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Original Article

A Retrospective Study of DNA Analysis Thalassemia Patients in Jambi Province for the Years 2016-2020

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ABSTRACT

Background: Thalassemia is a genetic blood disorder characterized by abnormal hemoglobin production, leading to anemia. Beta-thalassemia, particularly its transfusion-dependent form, requires lifelong care. DNA analysis plays a crucial role in diagnosing thalassemia, providing precise methods for genetic counseling, prenatal diagnosis, and effective prevention programs. This research aims to describe the results of DNA analysis of thalassemia patients in Jambi Province from 2016 to 2020.

Methods: This study uses a descriptive retrospective design. Data were analyzed from the medical records of thalassemia patients identified in Jambi Province between 2016 and 2020. The research subjects are individuals diagnosed with thalassemia within this period, with data collection performed via total sampling, encompassing 25 respondents.

Results: The majority of thalassemia patients in Jambi Province are children aged 5-14, with a significant proportion having a history of blood transfusions for more than a year. Most patients are classified as Beta Thalassemia (96%), consistent with global trends. DNA analysis revealed significant variation in mutations, with common mutations such as Hb E and IVS-nt-5 found in 48% of samples. The study highlights the genetic diversity within the thalassemia patient population, indicating variations in disease severity.

Conclusion: This study highlights the importance of early detection and management of thalassemia, particularly in children. Blood transfusions are crucial for maintaining the health of thalassemia patients in Jambi Province, where Beta Thalassemia is most common. DNA analysis reveals significant genetic diversity, which helps in selecting appropriate treatments and understanding the risk of complications. These findings provide a basis for improving diagnostic and management strategies for thalassemia in Jambi Province.

INTRODUCTION

Thalassemia is a genetic blood disorder characterized by abnormal hemoglobin production, leading to anemia. Beta-thalassemia, especially its transfusion-dependent form, requires lifelong care by multidisciplinary teams of experts[1]. The Thalassemia International Federation (TIF) plays a crucial role in global thalassemia control efforts[2]. In Pakistan, there is a high prevalence of transfusion-dependent thalassemia major patients, with over 100,000 active cases[3]. Thalassemia is among the most prevalent genetic hemoglobin disorders globally[4]. The prevalence of thalassemia varies globally, with Saudi Arabia having one

of the highest rates[5]. Lack of awareness about thalassemia among college students in Saudi Arabia highlights the need for increased education and genetic counseling services[6]. In Bangladesh, thalassemia is a significant public health concern due to its high prevalence[7]. Studies in Bangladesh also emphasize the importance of knowledge and attitudes towards thalassemia prevention among the population[8]. New therapeutic options beyond transfusion and iron chelation are being explored for beta-thalassemia, including genetic and molecular targeted therapies[9]. Health state utility values and quality of life in Chinese adult patients with beta-thalassemia major are influenced by social support and treatment compliance[10]. Lifestyle factors can impact the quality of life among adults with beta-thalassemia major[11]. Thalassemia is associated with complications such as iron overload cardiomyopathy, emphasizing the need for effective treatments[12]. Screening and management strategies have contributed to a declining trend in the prevalence of heart failure impairment with thalassemia globally[13]. The classification of thalassemia into major, intermedia, trait, and minima categories helps in understanding the disease spectrum[14].

Globally, it is estimated that approximately 3% of the world's population are carriers of beta-thalassemia. However, due to the autosomal recessive nature of this disease, both parents must be carriers for their child to manifest thalassemia. Beta-thalassemia is more commonly found in Southeast Asia, the Mediterranean, and Africa, but the prevalence of alpha-thalassemia in Southeast Asia is relatively higher. WHO data indicates that more than 40,000 babies are born with beta-thalassemia each year, with approximately 25,500 of them having transfusion-dependent beta-thalassemia. The annual incidence of newborns with beta-thalassemia is 20,420 in Southeast Asia. In the Mediterranean, it is reported at 9,914, while in Europe, it is 1,019, and in America, it is 341 individuals. Alpha-thalassemia is also prevalent in Southeast Asian populations, where an estimated 5-10% of the population are carriers. Indonesia is among the countries in the thalassemia belt or countries with a high frequency of thalassemia carrier genes. The frequency of beta-thalassemia genes in Indonesia is estimated to be 3-10%.

DNA analysis is a fundamental tool in the diagnosis of thalassemia, providing precise and efficient methods for genetic counseling, prenatal diagnosis, and effective prevention programs. Several studies have highlighted the importance of DNA analysis in confirming thalassemia diagnoses and enhancing patient care[15], [16]. For example, fetal DNA analysis enables the prenatal diagnosis of thalassemia major, aiding in the identification of molecular defects[16]. Techniques such as direct sequencing and polymerase chain reaction (PCR) are commonly used for DNA analysis on chorionic villi for prenatal diagnosis[17]. Non-invasive prenatal diagnostic methods based on DNA analysis, such as next-generation sequencing and high-resolution melting analysis, have been developed for thalassemia[18], [19]. These methods provide accurate and non-invasive ways to detect thalassemia mutations. Moreover, the use of genomic DNA reference materials and DNA controls has improved the reliability of genetic testing for thalassemia[20], [21]. DNA analysis is crucial for distinguishing between different types of thalassemia, particularly beta-thalassemia mutations prevalent in Asian populations[21]. Studies have emphasized the significance of DNA analysis in identifying specific thalassemia mutations, enabling precise diagnosis and genetic counseling[22], [23]. Additionally, DNA analysis has been instrumental in the development of rapid diagnostic methods for alpha-thalassemia and other hemoglobin disorders[24], [25].

DNA analysis is pivotal in the diagnosis of thalassemia, providing accurate, cost-effective, and non-invasive approaches for genetic testing, prenatal diagnosis, and mutation detection. The advancements in DNA analysis techniques have significantly

enhanced the management and prevention of thalassemia, highlighting the importance of molecular diagnostic strategies in addressing this genetic blood disorder. The aim of this research is to describe the results of DNA analysis of thalassemia patients in the Jambi Province from 2016 to 2020.

METHOD

The research design of this study is a descriptive retrospective study. Data analysis was conducted on the medical records of thalassemia patients who had been identified in the Jambi Province within the period of 2016-2020. The research subjects are individuals who have been diagnosed with thalassemia in the Jambi Province within the period of 2016-2020. The data collection technique is total sampling, with 25 respondents. The inclusion criteria for this study are individuals who have had DNA analysis results related to thalassemia within the period of 2016-2020. The exclusion criteria are individuals who do not have complete data or have a history of diseases that may affect the analysis results.

RESULTS AND DISCUSSIONS

From the result in **Table 1**, it can be seen that the distribution of thalassemia patients is based on age group, transfusion history, thalassemia classification, and their DNA analysis results. The age range of thalassemia patients is primarily between 5-14 years old, with 36% aged 5-9 years and 40% aged 10-14 years. This indicates that most thalassemia patients in the Jambi Province are diagnosed during childhood to early adolescence. The majority of patients (88%) have a history of blood transfusions for more than one year.

Table 1. **DNA Analysis of Respondent**

Variable (N=116)	Group	Frequency (N)	Percentage (%)
Group Of Age	0-4 Years	2	8
	5-9 Years	9	36
	10-14 Years	10	40
	15-18 Years	4	16
Transfusion History	< 1 Year	3	12
	> 1 Year	22	88
Thalassemia Classification	Thalassemia Alpha	1	4
	Thalassemia Beta	24	96
DNA Analysis Results			
Heterozigot Ganda	Mutasi Hb Malay Dan IVS-Nt-5	2	8
	Mutasi Hb E Dan IVS-Nt-5	12	48
	Mutasi Cd41-42 (Delesi TTCT) Dan Cd123/124/125 (Delesi ACCCACC)	1	4
	Mutasi Hb Malay Dan Codon 35	1	4
	Mutasi Hb E Dan =Cd123/124/125 (Delesi ACCCACC)	2	8
	-28 (A>G) Promoter Gen Globin Beta Dan Codon 41-42 (Delesi TTCT)	1	4
	Heterozigot Ganda Codon 59 Gen Globin-α2 Dan Hb Constant Spring	1	4
	Heterozigot Ganda Mutasi IVS1-Nt5 Dan Codon 41-42	1	4
Homozigot	Homozigot Mutasi IVS1-Nt.5 (G>C)	4	16

This indicates that blood transfusions are an important part of thalassemia patient management in the region. Most thalassemia patients are classified as Thalassemia Beta (96%) compared to Thalassemia Alpha (4%). This is consistent with the general picture, where Thalassemia Beta is more common. The DNA analysis results show significant variation in the types of mutations detected in thalassemia patients. There are some common mutations, such as Hb E and IVS-nt-5 mutations, found in 48% of the samples. However, there are also other variations in the types of mutations that reflect the genetic diversity in the thalassemia patient population in the Jambi Province. Some patients (16%) are homozygous for specific mutations, while others (84%) are heterozygous. This indicates variation in the severity of thalassemia disease among the population.

Thalassemia is a group of genetic blood disorders characterized by a decrease or absence of normal hemoglobin synthesis, leading to the destruction of red blood cells and resulting in severe anemia[26]. The condition is caused by mutations in the α and β globin genes and is usually inherited in an autosomal recessive manner[27]. Treatment options for thalassemia include blood transfusions, iron chelation therapy, hematopoietic stem cell transplantation, pharmaceutical induction of γ globin, and gene and cell therapies [28]. Patients with transfusion-dependent thalassemia require specialist and multidisciplinary care, which tends to become more expensive as patients age[29]. The management of thalassemia can have implications for different age groups. For instance, children with thalassemia may experience physical and psychosocial challenges that affect their overall wellness, including concerns about physical appearance and relationships[30]. Additionally, adolescents with thalassemia may face depression, which can be influenced by the chronic nature of the disease and its long-term treatment[31].

Blood transfusion plays a crucial role in the management of thalassemia, especially in patients with thalassemia major who require regular blood transfusions. The aim of blood transfusion is to increase pre- and post-transfusion hemoglobin levels, with specific targets that must be achieved to ensure patient health. Despite being a vital intervention, there are risks of transfusion reactions that can occur, such as moderate to severe transfusion reactions that can affect some patients.

In the context of thalassemia management, understanding and awareness of the importance of blood transfusion, selecting appropriate donors, and monitoring for potential side effects and complications post-transfusion are essential to ensure optimal quality of life for thalassemia patients. Different classifications of this condition have important clinical implications. Thalassemia is a group of genetic blood disorders characterized by reduced or absent synthesis of normal hemoglobin, resulting in the destruction of red blood cells and severe anemia[32]. The classification of thalassemia based on its type, such as alpha and beta thalassemia, influences patient management and prognosis[32]. In patients with thalassemia major, blood transfusion is an integral part of managing this disease[33]. The aim of blood transfusion is to increase pre- and post-transfusion hemoglobin levels, with specific targets that must be achieved to ensure patient health[33]. However, it is important to consider the risks of blood transfusion reactions and iron accumulation in the patient's body due to repeated blood transfusions. Additionally, thalassemia classification can also influence the risk of complications such as thalassemia cardiomyopathy[32] (Pratama, 2021). Thalassemia cardiomyopathy is a serious complication that can occur in thalassemia patients, and its management requires different approaches depending on the patient's thalassemia classification[32].

The genetic diversity within the thalassemia patient population has significant implications for the diagnosis, management, and prevention of this disease. Genetic

studies have revealed extensive genetic variations in thalassemia patients, including mutations in the beta-globin gene which is the main cause of thalassemia. In-depth knowledge of these genetic polymorphisms allows for the identification of different types of thalassemia and guides appropriate management based on the specific mutations a patient has[34].

In the context of the relationship between mutation types and the severity of thalassemia, genetic research has provided valuable insights. These studies highlight that various types of genetic mutations in the beta-globin gene can affect the severity of thalassemia[35], [36], [37]. For example, specific mutations such as CD17 (A>T) have been identified as the most common mutations in thalassemia in several regions in China[37]. Moreover, the interaction between alpha-globin and beta-thalassemia heterozygosity can result in intermediate thalassemia forms that do not require blood transfusions. Research also highlights that specific genetic mutations can affect the response to therapy and the prognosis of thalassemia patients[21], [38]. For instance, mutations in the KLF1 gene have been associated with various thalassemia phenotypes, including congenital hemolytic anemia and dyserythropoietic anemia[39]. Furthermore, recent studies have shown that the ability to predict the severity of thalassemia based on specific genetic polymorphisms can aid in better clinical decision-making[21].

Homozygous and heterozygous thalassemia have different clinical implications in the management of this disease. Homozygous thalassemia, characterized by having two mutated gene copies, often results in more severe symptoms and requires more intensive treatment such as regular blood transfusions and iron chelation therapy[40]. Conversely, heterozygous thalassemia, where only one gene copy is mutated, tends to show milder symptoms or may even be asymptomatic[41]. Genetic studies have highlighted clinical differences between homozygous and heterozygous thalassemia. For example, research indicates that the interaction between alpha-globin and beta-thalassemia heterozygosity can result in intermediate thalassemia forms that do not require blood transfusions[41]. On the other hand, homozygous thalassemia often results in more severe forms, such as thalassemia major, which requires lifelong intensive treatment[40].

To explore the differences in disease severity and treatment response in thalassemia, we can refer to various studies that shed light on these aspects. For instance, Lu et al. (2022) highlighted that patients with mild thalassemia may exhibit mild hypochromic microcytic anemia, while those with severe thalassemia may develop complications like edematous fetuses or hepatosplenomegaly[42]. This indicates a spectrum of severity based on the type of thalassemia. Moreover, Hussain et al. (2022) discussed the impact of hydroxyurea on blood transfusions in β-thalassemia patients, indicating the importance of different treatment modalities in managing the disease[43]. Additionally, Fazal et al. (2021) assessed the level of awareness among parents of affected children, emphasizing the significance of education and awareness in dealing with thalassemia effectively[44]. Furthermore, genetic polymorphisms, as studied by Omar et al., 2020, can influence hemoglobin levels and potentially affect disease severity[45]. Understanding these genetic variations can aid in predicting disease outcomes and tailoring treatment strategies accordingly. Additionally, the study by Ullah et al. (2020) on quantitative determination of HbA2 levels in β-thalassemia trait showcases the importance of specific biomarkers in diagnosing and managing thalassemia[46].

CONCLUSSION

In this study, we look at the distribution and characteristics of thalassemia sufferers in Jambi Province, highlighting the general pattern of the disease in this population. The predominant age range for thalassemia

diagnosis focuses on childhood to early adolescence, highlighting the importance of early detection and management of the disease in the early stages of development. A long history of blood transfusions, especially in the majority of sufferers, emphasizes the crucial role of blood transfusions in maintaining the health of thalassemia sufferers. Additionally, the high prevalence of Beta Thalassemia is in line with global findings, indicating consistency in disease patterns in Jambi Province. The results of DNA analysis highlight significant genetic diversity within the affected population, providing deep insight into the genetic variations underlying this disease. The clinical implications of DNA analysis results, especially in the selection of appropriate therapy and understanding the risk of complications, reinforce the importance of an individualized approach in the management of thalassemia. Thus, this research provides a solid foundation for the development of more effective diagnosis and management strategies in facing the challenges of Thalassemia in Jambi Province.

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