Original Article

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Assessment of Albuminuria, Estimated-Glomerular Filtration Rate and Uric Acid as Markers for Chronic Kidney Disease among Family Members of Sudanese Renal Failure Patients on Hemodialysis

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ABSTRACT

Background: Chronic kidney disease (CKD) is a global public health problem that increased rapidly throughout the world, and it was recommended that it should be discovered earlier especially among high risk population. **Objective:** To assess albuminuria, estimated glomerular filtration rate (eGFR) and uric acid as markers for CKD among first degree relatives (FDRs) of hemodialysis patients. **Materials and methods:** This is an analytical, case control study conducted at Khartoum state during May 2015 to May 2018, targeting 135 FDRs of end stage renal disease (ESRD) Sudanese patients on hemodialysis and other 161 healthy individuals serving as control group. Their plasma was prepared and analyzed for creatinine, uric acid, calcium, phosphate, and alkaline phosphatase. Also spot random urine sample was collected and analyzed for creatinine and micro albumin, from which albumin to creatinine ratio (ACR) was calculated. The plasma parameters were analyzed by Mendray BS 200 auto analyzer, while urine parameters were analyzed by using Cobas auto analyzer. **Results:** The mean levels of ACR and urine micro albumin were significantly increased while the mean levels of e-GFR and urine creatinine were significantly reduced in FDRs when compared to control group (The means ± SD were: 10 ± 4.4, 123.1 ± 68.2, 93.1 ± 25.6 and153.3 ± 115.3 versus 0.92±0.10, 14.9±2.05, 99.4±22.5 and 190.3±108.8, the p values were: 0.024, 0.001, 0.027 and 0.005 respectively). But there were no significant differences between means levels of calcium, phosphorus, uric acid and alkaline phosphatase when compared in FDRs versus control group. The correlation analysis showed significant positive correlation of serum uric acid with serum creatinine(r= 0.587, P value = 0.000). **Conclusion:** Albuminuria which was detected by ACR was significantly increased among FDRs of hemodialysis patients, while the eGFR was reduced, hence they are prone to develop CKD.

Key words: *Chronic kidney disease, Albuminuria, ACR, eGFR, FDRs, Uric acid*

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Introduction:

Chronic kidney disease (CKD) is a global public health problem [(1)], that increasing rapidly worldwide [(2)]. The estimates are that CKD affect more than 50 million people including over 1.1 million having ESRD, with an addition of 7% annually [(2), (3)]. Screening surveys performed in the United States, Europe, Australia, Asia, Japan and China, showed that, the prevalence of CKD ranged between 6 -11%. The prevalence of CKD in developing countries is scarce, and there are no reliable statistics of the prevalence of CKD in the majority of African countries [(4), (5)]. In Sudan, as it reported by Hassan Abu Aisha in his pilot study at 2009 the prevalence range was 7.7 - 11% [(4)]. It was recommended that; the CKD should be discovered earlier, through renal functions assessment, using newly adopted estimated glomerular filtration rate (eGFR) and measurement of albuminuria especially at high risk individuals to prevent its progression to ESRD [(6) , (7), (8)].

Several studies showed that there was positive screening for CKD among genetic relatives of patients in hemodialysis, also it was demonstrated that; the presence of a family history of ESRD was a risk factor for developing CKD [(9), (10)]. This study was focused on immediate family members of hemodialysis patients, having family history of ESRD to evaluate their renal status in order to detect the presence of CKD focusing on albuminuria, e-GFR and uric acid which fulfilled many criteria for validated biomarker in CKD, and observational data indicated a relationship between serum uric acid and CKD prevalence and progression [(11)].

Materials and Methods

Study design and study subjects*:*

This is an analytical case control study, established at Khartoum State, between May, 2015 and May, 2018. including 135 individuals of first degree relatives of Sudanese patients with chronic end stage renal failure on hemodialysis attending different dialysis centers, and other 161 healthy volunteers that matched for, age and gender served as a control group. All participants with ages ranged between 17- 60 years were included in this study. Participants having diabetes, hypertension, cancer, thyroid dysfunction, some undergoing glucocorticoid or thyroid hormone therapy, HIV infection, pregnancy, and of age more than 60 years were excluded from this study. The individuals were requested to fill a questionnaire, which includes some personal and medical information. The height in cm, weight in kg was measured for them, and then the BMI was calculated. The participant was considered to have CKD, if he showed albuminuria level (ACR>30mg/gm) and/or e-GFR less than 60 ml/min/1.73m^2.

Ethical approval:

The study was approved by the Medical Research Committees of Alneelain University and by the Training and Research Committees at the Ministry of Health in Khartoum State. The aim of the study was explained to all participants then verbal and undersigned consent was taken.

Specimens Collection & Lab measurements*:*

A five ml of venous blood was collected from each volunteer by venipuncture technique, using sterile disposable syringe, and then was drained into plain blood vacutainer, the plasma was obtained and used for measurement of creatinine, calcium, phosphate, uric acid and alkaline phosphatase, which were measured by Mind ray BS200 auto analyzer. Also about 20 ml of mid-stream single random urine sample was collected for creatinine and micro-albumin measurement, which were measured by Cobas auto analyzer, then albumin-creatinine ratio(ACR) was calculated by Medic al ® Scy med calculator, and expressed in mg/gm, ACR >30mg/gm was considered as positive for albuminuria. e-GFR was calculated by MDRD and CKD-EPI equations (reduced GFR was detected when eGFR<60 ml/min/1.73m^2). Uric acid level more than or equal 7mg/dl was considered increased.

Statistical analysis:

Descriptive statistic was used to show the demographic data for study population, which were presented in form of frequencies, percentages and (Mean ±SD). Student t. test was used to compare between the two means. Correlation analysis was used to detect the association between uric acid on one side and ACR, eGFR and creatinine on the other side. The level of significance was detected when the p value was ≤ 0 .05. The analysis was performed using SPSS software program version 21.

Results:

Two hundred and sixty nine individuals participated in this study. 135 individuals were first degree relatives (FDRs) of Sudanese patients with ESRD on hemodialysis and other 161 individuals resembled the healthy control group. Table 1 shows the demographic data for FDRs and control group, table 2 shows the comparison of biochemical parameters means between family members and control group in which urine micro albumin, urine creatinine, ACR and GFR-EPI showed significant differences between FDRs and the control group, with means ± SD:(123.1 ± 68.2), (153.3 ± 115.3), (10 ± 4.4), and (93.1 ± 25.6) for FDRs versus (14.9 ± 2.05), (190.3 ± 108.8),(0.92 ± 0.1) and (99.4 ± 22.5) for control group, and the p. values were 0.001, 0.005, 0.024 and 0.027 respectively. But there are no significant differences between means levels of calcium, phosphorus, uric acid and alkaline phosphatase when compared in FDRs versus control group. The correlation analysis showed significant positive correlation of serum uric with serum creatinine (r = 0.587, p = 0.000) and insignificant positive correlation with ACR and e-GFR.

Table 1: Characteristic and demographic data for family members of hemodialysis patients and the control group

Variables	FDRs (n = 135)	Control (n = 161)
	Frequency (%) or (Mean ± SD)	**Frequency (%) or** (Mean ± SD)
Gender: N (%)		
Male	49 (36.0%)	85 (52.8%)
Female	86 (64.0%)	76 (47.2%)
Age : (Mean ± SD)	(32.27 ± 14.4)	(32.65 ± 13.5)
Origin: N (%)		
North	42 (31.1%)	17 (10.6%)
West	17 (12.6%)	78 (48.4%)
East	8 (5.9 %)	7 (4.3%)
Central	68 (50.4 %)	59 (36.4 %)
Education level: N (%)		
Primary	20 (14.8 %)	60 (37.2 %)
Secondary	48 (35.6 %)	50 (31.1%)
Graduated	67 (49.6%)	51 (31.7 %)
Smoking: N (%)		
Smokers	8 (5.9 %)	7 (4.3 %)
Non smokers	127 (94.1 %)	154 (95.7 %)
BMI: (Mean ± SD)	(25.9 ± 6.62)	(23.7 ± 5.5)
Albuminuria: N (%)	23 (17 %)	7 (5 %)
Uric acid ≥ 7 mg/dl	14 (10.4 %)	17 (10.6 %)
Uric acid < 7 mg/dl	121 (89.6 %)	144 (89.4 %)
Estimated - GFR: N (%)		
≤ 60 ml/min/1.73m2	6 (4.4 %)	4 (2.5 %)
> 60 ml/min/1.73m2	129 (95.6 %)	157 (97.5 %)

Table 2: Comparison of biochemical parameters between family members of hemodialysis patients and control group

Parameters	Relatives (Mean ± SD)	Control (Mean ± SD)	*P-value*
ACR (mg/mmol)	10.0 ± 4.4	0.92±0.10	0.024
ACR (mg/gm)	88.8 ± 4.4	65.6 ± 7.2	0.036
U. microalbmin	123.1 ± 68.2	14.9 ± 2.05	0.001
U. Creatinine	153.3 ± 115.3	190.3 ± 108.8	0.005
Serum creatinine	0.94 ± 0.58	0.89 ± 0.20	0.269
Serum uric acid	4.68 ± 1.64	4.84 ± 1.51	0.407
Serum calcium	9.48 ± 1.5	9.56 ± 0.98	0.626
S. phosphate	3.55 ± 0.82	3.56 ± 0.83	0.924
ALP (U/L)	115.1 ± 73.8	130.1 ± 104.5	0.150
GFR- MDRD	85.1 ± 24.3	89.6 ± 22.7	0.104
GFR – EPI	93.1 ± 25.6	99.4 ± 22.5	0.027
Cr.C (ml/min)	102.3±35.5	100.1 ± 29.2	0.565

Table 3: Comparison of means of ACR, GFR and serum creatinine based on uric acid levels among patients relatives and control group

Parameters	Patients relatives		*P-value*
	Uric acid <7 (mg/dl) (Mean ± SD)	Uric acid >7(mg/dl) (Mean ± SD)	
ACR (mg/gm.)	18.15 ± 14.57	18.86 ± 15.58	0.920
ACR (mg/mmol)	9.76 ± 5.2	12.60 ± 4.29	0.845
GFR- MDRD	85.1 ± 24.4	85.29 ± 23.7	0.976
GFR - EPI	93.41 ± 25.8	90.79 ± 24.1	0.718
Serum creatinine	0.86 ± 0.18	1.10 ± 0.23	0.000
Control group			
ACR (mg/gm.)	8.60 ± 6.82	3.45 ± 2.39	0.000
ACR (mg/mmol)	0.97 ± 0.93	0.40 ± 0.26	0.098
GFR- MDRD	89.6 ± 23.11	89.1 ± 19.42	0.938
GFR - EPI	99.8 ± 22.94	94.4 ± 18.46	0.372
Serum creatinine	0.94 ± 0.61	0.99 ± 0.15	0.770

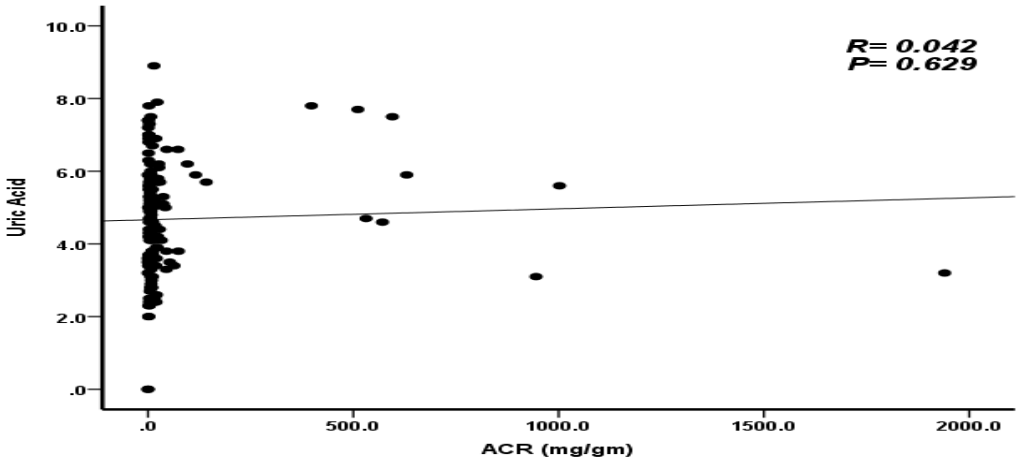

Figure (1): Correlation between serum uric acid and ACR

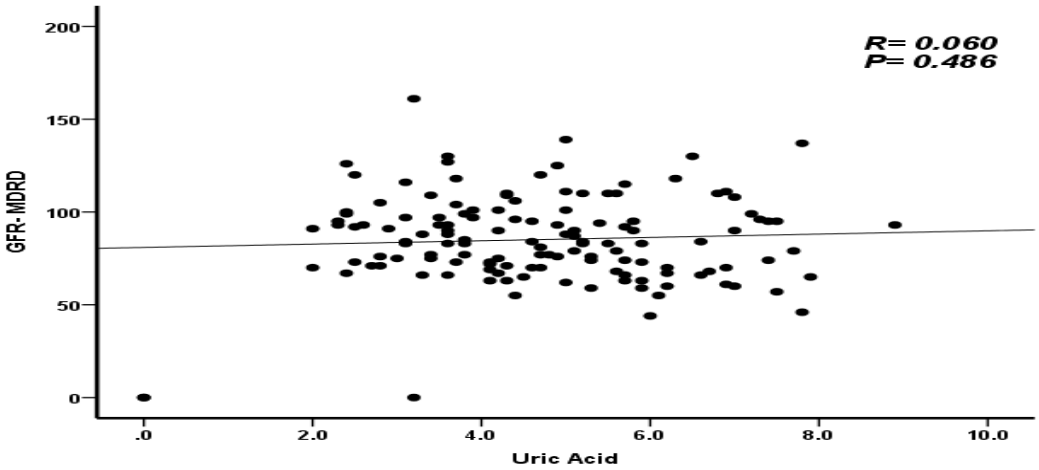

Figure (2): Correlation between serum uric acid and estimated-GFR

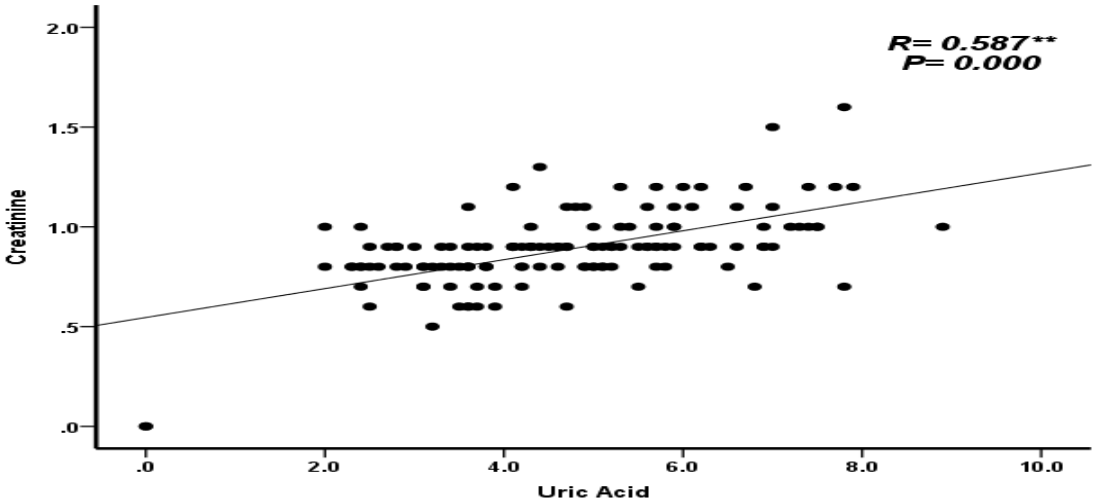

Figure (3): Correlation between serum uric acid and serum creatinine

DISCUSSION

In this study high prevalence of albuminuria (17%) was detected among FDRs against (5%) in control group. On the other hand the comparison of some biochemical parameters (ACR, urine creatinine and micro albumin, eGFR, serum creatinine, serum calcium, serum phosphate and serum alkaline phosphatase means between FDRs and control group showed significant differences. ACR and urine micro albumin were significantly increased while e-GFR and urine creatinine were significantly reduced among FDRs, these differences are considered to be logical and consistent with the information that is proven to indicate that these markers are affected among high risk groups to indicate presence of CKD, and many studies have shown that these parameters were affected by either increased or decreased as appropriate [12], [13].

The high prevalence of albuminuria and increase level of ACR which indicate the albuminuria was reported by different studies that targeting FDRs of CKD patients, such as study of Jer Chia Tsai, 2010 who reported high prevalence (10.7%) of albuminuria in hemodialysis relatives versus (4.1%) for control group [14], and Y R Raj who reported very high prevalence of albuminuria which is actually detected by increased level of ACR among 230 FDRs individuals [15]. This study goes in this direction and reported 17 % prevalence of albuminuria in FDRs compared to 5% for control group. On the other side the e-GFR showed significant decrease among FDRs, this is also in agreement with Y R Raj [15].

Although the uric acid is considered as important factor in progression of CKD among high risk groups, as it affect the kidneys by different mechanisms including: pre-glomerular arterial disease, renal inflammation and hyper tension and induction of proinflammatory cytokines. But this study showed no significant difference in the mean level of uric acid between FDRs and control group, no similar study assesses uric acid in FDRs, but to somehow this finding was in agreement with Kang D H *et al*, who found no association between uric acid and CKD. [16] Contrary to some studies that demonstrated this association in diabetics, normal, and hypertensive individuals, most of these studies found that hyper-uricemia to be an independent predictor for incidence CKD [17], [18], [19]. However the mean levels of ACR, GFR and creatinine in both FDRs and control group were compared based on uric acid levels which were divided into increased uric acid level (uric acid ≥ 7mg/dl) and not increased level (uric acid < 7mg/dl). Based on this division the serum creatinine mean level was significantly increased in case of increased uric acid (mean ± SD: 1.1 ± 0.23 vs. 0.86 ± 0.18 and the P.value = 0.00), but the mean levels of ACR was insignificantly increased, on the other hand the GFR was insignificantly reduced in case of increased uric acid level. Moreover among FDRs the correlation analysis showed significant positive correlation of serum uric with serum creatinine and insignificant positive correlation with ACR and e-GFR. These findings were in

agreement with several studies that targeting other high risk groups rather than FDRs, which demonstrated increased level of serum creatinine and ACR and reduced GFR, when they compare the means according to uric acid levels, these studies include study of international society of nephrology in Taiwan that showed significant correlation of serum uric acid with urinary ACR and calculated creatinine clearance and detected significant increase uric acid in diabetics with micro and macro albumin-uria(20).

Conclusion:

In conclusion the ACR was significantly increased among FDRs of Sudanese ESRD patients while e-GFR was reduced, and there was a positive significant correlation of uric acid with creatinine, these finding confirm that; the FDRS at risk and should be monitored for CKD.

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