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Research Article

### Molecular Characterization of Kidd Antigens Polymorphism (Jk) among Sudanese patients with Chronic Renal Failure in Khartoum State - Sudan

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#### ABSTRACT

**Background:** The Kidd glycoprotein is expressed in the kidney, where it enables the kidney to build up a high concentration of urea, which is needed for the kidney to produce concentrated urine. The urea transport across Kidd null RBC membranes is ~1000 times slower than across normal RBC membrane. Chronic kidney disease develops slowly and, initially, show few symptoms. CKD can be the long term consequence of irreversible acute disease or part of a disease progression. The most common causes of chronic renal failure are related to poorly controlled diabetes, poorly controlled high blood pressure.

**Objective:** the aim of this study was to assess the association between the Kidd antigen polymorphism and chronic kidney disease, in Sudan.

**Results:** The distribution of kidd blood group between chronic kidneydisease patient and control group were (49%) and (50%) for Jk (a + b-), 40% and 44% for Jk (a + b+) and 11% and 6% Jk (a - b+) respectively. also there were different in ten samples represented genomic typing (Jk ab ) but phenotyping represented as (Jka).

**Conclusion:** There were no obvious effects of kidd antigens polymorphism on kidney function .

**Keywords:** Kidd blood group, Genomic typing, Phenotyping, Chronic kidney disease.

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#### 1. INTRODUCTION

The kidneys are two bean-shaped organs found in vertebrates. They are located on the left and right in the back of the abdominal cavity. The kidneys play key roles in body function, not only by filtering the blood and getting rid of waste products, but also by balancing the electrolyte levels in the body, controlling blood pressure, and stimulating the production of red blood cells <sup>1</sup>. The Kidd glycoprotein is expressed in the kidney, where it enables the kidney to build up a high concentration of urea, which is needed for the kidney to produce concentrated urine. The *SLC14A1* gene (Solute carrier family 14, member 1) is a member of the urea-transporter gene family and is located on chromosome 18 (18q12-q21) <sup>1</sup>. Kidd antigens are located on a red blood cell urea transporter (aka human urea transporter 11-

HUT11 or UT-B1) <sup>2</sup>. The Jk<sup>a</sup>/Jk<sup>b</sup> polymorphism results from a 838G→A transition, resulting in an D280N substitution <sup>1</sup>.The Jk(a-b-) phenotype has no clinical defect, although two individuals with this phenotype have been reported to have mild urine-concentrating defects. The urea transport across Kidd null RBC membranes is ~1000 times slower than across normal RBC membrane <sup>3</sup>.

Chronic kidney disease (CKD) develops slowly and, initially, show few symptoms. CKD can be the long term consequence of irreversible acute disease or part of a disease progression <sup>4</sup>. The most common causes of chronic renal failure are related to poorly controlled diabetes, poorly controlled high blood pressure. The was no study done in Sudan relationship between the Kidd antigens and chronic kidney disease , the aim of this study was to detect the association of kidd

polymorphism phenotypes and genotype with the chronic kidney disease in Khartoum state.

**2. MATERIALS AND METHODS**

**2.1 Study design:**

A prospective cross-sectional case control study was conducted to assess the polymorphism of Kidd Antigens (JK), phenotypes and most probable genotypes among patients with Chronic Renal Failure in Khartoum State during the period of June 2016 to November 2018.

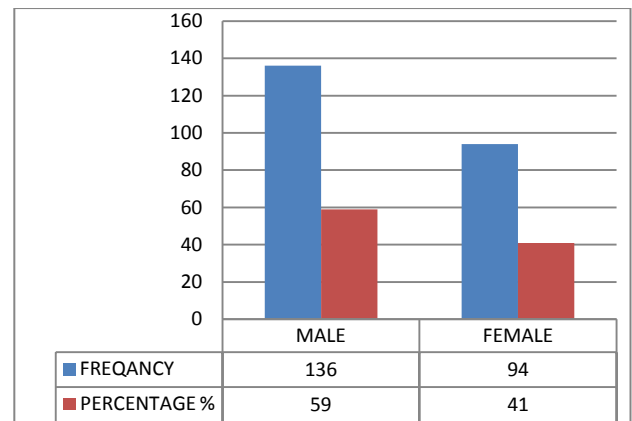
**2.2 Sample size:**

The sample size was calculated using software known as the survey system, available at <http://www.Surveystem.com.sscalc.htm>. The system inertly relies on the equation:  $n = z^2pq / d^2$  (n = sample size; z = the standard normal deviate, usually set at 1.96, which corresponds to the level of the 95% confidence level; p = the proportion to the target population i.e. percentage of the studied group, which is 0.11 in this study; q = 1.0 - p).

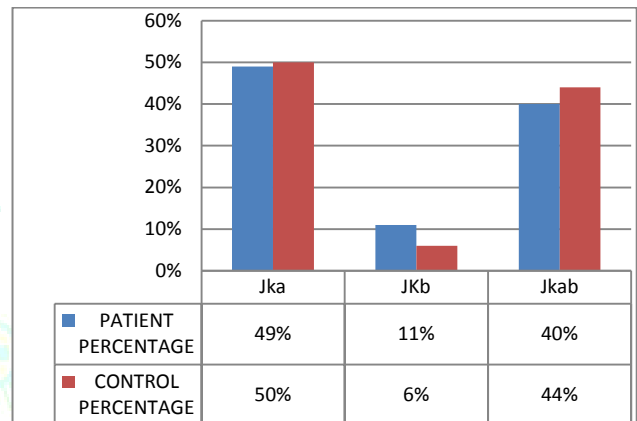
**2.3 Sample collection and analysis:**

Following standard protocol blood samples were collected from all patient and control group (5ml) in ethylene diamine tetra acetic acid (K2EDTA) anticoagulant. Kidd blood group was tested immediately by using serology technique and remain of samples used to extract DNA by G-DEX Genomic DNA extraction Kit protocol. After amplification, the PCR products and a DNA ladder size marker were loaded into the sample wells to aid in fragment size determination. PCR fragments were detected by size in the agarose gel. Electrophoresis was performed by using Electrophoresis power supply at 70 volts for 40 min at room temperature, and the DNA bands were visualized and documented using a UV trans-illuminator documentation system.

**3. RESULT**



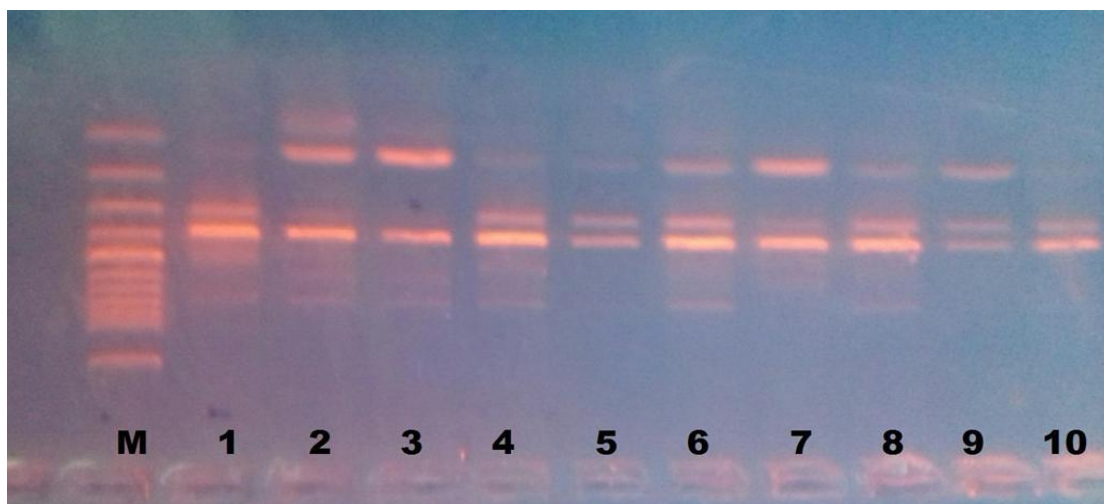
**Figure 1:** incidence of chronic Kidney disease according to Sex among case group.



**Figure 2:** Comparison the Kidd blood group percentage between case and control group.

**Table 1:** Different in Kidd blood group antigen between conventional serology group and Polymerase Chain Reaction (PCR) (n=460)

	JK <sup>a</sup>	JK <sup>b</sup>	JK <sup>ab</sup>
Conventional serology	49%	11%	40%
PCR	45%	11%	44%



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

#### 4. DISCUSSION

Distribution of sex in chronic kidney disease found the males group were slight more exposed to chronic kidney disease and ESRD than female but statistically insignificant different in gender group (male, female). The difference in control group found male more than female because social reasons that not mean female donor not accepted to donation but male more common donation.

The frequency of Kidd blood group phenotype in relation with chronic kidney disease Jk(a + b-), Jk(a + b+), Jk(a - b+) respectively that almost similar to distribution of control group that statistically found insignificant, in other hands there was no Kidd null represented that mean no relationship between Kidd null and chronic kidney disease. Caprioli et al. observed that no differences were between the Kidd phenotypes frequency distribution between patients with chronic kidney disease 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 agree with us<sup>5</sup>.

There were ten samples in phenotype serology technique represent as Jk<sup>a</sup> but in genotype molecular technique (PCR) found as Jk<sup>ab</sup> but all Jk<sup>b</sup>. found similar in both technique, suggest that may be there where weak Jk<sup>b</sup> in this ten different or actually molecular technique (PCR) was more sensitive than serology technique, but there were insignificant different between two technique. That was clarified with Ramsey *et al.* When investigated a 64-year-old Caucasian woman of Polish-Czech descent who developed anti-Jkb detected in solid-phase RBC adherence testing within 12 days after 7 units of RBCs were transfused. Her Kidd typing was JK\*A/JK\*B based on the Jka/Jkb single nucleotide polymorphism in exon 9 (c.838G>A, p.Asp280Asn). Genomic analysis and cDNA sequencing of her JK\*B allele revealed 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 percent of the expressed exons 4-11. This allele has been provisionally named JK\*02N.14<sup>6</sup>.

#### 5. CONCLUSION

Main distribution of chronic kidney disease in age 40-59 years old that may relate to hypertension or diabetes mellitus, on the other hand there were insignificant slight different observed in effect of chronic kidney disease on male rather than female.

No relationship between Kidd blood group polymorphism with chronic kidney disease because similar distribution with control group especially Kidd null that not detected in this study, in compared with result of PCR technique found some samples different from serology technique because premature stop of cDNA JK<sup>b</sup> that can lead to not appear by serology technique.

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