WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 7.523
Volume 6, Issue 13, 69-76. Research Article ISSN 2277– 7105

PHYSICAL GROWTH PATTERNS IN TRANSFUSION-DEPENDENT THALASSEMIC CHILDREN AT WASIT CITY

Dr. Safaa A. Faraj MD*[1], Dr. Ahmed I. Insaf MD[2] and Dr. Haider Nadhim Abd. MD MRCPCH[3]

[1]Consultant Pediatrics Hematooncologist, Department of Pediatrics, Faculty of Medicine, Wasit University.

[2,3]Pediatrics, Department of Pediatrics, Faculty of Medicine, Wasit University.

Article Received on
27 August 2017,

Revised on 17 Sept. 2017,
Accepted on 08 Oct. 2017

DOI: 10.20959/wjpr201713-9819

***Corresponding Author**
Dr. Safaa A. Faraj MD
Consultant Pediatrics Hematooncologist, Department of Pediatrics, Faculty of Medicine, Wasit University.

ABSTRACT

Objectives: Aim of Study: The main aim of this study is to determine the effects of age, type of chelation therapy, ferritin level and hemoglobin level on the physical growth of transfusion dependent thalassemia children. **Subjects and Methods:** This is a Cross sectional analysis for patients with thalassemia, registered at the thalassemia and hereditary anemia unit at Al-kut Maternity and child hospital, Wassit-Iraq- 2017. Growth parameters included height, weight, sexual maturity ratings according to tanner staging. Scores for weight, height were calculated using World Health Organization reference data. Laboratory parameters collected from patients records included: periodic Serum ferritin levels and pretransfusion Hemoglobin levels over the previous 2 years were calculated, type of chelating therapy, sex, age, presnceof endocrine disease were evaluated from patients records. Statistical analysis was carried out using SPSS. **Results:** Out of 200 patients registered at the thalassemia and hereditary anemia center at Al-Kut since 2006, 50 patients with thalassemia major and thalassemia intermedia included in the study. Their age ranging between 6-20 years of age with a mean age of 10.86 years. More than 75% of patients with thalassemia whose Hb levels below 10 g/dl were stunted growth. Most of the patients were treated with Deferasirox (Exjade) iron chelator (94%). Weight were found low in (50%) of patients whereas the height were found low in (74%) of patients. Both The Weight were significantly low (71%) and the Height (79%) were significantly low among patients with more than 10 years old. Also the Puberty was delayed in (100%) among16 patients whose age ≥ 14years. We found that the majority of our patients

with high serum ferritin (more than3000ng/ml) had underweight (77%) and short stature (92%) for their age. Endocrinopathies were found in (31%) of our patients aged less than 10 years old and increase to 42% with older children. **Conclusion:** Thalassemia patients are in very high risk for Growth retardation including underweight and short stature and endocrinopathy in our thalassemia patients in kut city. Low pretransfusionhemoglobin, high serum ferritin and increasing age are important risk facters. **Recomendations**: Social education and government health planning is urgently needed to reduce the number of new born baby with thalassemia through obligatory screening program for new marriages. Transfusion dependent Thalassemic patients should carefully monitored and supported to decrease their suffer and complications, further studies and larger samples are needed to document and evaluate this burden disease.

INTRODUCTION

Thalassemia is one of the commonest inherited disease in the whole world, and had severe deep complications for the patients, family and society.[1] Growth impairment is a common problem in homozygous B thalassemia.[2] About 6-10% of population in Iraq had hemoglobinapathy of which thalassemia is amajor part.[3] In Kut city to the south of Baghdad, the center of inherited blood diseases serves around two hundred regular registered patients, with daily attendance for follow up and to have blood transfusion of about 20-25 patients per day.

Growth retardation in thalassemic patients can occur as early as the first or second year of life but these abnormalities are more apparent after 6 to 8 years.[4]

In spite of modern treatment for thalasemic patients but still had many complications, the socio-economic background and parent education are important factors for irregular attendance and poor compliance to treatment leading to suboptimal growth resulting from chronic anemia, iron overload, bone dysplasia, multiple endocrine organ insufficiency.

PATIENTS AND METHOD

This study was conducted on 50 patients with Thalassemia, 41 patients had thalassemia major, 9 with thalassemia intermedia, (13 males and 37 females), age range ranging between 6-20 years of age with a mean age of 10.86 years. Cases of thalassemia minor and other hemoglobinopathies were excluded from the study. all information were obtained from medical file of the patients in AL Kut Maternity and Child hospital, unit of hereditary

anemia, and including age, sex, address, type of thalassemia, type of chelating agent, puberty and menarche states and presence of endocrine glands dysfunction. A mean level of hemoglobin and mean serum ferritin over the preceding two years were calculated for each child from his/her records . Weight and height t were compared with age on children growth charts of WHO percentile.

Complete clinical examination was also performed during this period. Height was recorded using a stadiometer to the nearest 0.1 cm, and weight was measured in minimal clothes to the nearest 0.1 kg. An assessment of sexual maturity rating (SMR) was done in all the patients 10 years or older. SMR staging was done for breast stage in girls and testicular volume in boys and for pubic hair in both. Delayed puberty was defined by non- appearance of breast buds or pubic hairs by 14 years of age in girls and no increase in testicle volume greater than 4 mL and no pubic hairs by 15 years of age in boys.

Delay secondary Sexual characters and menarche assessed for patients ≥14 years old. Data were entered into Statistical Package for Social science (SPSS) program version 17 for Windows 7. Quantitative variables were summarized by finding mean and qualitative variables were summarized by finding frequency and percentage.

RESULTS

From 50 patients with thalassemia, 37 (74%) patients were under 14 years of age. About three quarter of the patients were female gender, (74%). Most of the patients were treated with Deferasirox (Exjade) iron chelator.

Table 1: demographic data.

Variables			Patient No.	Percentage %
Age		≥ 14 years	13	26
		<14 years	37	74
Sex		Male	13	26
		Female	37	74
Address		urban	18	36
		Rural	32	64
Type of chelating agent		Deferasirox (Exjade)	47	94
		Deferoxamine (desferal)	3	6
Hb level (g/dl)		≥ 9	24	48
		<9	26	52
Growth patetern	**Wt/age**	**Weight above 5th centile**	24	48
		Weight below 5th centile	**26**	**52**
	Ht/age	**height above 5th centile**	13	26
		height below 5th centile	**37**	**74**

From 50 patients with thalassemia, 26(52%) patients were under weight. As show in table No. (2).

Table 2: Weight for age percentile of patients.

Weight / age	Patients No.	Percentage %
less than 5th percentile	**26**	**52**
5-90th percentile	24	48
Total	50	100

From 50 patients with thalassemia, 37 (74%) patients were short stature. As show in table No.(3).

Table 3: Height for age percentile of the Patients.

Height / age	Patients No.	Percentage %
less than 5th percentile	**37**	**74**
5-90th percentile	13	26
Total	50	100

All the patients with thalassemia whose ages above 14 years old were delayed puberty. As show in table No. (4).

Table 4: Distribution of Secondary sexual charachtristics and menarche in selected patients (age ≥ 14 years).

Secondary sexual characteristics'	Patients No.	Percentage %
Normal	0(0%)	0
Delayed	**16(100%)**	**100**
Total	16(100%)	16
Menarche	**Patients No.**	**Percentage %**
Normal	0	0
Delayed	**5**	**100**
Total	5	100

From 26 patients whose ages between 6-10 years old, 9(35 %) patients were under weight, 18(69%) patients were short stature and about one third of the patients had endocrinopathies (31%). on the other hand, reminder 24 patients whose ages above 10 years old, 17 (71%) patients were under weight, and Three quarter of the patients were short stature (79%) and 10(42%) patient had endocrinopathies As show in table No. (5).

Table 5: Physical Growth and Endocrinopathies with Related to Age Group.

Parameter	Age group	
	6-10 years No. = 26	>10 years No. = 24
Weight above 5th centile	17 (65%)	7 (29 %)
Weight below 5th centile	**9 (35%)**	**17 (71%)**
height above 5th centile	8(31%)	5(21%)
height below 5th centile	**18 (69%)**	**19 (79%)**
Endocrinopathies	**Positive (8) (31%)**	**Positive (10) (42%)**
	Negative (18) (69%)	Negative (14) (58%)

From 37 patients whose serum ferritin less than 3000ng/ml, 16 (43%) patients were under weight, 25(68%) patients were short stature and about one third of the patients had endocrinopathies (35%).On the other hand, reminder13 patients whose serum ferritin more than 3000 ng/ml, 10 (77%) patients were under weight, 12(92%)of the patients were short stature. and 5(38%) patient had endocrinopathies. As show in table No. (6)

Table 6: Physical Growth and Endocrinopathies with related to serum ferritin level.

Parameter	Serum ferritin ng/ml	
	< 3000 No. 37	≥3000 No. 13
Weight above 5th centile	21 (57%)	3 (23%)
Weight below 5th centile	**16 (43%)**	**(10 (77%)**
height above 5th centile	12 (32%)	1 (8%)
height below 5th centile	**25 (68%)**	**12 (92%)**
Endocrinopathies	**Positive (13) (35%)**	**Positive (5) (38%)**
	Negative (24) (65%)	Negative (8) (62%)

More than 75% of patients with thalassemia whose Hb levels below 10 g/dl were stanted growth compared to patients with Hb level above 10 g/ dl (50%).As show in table No. 7.

Table 7: Physical Growth with Related to mean Hb level.

Growth parameter	Hb level <10 g/dl No.=48	Hb level ≥10 g/dl No. = 2	P value
Weight below 5th centile	**25(96.2)**	**1(3.8)**	0.7
Weight above 5th centile	23(95.8)	1(4.2)	
height below 5th centile	**36(97.3)**	**1(2.7)**	0.4
height above 5th centile	12(92.3)	1(7.7)	

DISCUSSION

We conducted this study as there is no studies on physical growth in blood transfusions dependent thalassemics from kut city in south of Iraq and to direct the attention of ministry of health and the government of Iraq to give more medical, social and financial support for these

families and put a plan to prevent this terrible disease in the future such as obligatory hemoglobin electrophoresis testing for new marriages. Also to see the effect of mean pretransfusion hemoglobin, mean s. ferritin, type of chelating therapy and the progress of age on physical growth pattern.

"Growth failure is multifactorial in thalassemia, related to chronic hypoxia due to chronic anemia, chelation toxicity, low serum zinc level, hepatic iron overload with hepatic dysfunction and iron associated endocrinopathies such as hypogonadism, hypothyroidism, and growth hormone deficiency".[4]

In our study growth was adversely affected in thalassemics and the prevalence and severity of short stature was higher in thalassemics more than 10 years and this is similar to indian study in 2006,[2] this could be due to chronicity of disease and its complication.

Further, our study shows the Majority of the studied patients (More than 75%) whose Hb levels below 10 g/dl were stunted growth and this correlated with findings of some othersstudies, which show correlation between growth retardation and low pretransfusion hemoglobin levels, implicating chronic hypoxia as a cause of growth retardation,[5,6] and this not goes with other studies that shows growth retardation was inconsistently associated with the degree of anemia.[2,7,16]

Also, in our study, there is a relation between growth retardation and serum ferritin level, and this consistent with other studies showing iron overload had been implicated for contributing growth failure in thalassemics.[8,9,11,12] While other studies shows no significant association between s.ferritin levels and growth retardations.[2,5,10,16]

In spite of, we found that Physical growth retardation in thalassemics is mainly related to chronic anemia and iron overload. However, growth is influenced by other factors also, like ethnicity, genetic composition, hormonal milieu which we didn't under take in our study.

Around fifty percent of the studied patient were wasted and around three quarter were short stature, this goes with some other studies.[13,14]

The number of Thalassemic patients with short stature and under weight in our study is less than study[6]{(79%)(61%)}, This could be explained from patients age who included in this

study , were most of our patients (26/50) less the 10 years age in reverse to other study, where commonly done on patient who are above the age of 10 years.

In this study most patient whose ages above 10 years old, were more liable for stunted growth and endocrine dysfunction than other age group and this is in concordance with studies.[9,17]

In present study, secondary sexual characteristics and menarche in female were delayed in all assessed patients and this is in concordance with study[13] which concluded that Short stature and hypogonadism are extremely frequent in patients with thalassemia.

And this differ from a multicentre study in Italy, hypogonadism was present in 47% of girls older than 15years of age and secondary amenorrhoea in 23% menstrual irregularity in 14% and arrest of sexual maturation in 13%. Hypogonadism was present in half the male patients.[15]

A study from Tehran reported only delayed puberty in 12.4% of girls and 22.5% of boys with thalassemia major[16] and this may related to strict anemia and s. ferritin levels.

CONCLUSION

Growth failure (underweight and short stature), delayed puberty and endocrine dysfunction significantly occur in our blood transfusions thalassemic patients, this is due to low pretransfusion hemoglobin and iron over load, but these abnormalities are more apparent after 10 years.

REFERENCES

1. Najafi, Rabari and Sabzevari; The Effect of Family-Centered Empowerment Model on the Mothers Knowledge and Attitudes about Thalassemia Disorder; Iranian Journal of Pediatric Hematology oncology, 2006; 1(3).
2. Sunil Gomber and Pooja Dewan; Physical Growth Patterns and Dental Caries in Thalassemia; indian pediatrics, December 17, 2006; 43: 1064-1068.
3. Rasheed N. Ezzaddin and Ahmed S. Adnan, Effect of ß- Thalassemia on Some Biochemical Parameters. Middle East Journal of Family Medicine [on online], 2005. Available from: www.mejfm.com. [Accessed on 21/1/2010].
4. Moayeri, Oloomi; Prevalence of Growth and Puberty Failure with Respect to Growth Hormone and Gonadotropins Secretionin Beta-Thalassemia Major; Arch Iranian Med, 2006; 9(4): 329-334.

5. Rodda CP, Reid ED, Johnson S, Doery J,Mathews R, Bowden DK. Short stature inhomozygous beta-thalassemia is due todisproportionate truncal shortening. ClinEndocrinol (Oxf), 1995; 42: 587-592.
6. Ortolani M and Wolman IJ. Some clinical features of Cooley's anemia patients as related to transfusion schedules. Ann New York Acad of Sciences, 1969; 163: 407-414.
7. Tienboon P, Sanguansermesri T, Fuchs GJ.Malnutrition and growth abnormalities inchildren with beta thalassemia major. Southeast Asian J Trop Med Public Health, 1996; 27: 356-361.
8. Hamidah A, Rahman R, Azmi T, Aziz J, Jamal R. Short stature and truncal shortening transfusion dependent thalassemia center in Malaysia. Southeast Asian J Trop Med Public Health, 2001; 32: 625-630.
9. Chaim H. Pathogenesis and management of iron toxicity in thalassemia. Cooley's Anemia: Annals of the New York Academy of Sciences Volume 1202, Ninth Symposium, August 2010; 1.
10. Kaiagiorga-Lagana M, Papadokou-Lagovanni S, Pantelakis S, Lapatsanis P, Karaklis A. Body growth in Cooley's anemia in relation to the haemoglobin and ferritin levels. Iatrikri, 1980; 38: 30-36.
11. Nazar B., Abdulkader A., Alsaqy A., Alrabaty A., Growth Pattern and Sexual Maturation Rate in β-Thalassemia Major Patients from Thalassemia Center Erbil, The Iraqi Postgraduate Medical Journal, 2013: 12(1): 40-44.
12. Seema T, M. Kabra, N. Tandon, R. saxena, et-al. clinico hematological profile of thalassemia intermedia patients. int. J. hum Genets, 2003; 3251-58.
13. Ash M., Steven D. Delayed puberty. Gynaecology by Ten Teachers, 19th edition, 24.
14. Delvecchio M1, Cavallo L. Growth and endocrine function in thalassemia major in childhood and adolescence. J Endocrinol Invest, 2010 Jan; 33(1): 61-8.
15. Italian working group on endocrine complication in non endocrine disease. multicentre study on prevalence of endocrine complications in thalassemia major. clin endocrinol, 1995; 42: 581-586.
16. Shamshirsaz AA, Bekheirnia MR, Kamgar M, et al. Metabolic and endocrinologic coplicaitons in beta thalassemia major: A multicentric study in Tehran. BMC Endocr Disord, 2003; 3: 4–9.
17. Harish k pemde, jagdish chandra, divya gupta, et al physical growth in children with transfusion-dependent thalassemia Pediatric Health, Medicine and Therapeutics, 2011; 2: 13–19.