Risk Factors to Growth Retardation in Major Thalassemia

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Abstract

The increasing in the life span of patients with major thalassemia should be followed by increased quality of life. There are factors which can affect growth retardation in these patients. The aim of this study was to find out the risk factors for growth retardation in patients with major thalassemia. An analytical study with cross-sectional design was conducted at Pediatric Thalassemia Clinics of Dr.Hasan Sadikin Hospital, Bandung, in June to July 2006. The subjects of this study were patients with major thalassemia. Inclusion criteria's were age under 14 years old, had no chronic diseases like tuberculosis, cerebral palsy with complete medical records. Risk factors were the timing of diagnosis, initial and dose of deferoxamine, volume of transfused blood, mean pretransfusion hemoglobin level, family income, and age. Antropometric measurement indices were used to assess the growth which expressed in Z score. Growth evaluated based on height/age (H/A) and growth retardation if H/A <-2 SD. Risk factors for growth retardation were analyzed separately using chi-square test and odds ratio (OR) with 95% confidence interval (CI). Then they were analyzed simultaneously with logistic regression method. Subjects consisted of 152 patients with major thalassemia. Seventy three thalassemia patients were stunted. Analysis showed that age (OR: 5.42, 95% CI: 2.32–12.65, p <0.001), dosage of deferoxamine (OR: 4.0, 95% CI: 1.29–12.41, p: 0.016), and family income (OR: 2.32, 95% CI: 1.06–5.06, p: 0.036) were risks factors for growth retardation. Conclusion, risk factors for growth retardation in major thalassemia are age, dosage of deferoxamine, and family income. [**MKB.** 2011;43(1):21–5].

Key words: Major thalassemia, risk factors, stunted

Faktor Risiko terhadap Gangguan Tumbuh pada *Thalassemia Mayor*

Abstrak

Bertambahnya harapan hidup penderita *thalassemia*, seyogianya diikuti dengan kualitas hidup seperti anak normal. Terdapat berbagai faktor risiko yang mempengaruhi terjadinya gangguan tumbuh pada penderita *thalassemia mayor*. Tujuan penelitian ini untuk mengetahui berbagai faktor risiko terjadinya gangguan tumbuh pada penderita *thalassemia mayor*. Penelitian ini merupakan penelitian analitik dengan rancangan *cross sectional* di Poliklinik Anak *thalassemia* Dr. Hasan Sadikin, Bandung, pada bulan Juni–Juli 2006. Subjek penelitian ini adalah penderita *thalassemia mayor*. Kriteria inklusi adalah penderita berusia <14 tahun, tidak mempunyai penyakit kronik seperti tuberkulosis, palsi serebral, dan rekam medis yang lengkap. Faktor risiko adalah usia saat penegakan diagnosis, usia mulai menggunakan desferoksamin, dosis desferoksamin, volume darah yang telah diterima, kadar hemoglobin rata-rata sebelum transfusi, penghasilan keluarga, dan usia penderita. Dengan antropometri akan ditentukan pertumbuhan berdasarkan skor-Z. Pertumbuhan dinilai dari indeks tinggi badan/usia dan penderita yang mengalami gangguan tumbuh bila tinggi badan/usia <-2 SD. Faktor risiko gangguan tumbuh dianalisis menggunakan uji ki kuadrat dan rasio *odds* (RO) dengan interval kepercayaaan (IK) 95%, selanjutnya dilakukan analisis dengan metode regresi logistik. Subjek terdiri atas 152 penderita *thalassemia mayor*. Terdapat 73 penderita yang mengalami gangguan tumbuh. Hasil analisis menunjukkan usia penderita (RO 5,42; IK 95%: 2,32–12,65, p <0, 001), dosis desferoksamin (RO 4,0; IK95%:1,29–12,41, p: 0,016), dan penghasilan keluarga (RO 2,32; IK 95%:1,06–5,06, p: 0,036). merupakan faktor risiko terjadinya gangguan tumbuh. Simpulan, faktor risiko terjadinya gangguan tumbuh pada *thalassemia mayor* adalah usia, dosis desferoksamin, dan penghasilan keluarga.
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Kata kunci: Faktor risiko, gangguan tumbuh, *thalassemia mayor*

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Introduction

The increasing in the life span of patients with thalassemia should be followed by increased quality of life but almost all thalassemia patients had growth retardation.[1-4] Growth retardation in patients with thalassemia major is caused by multiple factors such as tissue hypoxia and iron overload. Nutrition is another important factor for growth.[5,6] Growth retardation can be evaluated based on height/age (H/A) <-2 SD (stunted).[7,8] Saxena[5] found five risk factors: low hemoglobin pretransfusion, high feritin, inoptimal iron chelating agent, poor socio economic background, and increasing age to growth retardation in thalassemia major patients. Study in Iran found there is association of initial deferoxamine treatment, dosage of deferoxamine, age, and maintenance level of hemoglobin <8.5 g/dL with growth retardation.[9,10] Andayani et al[11] found association between volume of transfused blood and growth retardation. Until this time, there has never been any study involving all seven factors simultaneously.

The aim of this study was to know the risk factors for growth retardation (the timing of diagnosis, initial deferoxamine treatment and dosage of deferoxamine, volume of transfused blood, mean pretransfusion hemoglobin level, family income, and age) in patients with major thalassemia. The study was initiated with the approval of Institutional Ethics Committee of Medical School, University of Padjadjaran, Hasan Sadikin Hospital Bandung, Indonesia and written informed consent of either parents was taken for inclusion of children.

Methods

An analytical study with cross-sectional design was conducted at the Clinics of Pediatric Thalassemia of Hasan Sadikin Hospital, Bandung. The subjects of this study were patients with major thalassemia visiting the clinic in June to July 2006. Inclusion criteria's were age under 14 years old, had no chronic diseases like tuberculosis, cerebral palsy, congenital heart diseases, and has complete medical records. This study involved only 152 subjects recruited consecutively due to limited time and fund.

Risk factors were the timing of diagnosis, initial and dosage deferoxamine treatment, volume of transfused blood, mean pretransfusion hemoglobin level, family income, and age. Outcome in this study was stunted.[7,8]

Anthropometric measurement indices were

Table 1 Characteristics Major Thalassemia Patient's

Characteristics	
Sex	
Male	78 (51.3%)
Female	74 (48.7%)
Age (months)	
Range	11–157
Weight (kg)	
SD	5.2
Range	7.1–32
Height (cm)	
SD	15.5
Range	66–145
The timing of diagnosis (months)	
Range	1–15
Initial deferoxamine treatment (years)	
Range	1–12.5
Dosage of deferoxamine	
Optimal	24 (16.9%)
In optimal	118 (83.1%)
Volume of transfused blood (mL)	
SD	12,754
Range	500–60,000
Mean pretransfusion hemoglobin level (g/dL)	
SD	1.14
Range	5–9
Family income (rupiah)	
Range	100,000–5,000,000

Table 2 Association of Risk Factors to Growth Retardation

Variable	Stunted (73)	Normal (79)	X^2	p Value	OR
Age (years)					
>10	34	10	21.22	<0.001*	2.14 (1.59–2.88)
≤10	39	69			
Timing of diagnosis (months)					
≥12	22	17	1.48	0.224	1.25 (0.88–1.76)
<12	51	62			
Initial deferoxamine treatment (years)					
<3 or >10	26	13	6.49	0.011	1.56 (1.14–2.14)
3–10	44	59			
Deferoxamine dosage					
Inoptimal	65	53	9.36	0.002*	2.64 (1.19–5.87)
Optimal	5	19			
Volume of transfused blood (mL)					
≥20,000	44	21	17.59	<0.001	2.03 (1.44–2.86)
<20,000	29	58			
Mean pretransfusion hemoglobin level (g/dL)					
<8.5	55	42	8.08	0.004	1.73 (1.14–2.63)
≥8.5	18	37			
Family income (rupiah)					
<850,000	54	43	6.26	0.012	1.61 (1.08–2.42)
≥850,000	19	36			

*X^2: Chi-square, OR: Odds Ratio

used to assess the growth which was expressed in Z-score. Growth evaluated based on H/A <-2 SD (stunted). Risk factors for growth retardation were identified by taking history and based on medical records.[7,8]

Patients with thalassemia major diagnosed by electrophoresis of blood. Timing of diagnosis was age the patients diagnosed thalassemia, divided into two groups, <12 months and ≥12 months. Initial deferoxamine treatment was age at the first deferoxamine uses, divided into two groups, <3 or >10 years and 3–10 years. Dosage of deferoxamine consisteded of optimal dosage and inoptimal dosage. Volume of transfused blood was divided into two groups, <20,000 mL and ≥20,000 mL. Mean pretransfusion hemoglobin level were mean hemoglobin level patients before transfusion, divided into two groups, <8.5 g/dL and ≥8.5 g/dL. Family income evaluated based on income/month, divided into two groups, < 850,000 and ≥850,000 rupiah.

Risk factors for growth disturbances and nutritional status were analyzed separately using chi-square test and odds ratio (OR) with 95% confidence interval (CI). They were analyzed concurrently with logistic regression method.[12] Data were analyzed using SPSS version 13.00 for windows SPSS inc., Chicago-Illinois, USA.

Results

There were 152 patients with thalassemia major enrolled in this study. Seventy three thalassemia patients were stunted. Characteristics of patients are shown in Table 1.

Based on univariate analysis, association of various risk factors with stunted were age >10 years, initial deferoxamine treatment <3 or >10 years, in optimal deferoxamine dosage, volume of transfused blood ≥20,000 mL, mean transfusion hemoglobin level <8.5 g/dL and family income < 850,000 rupiah shown in Table 2.

Logistic regression showed that age >10

Table 3 Risk Factors To Gowth Retardation In Patients with Major Thalassemia

Variable	Coefficient β	SE (β)	p* Value	OR (95% CI)
Age >10 years old	1.690	0.432	<0.001	5.422 (2.323–12.653)
Initial deferoxamine treatment <3 or >10 years old	0.746	0.463	0.107	2.108 (0.851–5.224)
Inoptimal deferoxamine dosage	0.386	0.578	0.016	4.0 (1.289–12.413)
Volume of tranfused blood ≥20,000 mL	0.418	0.465	0.368	1.519 (0.611–3.781)
Mean pre transfusion hemoglobin level <8.5 g/dL	0.275	0.420	0.513	1.317 (0.578–2.999)
Family income <850,000	0.841	0.400	0.036	2.318 (1.058–5.075)
Constanta	-1.671			

*Log regression

years old (odds ratio 5.42, p <0.001), in optimal deferoxamine dosage (odds ratio 4, p=0.016), and family income < 850,000 rupiah (odds ratio 2.32, p=0.036) were risk factors for stunted shown in Table 3.

Discussion

This study was expected to show risk factors for growth retardation in thalassemia patients. There were 152 children enrolled in this study consisted of 78 males (51.3%) and 74 females (48.7%). We found no significant difference in sex gender in association with growth retardation. It was in accordance with study in Iran, Turkey, and Hongkong.[13-15]

In this study growth retardation were assessed based on height/age. Our study showed 73 (48.0%) were stunted. These data was similar with previous report that showed almost all thalassemia patients were stunted. Karamifar et al[14] reported prevalence of stunted as 64% in patients with major thalassemia. In other study, Karamifar et al[15] concluded 62.9% of girls and 69% of boys were less than 2 SD below mean for normal height. Asadi Pooya et al[9] reported the height for age in 63% of patients with major thalassemia were lower than the 5th percentile. The exact mechanism of growth retardation in children with thalassemia major is unclear and seems to be multifactorial.[5,9, 14-16]

Saxena[5] found five risk factors: low hemoglobin pre transfusion, high feritin, inoptimal iron chelating agent, poor socio economic background, and increasing age to growth retardation in thalassemia major patients. In Iran found an association of initial deferoxamine treatment, dosage, age, and maintenance level of hemoglobin <8.5 g/dL with growth retardation.[9,10]

In our study, only three of seven risk factors for stunted were significant. There were three risk factors for stunted such as age >10 years old, inoptimal deferoxamine dosage, and family income <850,000 rupiah. If three risk factors were found together, the risk for stunted raised to 20.5%.

Similar with previous study from Pignatti et al[17] that found stunted was more frequent in pubertal patients. This was despite the fact that in pubertal children there may be a reduced growth spurt with marked deceleration and iron overload in endocrine glandular. The effect of in optimal deferoxamine dosage was similar with study from Saxena[5] which showed that growth retardation in India were led to high feritin. Level family income <850,000 rupiah was risk factor for stunted, the result was similar with study from Saxena[5]. Poor social economic states based on family income implies poor nutrition, hygiene, and social atmosphere.[5] Most of our patients suffered from poor control, inoptimal deferoxamine dosage, and low economic status.

In conclusion risk factors for growth retardation are age >10 years old, in optimal deferoxamine dosage, and family income <850,000 rupiah. The timing diagnosis, initial deferoxamine treatment, mean pretransfusion hemoglobin level, and volume of transfused blood clinically seemed to be the influencing factors, but the results was

not statistically significance, so they need to be explored further with larger sample.

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