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Original Article



# Prevalence of Kell Ag in Pregnant Women with Thalassemia Minor or Intermedia Beta in Medical Centers Affiliated to Shiraz University of Medical Sciences in 2019-2020

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## Abstract

**Background:** Kell Ag, the main antigen of kell system has the greatest antigenicity after Rh antigen and the associated antibodies are very important. These antibodies are mainly of the Ig G class and can cause side effects like Hemolytic disease of the Fetus and Newborn (HDFN) or Hemolytic Transfusion Reaction (HTR), especially in patients with chronic blood transfusions such as thalassemia patients. The aim of this study was to evaluate Kell antigen in pregnant women with thalassemia minor and intermedia and to determine the appropriate strategy for transfusion in this group of patients

**Methods:** This study is a cross-sectional study on pregnant women with thalassemia minor or intermedia. The samples were taken from patients of Shahid Motahari clinic and those with positive antigen were selected and statistically analyzed.

**Results:** The results showed that from the 64 patients who entered this study, the results of kell ag of 58 patients were negative and 6 were positive. Therefore, 91% of the pregnant women with beta thalassemia minor or intermedia were negative for ag kell and 9% were positive.

**Conclusion:** In summary, the results of this study indicated that a large percentage of pregnant women with beta-thalassemia minor or intermediate are Kell-negative, and due to the complications of alloimmunization, screening of pack cells and pregnant patients is very important.

**Keywords:** Beta thalassemia, Blood transfusion, Female, Pregnancy, Transfusion reaction

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## Introduction

Kell Ag (kell1) is the main antigen of the kell system (1). This antigen is made by the kell gene, which is located on chromosome seven. Unlike RH and ABO antigens, Kell's antigens are located on the red blood cell membrane glycoproteins. Kell Ag has the highest antigenicity after Rh Ag and associated antibodies are very important. These antibodies are mainly of the IgG class and can cause complications such as neonatal or Hemolytic Disease of the Fetus and Newborn (HDFN) or Hemolytic Transfusion-induced Reactions (HTR), especially in patients with chronic blood transfusions such as thalassemia.

According to studies, two-thirds of the alloantibodies produced in the body of thalassemia patients belong to the Rh or Kell subgroup (2). Thalassemia is a group of disorders in which the ratio of alpha globulin to beta production changes and these changes cause the destruction of red blood cells in the bone marrow and blood flow. It is the most common hemoglobinopathy in the world and is prevalent in parts of Africa, South Asia and the Mediterranean region. Mutations in beta globulin genes can reduce or not express this gene, and the severity of the disease or anemia is related to normal beta globulin levels. Beta thalassemia is divided into two categories: transfusion-dependent thalassemia (beta thalassemia major) and non-transfusion-dependent thalassemia (thalassemia minor and intermedia). It is noticeable that patients with non-transfusion dependent thalassemia in conditions such as specific infections or pregnancy and surgery may need a blood transfusion. For example, due to physiological anemia (dilute anemia) in pregnancy, anemia worsens and the chances of blood transfusions increase (3,4). According to surveys. Beta thalassemia is the most common inherited anemia in Iran, 10% of people living along the Caspian Sea and the Persian Gulf and about eight to ten percent of people living in Fars province have thalassemia (5,6).

In a study in Iran on Kell Ag by Farhoudi and Eftekhari in 1994, the frequency of *K* gene was detected at about 3.4% (7). In another study conducted in 2016 by Shahverdi and Moghadam, K – k + with 95% prevalence was recognized as the most common phenotype of the kell system in Iran (8). Evaluation of the Kell antigen in donated blood bags used in adult thalassemia clinic indicated that less than 4% of donors were positive for Kell antigen (2). These studies show that the majority of the subjects were negative for Kell antigen. Kell Ag is abundant in different geographical areas and different breeds. The prevalence of K antigen in northern Europe is approximately 9%. About 9% of whites and 2% of blacks are positive for K (9). Also, in a study in West Africa, the frequency of this antigen was about 0.77%. In the Netherlands, the prevalence of this antigen was reported to be 7.4%. The prevalence of this antigen is reported to be 5% in Senegal and 8% in Bangladesh (10-13). In a study conducted by Azarkeivan *et al*, 835 patients with thalassemia were evaluated for alloimmunization. 22 children and 79 adults were positive for the antibody. In 34 patients, anti-D was positive. This study showed a significant relationship between previous blood transfusions and alloimmunization (14). In the case report by Giannacopoulou *et al*, a pregnant woman who received a transfusion at 18 weeks developed alloimmunization during pregnancy and gave birth to a baby with severe anemia and hemoglobin 3 (15).

In a study by Sirchia *et al* in Italy, 1,435 patients with thalassemia major were enrolled in 19 centers, of which 6% were under 6 years old, 63% were between 6 and 15 years old, 19% were over 15 years old, and 41% had splenectomy. In this study, 5.2% of the patients had red cell alloantibodies, of which over half had more than one type of alloantibody and more than a quarter had more than two types of alloantibody. Among 136 alloantibodies obtained from 74 patients, the highest rates belonged to Rh, Kell, Kidd, and Duffy systems, respectively (16). In a study conducted by Karimi *et al* in Shiraz, blood samples were collected from 711 patients with beta thalassemia and evaluated for auto and alloantibodies. The most common types of antibodies were Anti-kell and Anti-Rh, respectively. In this study, the importance of cross match blood bags in terms of minor blood groups, especially kell and Rh, before transfusion were emphasized (17). A 2004 study in Malaysia examined 63 patients with thalassemia for alloantibodies and autoantibodies, and found autoantibodies in only one patient (18).

The aim of this study was to evaluate Kell antigen in pregnant women with minor and intermedia thalassemia and to determine the appropriate strategy

for transfusion in this group of patients. To the best our knowledge no study has been conducted in this field so far. Therefore, due to the lack of antigen testing in pregnant women and the high prevalence of thalassemia in the country and also risks of incompatible blood transfusions in patients with thalassemia, this study is justified.

## Materials and Methods

This study is a cross-sectional study performed by sampling the pregnant women with thalassemia minor or intermedia who referred to Motahhari clinic in 2019-2020. Minor thalassemia patients are diagnosed as having Microcytic Anemia, Hb A2 >3.5%, increased HbF (up to 30%) and normal Ferritin. Intermedia thalassemia diagnosis is based on normal Ferritin, increased RDW and HbF, splenomegally, and anisopoikilocytosis (19).

Sample size of the study was 64. The method of investigation of the population was through census. Samples were collected in tubes containing anticoagulants (EDTA, ACD). The test was performed as quickly as possible, using a Kell-mono-AEK4 and Kell-mono-M556 kit, otherwise the sample was kept at 2-8 °C, then a suspension of two to three percent of RBC was prepared in isotonic saline with a drop of Anti Kell IgM mixed and incubated for 10 to 15 minutes, and after one minute the sample was centrifuged for agglutination.

After receiving the test results, people with positive antigen were selected and entered in Excel software. The collected data were analyzed by IBM SPSS Statistics 22 (IBM Corp, Armonk, New York, USA) after descriptive evaluation.

## Results

Results show that out of the 64 patients who were entered in this study, the result of kell Ag was 58 negative samples and 6 positive samples. In other words, 91 percent of the pregnant women with beta thalassemia minor or intermedia were negative for kell Ag and 9 percent were positive. The age range of the patients varied from 20 to 35 years old (median age of 26).

## Discussion

Due to the high prevalence of thalassemia in the country and the fact that the antibodies of this system, which are mainly of the Ig G class and cause complications such as HDFN or reactions caused by blood transfusion (HTR), it is important to test kell Ag in pregnant women with thalassemia minor or intermediate prior to blood transfusions. Previous studies by Farhoudi and Eftekhari showed that the frequency of *K* gene on 291857 blood donors from 24 provinces of the country was about 3.4% (7). In another study conducted by Shahverdi and Moghaddam, K – k + with 95% prevalence was identified as the most common phenotype of the Kell system in Iran. The frequency of K + k + was approximately 4.8% (8). Also, in a study conducted to investigate the prevalence of Kell antigen in donated blood bags used in the clinic of adult thalassemia patients, less than 4% of the donors were positive for Kell antigen (2). The results of these studies indicate that compared to the present study, a lower percentage of subjects were positive for Kell antigen. This may be due to the large number of samples studied in previous studies and the fact that in this study, the focus was solely on pregnant women with thalassemia minor and intermedia.

The major limitation of our trial was the limited number of patients who entered in this study. Considering the high prevalence of thalassemia in the country and its implications, it is suggested that this study be conducted in a larger group of patients.

## Conclusion

In summary, the results of this study showed that a large percentage of pregnant women with beta-thalassemia minor or intermediate are Kell-negative, and due to the complications of alloimmunization, screening of pack cells and pregnant patients is very important.

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This study was approved by the ethics committee of Shiraz University of Medical Sciences (Ethics code: IR.SUMS.MED.REC.1400.243). We would like to thank all those who helped us in the implementation of the project. Authors would also like to appreciate the constructive comments of the anonymous reviewers which improved the quality of the manuscript.

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