

# Study of Transfusion Practices in Hereditary Anemia Patients Receiving Blood Transfusions at RAS Al Khaimah

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**Abstract:** *The population of the United Arab Emirates (UAE) is diverse, less than 20% are UAE nationals. Within this small group a variety of single gene defects occur, of which hereditary anemia, especially beta [ $\beta$ ]-thalassemia major; disorder of globin gene expression is one of the most prevalent. This is a transfusion-dependent severe anemia requiring lifelong blood transfusions to maintain life. It is also a major health problem in United Arab Emirates. Because of consanguinity, there are many homozygous thalassemia subjects who need special follow up and present a real health problem for their families and the community as a whole. A 5-year retrospective study from (2007-2011) of transfusion practices in hereditary anemia patients receiving multiple blood transfusions were done by analyzing the records from files of patients, available in blood bank of SAQR Hospital in Ras Al Khaimah. Our study comprised; 102 patients with hereditary anemia requiring blood transfusion, with the majority of cases being  $\beta$ -thalassemia major (60 cases). The age range of patients was 2-23 years, with mean being 10 years. It has been found more males (66%) being affected and consanguinity was found in 25% of parents of these patients and the major proportion of patients being Muslims and UAE nationals (62 cases). There was a linear relationship between the age of thalassemia major patients and total number of blood transfusions received and HCV positivity. Such a relation is expected, as due to worsening of the disease with progression of age.*

**Keywords:** Hepatitis C virus,  $\beta$ -thalassemia major, Hereditary anemia, Consanguinity

## 1. Introduction

The United Arab Emirates (UAE) is a federation of seven emirates situated on the Eastern Arabian Peninsula bordering Oman, Saudi Arabia and Qatar. In the north lie Iran and the Arabian Gulf. The population of the UAE is diverse is made up of immigrants from the Middle East, India, Pakistan, Iran and Europe. In the last two decades, the population of the UAE increased significantly of which only 20% are indigenous nationals. Approximately 80% of the UAE population is made up of expatriates, the majority of whom are Indians, Pakistanis, Iranians and Arab nationals.

The sharp increase in the UAE population is attributable to the rapid growth in economy, trade and tourism which attracted many foreign expats, to migrate to UAE for work. [1] The Ministry of Health, UAE rates genetic diseases as the fourth-highest cause of death in the country. There are 270 different kinds of these in the UAE alone, of which about 60 per cent are recessive disorders. One of the most plausible explanations for this observation would be the deep-rooted trend of consanguineous marriages widely practiced among the UAE Arab population. However, as children of consanguineous parents are more likely to enter into consanguineous marriages than children of non-consanguineous parents. As a result, attention should be directed towards identifying such families and providing them with genetic counseling and access to appropriate services [2].

In 2009 pre-marital genetic testing for couples with a family history of genetic diseases in cases of blood disorders like sickle cell anemia and thalassemia, was made compulsory. [1]. The UAEGDA's (UAE Genetic Diseases Association) first project was the nationally held campaign "UAE free Of Thalassemia by the Year 2012". The campaign aims to identify the carriers of Beta-Thalassemia and Sickle-cell Anemia throughout UAE's population, as part of the association's fight against Thalassemia, which comes in line with the United Arab Emirates federal governments' vision to free the country from new births of children with Thalassemia by the Year 2012.

### 1.1 Hereditary anemia can be due to:

Intrinsic causes can be due to Defects of red blood cell membrane production (as in hereditary spherocytosis and hereditary elliptocytosis or Defects in hemoglobin production (as in thalassemia, sickle-cell disease and congenital dyserythropoietic anemia) or Defective red cell metabolism (as in glucose-6-phosphate dehydrogenase deficiency and pyruvate kinase deficiency). Extrinsic causes are Acquired hemolytic anemia may be caused by immune-mediated causes, drugs and other miscellaneous causes [3].

### 1.2 $\beta$ -Thalassemia

Hereditary anemia, especially beta [ $\beta$ ]-thalassemia major; is a transfusion-dependent severe anemia requiring lifelong

blood transfusions to maintain life. It is also a major health problem in United Arab Emirates. Thalassemia ( $\beta$ -thal) is one of the most common single gene disorders affecting almost all the countries in the Mediterranean Basin, the Middle East, South East Asia, Far East, Australasia, America and Africa. [4, 5] It is characterized by the deficiency or absence of  $\beta$ -globin chain production. More than 200 different mutations have so far been reported that result in  $\beta$ -thalassemia (Huisman et al., 1997). According to the literature, recessively inherited disorders constitute the overwhelming majority of genetic disorders in the UAE population. One of the most plausible explanations for this observation would be the deep-rooted trend of consanguineous marriages widely practiced among the UAE Arab population. [1].

The word thalassemia comes from the Greek “thalassa”, sea referring to the Mediterranean and “haima”, blood which means blood disease of the sea. [ 6,7,8] The first description of severe thalassemia as a unique disorder was described in 1925 by a Detroit pediatrician “Thomas Cooley” who described a severe type of anemia in children of Italian origin which was later named after him(3).

The underlying abnormality in the thalassemia is thought to be absence or reduction in production of globin chain is affected by genetic mutation or deletion. This can cause red blood cells not to last as long in the blood, not be as effective transporting oxygen from the lungs to different parts of the body, or not be created at all. [ 9,10]. There are 2 types of thalassemia - alpha [ $\alpha$ ] when  $\alpha$  chain production is decreased relative to  $\beta$  and beta [ $\beta$ ] when  $\beta$ - chain production is decreased relative to  $\alpha$ -chain. [9, 5, 10]. The  $\beta$ -thalassemia major results in severe anemia, which needs regular blood transfusion. The combination of transfusion and chelating therapy has dramatically extended the life expectancy of thalassemic patients. [ 11,12] On the other hand, frequent blood transfusion in turn can lead to iron overload resulting in metabolic and endocrine abnormalities like hypogonadism, diabetes mellitus, hypothyroidism, hypoparathyroidism and zinc and copper deficiency [13,14,15] and transmission of infections such as HIV, HCV, and HBsAg which ultimately curtail their life span. [16, 17] On the other hand, inadequate transfusions lead to severe anemia and general fatigue and debility.

## 2. Aims and Objectives

A 5-year retrospective study from (2007-2011) of transfusion practices in hereditary anemia patients receiving multiple blood transfusions were done in Ras Al Khaimah. The information was obtained by analyzing the records from files of patients, available in blood bank of SAQR Hospital. Information regarding transfusion of blood components was obtained using the Blood Bank Database. Patient variables studied include age, gender, nationality, types and number of units of blood products transfused.

## 3. Results

Our study comprised: 102 patients with hereditary anemia requiring blood transfusion, with the majority of cases being  $\beta$ -thalassemia major (60cases) [Figure 1]. The age range of patients was 2-23 years, with mean being 10years. It has

been found more males (66%) being affected than females (34%) and consanguinity was found in 25% of parents of these patients and the major proportion of patients being Muslims and UAE nationals (62cases) [Figure 2]. There was a linear relationship between the age of thalassemia major patients and total number of blood transfusions received so far. Percentages for those receiving 2 and 3 transfusions per month were 43% and 50% respectively. We studied the prevalence of three important TTIs; 3% of patients were found to be HCV positive. Other two HIV, Hepatitis B were not found to be positive [Figure 3].

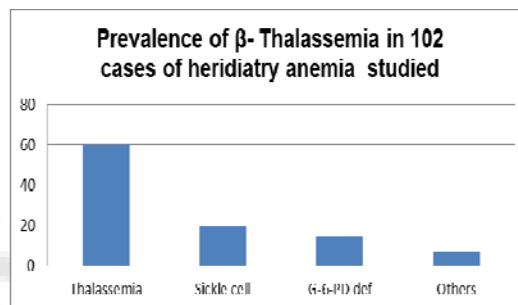


Figure 1: Prevalence of  $\beta$ -Thalassemia in 102 cases of hereditary anemia

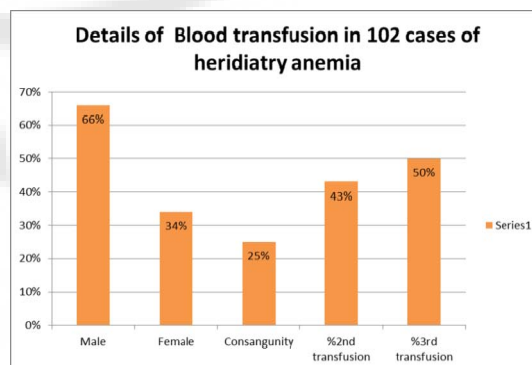


Figure 2: Blood transfusion details in 102 cases of hereditary anemia

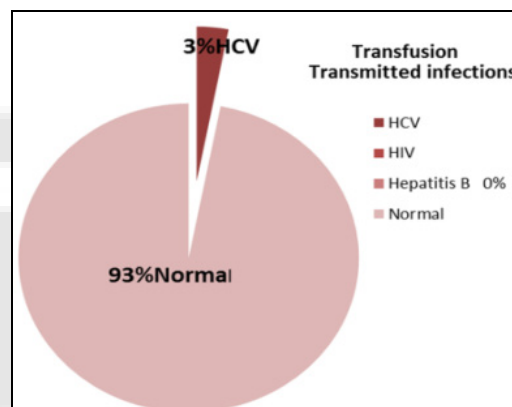


Figure 3: Prevalence of transfusion transmitted infections

## 4. Discussion

Thalassemia is a genetic disease that exhibits autosomal recessive inheritance, usually inherited from both parents who are usually symptom-free and are carriers. There is 25% chance of their child getting the disease, and 50% chance of the child being a carrier, and 25% chance of neither having the disease nor carrier state. Male or females get the disease equally.

The mutation analysis among the UAE national and expatriate  $\beta$ -thal patients clearly demonstrates that the UAE has the most heterogeneous  $\beta$ -thal population in the world with 50 different  $\beta$ -thal mutations reported to date. It is important to note that the majority of the  $\beta$ -thal mutations in the UAE are very severe. Most of the mutations are of severe  $\beta^0$ -thal type. The high degree of consanguinity, especially between the first cousin marriages, resulted in significant number of homozygotes who are on regular blood transfusion and chelation therapy. The high level of endogamy originates from centuries old socio-cultural and religious traditions in the Arab societies. Similar observations were made in the expatriate patient population most of whom are Muslims (Bener et al., 1996; Al-Gazali et al., 1997) [18]. The IVSI-5 (G-C) mutation was found to be present in 66%, while six other alleles occurred at the much lower frequencies. It is proposed that IVSI-5 and other Asian Indian mutations were introduced into the UAE by population migration. [18]

The [B+ IVSI-5 (G-C) mutation is interesting because it has been previously found in the Chinese [19] and Asian Indian populations [20] but has rarely been reported among Mediterranean Arabs. [20] With its high frequency in the UAE population, it may be that this allele was introduced into the UAE by gene flow from the Asian subcontinent. The recommended treatment for thalassemia major involves lifelong regular blood transfusions, usually administered every two to five weeks, to maintain the pre-transfusion hemoglobin level above 9–10.5g/dl.

#### 4.1 Appropriate goals of transfusion therapy to patients with thalassemia are

1. Use of donor erythrocytes with a normal recovery and half-life in the recipient
2. Achievement of appropriate hemoglobin level
3. Avoidance of adverse reactions, including transmission of infectious agents [21]
4. Packed red cells are obtained by leukoreduction of whole blood may be beneficial for patients with thalassemia [22].

In the present study majority usage of blood products was packed RBC's. The moderate transfusion regimen practiced correctly has been shown to ensure normal growth without excessive expansion of erythropoiesis, and with effective prevention of iron overload.[23] The inevitable consequence of regular life-saving transfusions in thalassemia major is the accumulation of excess iron within tissues. This causes progressive organ damage and dysfunction which, without treatment, can lead to an increase in morbidity and mortality. [24] For patients requiring regular blood transfusions, iron chelation may represent life-saving therapy. The optimal age for initiating iron chelation therapy in patients with severe thalassemia remains uncertain, although in theory it should begin as early as possible to prevent growth and developmental defects. Guidelines from the Thalassemia International Federation recommend that chelation therapy is initiated when serum ferritin levels reach approximately 1000 ng/mL, which usually occurs after the first 10 to 20 transfusions or around 2-3 years of age. [25, 26]

Patients receiving multiple transfusions are at a high risk for transfusion-associated diseases such as HIV, HBsAg, and

HCV, and thalassemic children form one such high-risk group. After the discovery of hepatitis C virus (HCV) in 1989 which is an enveloped virus of size 30-60 nm, and it gets transmitted through the parenteral route, it has proved to be the major cause of transfusion-associated hepatitis in the world. [27] Thus, chronic blood transfusion in thalassemic patients is a double-edged sword.

Since a large proportion of patients are HCV positive, we have analyzed our data by finding correlation between, HCV positivity and age, with age the number of blood transfusions received increases and so does the risk of acquiring TTIs. A linear relationship between age and HCV positivity was observed which indicates that the more the age of the patient the more is the chance of him/her being HCV positive.

A striking 3% of the patients are HCV positive which is significantly more than the prevalence in general population ( $P < 0.001$ ). The prevalence of HIV and HbsAg positivity is not statistically significant compared to the general population. With the increase in age, frequency of blood transfusions received per month also goes up. Such a relation is expected, as due to worsening of the disease with progression of age, the requirement for blood transfusions will increase.

A three-years prospective study from India by Choudhury et al.[28] observed that anti-HCV prevalence in the same number of thalassemia major patients was 23%, 30.7%, and 35.9% each year, respectively. The present study showed similar result as described by Choudhury et al.[28]. Prevalence studies have found that common infections occurring in thalassemic patients are Hepatitis C (2.2%-44%), followed by Hepatitis B (1.2%-7.4%) and HIV (0%-9%).[28,29,30,32] Karimi et al.[34] found the prevalence of HCV to be 15.7%, Prati et al [33] found it to be 14.8%, and Singh et al [30] found a high prevalence of HCV (20%) in multiply transfused thalassemia major patients. Results in the present study showed prevalence of HCV (3%).

## 5. Conclusions

The present study critically evaluated the current transfusion regime, multiple transfusions in terms of prevalence of three major transfusion-associated infections, namely infections by HIV, HCV, and HBV in thalassemia major patients enrolled at RAK in UAE. Majority usage of blood products was packed RBC's and 3% prevalence of HCV positivity among children. It is concluded that HCV is the current major problem in multi-transfused children with thalassemia major and more careful pretransfusion screening of blood for anti-HCV must be introduced in blood centers. It is suggested that efforts should be made to identify the real reasons for higher prevalence of HCV which might include comparison of ELISA kits of different manufacturers, rigid implementation of quality control measures while testing, and use of more specific and sensitive methods like NAT testing for HCV. In patients with thalassemia major, a remarkable improvement in life may be attributed to several key factors, including improved methods of blood transfusion, better understanding of iron toxicity, and a continuous improvement in iron chelation therapy. Recent progress in thalassemia major treatments that may improve life expectancy include hematopoietic stem cell

transplantation, [34, 35] the use of cardiac T2\* measurements and chelation regimens targeted on cardiac iron overload. [36, 37, 38]

## 6. Future Scope

A report by the Dubai-based Centre for Arab Genomic Studies (CAGS) in September 2009 found that Arabs have one of the world's highest rates of genetic disorders, of which nearly two-thirds are linked to consanguinity. Children born from these unions have an increased frequency of recessive disorders. Becoming aware of the health risks of consanguineous marriages, even though this is an ongoing debate, and a sensitive issue many feel that high school children should be informed about the health risks as well as the importance of genetic testing in order for them to make informed decisions one day.

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