Short communication

Molecular organisation of Kell (KEL) red blood cell variants among voluntary blood donors at the National Blood Grouping Testing Laboratory, Kenya

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A variant is an alternative nucleotide located at a specific region of a gene. 48 genes encode for human red cell blood group systems. Variants within these genes encode for alleles, which can be highly polymorphic. The blood group gene loci jointly display all types of inherited variants to include single nucleotide variants (SNVs), insertions/deletions (indels), and structural variants. In Africa, there is limited information on the red cell variants. The aim of the study was to determine the incidence of Kell red blood cell variants among the Kenyans. Blood donor’s samples that were used for routine grouping process were identified for this study. Next generation sequencing method was employed to predict the Kell red cell variants in blood donor samples. Descriptive statistics was applied and the result was presented in form of tables. The study reveals that Kell system has six variants with two major phenotypes and genotypes. The most common phenotype genotyped was KEL2 (KEL*02/KEL*02) 79% (85/108) followed by KEL2 KEL6 KEL7 (KEL*02.06/KEL*02) 16.7% (18/108). The rest were found to be of low frequency and all were associated with KEL2. The study recommends an extended study with a large sample size and introduction of extended phenotyping to aid Kell antigens identification in the donor population.

Key words: Kell, variant, allele, KEL, KEL*02/KEL*02, molecular, genome, gene, next generation sequencing.

INTRODUCTION

A variant is an alternative nucleotide whose location is at a specific region within a gene or genome. A gene variant is a permanent change in the DNA sequence that makes up a gene. 48 genes encode for human red cell blood

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Table 1. The frequency and association of predicted KELL phenotypes and variants.

<table>
<thead>
<tr>
<th>System</th>
<th>Genotype</th>
<th>Predicated Phenotype</th>
<th>n</th>
<th>Frequency (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>KEL</td>
<td>KEL<em>02/KEL</em>02</td>
<td>KEL2</td>
<td>85</td>
<td>78.7</td>
</tr>
<tr>
<td></td>
<td>KEL<em>02.06/KEL</em>02</td>
<td>KEL2 KEL6 KEL7</td>
<td>18</td>
<td>16.67</td>
</tr>
<tr>
<td></td>
<td>KEL<em>02/KEL</em>02.00.02</td>
<td>KEL2</td>
<td>2</td>
<td>1.85%</td>
</tr>
<tr>
<td></td>
<td>KEL<em>02.19/KEL</em>02</td>
<td>KEL2 KEL19</td>
<td>1</td>
<td>0.93%</td>
</tr>
<tr>
<td></td>
<td>KEL<em>02/KEL</em>02.02.21/</td>
<td>KEL2 KEL3 KEL4 KEL21</td>
<td>1</td>
<td>0.93%</td>
</tr>
<tr>
<td></td>
<td>KEL<em>02.19/KEL</em>02.02.06</td>
<td>KEL2 KEL6 KEL7 KEL19</td>
<td>1</td>
<td>0.93%</td>
</tr>
</tbody>
</table>

Frequency of KEL phenotypes inferred from the genotype data presented in this report. KEL*02/KEL*02 predicting the k (KEL2) phenotype was the most common genotype. Variants at other locations in the KEL protein were most frequently associated with the KEL*02/KEL*02 variant at the K/k site.

Source: Authors

A total of 108 anonymous left over blood samples collected in EDTA vacutainers were identified, selected and prepared for molecular genotyping. Manual Genomic DNA extraction was accomplished by using QIAamp whole blood DNA mini kit (250 51106) as per manufacturer's instructions (Qaigen Germany). Library preparation was performed using a custom blood grouping enrichment panel (Roulis et al., 2020), and the Illumina DNA prep Enrichment protocol as per manufacturer's instructions (Illumina Inc., San Diego, CA, USA).

Inclusion criteria

Samples collected in 4 ml EDTA tubes that were non-reactive for transfusion transmission infections (TTIs), with no haemolysis.

Exclusion criteria

All samples that failed the required inclusion criteria in preparation for the manual DNA extraction.

RESULTS

The study reveals that Kell system has six variants with two major phenotypes and genotypes. The most common phenotype was KEL2 (KEL*02/KEL*02) 79% (85/108) followed by KEL2, KEL6, KEL7 (KEL*02.06/KEL*02) 16.7% (18/108). The rest were found to be of low frequency and all were associated with KEL2 as shown in Table 1.

DISCUSSION

The study reveals that Kell system has six variants and their predicted phenotypes. Most common was KEL2 (KEL*02/KEL*02) 85 (79%) followed by KEL2 KEL6 KEL7 (KEL*02.06/KEL*02) 18 (16.7%). The rest were found to be of low frequency 2-1% and all were associated with KEL2 (k+).

The study outcome has shown that indeed there is heterogeneity in the distribution patterns of Kell variants and phenotypes globally. It has also shown that k+ is the most occurring in the donor population of Kenya. This k+
is implicated in red cell alloimmunisation, thrombocytopenia, and fetomaternal hemorrhage, new natal and infants breeding and organ rejections, thus it is of clinical significance in the transfusion and transplantation therapy. Having this information is very important for supporting resolving complex cases associated with red cell therapy. Comparing the results with similar studies, there is variance in different populations as observed by Dean (2005). KEL2 (k+) was found to be 91% in the white population, and 98% in the people of black colour. KEL1 (K) was recorded as having a low frequency of 0.2% in whites and very rare in the dark population. KEL1/KEL2 (K+k+) 8.8% in whites and 2% in people of black colour (Dean, 2005).

In the Chinese community, K (KEL1) frequency was 3.5% and k (KEL2) 99.97% (Liu et al., 2012). In Indian study, KEL2 (k+) frequency is 96.5%, whites is 91% and dark colour (blacks) is 98% and 100% in Chinese populace (Makroo et al., 2013). In Northern India, the incidence of Kell types have shown as KEL1 (K) 2.57% whereas KEL2 (k+) as 97.43% (Mangwana et al., 2021; Thakral et al., 2010).

In the Japanese population, the study revealed KEL*01/KEL*02 as 0.48%; KEL*02/KEL*02 as 99.52%, KEL*02 as 99.76% and KEL*01.01 as 0.024% (Flóres et al., 2013). Study from Saudi Arabia indicates that KEL2 (k+ Cellano) was the most common (100%) whereas KEL1 (K) recorded 8% (Amani et al., 2020).

A study from Morocco, KEL1 (K) is 0.19% whereas KEL2 is 99.80% (Benahadi et al., 2014). Similar study conducted in Southern Brazil documented the frequencies as KEL*02/KEL*02: 94 (75%), KEL*01/KEL*02: 5.0%, while KEL*01/KEL*01 was 0.25% (Guelsin et al., 2011; Flóres et al., 2014).

**Conclusion**

The study has revealed the organization of Kell red cell variants in the donor population of Kenya. It has also shown that k+ (KEL2) is the most prevalent phenotype. These findings are also the first of this kind in Kenya. In addition to confirmed presence of Kell red cell variants, valuable knowledge is presented on the basis for improved investigations of these variants. The generated evidence is useful in forming a base for the preparation of red cell antigen panels, advocacy for the initiation for extended phenotyping and in the generation of a red cell genomic library/gene reference for Kenya and her neighboring countries.

**RECOMMENDATION**

Considering the clinical implications associated with Kell antigens (transfusion reactions, infants breeding, thrombocytopenia and organ rejections); this outcome is very beneficial in resolving cases associated with adverse transfusion reaction especially in ongoing and massively transfused patients (Sickle cells, cancer cases among others) matching and as a base for a reference gene bank in Kenya. The results of this study in combination with others related to other blood groups red cell variants will be useful in instituting a blood grouping molecular reference laboratory in Kenya and support for East Africa community. It will also be useful evidence while considering the use of extended phenotyping in blood bank and tissue transplant laboratories both in Kenya and East Africa in the identification of rare phenotypes that are of clinical significance in transfusion and transplantation medicine. More research on this field in Kenya and East Africa will augment the gene data base and support the blood grouping laboratories in the investigations of complicated complex cases as well as enhance collaborations nationally and internationally.

**CONFLICT OF INTERESTS**

The authors have not declared any conflict of interests.

**ACKNOWLEDGEMENTS**

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**ABBREVIATIONS**

EDTA, Ethylenediaminetetraacetic acid; HDFN, haemolytic disease of the fetus and the new born; HTR, haemolytic transfusion reaction; KNBTS, Kenya National Blood Transfusion Service; RBBCs, red blood cells; SNVs, single nucleotide variants; MKU, Mount Kenya University; NGS, next generation sequencing.

**REFERENCES**


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