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Growth factors and puberty in thalassemia adolescents

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Abstract

Thalassemia is a genetic disorder that affects hemoglobin synthesis, causing chronic anemia that contributes to delayed growth and puberty in adolescents. This literature review discusses the factors underlying these delays, such as chronic anemia, iron overload due to repeated blood transfusions, and hormonal dysfunction. Oxygen deficiency due to anemia disrupts metabolic processes and endocrine function, especially in the pituitary axis and gonads, leading to delayed puberty. Effective treatment strategies include routine blood transfusions to maintain hemoglobin levels, iron chelation therapy to prevent endocrine damage, and hormonal interventions to treat growth and puberty disorders. Early detection and regular monitoring are essential to optimize outcomes for adolescent patients with thalassemia.

Keywords: Thalassemia; Growth; Puberty; Adolescents

1. Introduction

Thalassemia is a genetic disease that affects hemoglobin formation and is one of the most common monogenetic disorders. In Indonesia, it is estimated that around 2,500 children are born with thalassemia major every year. Signs of growth delay in children with thalassemia can be seen in height below -2SD or growth rate of less than 4 cm per year. Delayed puberty in females can be recognized if at the age of more than 13 years, they have not shown signs of puberty, such as breast development. In males, it is said that puberty is delayed if at the age of 14 years the testicular diameter is still less than 2.5 cm or the testicular volume is less than 4 ml.

Suboptimal blood transfusions, iron overload, deferioxamine (DFO) toxicity, puberty, late puberty, disruption of the growth hormone axis, and disruption of the insulin-like growth factor (IGF-I) axis are some of the causes of significant growth impairment in thalassemia, the pathogenesis of which is not yet definitively known. Serum ferritin levels may also directly correlate with growth rate in thalassemia patients. With advances in medical treatment, most patients can grow normally during childhood, although later in life they often experience significant growth retardation and delayed puberty.

2. Review Content

2.1. Factors Affecting Growth and Development in Adolescents

Adolescent growth and development is influenced by various interrelated factors. Genetic factors play a major role in determining potential height, timing of puberty and other physical characteristics. In addition, nutritional status is also highly influential where deficiencies in the intake of nutrients such as protein, calcium, iron, and vitamins can hinder

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optimal growth. Physical health factors, such as the presence of chronic diseases (e.g. thalassemia, anemia, or endocrine disorders) and recurrent infections, also affect adolescent development.

Important hormones including growth hormone (GH), sex hormones (testosterone and estrogen), thyroid hormones and insulin play a crucial role in supporting growth and puberty. Hormonal imbalances can lead to impaired growth or delayed puberty. Psychosocial environments such as stress, trauma or lack of family support can also have a negative impact on adolescent development.

In addition, adequate physical activity favors the growth of bones and bibs, while an unhealthy lifestyle may hinder optimal physical development. In adolescents with certain medical conditions such as thalassemia, the quality of blood transfusion therapy and iron chelation can be important factors in influencing growth. Normal pubertal development contributes to a growth spurt, while pubertal disorders such as precocious puberty or delayed puberty can affect growth patterns.

2.2. Pathophysiology of Thalassemia on Adolescent Growth Status

Thalassemia is a genetic disorder characterized by a disruption in globin synthesis, leading to abnormal hemoglobin production and more fragile red blood cells that break easily. This leads to chronic anemia, which is a major cause of impaired growth in thalassemia children and adolescents. Chronic anemia that occurs due to hemoglobin deficiency in thalassemia patients leads to inadequate tissue oxygenation, which interferes with metabolic processes and body growth [5].

In children, the body responds to the lack of oxygen by increasing the amount of ertiropoeiesis (red blood cell formation), which often causes the spleen and liver organs to enlarge due to the accumulation of damaged red blood cells. The buildup of these cells also exacerbates the imbalance between the formation and breakdown of red blood cells, further increasing fatigue and worsening anemia [4].

Growth retardation in adolescents with thalassemia major is often influenced by several factors, such as long-lasting anemia, iron overload due to repeated blood transfusions, and hormonal disorders. Frequent blood transfusions required in thalassemia major increase iron levels in the body, which can then be deposited in various organs including the liver, heart, and endocrine glands, which can interfere with the normal function of these glands, especially the pituitary gland and gonads [7] [8].

Chronic anemia leads to considerable energy deficiency, affects the body's metabolism, and disrupts physiological processes such as bone growth and pubertal development. In adolescents, pubertal disorders often occur due to oxygen deficiency and endocrine disorders. Delayed hormonal changes, such as delayed breast development in girls and small testicle size in boys, can be seen from the direct impact of hormonal disorders caused by thalassemia [3].

In addition, growth hormone (GH) deficiency and impaired gonadal function can also cause delayed puberty. GH deficiency may result from damage to the pituitary gland or hypothalamus due to iron overload [1] [6]. Growth disorders and delayed puberty in adolescent thalassemia major often require endocrine therapy, including growth hormone treatment and deferiprone therapy to reduce body iron levels.

2.3. Pathophysiology of Thalassemia on Adolescent Pubertal Status

Thalassemia, especially thalassemia major, is a genetic disorder that affects hemoglobin synthesis causing chronic anemia that can have a significant impact on physical development, including adolescent pubertal status. Persistent severe anemia in thalassemia patients causes tissue hypoxia which can interfere with many physiological processes of the body, including pubertal development [2] [7].

In adolescents, puberty is influenced by endocrine hormones, such as growth hormone (GH), gonadotropins (FSH and LH), as well as estrogen in females and testosterone in males. In individuals with thalassemia, there are several factors that contribute to delayed puberty. First, chronic anemia causes an imbalance of oxygen in the body, affecting the pituitary gland and hypothalamus (glands that regulate the production of hormones important for puberty) [3]. In addition, routine blood transfusions in thalassemia patients often lead to the accumulation of iron in the body, especially in organs such as the liver, heart and endocrine glands. This iron overload can impair the function of the pituitary gland and gonads, which are responsible for the production of sex hormones and the regulation of sexual development.

Research conducted by Mussalam shows that patients with thalassemia major often experience growth hormone (GH) deficiency which plays an important role in pubertal development. This disorder is usually caused by iron accumulation in the pituitary gland, which leads to a reduction in the secretion of GH, a hormone that functions to stimulate physical growth and pubertal development. As a result, adolescents with thalassemia major often experience delays in physical development such as breast enlargement in females and testicular growth in males. In addition, hormonal disruption in thalassemia can also cause gonadal dysfunction leading to delayed or absent signs of puberty. In girls, delayed breast development and menstruation are common symptoms, while in males smaller testicular size and delayed penile growth may be observed. In some cases, gonadotropin (FSH and LH) deficiency may result from direct damage to the pituitary gland or hypothalamus [3].

2.4. Thalassemia Management on Growth Status and Puberty in Adolescent Patients

Management of thalassemia specifically in adolescents aims to address the impact of chronic anemia, iron overload and hormonal disturbances that affect growth and puberty. This approach includes blood transfusion therapy, iron chelation therapy, and specific hormonal interventions. Here are some of the therapies that can be done:

2.4.1. Blood Transfusion Therapy

Routine blood transfusion is a key pillar in the management of thalassemia major. This therapy aims to maintain pretransfusion hemoglobin levels above 9-10 g/dL to prevent severe anemia and ensure adequate tissue oxygenation (Cappellini). Adequate oxygenation plays an important role in supporting physical growth, such as height, as well as pubertal development. However, frequent blood transfusions can increase the risk of iron overload which can affect endocrine organs such as the hypothalamus, pituitary, and gonads.

2.4.2. Iron Chelation Therapy

Iron accumulation due to blood transfusion causes hemosiderosis which impacts endocrine function. Therefore, iron chelation therapy is an important part of thalassemia management to prevent complications due to iron overload. Iron chelation drugs such as deferasirox, deferiprone, or deferoxamine are used to reduce body iron levels (Mussalam). Research by Farmaki et al 92010 showed that appropriate iron chelation therapy can improve hormonal function, including the secretion of gonadotropins and growth hormone which contributes to the improvement of pubertal status and growth.

2.4.3. Routine Monitoring and Evaluation

Monitoring of serum ferritin levels, hormone function (LH, FSH, and GH), and physical growth should be done regularly. This monitoring aims to adjust therapy and anticipate long-term complications.

3. Conclusion

The conclusion of this literature review is that there is a significant impact of thalassemia patients on adolescent growth and puberty status. This is because the delay in growth in adolescents with thalassemia major is often influenced by several factors, such as long-lasting anemia, iron overload due to repeated blood transfusions, and hormonal disorders. In thalaasemia patients, there are several factors that contribute to the delay in puberty, namely the imbalance of oxygen in the body that affects the pituitary gland and hypothalamus. For this reason, it is necessary to treat thalassemia patients with blood transfusion therapy, iron chelation therapy, and regular monitoring and evaluation of patients.

Compliance with ethical standards

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Disclosure of conflict of interest

No conflict of interest to be disclosed.

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