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Bone Health Status among Thalassemia Children

Yeo Pei Sien[1]*, Noor Aini Mohd Yusoff[2], Suzana Shahar[2] and Roslee Rajikan[2]

[1] Institute for Public Health, Ministry of Health, Malaysia.
[2] Dietetics Program, Faculty of Health Sciences, Universiti Kebangsaan Malaysia, Malaysia.

**For reprint and all correspondence: Yeo Pei Sien, Institute for Public Health, Jalan Bangsar, 50290 Kuala Lumpur, Malaysia.*
Email: yeops@moh.gov.my

ABSTRACT

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Introduction Low bone mineral density is a significant problem in children with Thalassemia which may lead to increased risk for fragility fractures and suboptimal peak bone mass. This cross-sectional study was conducted to determine the bone health status of Thalassemia children Universiti Kebangsaan Malaysia Medical Centre and Paediatrics Insititute Kuala Lumpur Hospital.

Methods A total of 81 respondents diagnosed with transfusion dependant beta Thalassemia (41 boys and 40 girls) aged between 7 to 19 years old completed the study. The data collected were demographic information, anthropometric measurements, dairy frequency questionnaires, dietary habits of the respondents and their parents, dietary intakes and bone densitometry using Ultrasound Bone Densitometer.

Results For Quantitative Ultrasound (QUS) parameters, T-score of 9.8% participants were lower than -1.0 and 30.9% of the participants had lower Speed of Sound (SOS) than healthy SOS. This study showed there was no difference in bone density by sex ($p>0.05$). The median bone density of boys was 1616.00 m/ sec (IQR= 39.00) and girls' was 1579.00 m/ sec (IQR= 116.00). SOS was not increased with age, height and weight; but girls' Body Mass Index (BMI). Malay children had significantly higher SOS than non-Malay children.

Conclusions This study highlights a need of proper intervention for the high risk group to achieve optimal bone health.

Keywords Thalassemia children - Bone mineral density - Bone health status - QUS - Malaysia.

INTRODUCTION

Low bone mineral density is a significant problem in patients with thalassemia which leads to decreased quality of life. Regular transfusions and increased compliance with iron chelation therapy are often accompanied by a series of serious complications including growth failure, osteopenia and osteoporosis in later life[1].

Children with thalassemia major who were fully treated with transfusion and chelation therapy, were found to have reduced bone mineral density (BMD) at diagnosis and showed further reductions at follow-up[2,3]. These children may be at increased risk for fragility fractures and suboptimal peak bone mass[1].

Thalassemias are particularly associated with people of Mediterranean origin, Arabs, and Asians. The estimated prevalence is 16% in people from Cyprus, 1% in Thailand, and 3-8% in populations from Bangladesh, China, India, Malaysia and Pakistan. In Malaysia, about 4.5% of the people are heterozygous carriers for beta thalassemia and these couples are at risk of producing a child with beta thalassemia major where affected births annually would be 2.1/ 1000[4].

A study in Iran found that the prevalence of lumbar osteoporosis and osteopenia in beta-thalassemia major patients were 50.7% and 39.4%, while lumbar BMD abnormalities were associated with duration of chelation therapy. Femoral osteoporosis and osteopenia were present in 10.8% and 36.9% of the patients[5].

As the combination of transfusion and chelation therapy has extended the life expectancy of thalassemia patients, improved survival of patients has allowed for adult complications that have a major impact on the quality of life. The objective of this study was to determine bone health status of thalassemic children using bone densitometry.

METHODS

This was a cross-sectional study conducted in paediatric thalassemic patients aged between 8-19 years admitted as in-patient or out-patient at the Paediatrics Institute Kuala Lumpur Hospital (PIKLH) and Universiti Kebangsaan Malaysia Medical Centre (UKMMC), Kuala Lumpur. Data were collected from May 2009 until August 2009. Ethical approval for this study was obtained from the Medical Research Secretariat, Universiti Kebangsaan Malaysia Medical Centre, Clinical Research Centre (CRC) and the Ministry of Health Research& Ethics Committee (MREC), Malaysia (Reference Ethical Approval No.: FF-290-2008).

Sampling

Convenience sampling of 158 thalassemic patients diagnosed with transfusion dependant beta thalassemia (major, intermediate) who met the inclusion criteria been chosen. The lists of thalassemia patients were obtained from the Daycare Centre in the two hospitals. This study was done over a period of 4 months. Eighty four (84) participants agreed to participate. *Inclusion criteria:* (a) Patients with thalassemia syndrome (including transfusion dependent beta-thalassemia, E/beta-thalassemia major and intermediate); and (b) age 7-19 years old. *Exclusion criteria:* (a) Thalassemic patients with malabsorption diseases, other gastrointestinal problems, asthma, or on any other medications; (b) patients currently taking a bisphosphonate medication for osteopenia. (c) patients who have had a bone marrow transplant. (d) chronic use of systemic corticosteroids; and (f) patients currently use calcium supplement.

After the written consent was obtained from the parent, each participant was interviewed for demographic information, dairy frequency questionnaires, dietary habits of subjects and their parents, and dietary intakes. Body weight and height of participants were measured.

Ultra Sound Bone Densitometry

Bone densitometry test was performed by using Ultrasound Bone Densitometer CM-200 (Furuno Electric Co., Ltd., Japan) to measure participants' bone mineral density (BMD). QUS parameters that had been assessed were Speed of Sound (SOS) and T-score. SOS is a measurement which the sound velocity in cancellous bone is calculated from Time of Flight (TOF) measurement by transmission ultrasound methods[6]. The TOF method measures the sound travel time through coupled medium (gel), soft tissue and bone sample, between fixed ultrasound transducer separations. The calcaneal QUS values in mainland Chinese children and adolescents were used as reference SOS[7]. T-score is a comparison of a patient's BMD to that of a healthy thirty-year-old of the same sex and ethnicity[8].

Statistical analyses

All statistical analyses were done with SPSS software, version 16.0. Mann-Whitney U test was used to determine difference between QUS parameters and age groups. Spearman Correlation was used to determine the relationship between SOS and anthropometry data.

RESULTS

A total of 84 subjects participated in the study (response rate 53.2%). However, data from 3 participants had to be excluded in this report due to missing data and withdrawal. Forty one (50.6%) participants were boys and 40 participants (49.4%) were girls. Median age of participants was 13 (IQR=5) years old. The proportion of ethnicity was 69.1% Malays, 25.9% Chinese, 1.2% Indian and 3.7% others.

Bone health status of participants was measured using QUS parameters, i.e. Speed of Sound (SOS) dan *T-score*. Median SOS dan *T-score* for boys were 1616.00 m/second (IQR= 39.00) and 2.23 (IQR= 1.12) respectively. Where else, the median SOS and *T-score* of girls were 1579.00 m/second (IQR= 116.00) and 1.24 (IQR= 3.52) respectively. QUS paremeters of participants by age groups and sex was shown in Table 1. For the purpose of comparison with the age groups as the Recommended Nutrient Intakes for Malaysia[9], the ages were grouped as such. Result showed that there was no difference in bone density by sex.

Table 2 shows the relationship between SOS with participants' age, height, weight and BMI. Age, weight and height were not associated with QUS parameters among boys and girls.

Malay participants had higher SOS compared to other ethnic groups. The association by participants' ethnicity, family income, frequency of transfusion, chelation and anthropometry data with SOS was shown in Table 3. There was no association found between SOS and those variables.

Table 1 QUS parameter by sex and age group

Age Group (years)	n	SOS (m/sec)			T-score		
		Median (IQR)	x^2	p	Median (IQR)	x^2	p
Boys							
7-9	12	1606.50 (36.25)	3.079 (4)	0.545	1.96 (1.03)	3.079 (4)	0.545
10-12	7	1612.00 (73.00)			2.11 (2.08)		
13-15	13	1621.00 (40.00)			2.37 (1.15)		
16-18	5	1598.00(162.00)			1.71 (4.63)		
19-20*	2	1629.50 (0)			2.62 (0)		
Total	39						
Girls							
7-9	5	1612.00(100.50)	5.131 (4)	0.274	2.24 (3.05)	5.058(4)	0.281
10-12	12	1551.00(121.25)			0.40 (3.68)		
13-15	13	1607.00(100.50)			2.09 (3.09)		
16-18	7	1527.50(139.75)			-0.32 (4.23)		
19-20**	1						
Total	39						

* IQR could not be obtained since n=2
**Analysis was omitted since n=1

Table 2 Relationship of age, height, weight and BMI with SOS among boys and girls

	SOS			
	Boys (n=39)		Girls (n=39)	
	R	p	r	P
Age	0.003	0.985	-0.271	0.095
Height	0.096	0.559	-0.207	0.207
Weight	0.110	0.506	-0.299	0.065
BMI	0.124	0.453	-0.320	0.047*

* $p < 0.05$

Table 3 Relationship with SOS by participants' ethnicity, family income, frequency of transfusion, chelation therapy and anthroppometry data

	SOS			
	Low (n/ %)	High (n/ %)	χ^2	p
Ethnicity				
Malay	12/ 15.6	40/ 51.9	8.183	0.004**
Non Malay	14/ 18.2	11/ 14.3		

Family income				
<RM1500	7/ 10.1	7/ 10.1	2.654	0.120
≥RM1500	15/ 21.8	40/ 58.0		
Frequency of transfusion				
≤ 1/ bulan	25/ 32.5	44/ 57.1	1.805	0.254
> 1/ bulan	1/ 1.3	7/ 9.1		
Chelation				
Yes	0/ 0	10/ 13.3	-	-
No	25/ 33.3	40/ 53.4		
Height-for-age				
Stunted	10/ 13.0	25/ 32.5	0.774	0.379
Normal	16/ 20.8	26/ 33.7		
Weight-for-age				
Malnutrition	10/ 13.0	28/ 36.3	1.862	0.172
Normal	16/ 20.8	23/ 29.9		
BMI-for-age				
Underweight	6/ 7.8	16/ 20.8	0.581	0.446
Normal	20/ 26.0	35/ 45.4		

** $p < 0.05$

DISCUSSION

In this study, we found no difference between BMD of boys and girls. This was in contrast to the findings of Jensen et. al. who reported that the bone lesions in thalassemic patients were more frequent and more prominent in males[5], but in agreement with the some previous reports[10-12]. A study in Southeast Asian Thalassemia children also found broadband ultrasound attenuation and SOS were independent on sex[13]. Our finding might be influenced by the small number of participants in this study.

SOS of participants was compared with the calcaneal QUS values in mainland Chinese children and adolescents[7]. There was 30.9% of participants' SOS lower than the reference SOS while 80% of them were girls. Low SOS was found in the age group of 7 to 9 years old. The participants whose *T-Score* less than -1.0 were among those aged between 12 until 19 years old (9.8%) and 87.5% of them were girls.

However, *T-score* is not appopriate to make the comparison because it is the bone mineral density at the site when compared to the young normal reference mean. Hence, T-score might over predict the osteopenia among children. The Z-score would be a better value to be used as it is the number of standard deviations a patient's BMD differs from the average BMD of their age, sex, and ethnicity[14].

There were no relationships found between SOS and the anthropometry data of participants in our study, except for girls' BMI. However, Zhu (2007) found the age, height and body weight of participants were related with SOS, except for the boys' weight& BMI and girls' height were not correlated with SOS in China[7]. Wünche (2000) in Germany also found SOS was correlated with increasing of age, height and weight[15].

This study found that there was a significant difference between ethnicity and the bone health status, but could find no significant the relation among family income, frequency of transfusion, chelation, height-for-age, weight-for-age and BMI-for-age. Previous studies found bone density is lower in Chinese and Japanese, and higher in black subjects when compared with white subjects[16-17]. The body proportions are different for different ethnic groups. Further more, the complex interactions between genetic, geographical differences and environmental factors also determine the formation of bone[18-20].

Ultrasound Bone Densitometer was used in the study though DEXA (Dual Energy X-ray Absorptiometry) is considered as a reference standard to measure bone density. Ultrasound Bone Densitometer is safe for children due to not using any radioactive X-ray for detecting BMD, and has high correlativity with DEXA[21]. Ultrasound method also has other advantages such as simpler to use, more cost-effective, and reproducibility[22-23]. Besides that, QUS technology is also able to assess bone changes in the growing bone[24].

There are some limitations should be considered in this study. Firstly, the dimension of the subjects' feet was not examined which may affect the result of QUS because its location between the transducer was not guaranteed. Additionally, the pubertal status of subjects was not assessed using Tanner's Method. As children with chronic disease have delayed growth or delayed maturity in bone, QUS at calcaneus is influenced by the growth process and may cause the incorrect interpretation. Further studies are warranted to

investigate the confounding factors that may influence QUS result.

CONCLUSIONS

There was no difference between BMD of boys and girls. This study found that there was significant difference between ethnicity and the bone health status. QUS can be an useful screening or assessment tool to improve the care for thalassemia children.

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