotein cholesterol (LDL-C) determination: LDL-C (mmol/l) was calculated according to Friedwald's formula in accordance to the manufacturer's instructions i.e. LDL-C = TC- TG/2-HDL-C.

### Measurement of Oxidative Stress

Parameters measured included; Malondialdehyde (MDA) (µmol/l), Vitamin C (Vit C) (mg/ml), Catalase (CAT) (units/ml) and Vitamin A (Vit A) (µg/ml).

### Malondialdehyde (MDA)

Malondialdehyde (MDA) levels were determined by the MDA thiobarbituric acid (TBA) test which is the colorimetric reaction of MDA and TBA in acid solution. MDA, a secondary product of lipid peroxidation, reacts with thiobarbituric acid (TBA) to generate a red-coloured product, which was detected spectrophotometrically at 535 nm. The protocol used in this study was the Kamal *et al.,* (1989) modification of the Shlafer and

Shepard (1984) protocol. The absorbance of the mixture was measured at 535 nm with a spectrophotometer (Biomate 3S UV Visible spectrophotometer, Thermoelectron Inc USA) and the results were expressed as μmol/l, using the extinction coefficient of $1.56\times10^5$ L $mmol^{-1}$ $cm^{-1}$.

**Vitamin C**
Vitamin C was determined by the method of Omaye *et al.,* (1979) at most 3 hours after sample collection. Ascorbic acid in plasma is oxidized by Cu (II) to form dehydroascorbic acid, which reacts with acidic 2,4- dinitrophenylhydrazine to form a red dihydrazone which is measured at 520 nm with a spectrophotometer.

**Catalase**
Catalase was assayed by the method of Takahara *et al.*, (1960). To 1.2 ml of 50 mM phosphate buffer (pH 7.0), 0.2 ml of plasma was added and the enzyme reaction was started by the addition of 1.0 ml of 30 mM $H_2O_2$ solution. The decrease in absorbance was measured at 240 nm at 30 second intervals for 3 minutes with an ultra violet-visible spectrophotometer. The enzyme blank was run simultaneously with 1.0 ml of distilled water instead of hydrogen peroxide. The enzyme activity was expressed as units/ml.

**Vitamin A**
Plasma- retinol (vitamin A) was determined by reverse phase high performance liquid chromatography (HPLC) (Zaman *et al.*, 1993).

**Proteinuria**
Early morning urine was collected in plastic containers from the respondents and urine protein was determined using the dip-stick qualitative method (CYBOW™ DFI Co Ltd, Gimhae-City, Republic of Korea).

**Anthropometric variables**
Anthropometric measurements included height to the nearest centimetre without shoes and weight to nearest 0.1 kg in light clothing. Subjects were weighed on a bathroom scale (Zhongshan Camry Electronic Co. Ltd, Guangdong, China) and their height measured with a wall -mounted ruler. BMI was calculated by dividing weight (kg) by height squared ($m^2$).

**Estimation of GFR**
The 4-variable Modification of diet in renal disease (4v-MDRD) equation (Levey *et al.*, 1999) was used to estimate the GFR of both subjects and controls using serum creatinine.

$$4v-MDRD = 186 \times SCr^{-1.154} \times age^{-0.203}$$

The equation is multiply by 1.212 if black and 0.742 if female

The GFR results from the equations was used to divide the study population into five categories corresponding with the five stages of CKD in the kidney disease outcome quality initiative (K/DOQI) CKD classification (National Kidney Foundation, 2002).

The staging classified GFR ≥ 90 ml/min/1.73 $m^2$ as stage 1; 60-89 ml/min/1.73 $m^2$ as stage 2; 30-59 ml/min/1.73 $m^2$ as stage 3; 15-29 ml/min/1.73 $m^2$ as stage 4; and < 15 ml/min/1.73 $m^2$ as stage 5.

**Blood pressure**
Blood pressure was measured by trained personnel using a mercury sphygmomanometer and stethoscope. Measurements were taken from the left upper arm after subjects had been sitting for >5 min in accordance with the recommendation of the American Heart Association (Kirkendall *et al.*, 1967). Duplicate measurements were taken with a 5 min interval between measurements and the mean value was recorded to the nearest 2.0 mmHg.

**Statistical analysis**
The results are expressed as Means ± SEM. Unpaired t-test was used to compare mean values of continuous variables and $\chi^2$ was used to compare discontinuous variables. Correlation was assessed by the Pearson's method. A level of $p<0.05$ was considered as statistically significant. GraphPad Prism version 5.00 for windows was used for the statistical analysis (GraphPad software, San Diego California USA, www.graphpad.com).

## RESULTS

Demographic and clinical characteristics of the study population are shown in Table 1. The mean age of the 146 participants involved in this study was 50.18 ± 1.14 ($p=0.0720$) with 45.2% of the participants being males. Apart from estimated GFR (eGFR) and haemoglobin (HGB) which were significantly decreased as compared to the control, lipid fractions (LDL-C, TC, TG) (except HDL-C), fasting blood glucose (FBG), blood pressure (SBP and DBP), creatinine (CRT), blood urea nitrogen (BUN) and proteinuria (PRT) were significantly increased in the CKD subjects compared to the control group. Marker of oxidative stress (MDA) increased significantly in the CKD patients compared to the controls. Apart from Vit C which decreased significantly in the

CKD group compared to the controls, the other antioxidants (Vit A, CAT and uric acid) showed a significant

**Table 1. Demographic, clinical and biochemical characteristics of study population.**

| Parameters | Control (n=80) | CKD (n=146) | P value |
|---|---|---|---|
| Age (yrs) | 46.35 ± 1.96 | 50.18 ± 1.14 | 0.0720 |
| BMI (kg $m^{-2}$) | 24.66 ± 0.80 | 24.44 ± 0.44 | 0.8021 |
| SBP (mmHg) | 120.7 0 ± 1.82 | 140.40 ± 3.84 | 0.0001 |
| DBP (mmHg) | 70.42 ± 1.25 | 90.32 ± 2.61 | 0.0001 |
| PRT (g/l) | 0.04 ± 0.02 | 1.17 ± 0.26 | 0.0001 |
| ***Biochemical assays*** | | | |
| CRT (µmol/l) | 105.90 ± 3.96 | 268.00 ± 25.60 | 0.0001 |
| BUN (mmol/l) | 3.51 ± 0.17 | 15.45 ± 2.80 | 0.0001 |
| FBG (mmol/l) | 5.31 ± 0.17 | 8.75 ± 0.33 | 0.0001 |
| TC (mmol/l) | 4.54 ± 0.13 | 5.63 ± 0.13 | 0.0274 |
| TG (mmol/l) | 1.52 ± 0.08 | 1.84 ± 0.09 | 0.0086 |
| HDL-C (mmol/l) | 1.35 ± 0.05 | 1.61 ± 0.20 | 0.2114 |
| LDL-C (mmol/l) | 2.75 ± 0.10 | 3.30 ± 0.14 | 0.0134 |
| eGFR (ml/min/173 m2) | 92.40 ± 5.67 | 57.61 ± 4.15 | 0.0001 |
| ***Oxidative stress markers*** | | | |
| VIT C (mg/ml) | 0.54 ± 0.02 | 0.34 ± 0.05 | 0.0001 |
| VIT A (µmol/l) | 9.76 ± 3.03 | 16.17 ± 5.21 | 0.0012 |
| MDA (µmol/l) | 1.22 ± 0.10 | 2.66 ± 0.07 | 0.0001 |
| Uric acid (µmol/l) | 266.68 ± 11.00 | 333.90 ± 10.02 | <0.0001 |
| CAT (units/ml) | 57.49 ± 1.18 | 71.98 ± 2.91 | 0.0001 |

***BMI=Body mass index, SBP=Systolic blood pressure, DBP=Diastolic blood pressure, PRT=Proteinuria, TC=Cholesterol, HDL-C=High density lipoprotein, TG=Triglyceride, LDL-C= Low density lipoprotein, CRT=Creatinine, BUN=Blood urea nitrogen, FBG=fasting blood glucose, eGFR=Glomerular filtration rate, CAT=Catalase.***

increase in CKD patients compared to controls as shown in Table 1.

Table 2 represents demographic, clinical and biochemical parameters during various stages of CKD. Apart from eGFR which decreased significantly among the CKD subjects as the condition progressed from stage 1 to 5; CRT, BUN, PRT, SBP and DBP, increased significantly at some stages of CKD. With the exception of LDL and HDL, the other lipid fractions (TC and TG) increased significantly as the condition progressed with TG increasing significantly at stage 5. The marker of oxidative stress (MDA) increased significantly with the severity of CKD, whereas with the exception of Vit C which decreased as the condition progressed, the antioxidant (Vit A, CAT, Uric acid) increased with the severity of the condition.

From the Pearson correlation analysis in Table 3, there is a positive correlation between blood pressure (SBP and DBP) and the various oxidative stress parameters (MDA, Vit C, uric acid and Catalase) among the CKD group. Furthermore, with the exception of uric acid, Vit A and CAT which showed generally a positive correlation with eGFR, the other antioxidant (Vit C) showed a negative but significant correlation with eGFR. Again there was significant negative correlation between FBG and MDA among CKD subjects. Furthermore, there was a significant negative correlation between eGFR and FBG and between CRT and eGFR among subjects with CKD.

Figure 1 represents levels of plasma MDA (A), catalase activity (B), uric acid (C), and albumin (D) in controls and CKD patients. Apart from albumin (1D) which

**Table 2. Demographic, blood pressure and biochemical parameters during various stages of chronic kidney disease**

| Parameters | CKD STAGE | | | | | | |
|---|---|---|---|---|---|---|---|
| | Controls (n=80) | 1 (n=25) | 2 (n=35) | 3 (n=37) | 4 (n=25) | 5 (n=24) | P Value |
| **Anthropometric data** | | | | | | | |
| Age (yrs) | 46.35 ± 1.96 | 48.08 ± 3.72 | 50.45 ± 2.20 | 52.76 ± 2.13 | 50.12 ± 2.31 | 47.67 ± 2.50 | 0.3793 |
| Sex (Males) | 30 (37.5%) | 10 (40.0%) | 13 (37.1%) | 15 (40.5%) | 9 (36.0%) | 10 (41.6%) | 0.0149 |
| BMI (kg/m2) | 24.66 ± 0.80 | 25.97 ± 0.92 | 25.60 ± 1.54 | 24.60 ± 0.98 | 24.11 ± 0.81 | 23.56 ± 0.75 | 0.7815 |
| SBP (mmHg) | 120.70 ± 1.82 | 129.1 ± 3.38* | 126.00 ± 3.70 | 134.3 ± 3.82* | 135.6 ± 4.36 | 136.00 ± 4.36* | 0.005 |
| DBP (mmHg) | 70.21 ± 1.26 | 79.2 ± 2.70*** | 78.92 ± 1.85* | 79.43 ± 1.87* | 84.20 ± 2.80 | 90.50 ± 4.94*** | 0.0001 |
| PRT (g/l) | 0.04 ± 0.02 | 0.29 ± 0.06 | 0.82 ± 0.26 | 1.13 ± 0.29 | 1.27 ± 0.38 | 1.49 ± 0.40 | 0.0001 |
| **Biochemical assay** | | | | | | | |
| CRT (µmol/l) | 105.90 ± 3.96 | 62.19 ± 3.26 | 110.30 ± 2.25 | 160.00 ± 3.73 | 302.90 ±12.22** | 835.50 ± 79.42** | 0.0001 |
| BUN (mmol/l) | 3.51 ± 0.17 | 4.91 ± 0.64 | 4.48 ± 0.48 | 10.85 ± 1.95 | 15.40 ± 5.33 | 46.49 ± 6.37*** | 0.0001 |
| FBG (mmol/l) | 5.31 ± 0.17 | 8.19 ± 0.81 | 8.55 ± 0.85 | 8.95 ± 0.70 | 10.66 ± 0.93* | 7.28 ± 0.71 | 0.0001 |
| TC (mmol/l) | 4.54 ± 0.13 | 5.56 ± 0.28 | 5.65 ± 0.25 | 5.75 ± 0.39 | 5.98 ± 0.24 | 6.55 ± 0.26 | 0.0172 |
| TG (mmol/l) | 1.52 ± 0.08 | 1.05 ± 0.26 | 1.07 ± 0.02 | 1.53 ± 0.37 | 1.83 ± 0.25 | 2.69 ± 0.46** | 0.0013 |
| HDL (mmol/l) | 1.35 ± 0.05 | 1.73 ± 0.28 | 1.09 ± 0.16 | 1.76 ± 0.25 | 1.32 ± 0.16 | 1.23 ± 0.10 | 0.0660 |
| LDL (mmol/l) | 2.74 ± 0.10 | 3.45 ± 0.53 | 3.90 ± 0.38 | 4.11 ± 1.00 | 2.77 ± 0.28 | 2.45. ± 0.50 | 0.1423 |
| **Oxidative markers** | | | | | | | |
| Uric acid (µmol/l) | 266.68 ± 11.00 | 255.70 ± 17.83 | 266.20 ± 17.12 | 277.70 ± 19.83 | 324.50 ± 29.5 | 309.70 ± 21.41 | 0.7363 |
| MDA (µmol/l) | 1.22 ± 0.10 | 2.41 ± 0.15* | 2.45 ± 0.13** | 2.59 ± 0.17** | 2.67 ± 0.15*** | 2.87 ± 0.18*** | 0.0001 |
| CAT(units/ml) | 57.49 ± 1.18 | 58.58 ± 2.61 | 59.25 ± 4.77 | 60.00 ± 5.00 | 71.63 ± 6.88 | 79.72 ± 8.45*** | 0.0001 |
| VIT C (mg/ml) | 0.54 ± 0.02 | 0.54 ± 0.07 | 0.34 ± 0.03** | 0.30 ± 0.04** | 0.33 ± 0.06** | 0.21 ± 0.02*** | 0.0001 |
| VIT A (µmol/l) | 9.76 ± 3.03 | 8.79 ± 1.04 | 9.94 ± 2.20 | 19.42 ± 2.10** | 8.72 ± 1.08 | 33.98 ± 1.22*** | 0.0001 |
| e GFR(ml/min/173m2) | 92.40 ± 5.67 | 150.50 ± 9.22** | 67.47 ± 1.34 | 44.34 ± 1.35*** | 21.50 ± 0.98*** | 8.45 ± 0.67*** | 0.0001 |

***=p<0.05; **p< 0.01; ***p<0.001. BMI = Body mass index, SBP=Systolic blood pressure, DBP= Diastolic blood pressure, PRT = Proteinuria, TC= Total Cholesterol, HDL-C=High density lipoprotein cholesterol, TG= Triglyceride, LDL-C= Low density lipoprotein cholesterol; CRT = Creatinine, BUN= Blood urea nitrogen, GFR=Glomerular filtration rate, FBG= fasting blood glucose, MDA= Malondialdehyde, Vit C=Vitamin C, Vit A=Vitamin A, CAT= Catalase. Stage 1 = eGFR ≥90 mL/min/1.73m²; stage 2 = eGFR 60-89 mL/min/1.73m²; stage 3 = eGFR 30-59 mL/min/1.73m²; stage 4 = eGFR 16-29 mL/min/1.73m²; stage 5 = eGFR<15 mL/min/1.73m² or dialysis..***

**Table 3. Pearson correlation coefficients of clinical variables and biochemical parameters for CKD subjects**

| Variables | DPB | TC | TG | HDL | LDL | CRT | eGFR | FBG | MDA | Vit C | Vit A | CAT | UA |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| SBP | 0.76*** | -0.23 | -0.19 | -0.37** | -0.14 | 0.05 | -0.05 | -0.23 | 0.16 | 0.13 | 0.16 | 0.07 | 0.21 |
| DBP | | -0.21 | -0.14 | -0.18 | -0.17 | 0.03 | 0.05 | -0.30* | 0.19 | 0.09 | 0.19 | 0.16 | 0.15 |
| TC | | | 0.02 | 0.32* | 0.96*** | -0.24 | 0.19 | 0.17 | -0.15 | -0.08 | -0.1 | -0.16 | 0.11 |
| TG | | | | -0.43** | -0.17 | 0.22 | -0.10 | -0.06 | -0.21 | 0.04 | -0.04 | -0.01 | -0.27 |
| HDL | | | | | 0.28* | -0.03 | -0.06 | 0.06 | 0.01 | -0.26 | -0.17 | -0.08 | 0.02 |
| LDL | | | | | | -0.24 | 0.17 | 0.20 | -0.08 | -0.05 | -0.10 | -0.12 | 0.19 |
| CRT | | | | | | | -0.70*** | -0.28* | 0.17 | -0.29* | 0.14 | 0.32* | -0.13 |
| eGFR | | | | | | | | 0.34* | -0.31* | 0.05 | -0.25* | 0.08 | -0.05 |
| FBG | | | | | | | | | -0.11 | -0.30* | 0.03 | -0.12 | -0.07 |
| MDA | | | | | | | | | | -0.31* | 0.11 | 0.22 | 0.22 |
| Vit C | | | | | | | | | | | -0.29* | 0.59*** | -0.03 |
| Vit A | | | | | | | | | | | | 0.22 | -0.08 |
| CAT | | | | | | | | | | | | | -0.14 |

****.Correlation is significant at the 0.05 level (2-tailed), **.Correlation is significant at the 0.01 level (2-tailed), ***.Correlation is significant at the 0.001 level (2-tailed). eGFR= Estimated Glomerular filtration rate, UA= Uric acid, MDA= Malondialdehyde, CAT= Catalase.***

showed a significant decrease in the CKD subjects compared to the controls, MDA (1A), uric acid (1C) and catalase (1B) generally increased significantly in the CKD subjects compared to the controls.

## DISCUSSION

Renal disease, in early as well as advanced stages, is associated with abnormalities in lipoprotein metabolism. These abnormalities have been reported to be characterized by low plasma concentrations of HDL-C, high concentrations of TG, LDL-C particles, and TC (de Sain-van der Velden *et al.*, 1998; Vaziri, 2006) as confirmed by this study except for HDL-C which was not significantly different from the controls. However, the level of HDL in CKD is inconsistent as some researchers have shown that it can either decrease (Vaziri, 2006) or remain unchanged (Shah *et al.*, 1994).

The alteration in lipid metabolism has been proposed to accelerate the progression of CKD through various mechanisms. First, reabsorption of fatty acids, phospholipids, and cholesterol contained in the filtered proteins (albumin and lipoproteins) by tubular epithelial cells can stimulate tubulointerstitial inflammation, foam cell formation, and tissue injury (Magil, 1999). Secondly, accumulation of lipoproteins in glomerular mesangium can promote matrix production and glomerulosclerosis (Wheeler and Chana, 1993). In this context, native and oxidized lipoproteins, particularly LDL, stimulate production of matrix proteins by cultured mesangial cells and promote generation of proinflammatory cytokines, which can lead to recruitment and activation of circulating and resident macrophages (Rovin and Tan, 1993).

Furthermore, dyslipidaemia is an important risk factor for the development of cardiovascular events in CKD patients and it requires intervention like the use of statins to avoid or minimize the sequel of these complications (Kasiske, 2003). The effects of dyslipidaemia on the kidney are mainly observed in those with other risk factors for renal disease progression such as hypertension, diabetes and proteinuria (Keane 2000).

Oxidative stress status among the CKD patients was evaluated by measuring plasma lipid peroxidation end product MDA, whereas antioxidant vitamins (vitamin A and C), uric acid and catalase evaluated the antioxidant status. The increase in MDA found in this study is in agreement with the results of other studies (Rutkowski *et al.*, 2006) which support the observation that MDA is increased in CKD patients compared to controls. This gives an indication of the state of oxidative stress to

which the patients are subjected. Furthermore, levels of MDA increased with the progression of disease from stage 1 to stage 5. This is in accordance with the study of Yilmaz *et al.,* (2006). Lipid peroxidation products may contribute to endothelial injury and may be involved in intensive oxidative modifications of LDL (Esterbauer *et al.*, 1992) and in the development of atherosclerosis (Basha and Sowers, 1996).

Moreover, MDA altered LDL-C (Ox LDL) leads to cholesterol ester accumulation within human monocyte macrophages and it has been hypothesized that modification of native LDL may be a prerequisite for the accumulation of cholesteryl esters within the cells of atherosclerotic lesion (Fogelman *et al.*, 1980). Secondly, increased lipid peroxidation causes endothelial dysfunction through the breakdown of nitric oxide (Taddei *et al.*, 1998). Consequently, the endothelial cells lose their ability to protect the vessel wall and become atheroscle-

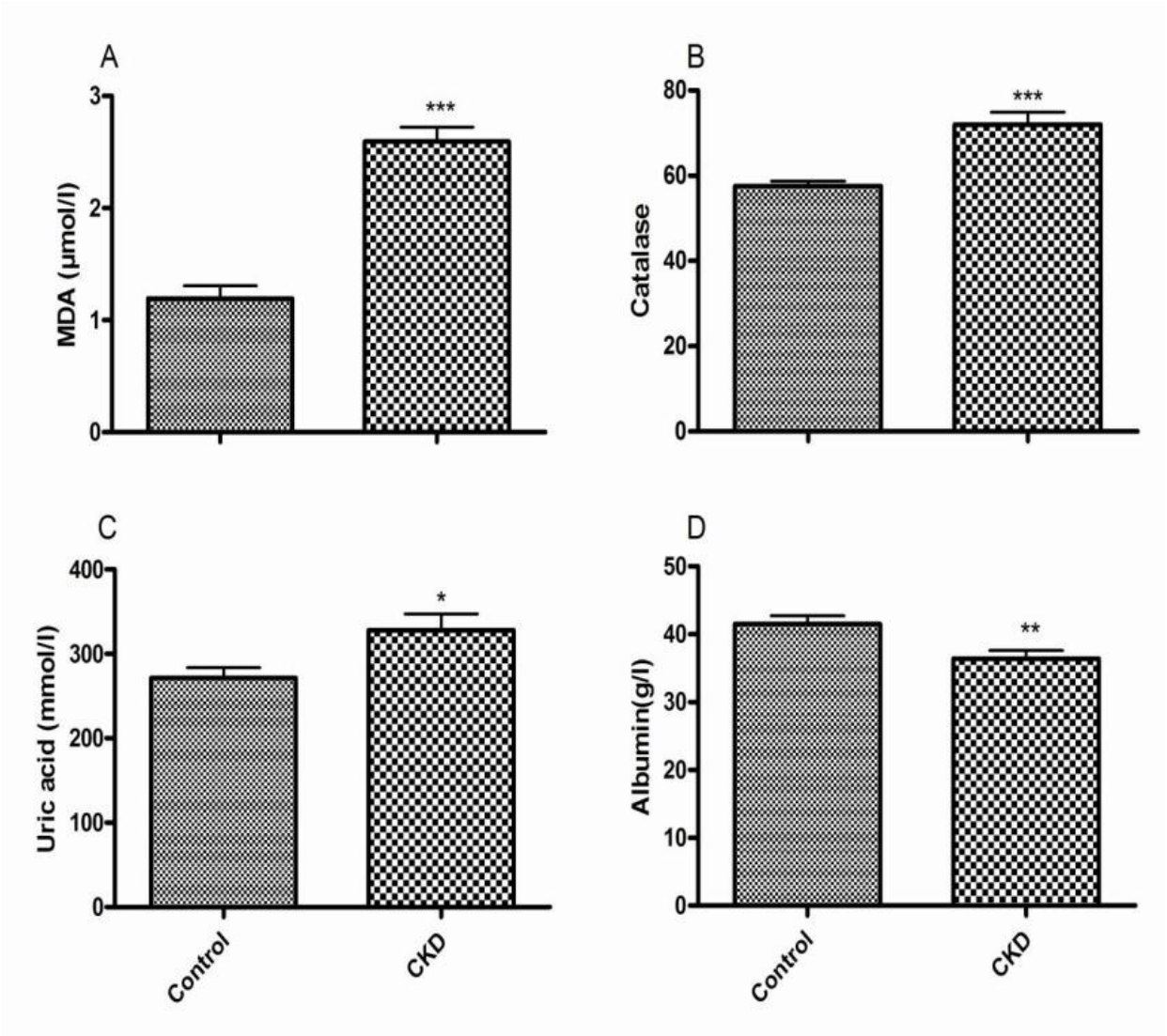


***Figure 1. Levels of plasma MDA (A), catalase activity (B), uric acid (C), and albumin (D) in controls and CKD patients. Results are means ± SEM.. Values significantly different from controls *=p<0.05, **=p<0.01, ***p<0.001***

rotic promoters (Lüscher and Vanhoutte, 1990). Thus lipid peroxidation marked by an increased MDA level may also contribute to the high incidence of premature atherosclerosis in CKD patients.

Catalase is a haemoprotein catalyzing the reduction of hydrogen peroxides and protects against the formation of highly reactive hydroxyls. The plasma concentrations of catalase increased significantly in the CKD patients compared with the controls, and increased with the severity of the condition. This observation is however contrary to the findings made in other studies elsewhere (Chen *et al.*, 1997) and may thus require further scientific enquiry.

Ascorbic acid represents one of the most prominent antioxidants, exerting beneficial effects by an inhibition of lipid peroxidation and by reducing endothelial dysfunction (Deicher and Horl, 2003). The significant decrease in the plasma concentration of Vitamin C observed in this study is consistent with the observations made in other studies (Bakaev *et al.*, 1999). Although in CKD deficiency of vitamin C can be observed, its administration in these patients requires caution.

The elevated plasma retinol (Vitamin A), an antioxidant fat-soluble vitamin, observed among the CKD patients in this study is consistent with the findings of Hala *et al.,* (2000). The high level of plasma retinol in CKD may be due to the increased levels of RBP (retinol binding protein), reduced vitamin excretion and decreased conversion of retinol to retinoic acid in the whole blood (Gerlach and Zile, 1990). In renal dysfunction both the excretory and tubular catabolism of RBP are reduced which results in the accumulation of these proteins in the blood (Smith and Goodman, 1976). In this study there was a negative correlation between eGFR and plasma retinol. Ayatse, (1991) however observed a positive correlation between serum creatinine and plasma retinol.

Uric acid is generated in the human body by the degradation of purines. It has been found that uric acid is a powerful antioxidant and is a scavenger of singlet oxygen and other radicals (Grootveld and Halliwell, 1987). In this study, the significantly higher plasma uric acid concentration that was found compared to the control, is probably a consequence of the failure of the excretory function of the kidneys as well as increased protein catabolism as part of the hypercatabolic state in CKD (Davison *et al.*, 1999). Hyperuricaemia is often present and associated with an increased prevalence of gouty arthritis and tophi in CKD. It also acts as an independent factor in the progression of renal disease and cardiovascular risk factor as well. High uric acid levels induce vasoconstriction, inflammation and intrarenal generation of angiotensin II, all of which promote hypertension (Johnson *et al.*, 2005).

## CONCLUSION

It has been established by this study that dyslipidaemia and increased lipid peroxidation (oxidative stress) with abnormal antioxidant levels are common in CKD patients. Based on the findings in this study, it may seem reasonable to propose that therapeutic regimens aimed at strengthening the antioxidant defenses as well as normalizing lipid concentrations would be useful in protecting CKD patients against lipid peroxidation (oxidative stress) and any related complications.

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