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Correlation between Kidd blood group (Jk) and renal function tests in the End Stage of Chronic Kidney Disease (ESCKD) patients

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ABSTRACT

Background and Objective: Along with erythrocytes, the Kidd glycoprotein exists in the kidney, where it enables the kidney to accumulate an elevated urea concentration, which is required for the kidney to produce concentrated urine. The primary objective of this research is to look for Kidd genes (Jk) in patients with end-stage chronic kidney disease. *Materials and Methods:* This is a prospective cross-sectional study of 200 patients with chronic renal failure in Khartoum in the period from June 2018 to November 2021. The patients were being monitored in clinic and the majority of them were nearing the end of their chronic kidney disease (ESCKD). *Results:* When the positive and negative Jk Kidd antigens in ESCKD patients were compared, it was discovered that there were significant differences in urea (P-value 0.001), creatinine (P-value 0.001) and uric acid (P-value 0.04), but no difference in sodium or potassium. *Conclusion:* Kidd blood group influences serum urea, creatinine and uric acid levels significantly. This effect was observed in different Kidd blood group antigens, including Jka+, Jkb+ and Jka+b+. This means that the Jk group is important in estimating the severity of ESCKD; this discovery could be useful in determining dialysis time and treatment response.

Keywords: Phenotype, Kidd antigens (Jk), renal function test, end stage chronic kidney disease

1. INTRODUCTION

Kidney failure is a medical condition in which the kidneys perform poorly to filter waste from the plasma. The two main types are acute kidney injury, which is often reversible with proper treatment and chronic kidney disease.

Acute renal disease is a quickly progressive decline of kidney function defined by oliguria (Klein et al., 2018) and dialysis may be needed to connect the time gap required for treating these underlying causes. Chronic kidney disease (CKD) also can progress slowly and with few symptoms. CKD could be the lengthy result of an irreversible acute disease or a constituent of disease progression (Moore et al., 2012; Alreshidi et al., 2022).

The Kidd proteins are the red cell urea transporter. It is found in the membrane and carry the urea in red cells while preserving the red cells s osmotic stability and form. Also is demonstrated in the kidney, allowing it to accumulate an elevated urea concentration, which is important for kidney to generate concentrated urine Individuals who do not generate the Kidd glycoprotein have a lower ability to concentrate urine but are otherwise healthy, with normal erythrocyte shape and life span. SLC14A1 (Solute carrier family 14, member 1) is a urea transporter gene located on chromosome 18 (18q12-q21). The gene is divided into 11 exons spanning more than 30kb of DNA. Exons 1-3 and a portion of exon 4 do not encode the mature Kidd protein; exons 4-11 do. The Jka and Jkb antigens are the outcome of two alleles co-dominantly inherited. An 838GA transition results in a D280N substitution, which causes the Jka/Jkb polymorphism (Halawani et al., 2022).

The Jk (a-b-) phenotype is normally inherited as a recessive trait, with a variety of mutations implicated (Irshaid et al., 2000). The finding that RBCs from Jk (a-b-) individuals lacking Kidd antigens were more resistant to lysis in aqueous 2M urea raised the possibility that urea transport of human RBCs was related to Kidd blood group antigens (Barros, 2017; Lawicki et al., 2017). Cells have a urea transport deformity, but their permeability to chloride, water and ethylene glycol is normal (Yang, 2014). The primary goal of this study is to evaluate the Kidd antigens (Jk) found in (ESCKD) patients.

2. MATERIAL AND METHODS

Study design

The study is a prospective cross-sectional study of patients with chronic renal failure in Khartoum state during Jun 2018 to Nov 2021.

Population of the study

This study, which took place in Khartoum hospitals and dialysis centers, included 200 ESCKD patients (Soba University Hospital, Princess Nora Pediatric Dialysis Center, Ibn Sina Hospital, Ahmed Gasim Teaching Hospital, Jafer Ibn Auf Pediatric Hospital and The Sudanese Kidney Transplant Association). The patients were being monitored in clinic and they all had ESCKD.

Inclusion criteria

Patients in Khartoum state who have had ESCKD for more than six months.

Exclusion criteria

The study excluded all patients with acute renal failure who were on dialysis.

Sample collection

To detect renal function, blood specimens were taken as 5 ml and divided into 2 ml for blood groups and PCR and 3 ml for result serum that was free of hemolysis and gross lipemia Kidd blood group determination via tube technique. Kidd antigens are protein chains located on red blood cell surfaces. Anti-Jk^a and Anti-Jk^b Mono-Type are monoclonal antisera used in tube and microplate tests to detect Jk^a and Jk^b antigens on red cells. Grifols Diagnosis, based in Barcelona, Spain, produces monoclonal antibodies against Jk^a and Jk^b.

Renal function tests

All ESCKD patients and donor samples were tested for urea, creatinine, uric acid, sodium and potassium at the Sudanese Kidney Transplant Association using the Cobas C311, Roche, Grenzach-Wyhlen, Germany.

Molecular analysis

DNA extraction (G-DEX Genomic DNA extraction Kit from Therm Fisher scientific Rochester, NY, USA) for both the Jk^a and Jk^b PCR assays, the following profile was used.

PCR Kidd blood group

The master mix was made according to the recipe above for the number of samples to be amplified, plus one extra for petting errors and 15 l of the master mix was added to each 0.2 l PCR tube, followed by 5 l of DNA in each tube for each sample incubated at the PCR temperature profile in the BIO-RAD thermo-cycler, California, USA.

Data analysis

The data was managed using the Statistical Package for Social Sciences (SPSS version 21.0). SPSS was used for analysis and the Pearson Chi-square test for statistical significance (P value) and the Z test for two proportions at 95% confidence level were used to test for significant differences in Kidd relationships observed in this study, with the result revealing statistical significance at P value< 0.05.

3. RESULTS

Renal function tests were used to identify the variation and resemblance of Kidd genes in ESCKD with positivity and negativity. The percentage of Kidd blood group in chronic kidney disease patients and healthy group was found to be 49% for Jk^{a-} kidd genes and 50% for Jk^{a+} genes, 40% for Jk^{a-b-} kidd genes and 44% for Jka^{+b+} genes and 6% for Jk^{b-} kidd genes (Figure 1). Polymerase chain reaction was used to demonstrate the polymorphism of the Kidd genotype and was run in 3%agarose gel electrophoresis (Figure 2). Kidd blood group determination using two distinct techniques Traditional serology antisera used to detect Jk^{a+}, Jk^{b+} and Jk^{a+b+} by anti-Jk^{a} and anti-Jk^{b} were nearly identical to the molecular technique polymerase chain reaction (PCR) (Table 1).

When assessing the variation in Jk^{a+} Kidd gees in ESCKD patients, it was discovered that there were significant differences in urea with P-value 0.001, creatinine values with P-value 0.001 and uric acid with P-value 0.04, on the other hand there were no significant differences (Table 2).

Jk^{b} Kidd genes gathering was demonstrated extraordinary (noteworthy variety) in urea (P-value <0.001), creatinine (P-value < 0.001) and uric acid (P-value 0.05). Generally, comparability (unimportant variety) was found in sodium and Potassium (p value ≥ 0.05) that appeared in (Table 3).

When Jk^{a-b-} and Jk^{a+b+} Kidd genes compared, the unique (critical variety) speak to obviously in urea (P-value < 0.001), creatinine separately with P-value < 0.001, different tests show insignificant results such as sodium, potassium and uric acid (Table 4).

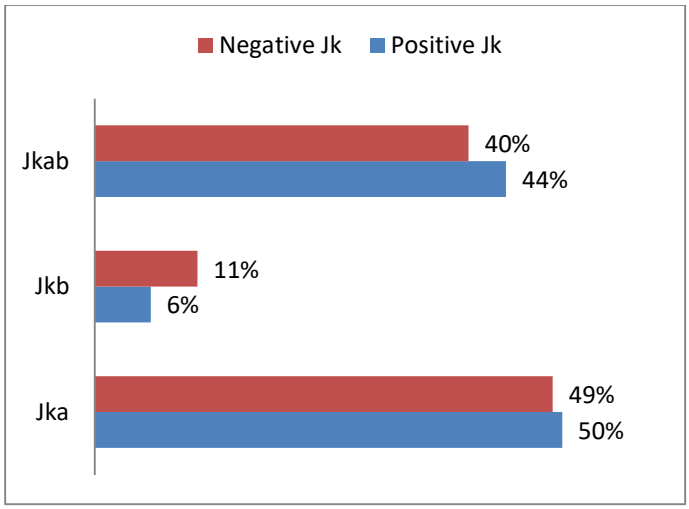

Figure 1 The percentage of positive and negative Kidd antigen phenotypes in chronic kidney disease patients

Table 1 Shows the identical results of renal function test in Kidd group using conventional serology method and PCR

	Urea mg/dl	Creatinine mg/dl	Sodium mmol/l	Potassium mmol/l	Uric acid mg/dl
Jk^{a+}	98±25.7	98±25.7	98±25.7	98±25.7	98±25.7
Jk^{b+}	107±27	107±27	107±27	107±27	107±27
Jk^{a+b+}	104±23.7	104±23.7	104±23.7	104±23.7	104±23.7

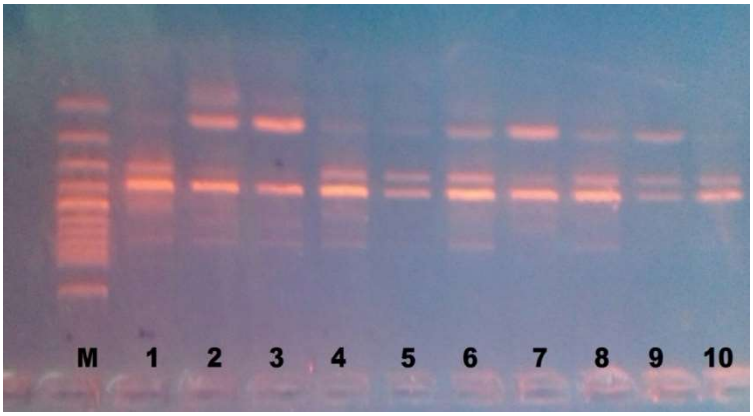

Figure 2 DNA polymorphism of Kidd antigen in 3% agarose gel electrophoresis M represents molecular size marker 100bp, Jk-781-F3/ Jka864-F1 primer mixes and Jkb843-R2/ JK-943-R3 primer mixes were used to amplification Lane 1,4,5,10 display Jk (a+b-), lane 2-3 show Jk (a-b+), lane 6,7,8,9 illustrate Jk (a+b+), lane 5, 7and 9 show Jk (a+b-) and lane 10 shows Jk (a-b-)

Table 2 The mean± SD of renal function tests among patients with ESCKD for individuals with negative Jk^a and positive Jk^a Kidd blood group

Renal function tests	Jk^{a-} Mean± SD	Jk^{a+} Mean± SD	P value
Urea mg/dl	130±57.7	98±25.7	0. 001*
Creatinine mg/dl	9.3±4.6	5.8±2.49	0. 001*
Sodium mmol/l	135±5.0	138±2.4	0.13
Potassium mmol/l	4.5±0.88	4.0±0.28	0.16
Uric acid mg/dl	7.5±2.5	5.3±2.1	0.04*

Table 3 The mean± SD of renal function tests among patients with ESCKD in negative Jk^b individuals with positive Jk^b blood group

Renal function tests	Jk^{b-} Mean± SD	Jk^{b+} Mean± SD	P value
Urea mg/dl	143±54	107±27	0.001*
Creatinine mg/dl	10.4±4.2	6.7±2.08	0.001*
Sodium mmol/l	134±4.8	137±2.7	0.72
Potssium mmol/l	4.5±1.0	3.7±0.38	0.41
Uric acid mg/dl	7.0±2.9	4.6±0.9	0.05*

Table 4 The mean± SD of renal function tests among patients with ESCKD negative Jk^{a-b-} individual with positive Jk^{a+b+} blood group

Renal function tests	Jk^{a-b-} Mean± SD	Jk^{a+b+} Mean± SD	P value
Urea mg/dl	119±47.1	104±23.7	0.001*
Creatinine mg/dl	9.4±3.7	4.7±1.16	0.001*
Sodium mmol/l	134±4.25	139±5.5	0.89
Potssium mmol/l	4.5±0.81	3.8±0.36	0.64
Uric acid mg/dl	6.7±2.2	5.1±0.8	0.16

4. DISCUSSION

Due to its unknown etiology, chronic renal failure is most complicated diseases. It can also occur as a side effect of other chronic diseases such as diabetes mellitus, hypertension and cardiac disease, eventually leading to ESRD (Obrador et al., 2017). In this study, we hypothesize that the Kidd blood group, as a member of the urea transport family-B1, is associated with chronic renal failure (Sands, 2003).

When we started this research in November 2019, there was no research on Kidd blood group and chronic kidney disease. In present study the percentage of the Kidd genes in Sudanese people was 50 % (a+ b-), then 44 % (a+b+) and finally 6% (a-b+). Previous study was conducted by Capriolli et al., (2017) discovered no differences in the frequency distribution of Kidd phenotypes between chronic patients and blood donors. Jk (a- b+) = 22.3 and 27.2 %; Jk (a + b-) = 30.5 and 24.3 %; Jk (a + b+) = 47.25 and 48.4%, respectively, that quitely similar to our study.

Jk (a+ b+) concur: Jk (a+ b-): 50 percent Caucasians, 41 % Blacks, 49% Asians JK (a-b+): 26% Caucasians, 51% Blacks, 23% Asians, JK (a-b-): 26% Caucasians, 8% Blacks, 27% Asians, JK (a-b-): 26% Caucasians, 8% Blacks, 27% Asians, JK (a-b-) Rare in most populations, but found in 0.9% of Polynesians (Reid et al., 2012).

In this research, the relationship between Kidd group and renal function test results in ESCKD patients, in Jka Kidd genes we discovered a significant difference between Jka+ and Jka- groups in urea, creatinine and uric acid, but not in sodium and potassium, and in Jkb+ and Jkb- Kidd genes we found a significant difference in urea, creatinine and uric acid, but not in sodium and potassium. According to previous study, sodium and potassium concentrations in serum of ESCKD patients were determined and the results show no significant differences in serum of pre-hemodialysis patients when compared to the control group (Al-Abachi et al., 2012). Creatinine and urea biochemical analysis in renal failure hemo dialysis patients agree with our study that statistically significant differences in mean creatinine and urea values were noticed in all age groups in comparison with the normal ranges (Amin et al., 2014). All significant differences in urea and creatinine are commonly present, but the cause of insignificant sodium and potassium differences is due to the dialysis maintenance supplement.

Kidd blood group determination using two distinct techniques traditional serology antisera to detect Jk^a, Jk^b, Jk^{ab} were almost identical to molecular technique (PCR), There were ten samples in serology technique represented as Jk^a but in molecular technique (PCR) found as Jk^{ab} but all Jkb found similar in both technique, indicating that there could be weak Jk^b in these ten different or certainly molecular technique (PCR) was more sensitive than serology technique, however the difference was insignificant.

Ramsey et al., (2016) clarified this by discovering anti-Jkb in solid-phase red cell adherence testing 12 days after transfusing 7 units of red cells. The genomic and cDNA sequencing of the JK*B allele demonstrated a novel single-nucleotide deletion of c.1038G in exon 11, predicting a frame shift and premature stop (p.Thr346Thrfs*5) after translation of nearly 90% of the expressed exons 4-11. This allele's tentative name is JK*02N.14.

More research should be done, such as sequencing the samples that show Jka in serology and Jkab in PCR, to determine the cause of immature genes expressing Jkb and the impact of these phenomena on diseases. Furthermore, more research should be conducted to distinguish the relationship between Kidd genes and levels of renal function test in ESCKD, especially the reason for Jkb Kidd blood collection being the most increased level in serum urea and creatinine.

5. CONCLUSION

Kidd blood group has significant effect in serum urea, creatinine and uric acid levels. This effect was similar in different Kidd blood group antigens Jk^{a+}, Jk^{b+}, Jk^{a+b+}. This means that Jk group play critical role in estimated the severity of ESCKD; this finding may be useful in determining dialysis time and treatment response.

Significance statement

This study discovers that Kidd blood group antigens have potential effect in serum urea, creatinine and uric acid levels. Jk genes have crucial function in ESCKD. This study will help the researcher to uncover the importance of Jk blood group in establishing dialysis time and therapy response.

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Authors Contributions

AOIA, FMHG and MHAA conceived and designed the study. AOIA, FMHG, MHAA, RHE and HAW wrote the initial draft. KAM, AKS and AMB wrote the final draft of the manuscript. All authors critically read, revised and approved the final draft of the manuscript submitted to the journal.

Ethical approval

This study was approved by the Research and Ethics Committee of the Ibn Sina Specialized Hospital (ethical approval number M/A/S/B/70).

Informed consent

Oral informed consent was obtained from all individual participants included in the study.

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Conflict of interest

The authors declare that there is no conflict of interests.

Data and materials availability

All data sets collected during this study are available upon reasonable request from the corresponding author.

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