Comparison of *Axial Length, Anterior Chamber Depth, Lens Thickness* Measurement Using Biometry in Thalassemia β Mayor Children toward Emmetropia Children

Elyani Rahman[1], Aryani Atiyatul Amra[1], Fithria Aldy[1], Masitha Dewi Sari[1], Bidasari Lubis[2]
[1]Ophthalmology Department, Faculty of Medicine Sumatera Utara University
[2]Pediatric Department, Faculty of Medicine Sumatera Utara University

ABSTRACT

Background : Thalassemia β major may reduce the quality of life of patients, one of them is a eyesight problem. Refractive errors are the most common problems. This disorder may occur due to changes in biometry arising from changes in craniofacial structures caused by chronic anemia. However, not all children with thalassemia β major experience refractive disorder.

Aim : To compare biometry measurement result of axial length, anterior chamber depth and lens thickness between thalassemia β major and emmetropia children.

Methods : A prospective, analytical observational with cross sectional study. The data obtained were Thalassemia β major pediatric patients from One Day Care Thalassemia Unit of Haji Adam Malik General Hospital and the emmetropia pediatric patients from University of North Sumatera Hospital from December 2017 to January 2018 after approved by the Ethics Committee for Health Research Sumatera Utara University. Thirty four children with β-thalassemia major group (68 eyes) and thirty four children with emetropia (68 eyes) as a control with age-matched subjects. Underwent a complete ophthalmological examination with biometry for measure axial length, anterior chamber depth and lens thickness

Results : There were significant differences in anterior chamber depth (p=0.0001*) and lens thickness (p=0.01*) in β-thalassemia major group compare to control group. . The average of axial length shorter in thalassemia group compare to control group but from statistical, there was no significant differences (p=0.35).

Conclusion : β-thalassemia major as accompanied by typical bone growth disorders, especially craniofacial may cause abnormal orbital bone growth and considered to evaluating biometric examination .axial length, anterior chamber depth and lens thickness

Keywords: β-Thalassemia Major, Biometry, Axial Length, Anterior Chamber Depth, Lens Thickness

Background

Thalassemia is a hemoglobinopathy characterized by a disruption in the production of α and β-globin chains. The defect in the α-globin chain synthesis is called α-thalassemia, whereas the defect in the β-globin chain synthesis is called β-thalassemia. Epidemiologically, β-thalassemia is the most common type of thalassemia (with an incidence of up to 14 percent in some populations) which is autosomal recessively inherited. Disturbances in the biosynthesis of β-globin reduce the production of tetramer hemoglobin, resulting in hypochromia and microcytosis in peripheral blood cells. Hemoglobin is essential for oxygen delivery to the tissues. In β-thalassemia found HbF levels of 95-98%, HbA2 is about 2-5% and HbA is not present.[1] About seven percent of the world's total population is the carriers of hemoglobinopathy. The frequency of thalassemia carriers in Indonesia is between 3-10%.[2]

Patients with β-thalassemia major are always accompanied by typical bone growth disorders, especially in craniofacial and long bone. The craniofacial changes encountered were skull fractures, protrusion of the maxillary bone, depression of the bridge of the nose, and changes in the orbital bone. Ocular growth is closely related to orbital bone growth. In principle, craniofacial changes in major thalassemia patients may cause abnormal orbital bone growth and may subsequently lead to changes in biometric examination.[3] The purpose of this study was to compare axial length, anterior chamber depth, lens thickness with biometric examination in the children with β-thalassemia major and the children with emmetropia.

Methods

Subjects

This was a prospective, an observational analytic study with cross sectional study comprising 34 β-thalassemia major group (68 eyes) from Thalassemia One Day Care unit Department of Child Health in the Haji Adam Malik General Hospital Medan and 34 emetropia (68 eyes) from Pediatric Eye Clinic of University of Sumatera Utara General Hospital as a control group with the same age range and sex.

Ethical approval was obtained from University Sumatera Utara ethics committee. The aims and objectives of our study were explained to all participants in accordance to the Declaration of Helsinki. A written consent was obtained from all patients by the reaearchers.

Patients medical history was recorded, visual acuity was measured with the best possible correction.

Inclusion criteria: we included al patients who fulfilled the following criteria: range age 6-15 years old, Patient diagnose as B thalassemia major and emetropia as a control, visual acuity with the best possible correction, and axial length, anterior chamber depth and lens thickness measured by biometry.

Exclusion criteria: Minor thalassemia, intermediate thalassemia and α thalassemia.

A biometric examination was performed prior to the examination using a Snellen chart. The biometry used was Tomey AL 100. Shortly before the biometric measurement, the eyes examined were dripped with 1 drop of 0.5% pantocaine, biometric examination was performed, then dripped with 1 drop of ofloxacin 3 mg to avoid secondary infection. The axial length is the distance between the surface of the cornea and the anterior surface of the lens. Anterior chamber depth is the distance between the anterior surface of the cornea and the anterior surface of the lens. While the lens thickness is the distance between the anterior surface of the lens with the posterior surface of the lens.[3]

Statistical Analysis

The collected data write in the research publication and keep in the computer. The collected data keeped in compuyer analysed by using the statistical software. To compare quantitative variables (axial length, anterior chamber depth , lens thickness) between the two groups, Independent T-Test was used. To compare refraction problem between the two groups, Chi square was used. Statistical analysis were performed with SPSS 19,0 and the level significance was=0,05 in all statistical test.

Results

The average sample of the children with β-thalassemia major is the children who have received multiple transfusions. Demographic characteristics in the study are presented in Table 1

Table 1. Characteristics of Research Subjects In the Children with β-Thalassemia Major and the Children with Emmetropia

The Characteristic	Group				P value
	n	β-Thalassemia Major x̄ ± SD	N	Emmetropia x̄ ± SD	
Age	34	11.85 ± 3.807	34	11.76 ± 3.191	0.918
Height	34	134.15 ± 18.715	34	145.59 ± 15.351	0.008*
Weight	34	29.50 ± 13.567	34	38.94 ± 11.238	0.003*
Head Circumference	34	51.03 ± 1.586	34	52.71 ± 1.292	0.0001*
HB Before Blood Transfusion	34	6.7 ± 1.247			

* *T-Test Independent*, significant < 0.05

In table 1, based on clinical characteristic showed there was significant differences of height, weight and head circumference between the two groups (p<0,05).

Table 2. Characteristics of Research Subjects In Children with β-Thalassemia Major and Emmetropia Based on Sex

Sex	Group		Total n(%)	P value
	β-Thalassemia Major n(%)	Emmetropia n(%)		
Male	17 (58.6 %)	12 (41.4 %)	29 (100 %)	0.220
Female	17 (43.6 %)	22 (56.4 %)	39 (100 %)	

Chi-Square test

Table 2 showed there was no signifant differences based on age between the two group (p<0,05)

Table 3. Differences of the Eyesight In Children with β-Thalassemia Major and Emmetropia

Eyesight	Group		Total n(%)	P value
	β-Thalassemia Major n(%)	Emmetropia n(%)		
Right Eye (OD)				
- Normal	14 (29,2 %)	34 (70,8 %)	48 (100 %)	0.0001*
- Not normal	20 (100 %)	0 (0 %)	20 (100 %)	
Left Eye (OS)				
- Normal	16 (32 %)	34 (68 %)	50 (100 %)	0.0001*
- Not normal	18 (100 %)	0 (0 %)	18 (100 %)	

* Chi-Square test, significant < 0.05

Table 3 showed there was significant differences based on eyesight between the two group (p<0,05)

Table 4. Differences of Axial Length, Anterior Chamber Depth, Lens Thickness In Children with β-Thalassemia Major and Emmetropia

Biometry	Group				P value
	N	Thalassemia $\bar{x} \pm SD$	n	Emmetropia $\bar{x} \pm SD$	
Axial Length (mm)	68	22.54 ± 0.984	68	22.69 ± 0.939	0.350
Anterior Chamber Depth (mm)	68	2.89 ± 0.410	68	3.15 ± 0.331	0.0001*
Lens Thickness (mm)	68	3.73 ± 0.306	68	3.58 ± 0.367	0.010*

* *T-Test Independent*, significant < 0.05

In Table 4 showed there was a significant differences in anterior chamber depth and lens thickness between the two groups (p<0,05). In axial length the average of axial length was shorter in thalassemia group compared to control group. but from the statistical not significant differences (p>0,05).

Discussion

Thalassemia is a hemoglobinopathy characterized by a disruption in the production of α and β-globin chains. Patients with β-thalassemia major are always accompanied by typical bone growth disorders, especially in craniofacial and long bone. The craniofacial changes encountered were skull fractures, protrusion of the maxillary bone, depression of the bridge of the nose, and changes in the orbital bone. Ocular growth is closely related to orbital bone growth. In principle, craniofacial changes in major thalassemia patients may cause abnormal orbital bone growth and may subsequently lead to changes in biometric examination[3]. In our study, we observed comparison axial length, anterior chamber depth, lens thickness with biometric examination in the children with β-thalassemia major and the children with emmetropia.

From Table 1 showed there was a significance differences in heigh, weight, and head circumference between the two groups (p<0,05). In this study, the height of the β-thalassemia major patients was shorter than emmetropia patients. At body weight the β-thalassemia major patients appeared to be thinner than the emmetropia patients. In head circumference, the head circumference of the β-thalassemia major patients appeared to be smaller than the emmetropia patients.. body weight in the children with β-Thalassemia Major group with emmetropia children. This is suitable with research by De Sanctis V et al in Italy in 2013, found significant differences, between height and weight of Children with β-Thalassemia Major with emmetropia children. Where the children with β-Thalassemia Major appeared shorter and thinner than in the children with emmetropia.[4] Lack of weight in children with thalassemia is associated with high body metabolism. Chronic anemia will cause oxygen delivery to be low, so the body will increase metabolism to produce catecholamines. The resulting catecholamine is used to increase heart frequency that directly affects cardiac output.[2]

The study also showed a significant differences (p <0.05) between the head circumference of the children with β-Thalassemia Major group with children with emmetropia. Children with β-thalassemia major will experience changes in craniofacial structures such as frontal bossing that should have an effect on head circumference.[5] However, in this study, the head circumference was found smaller in children with β-Thalassemia Major. This is suitable with the study of Karakas et al in Turkey in 2016 involving 43 Children with β-Thalassemia Major and 43 children of emmetropia as the control explained that there were significant differences in terms of head circumference. The study showed that head circumference in children with thalassemia seen smaller than the control.[6] The study of Elkitkat RS et al in Egypt in 2016 involving 100 Children with β-Thalassemia Major and 100 children of emmetropia as the controls explained there was a significant difference in terms of head circumference. The study showed that head circumference in Children with β-Thalassemia Major appeared to be smaller than the controls, but not statistically significant.[7] Genetic mutations occurring in thalassemia vary widely, which is directly related to the phenotypic expression of the disease. Anatomic changes in the circumference of head circumference may not necessarily occur uniformly in all child populations in the world.[6]

Mean Hb in the β-thalassemia major patients was 6.7 ± 1.24 g/dl. The Hb was the Hb before blood transfusion was performed. All of the β-thalassemia major patient samples have received multiple blood transfusions, unfortunately, it is not recorded how many times each patient receives a blood transfusion. The given transfusion is a packed red blood cell component (PRC).[7] The Hb condition of the β-thalassemia major patients in this study was consistent with the mean height and weight which were lower than the emmetropia patients, reflecting the presence of growth disorders in this sample, but from statistical there was no significant differences between the two groups (p>0,05)

Table 2 shows no significant difference between the sex of Children between the two groups (p>0,05).. Ain et al's study in Pakistan in 2011 involving 300 of β-thalassemia children consisting of 97% of β-thalassemia major and 3% of intermedia thalassemia, despite having equal opportunities, but males were significantly higher in proportion suffering from β-thalassemia major. According to the theory, the proportion of males suffering from β-thalassemia major will increase if the first cousin marriage takes place (1st cousin).[8]

Table 3 shows a significant difference eyesight between the two groups (p<0,05), where the eyesight of the

children with β-Thalassemia Major looked worse than children with emmetropia.[9] This is suitable with Merchant et al's study in India (2017) involving 60 Children with β-Thalassemia Major and 60 emmetropia children as the controls showed a significant difference in eyesight, where the eyesight of the children with β-Thalassemia Major looked worse than children with emmetropia.[9]The study of Aksoy et al in Turkey (2014) involved 43 Children with β-Thalassemia Major and 47 emmetropia children as controls showed a significant difference in eyesight, where the eyesight of children with β-Thalassemia Major was worse than that of emmetropia children.[10] On the other hand, Heydarian S et al's study in Iran (2016) from 54 Children with β-Thalassemia Major and 54 emmetropia children as the controls showed no significant difference in refractive abnormalities between the two groups but had significant differences in biometric parameters.[11] Refractive disorders are due to axial length shortening that is likely to be found in children with β-Thalassemia Major. Abnormal perfusion will cause growth restriction on craniofacial bone then directly inhibits orbital bone growth. This situation will make the growth of orbita space is limited, thus suppressing the growth of eye tissue. This condition is evidenced by studies showing a smaller eye volume in thalassemia children when compared with normal children.[12]

Table 4 showed there was a significance differences in anterior chamber depth and lens thickness between the two groups (p<0,05). In axial length the average of axial length was shorter in thalassemia group compared to control group, but no from statistical there was no significant differences (p>0,05). Aksoy et al in Turkey (2014) study involving 43 major thalassemia children and 47 emmetropia children as the controls explained no difference between axial length in thalassemia and the control children. However, significant differences were found in the eyesight and Schirmer test values. Subjects in this study had an average age of eight to fourteen years old, both in the children with β-Thalassemia Major and emmetropia. Based on the axial length growth curve of American Academy of Ophthalmology in children aged 8-14 years old, having axial length of 23-24 mm.[13] While the results of this study showed the average axial length was 21-23 mm. Asian and European posture differences may be able to explain the axial length discrepancy in this study. Large scale studies are needed to determine the standard deviation of axial length growth in Asian people, especially

Anterior chamber depth in the children with β-Thalassemia Major looked more superficial than emmetropic children. Heydarian S et al in Iran (2016) involved 54 Children with β-Thalassemia Major and 54 emmetropia children as the controls that found significant differences in terms of axial length, anterior chamber depth and magnitude of keratometry values, where the Children with β-Thalassemia Major has a short axial length, a shallow anterior chamber depth, and a smaller keratometry value.[11] Elkitkat RS et al in Egypt (2016) involved 100 Children with β-Thalassemia Major and 100 emmetropia children as the controls showed that there was a significant difference in terms of biometric parameters. There was a significant difference, in which children with β-Thalassemia Major had a short axial length, a shallow anterior chamber depth and thicker lens.[7]

The shallow anterior chamber depth is directly proportional to the thickening of the crystalline lens. The average anterior chamber depth in emmetropia children ages 8-14 years old is 3.30-3.44 mm.[13] However, the average anterior chamber depth obtained from this study was 2.8-3.48 mm. No standard deviation curve has yet been found for the anterior chamber depth for Asian populations to be a problem that needs to be immediately solved.

This study also showed a significant differences of lens thickness between the two groups (P <0.05), where the lens thickness of the children with β-Thalassemia Major looks thicker than emmetropia children. Kundu et al's study in India (2017) involved 502 Children with β-Thalassemia Major and 523 emmetropia children respectively found significant differences in terms of axial length, lens thickness and value keratometry. Children with β-Thalassemia Major has a short axial length, thicker lens and steeper corneal curvature, characterized by smaller keratometry values. This difference is caused by changes in craniofacial bone structures found in thalassemia children lead to changes in biometric examination.[3]

The weakness of this study is the lack of the samples. There is still neeed for the similar study with prospective designs to monitor the growth of axial length, anterior chamber depth and lens thickness in the children with β-Thalassemia Major. The absence of standard deviation curves of normal growth of biometric parameters for the Indonesian nation presents a special challenge in the future for an immediate solution.

Conclusion

β-thalassemia major as accompanied by typical bone growth disorders, especially craniofacial may cause abnormal orbital bone growth and considered to evaluating biometric examination .axial length, anterior chamber depth and lens thickness Well design, good quality prospective longitudinal study on larger populations are therefore needed.

Disclosure

Patients have been approved prior to the study conducted and cost involved in this research is borne by researcher.

References

1. DeBaun MR, Frei-Jones MJ, Vichinsky EP. Thalassemia Syndromes. In: Kliegman MR, Stanton BF, St Geme JW, Schor NF, editors. Nelson textbook of Pediatrics. 20th ed. Philadelphia: Elsevier; 2016. p. 2349-53.

2. Wahidiyat I, Wahidiyat PA. Genetic Problems At Present And Their Challenges in The Future: Thalassemia as A Model. Pediatr Indones. 2006; 46: 189-94.
3. Kundu A, Ganguly P, Sinharay A, Patil P, Sharma K, Bandyopadhyay M. A Study To Assess The Ocular Biometric Parameters And Prevalence Of Refractive Errors Among Thalassemia Children In A Rural Based Tertiary Hospital. IJHSR. 2017; 7(4): 160-5.
4. De Sanctis V, Soliman AT, Elsedfy H, Skordis N, Kattamis C, Angastiniotis M, et al. Growth And Endocrine Disorders In Thalassemia: The International Network on Endocrine Complications In Thalassemia (I-CET) Position Statement And Guidelines. Indian J Endocr Metab. 2013; 17(1): 8-18.
5. Kwiatkowski JL. Thalassemia. In: Lanzkowsky P, Lipton JM, Fish JD, editors. Lanzkowsky's Manual Of Pediatric Hematology And Oncology. 6th ed. Amsterdam: Elsevier; 2016. 186-95.
6. Karakas S, Tellioglu AM, Bligin M, Omurlu IK, Caliskan S, Coskun S. Craniofacials Characteristics of Thalassemia Major Patients. Eurasian J Med. 2016; 48 : 204-8.
7. Elkitkat RS, El Shazly AA, Ebeid WM, Deghedy MR. Relation of Anthropometric Mesurements to Ocular Biometric Changes and Refractive Error in Children With Thalassemia. Eur J Ophthalmol. 2016; 5: 212-9.
8. Ain Q, Ahmad L, Hassan M, Rana SM, Jabeen F. Prevalence of Beta Thalassemic Patients Associated With Consanguinity and Anti HCV-Antibody Positivity- A Cross Sectional Study. Pakistan J.ZOOL. 2011; 43(1) : 29-36.
9. Merchant RH, Punde H, Thacker N, Bhatt D. Ophthalmic Evaluation in Beta-Thalassemia. Indian J Pediatr. 2016; 22:190-5.
10. Aksoy A, Aslankurt M, Aslan L, Gul O, Garipadic M, Celik O, et al. Ocular Findings In Children With Thalassemia Major In Eastern Mediterranean. Int J Ophthalmol. 2014; 7(1): 118-21.
11. Heydarian S, Jafari R, Karami H. Refractive Errors And Ocular Biometry Components In Thalassemia Major Patients. Int Ophthalmol. 2016; 36: 267–7.
12. Nowroozzadeh MH, Kalantari Z, Namvar K, Meshkilbaf MH. Ocular Refractive And Biometric Characteristics in Patients with Thalassaemia Major. Clin Exp Optom. 2011; 94(4): 361–6.
13. Gul A, Caglar C, Cinal A, Yasar T, Kilic A. Ocular Biometry And Central Corneal Thickness In Children: A Hospital-Based Study. Arq Bras Ophthalmol. 2014; 77(3):152-4.