# Decoding Kidd (JK) Blood System Phenotype in Kenya: Unveiling the Diversity with Cutting-Edge Next-Generation Sequencing Technology

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**Abstract**

**Background:** The Kidd blood group system plays a crucial role in transfusion medicine, and understanding the molecular basis of Kidd red cell alleles is essential for effective blood matching and preventing alloimmunization. In Africa there are limited reports on the phenotype distribution for the 45 blood group systems recognized by the ISBT. Most of the blood group determination is via serological methods however, only the major blood groups antigens are identified (ABO & RhD) despite the evidence of some of the rare blood group antigens such as Kidd types being associated with clinical significance in transfusions, pregnancy and transplantation. In adverse complicated undetermined cases, genomic typing has become useful in determining the involved red cell variant. The study sought to investigate the genotypic and phenotypic distribution of Kidd blood group alleles in the blood donor population to enhance safety in transfusion practice.

**Methods:** The study site was Kenya National Blood Transfusion Service and Red Cross lifeblood Brisbane, experimental design was employed, sample size determination was by Slovin's Formula Sampling Techniques, and purposeful sampling method was employed to achieve a representative sample. Molecular genotyping were employed to determine red cell genotypes and phenotypes. Sequencing was performed using the Illumina MiSeq platform with 12-plex pools and standard 300-cycle V2 chemistry.

**Results:** Of the 119 samples sequenced, thirteen JK genotype combinations were identified in the cohort, with the following predicted phenotype distribution: Jk(a+b-) 45.5%, Jk(a+b+) 25.7%, Jk(a+wb+) or Jk(a+b+w) 9.9%, Jk(a-b+) 9.4%, Jk(a+wb-) 5.8%, Jk(a+wb-) or Jk(a+b-) 2.1%, and Jk(a+wb+) 1.6%. These frequencies are consistent with global and sub-Saharan Kidd frequencies, highlighting the importance of population-specific data. Accurate genotyping and phenotype matching are essential to ensure safe and effective transfusions.

**Conclusion:** The study findings elucidated the genotypes that are responsible for the Kidd thirteen phenotypes in the identified Kenyan population. This data forms the basis or evidence to advocate for a blood group reference laboratory and a red cell panel that is African specific.

**Keywords:** Kidd blood group, alleles, JK (a, b), antigens, genotyping, phenotype distribution, transfusion medicine

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## 1. Introduction

Blood groups are molecules that are organized on the erythrocytes (red blood cells) surface membranes. They are either polypeptides, glycolipids or carbohydrate. They constitute portions of the erythrocytes cover, allow communication with the immune system and give rise to phenotypes. The Kidd blood group system plays a crucial role in transfusion medicine, and understanding the molecular basis of Kidd red cell alleles is essential for effective blood matching and preventing alloimmunization. The Kidd blood group system, comprising the Jk(a) and Jk(b) antigens, is one of the clinically significant blood group systems in transfusion medicine. The molecular basis of Kidd red cell alleles influences antigen expression, making accurate genotyping crucial for appropriate blood matching. The Kidd antigens are encoded by the SLC14A1 gene on chromosome 18q12.1 and exhibit diverse allele variations worldwide. Global studies have revealed variations in Kidd allele frequencies across populations, with some regions showing high frequencies of specific phenotypes. For instance, sub-Saharan Africa has been reported to have a high frequency of Jk (a+b-) phenotype individuals, accounting for approximately 40-50% of the population. Understanding the distribution and properties of Kidd alleles is essential for optimizing transfusion strategies, preventing alloimmunization, and ensuring the safety and efficacy of blood transfusions.

## 2. Materials and methods

### 2.1 Study site

The research was conducted at the Kenya National Blood Transfusion Service (KNBTS), which serves as a pivotal institution in the country's healthcare system, responsible for ensuring an adequate and safe supply of blood for medical purposes. KNBTS operates through various regional centers and blood donation drives across Kenya, facilitating blood collection, testing, processing, and distribution.

### 2.2 Target population

The study focused on volunteer donors who contributed blood to KNBTS. Additionally, the research included donated blood samples that were leftover from routine blood collection procedures. These samples are valuable resources for scientific investigation, providing insights into various aspects

 

of blood physiology, transfusion medicine, and disease detection.

**2.3 Study design**

An experimental design type was employed for this study. Experimental designs are characterized by the manipulation of independent variables to observe their effects on dependent variables. In the context of blood transfusion research, experimental designs allow researchers to investigate interventions, treatments, or procedural changes aimed at improving blood safety and efficacy.

**2.4 Sample size determination**

The study employed purposeful sampling method to achieve the sample size

n = N/(1 + Ne2)

Where:

n = Number of samples=120

N = Total population = 5%

e = Error tolerance (level)

n = 120(total samples)

N = 5% (0.005) (CI)

120/(1+120*0.05)=120/(1+121*0.05*0.05)

=120/1.3025=92.1305

Sample size =92

Samples collected in 4mls ETDA tubes, weak D positive and D negative, non-reactive for transfusion transmission infections (TTIs), with no haemolysis were selected for the study

**2.5 Sampling procedure**

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**2.6 Data collection, assurance and control**

In this study, the integrity and volume of samples (4mls of blood samples collected in ETDA were assessed for consistency and conformity; data quality management was adhered to during data collection, storage, processing, analysis and publication. The collection processes involved selection and acquisition of blood donor samples. Unique codes were generated for labeling the selected samples which were entered into an excel sheet ensuring the right codes were indicated correctly. These unique codes were used and maintained throughout the sample handling and processing (manual genomic DNA extraction), samples shipment, quantification, sequencing, annotating, analysis, result interpretation, publication and storage.

**2.7 Data Management, analysis and presentation**

Sequencing data Read mapping and variant prediction was performed on board the MiSeq using BWA-MEM (Li H. 2013) and GATK (McKenna A et al., 2010), generating BAM and VCF files respectively. BAM and VCF files were submitted to the RBCeq webserver for analysis and reporting of blood group variants, alleles and phenotypes (Jadhao et al., 2022) and results displayed in table and figure forms.

**2.8 Ethical Considerations**

Study was conducted in accordance with the ethical guidelines and regulations of Mount Kenya University Ethical Review Committee, Ministry of Health Kenya, Australia Red Cross and National Commission for Science, Technology and Innovation (NACOSTI).

**3. Results and Discussion**

Thirteen JK genotype combinations were detected in cohort (Figure 1). The predicted phenotype distribution of the Kidd blood group system was as follows: Jk(a+b-) 45.5%, Jk(a+b+) 25.7%, Jk(a+wb+) or Jk(a+b+w) 9.9%, Jk(a-b+) 9.4%, Jk(a+wb-) 5.8%, Jk(a+wb-) or Jk(a+b-) 2.1%, and Jk(a+wb+) 1.6%. These findings are consistent with global and sub-Saharan Kidd frequencies, indicating the representation of diverse alleles in the studied population.

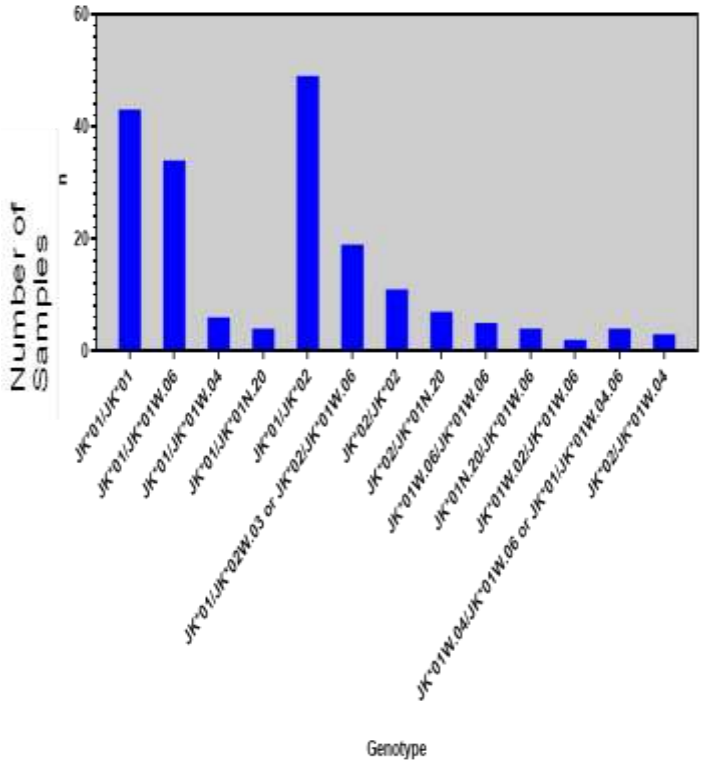


**Fig 1: Showing the JK genotypes/Alleles**

 

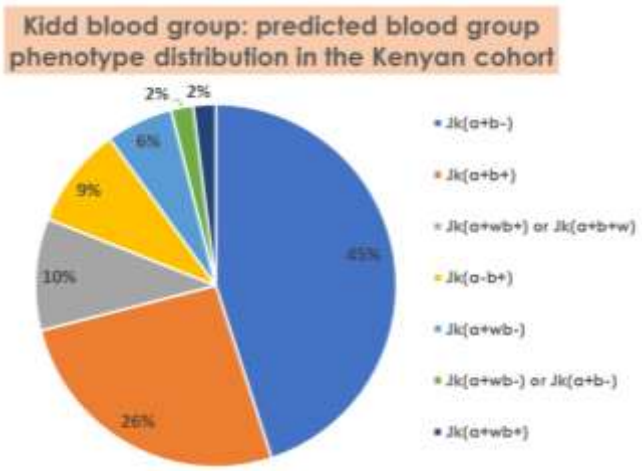


**Fig 2: Showing the JK predicated phenotypes in percentages**

## 4. Discussion

The observed distribution of Kidd genotypes and phenotypes in this cohort aligns with previous studies in other populations. The high frequency of the Jk(a+b-) phenotype is consistent with the known prevalence in sub-Saharan Africa. The diversity of JK genotype combinations reflects the complex nature of Kidd allele variations and the importance of accurate genotyping in transfusion medicine Moreover, the results highlight the significance of population-specific data when considering transfusion practices. Understanding the distribution of Kidd alleles in different populations allows for tailored transfusion strategies and minimizes the risk of alloimmunization. Additionally, the genotypic and phenotypic information obtained from study can contribute to the prediction of rare phenotypes and improve donor selection for individuals with specific Kidd antigen requirements. The findings also emphasize the importance of accurate genotyping in transfusion practice. Precise identification of Kidd alleles and phenotypes ensures compatibility between donors and recipients, reducing the risk of adverse reactions and promoting transfusion safety. Incorporating advanced genotyping techniques, such as high-throughput next-generation sequencing, can enhance the efficiency and accuracy of Kidd allele identification, particularly in cases where rare variants or novel alleles are present.

The molecular basis of Kidd alleles provides valuable insights into antigen expression properties. Variations in allele sequences can lead to altered antigen phenotypes and affect transfusion compatibility. The identification of novel variants, as demonstrated in study, underscores the ongoing need for comprehensive characterization of Kidd alleles. Continued research in area will contribute to expanding this understanding of the Kidd blood group system and enable the development of improved strategies for blood matching and transfusion practice.

## Conclusion

In cohort, the Kidd phenotype distribution pattern was consistent with that reported elsewhere in Africa of Jk (a+b-)>Jk (a+b+)>Jk(a-b+)[1, 2]. Frequency pattern is also observed in Sub-Saharan Africa including Ghana, Mali, Nigeria, Burkina Faso[2,3,4] and an Egyptian population[2,5]. Surprisingly 3 genotypes were associated with weak Kidd antigen expression and such samples can be missed by serological typing. Variants encoding Kidd alleles had similar frequencies to reports for the African population, however variants for weak alleles JK*01W.02 and JK*01W.03 had lower frequencies. No null variants were detected, as expected for an African population[1]. The study provides the basis for further research into tools and infrastructures that can be used for extended red cell serological and genotyping in the KNBTS, to improve transfusion practices and develop a genomic reference library.

## Recommendations

Based on the findings of study, the following recommendations are proposed; continued monitoring and analysis of Kidd allele frequencies in diverse populations to ensure up-to-date and accurate transfusion practices. Implementation of advanced genotyping techniques, such as high-throughput next-generation sequencing, to improve the accuracy and efficiency of Kidd allele identification. Collaboration between transfusion centers and research institutions to establish comprehensive databases of Kidd allele variations and their associated phenotypes. Need to engage the training institutions to review existing training curriculums in line with current technological advancement. Capacity building of healthcare professionals involved in transfusion medicine to raise awareness of the importance of accurate genotyping and phenotype matching in blood transfusions and also to review the training curriculum to align with current technological advancement. Further investigation into the functional significance of Kidd allele variations and their impact on antigen expression and transfusion compatibility.

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**Conflict of Interest:**

The authors declare no conflicts of interest.

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