Editorial

Ensuring the safety of blood donations from donors with thalassemia traits: addressing critical issues in Thailand

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Introduction

In Thailand, ensuring the safety and adequacy of the blood supply is vital for maintaining a healthcare system. However, a significant challenge lies in the high prevalence of thalassemia traits among potential blood donors. Approximately 30-40% of the Thai population carries some form of thalassemia, an inherited blood disorder affecting hemoglobin production.[1] While individuals with thalassemia traits are usually asymptomatic, their blood may pose unique safety concerns when used for transfusions. This article focuses on the safety concerns associated with blood donations from donors with thalassemia traits and explores the critical issues that blood banks in Thailand face when balancing donor safety and ensuring a sufficient blood supply.

Overview of thalassemia

Alpha thalassemia

Alpha thalassemia is caused by mutations or deletions in the genes that produce alpha-globin, one of the two protein chains that make up hemoglobin, the molecule in red blood cells responsible for transporting oxygen. Humans have four alpha-globin genes (two on each chromosome 16). The severity of alpha thalassemia depends on how many of these genes are affected:

1. **Silent carrier (1 gene deletion):** Only one of the four alpha-globin genes is missing. Individuals with this condition do not show symptoms and often have completely normal blood test results. These individuals are often undiagnosed unless they undergo genetic testing.

2. **Alpha thalassemia trait (2 gene deletions):** People with two missing alpha-globin genes are referred to as having the alpha thalassemia trait or being carriers. They may have mild anemia but usually no significant health problems. Their red blood cells tend to be smaller than normal (microcytic), with reduced hemoglobin (hypochromic), but they generally lead healthy lives without the need for treatment. However, their altered red blood cell morphology can affect their suitability as blood donors.

3. **Hemoglobin H disease (3 gene deletions):** If three of the four alpha-globin genes are missing, a person develops hemoglobin H disease. This condition causes moderate to severe anemia, as the body forms abnormal hemoglobin called hemoglobin H (composed of four beta-globin chains).[2,3] Hemoglobin H is unstable and does not transport oxygen effectively, leading to anemia, jaundice, and an enlarged spleen. These patients often require medical care, and their red blood cells are significantly abnormal, making them unsuitable as blood donors.[4]

4. **Alpha thalassemia major or hydrops fetalis (4 gene deletions):** This is the most severe form of alpha thalassemia, where all four alpha-globin genes are deleted. It usually results in the death of the fetus during pregnancy or shortly after birth.[5] In rare cases where the condition is diagnosed early, prenatal treatments like intrauterine transfusions may be needed, but the prognosis is generally poor.[3]

Beta thalassemia

Beta thalassemia is caused by mutations in the beta-globin gene on chromosome 11. Unlike alpha thalassemia, where gene deletions are common, beta thalassemia results from mutations that reduce or stop the production of beta-globin chains. The severity of beta

thalassemia depends on whether one or both beta-globin genes are affected, and whether the mutations reduce beta-globin production (beta-plus) or stop it entirely (beta-zero)[6]:

1. **Beta thalassemia trait (beta thalassemia minor):** This occurs when only one of the two beta-globin genes is mutated. People with beta thalassemia trait are typically asymptomatic or have mild anemia.[7] They may have microcytosis and hypochromia, but their overall health is generally unaffected. Despite their good health, the abnormal characteristics of their red blood cells can still pose challenges in blood donation, as they may not be suitable for patients with high oxygen demands or those requiring regular transfusions.

2. **Beta thalassemia intermedia:** This form of beta thalassemia occurs when both beta-globin genes are affected, but some beta-globin is still produced (usually a combination of beta-plus mutations). These individuals experience moderate anemia and may require occasional blood transfusions, particularly during periods of stress or illness.[2] While not as severe as beta thalassemia major, their red blood cells are abnormal, and they often suffer from complications such as splenomegaly and bone deformities. They are not considered suitable blood donors due to the significant changes in their blood.

3. **Beta thalassemia major (Cooley's anemia):** This is the most severe form of beta thalassemia, occurring when both beta-globin genes are either severely mutated or entirely non-functional (usually two beta-zero mutations). Individuals with beta thalassemia major are unable to produce enough beta-globin, leading to severe anemia that manifests within the first two years of life. They require regular blood transfusions throughout their lives to survive. Iron overload from frequent transfusions is a major complication, requiring chelation therapy to remove excess iron from the body. Patients with beta thalassemia major are recipients of blood transfusions and, therefore, not blood donors.

Compound heterozygosity: alpha and beta thalassemia

Compound heterozygosity refers to the inheritance of both alpha and beta thalassemia traits from different parents. While this is less common than inheriting either alpha or beta thalassemia alone, it presents a unique set of challenges. Individuals with compound heterozygosity usually have abnormal red blood cell morphology, with microcytosis (small red blood cells) and hypochromia (pale red blood cells). However, the severity of their symptoms can vary depending on the specific combination of alpha and beta thalassemia mutations they inherit.[1,3,4]

1. **Mild to moderate anemia:** Most compound heterozygous individuals experience mild to moderate anemia. While they may not require regular medical treatment, their red blood cells are often abnormal, which affects their ability to donate blood, as their blood may not provide the necessary oxygen-carrying capacity for recipients.

2. **Screening challenges:** Blood donation centers need to carefully screen donors with compound heterozygous thalassemia to ensure their red blood cells meet transfusion standards. This adds complexity to the already rigorous screening process required to maintain a safe and effective blood supply.

Importance of screening and implications for blood donation

Screening for thalassemia traits is critical to maintaining the quality of blood donations in Thailand, where a high percentage of the population carries alpha or beta thalassemia traits.[8] While people with thalassemia traits can donate blood, their donations are not always ideal for certain patients due to the altered structure and function of their red blood cells.[9]

1. **Blood component requirements:** Many patients, such as those undergoing surgeries, trauma victims, or individuals with severe anemia, require red blood cells that can deliver sufficient oxygen to tissues. Blood from donors with thalassemia traits may have a reduced capacity to do so, limiting its effectiveness in these cases.

2. Longer-term effects: Even if blood from a thalassemia trait donor is deemed safe for transfusion, the altered red blood cells may have a shorter lifespan in the recipient's circulation. This could necessitate more frequent transfusions for the patient, increasing the overall demand for blood.

Blood donation and thalassemia traits

The availability of safe and adequate blood supplies is a cornerstone of healthcare systems worldwide. In Thailand, a nation with a relatively high prevalence of thalassemia, managing the blood donation process presents a unique set of challenges. One of the most significant hurdles lies in determining the suitability of blood donations from individuals with thalassemia traits. Thalassemia is an inherited blood disorder that affects hemoglobin production, and while carriers of the condition, also known as individuals with thalassemia traits, are typically asymptomatic, the quality of their blood may not always meet the standards required for transfusion. This issue is particularly critical for patients with chronic conditions like thalassemia major, who depend on frequent and precise transfusions of healthy red blood cells (RBCs) to survive. The following outlines the key challenges posed by thalassemia carriers in maintaining a safe and efficient blood supply for such patients and other vulnerable populations in Thailand.[9]

1. Reduced hemoglobin content and its impact on transfusion

One of the primary challenges in accepting blood donations from thalassemia carriers is the reduced hemoglobin content typically observed in their red blood cells. Thalassemia carriers often have microcytic (smaller than normal) and hypochromic (paler than normal) RBCs. These abnormal red blood cells carry less hemoglobin, the protein responsible for transporting oxygen throughout the body.

For transfusion recipients, particularly those with severe anemia, trauma, or chronic blood disorders like thalassemia major, red blood cells with optimal oxygen-carrying capacity are essential for improving health outcomes. When donors with thalassemia traits provide blood with lower-than-average hemoglobin levels, the transfused blood may not meet the oxygen needs of the recipient, leading to suboptimal treatment outcomes. This poses a significant challenge for blood banks in Thailand, where a careful balance must be maintained between accepting enough donations to meet demand and ensuring that every unit of blood is of high enough quality to effectively treat patients.

2. Altered red blood cell morphology and its consequences

In addition to having reduced hemoglobin content, the morphology, or shape, of red blood cells from individuals with thalassemia traits is often abnormal. Common morphological changes include the presence of target cells (RBCs with a bullseye appearance) or elliptocytes (oval-shaped RBCs). These altered shapes reduce the lifespan of transfused RBCs, meaning that they do not circulate in the recipient's bloodstream for as long as normal red blood cells.[10] For patients who rely on regular transfusions, such as those with thalassemia major or other hematologic disorders, transfusions of RBCs with a shortened lifespan can result in the need for more frequent transfusions. This, in turn, increases the burden on both the healthcare system and the blood donor pool. As blood supplies are often limited, particularly during times of crisis or low donation periods, the inability to provide long-lasting, effective red blood cells can compromise patient care. It also raises the need for more intensive donor recruitment efforts, which are already challenging in regions with high carrier rates of thalassemia.[11]

3. The screening and deferral process in blood donation centers

The issue of screening blood donors for thalassemia traits is another key challenge faced by blood donation centers in Thailand. While individuals with thalassemia traits are not automatically disqualified from donating

blood, careful screening is required to determine whether their blood is suitable for specific patient populations. For example, patients with severe anemia, cardiovascular conditions, or those undergoing extensive surgeries require red blood cells that have a high oxygen-carrying capacity and a normal lifespan in the bloodstream. Blood donation centers in Thailand commonly perform complete blood count (CBC) to detect the presence of thalassemia traits, in donors with low Hb from hemoglobinometer. Donors with low Hb are deferred. However, this deferral process further reduces the already limited pool of potential donors, creating a dilemma for blood banks. In a country where the prevalence of thalassemia traits is relatively high, the exclusion of these individuals from donating can exacerbate shortages of blood supplies, particularly during periods of high demand, such as during public health emergencies or natural disasters.

Moreover, screening for thalassemia traits adds another layer of complexity and cost to blood donation services. Extensive laboratory testing is required to accurately assess donor eligibility, and this adds pressure on healthcare budgets and blood donation infrastructures, especially in rural or underfunded areas of Thailand. Developing efficient and cost-effective screening methods is critical for managing these challenges and ensuring the long-term sustainability of blood donation services in the country.

4. The broader implications for public health and blood donation strategies

The issue of blood donation from thalassemia carriers is not only a challenge for managing current blood supplies, but it also highlights broader public health concerns. Thailand has one of the highest rates of thalassemia carriers in the world, with an estimated 30-40% of the population carrying some form of the trait. This high carrier rate makes it difficult to exclude all thalassemia carriers from donating blood without creating significant shortages. Addressing these challenges will require a multifaceted approach, including public education campaigns to raise awareness about the importance of blood donation and the specific challenges posed by thalassemia traits. Encouraging more widespread genetic screening and counseling for thalassemia could also help potential donors make informed decisions about their eligibility to donate. Additionally, investments in research and development to improve screening techniques and refine transfusion protocols are crucial to ensuring that blood donations from carriers of thalassemia traits can still be utilized safely and effectively in certain contexts.[13,14]

Impact on blood supply sufficiency

The high prevalence of thalassemia traits in the Thai population has direct implications for the sufficiency of the blood supply. As individuals with alpha or beta thalassemia traits represent a large proportion of the potential donor pool, their blood's suitability for transfusion must be carefully evaluated. This poses challenges in several areas:

Limited donor pool: The deferral of blood donors with significant microcytosis or hemoglobinopathies reduces the number of available donors. This is especially problematic during times of increased demand for blood products, such as during natural disasters, epidemics, or public holidays.

Increased screening costs: Extensive screening for thalassemia traits and other hemoglobinopathies increases the cost of maintaining a safe blood supply. Blood donation centers need to invest in specialized testing, such as hemoglobin electrophoresis, to accurately identify carriers and determine the suitability of their blood for transfusion.

Blood component availability: Patients with thalassemia major and other conditions that require regular transfusions rely on specific blood components, such as red blood cells with high hemoglobin content. The reduced viability of blood from thalassemia trait donors limits the availability of these critical components, placing additional strain on blood banks.

Transfusion safety concerns

Blood donations from individuals with thalassemia traits, though often considered safe for many patients, pose several transfusion safety concerns that warrant careful attention. One of the primary issues is the lower hemoglobin content and altered red blood cell morphology found in thalassemia trait donors. These red blood cells are typically microcytic (smaller than normal) and hypochromic (paler due to less hemoglobin), which can lead to ineffective transfusions. For patients with severe anemia or those who require blood with a higher oxygen-carrying capacity, this may result in inadequate oxygen delivery to tissues and organs, potentially complicating their recovery.

Another major concern is the risk of alloimmunization. This occurs when the recipient's immune system recognizes the transfused blood as foreign and mounts an immune response, producing antibodies against the donor's red blood cells. Patients with thalassemia major are particularly vulnerable to this, as they require regular blood transfusions over their lifetime. Frequent exposure to different donor blood types increases the likelihood of developing alloantibodies, which can complicate future transfusions, limit compatible donor options, and potentially lead to transfusion reactions.

In addition, although uncommon, there is a risk of adverse transfusion reactions when using blood from thalassemia trait donors. These reactions can range from mild febrile responses, where the patient experiences fever or chills post-transfusion, to more serious complications such as transfusion-related acute lung injury (TRALI). TRALI is a rare but serious condition where the recipient's lungs are affected following a transfusion, leading to respiratory distress. Given these risks, blood banks must ensure meticulous screening processes, carefully assessing the suitability of blood from thalassemia trait donors to avoid potential complications and ensure the safest possible outcome for transfusion recipients.

Conclusion

The challenge of maintaining a safe and sufficient blood supply in Thailand is compounded by the high prevalence of thalassemia traits. While individuals with alpha, beta, or compound heterozygous thalassemia traits are typically healthy, their blood may not always be ideal for transfusion due to reduced hemoglobin content and abnormal red blood cell morphology. Addressing these challenges requires a multifaceted approach that includes public education, improved screening, and research into alternative blood sources. By tackling these issues, Thailand can work towards ensuring a safe, sufficient, and sustainable blood supply for all its citizens.

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