

Original Article

The occurrence of pulmonary hypertension in patients with thalassemia major

Hasan Basri, MD; Armijn Firman, MD; Kusnandi Rusmil, MD; Eddy Fadlyana, MD

ABSTRACT

Background The life of patients with thalassemia major depends on blood transfusions, while repeated blood transfusions may cause adverse effects such as iron deposition in various organs, including heart and lungs, which eventually increases the pulmonary arterial pressure.

Objective This study was proposed to know the occurrence of pulmonary hypertension in patients with thalassemia major, measured by echocardiography in the Thalassemia Clinic, Department of Child Health, Medical School, Padjadjaran University/Hasan Sadikin Hospital, Bandung.

Methods A descriptive cross-sectional study was carried out on 30 patients with thalassemia major, aged 10-14 year-old who received repeated blood transfusions. The study was conducted from April to May 2002. Subjects were examined right after a blood transfusion completed and the pulmonary arterial pressure was assessed using Doppler–echocardiography and 2-D echocardiography.

Results Twenty two out of 30 subjects showed pulmonary hypertension, with pulmonary arterial pressure ranged between 32.3 to 46.2 mmHg. According to the age group, pulmonary hypertension was found in 12 out of 17 subjects aged 10-12 years old and 10 out of 13 subjects aged 13-14 years old.

Conclusion The occurrence of pulmonary hypertension in patients with thalassemia major at Hasan Sadikin Hospital was 22/30 and seemed to increase with the age of the patients [*Paediatr Indones* 2003;43:162-164].

Keywords: *pulmonary hypertension, thalassemia major, blood transfusion, echocardiography*

Thalassemia is a hematologic disease caused by an inherited genetic defect in the production of globin polypeptide chain. Thalassemia major is a variant of thalassemia, clinically manifests as severe chronic

anemia. Until now, there is no causal therapy for the disease.¹⁻⁴ The patient usually dies before ten year-old because of severe anemia, malnutrition, and infection.⁵⁻⁷ Since transfusion therapy has been developed, the life expectancy of patients with thalassemia major increases, but repeated blood transfusions cause iron excess in the body.^{4,5} The excessive iron will be deposited in various organs, including heart and lungs. Chronic anemia and iron deposition in heart and lungs for a long period may cause cellular and tissue malfunction leading to complications. Heart failure due to myocardial hemosiderosis, myocarditis, and pulmonary hypertension is the most common cause of death in patients with thalassemia major.⁷⁻¹⁰ The mortality rate of 10-14 year-old thalassemia major patients caused by heart failure is approximately 41%.⁷ Until today, the pathogenesis is still controversial. Iron deposit in the heart might affect the contractility of myocardial cells and lead to left and right ventricular dysfunction.^{8,9} Several studies suggested that the heart failure might be associated with myocarditis. The occurrence of pulmonary hypertension increased recently and may play an important role in the pathogenesis of heart failure or cardiogenic death in patients with thalassemia major.⁹

From the Department of Child Health, Medical School, Padjadjaran University, Hasan Sadikin Hospital, Bandung.

Reprint requests to: Hasan Basri, MD, Department of Child Health, Medical School, Padjadjaran University, Hasan Sadikin Hospital, Bandung, Indonesia. Tel. 62-22-2011282, Fax.62-22-2032216.

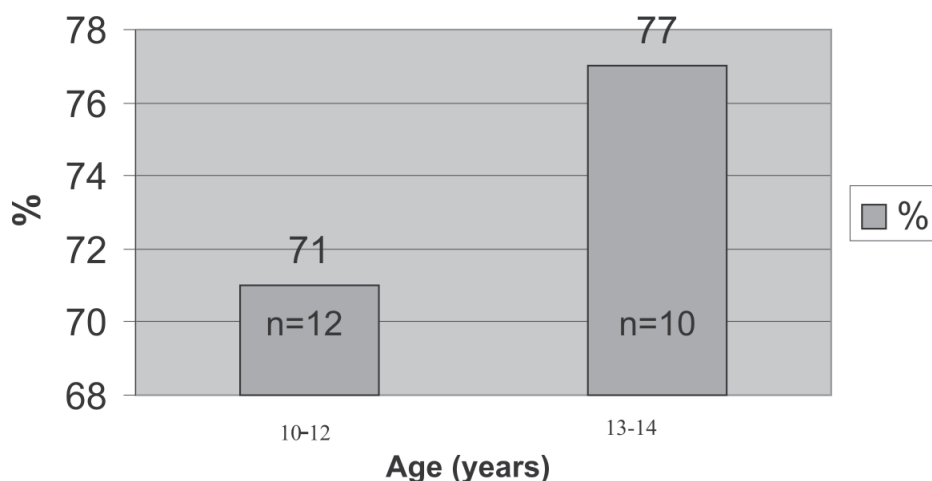


Figure. The comparison of pulmonary hypertension occurrence based on age group

The pulmonary arterial pressure can be measured by catheterization, but this technique is less preferable due to its invasiveness. Non-invasive technique is chosen such as echocardiography by measuring tricuspid regurgitation and doppler flow of the pulmonary artery. Echocardiography has been proven to be an accurate and reliable method to assess pulmonary arterial pressure.⁹⁻¹⁶ The objective of this study was to know the occurrence of pulmonary hypertension in patients with thalassemia major measured by echocardiography at the Outpatient Thalassemia Clinic, Department of Child Health, Hasan Sadikin Hospital.

Methods

This was a descriptive study with cross-sectional design, conducted from April to May 2002 in the Outpatient Thalassemia Clinic. Sample size was determined with 95% confidence interval, $Z\alpha$ score of 1.96, degree of absolute proximity of 15% (d), and disease proportion of 80% (P). From sample size formula ($n = Z\alpha^2 PQ/d^2$), the minimum sample size was 30 children.¹⁷ Subjects were determined by consecutive admission of patients with thalassemia major who underwent periodic transfusions and fulfilled the inclusion criteria i.e., aged 10-14 years, did not suffer from congenital heart disease, and had informed consent from parents. All subjects who fulfilled the criteria were recorded by name, age, and sex. Data were presented descriptively.

Echocardiography examination was performed right after the patient completed a transfusion, by using echocardiograph Logic 500 series, made by General Electric, with 2.5 MHz transducer. Complete echocardiography examination was performed to exclude congenital heart disease. Pulmonary arterial pressure was measured by examining maximal velocity of the tricuspid regurgitation (V_{max}) with Doppler echo at short apical axis -4 chamber view, cursor was placed at tricuspid valve. To calculate Transtricuspid gradient, modified Bernoulli equation ($\Delta P = 4 V^2$) was used. Pulmonary arterial systolic pressure was the additional sum of transtricuspid gradient with right atrial pressure of 10 mmHg. The patient was considered had pulmonary hypertension when the sum exceeds 25 mmHg.⁹⁻¹⁶

Results

From 30 subjects who fulfilled the inclusion criteria, 17 were male and 13 were female. Seventeen subjects aged 10-12 year-old (primary school) and 13 subjects aged 13-14 year-old (junior high school). Three subjects had undergone splenectomy.

Twenty two subjects had pulmonary hypertension consisting of 15 male and 7 female subjects, with pulmonary arterial pressure between 32.4-46.2 mmHg. The occurrence of pulmonary hypertension based on age group can be seen in **Figure** below.

Discussion

The occurrence of pulmonary hypertension in patients with thalassemia major in this study was quite high. This might be caused by repeated blood transfusions for such long period of time leading to the deposition of iron in the lungs and heart, prolonged hypoxia, and irregular or absence of chelating therapy using desferoxamine.⁹

Irregular use of chelating therapy was caused by its expensiveness and limited equipment to administer this agent. This was similar to other study which found that the prevalence of pulmonary hypertension was as high as 81.5% in patients with thalassemia major aged >10 year-old.⁹ This condition might be caused by the delayed administration of chelating therapy. However, it was different from the study of Derchi who found pulmonary hypertension in only 10% of patients with thalassemia major. In these patients, chelating therapy begun at the age of 3 ± 2 years old.^{9,10}

In conclusion, the occurrence of pulmonary hypertension in thalassemia major patients at Hasan Sadikin Hospital, Bandung was 22/30 and seemed to increase with the age of the patients. We suggested that echocardiography examination should be done before the age of 10 year-old for early detection of pulmonary hypertension. A study of pulmonary hypertension in patients with thalassemia major aged less than 10 year-old is needed. Further study is needed to know the influencing factors of the occurrence of pulmonary hypertension in patients with thalassemia major.

References

- Giardina PJ, Hilgartner MW. Update on thalassemia. *Pediatric in review* 1992;13:55-63.
- Benz EJ, Giardina PJV. Thalassemia syndrome. In: Miller DR, editor. *Blood diseases of infancy and childhood*. Mosby Year book Inc. St Louis; 1995. p. 460-98.
- Honig GR. Hemoglobin Disorders. In: Behrman, Kleigman, Arvin, editors. *Nelson textbook of pediatrics*. 15th ed. Philadelphia WB Saunders Co; 1996. p. 1401-5
- Olivieri NF. The beta thalassemias. *N Engl J Med* 1999;341:99-109.
- Olivieri NF, Nathan DG, MacMillan JH, Wayne AS, Liu PP, Mc Gee A, *et al.* Survival in medically treated patients with homozygous beta – thalassemia. *N Eng J Med* 1994;331:574-8.
- Leon MB, Borer JS, Bacharach SL, Green MV, Benz EJ Jr, Griffith P, *et al.* Detection of early cardiac dysfunction in patients with severe beta-thalassemia and chronic iron overload. *N Eng J Med* 1979;301:1143-8.
- Zurlo MG, De Stefano S, Borgna-Pignatti C, Di Palma A, Piga A, Melevendi C, *et al.* Survival and causes of death in thalassemia major. *Lancet* 1989;2:27-30.
- Merault JM, Escamilla R, Degano B, Guittard J, Herman C, Krempf M. Pulmonary hypertension in patients with thalassemia major. *Rev Mal Respir* 2000; 17:689-91.
- Du ZD, Roguin N, Milgram E, Saab K, Koren A. Pulmonary hypertension in patients with thalassemia major. *Am Heart J* 1997;134:532-7.
- Derchi G, Fonti A, Forni GL, Galliera EO, Cappelini MD, Turoti F, *et al.* Pulmonary hypertension in patients with thalassemia major. *Am Heart J* 1999;138:384
- Alverson DC, Eldridge M, Dillon T, Yabek SM, Berman W. Non invasive pulsed doppler determination of cardiac output in neonate and children. *J Pediatr* 1982;101:46-50.
- Ehler KH, Giardina PJ, Lesser ML, Engle MA, Hilgartner MW. Prolonged survival in patients with beta-thalassemia major treated with desferoxamine. *J Pediatr* 1991;118:540-5.
- Heger JW, Roth FR, Niemann JT, Criley JM. Echocardiography. In: *Cardiology*. Baltimore: William & Wilkins; 1994. p. 93-118
- Kulik TJ. Pulmonary hypertension. In: Fyler DC, editor. *Nadas pediatric cardiology*. Philadelphia: Hanley & Belfus; 1992. p. 83-100
- Park MK. Pulmonary hypertension. In: *Pediatric cardiology for practitioners*. 3rd ed. St Louis: Mosby; 1996. p. 420-9.
- Park MK. Noninvasive techniques. In: *Pediatric cardiology for practitioners*. 3rd ed. St Louis: Mosby; 1996. p. 67-82.
- Madiyono B, Moeslichan S, Sastroasmoro S, Budiman I, Purwanto SH. Perkiraan besar sampel. In: Sastroasmoro S, Ismael S, editors. *Dasar-dasar metodologi penelitian klinis*. Jakarta: Bina Rupa Aksara; 1995. p. 187-212