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Prevalence of osteoporosis & osteopenia in transfusion-dependent thalassemia in Sulaimaniyah city, Iraq

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Abstract

Background and objectives: Although blood transfusion and iron chelation increase the lifespan of thalassemic patients, these patients face many complications, including osteoporosis and osteopenia. Thus, we aimed to determine prevalence rates of osteoporosis/osteopenia using Dual Energy X-Ray Absorptiometry in transfusion-dependent thalassemia patients and its relationship with chelation agents and body mass index.

Methods: This retrospective study included 150 patients with transfusion-dependent thalassemia in the Thalassemia and Congenital Blood Disorders Center, Sulaimaniyah, Iraq, from December 2021 to July 2022. The participant's information was collected from the hospital database, including sociodemographic characteristics, bone mineral density status, and the number of items used for chelation. A Dual Energy X-Ray Absorptiometry bone scan was used to check the bone mineral density.

Results: The mean age of patients was 19.59±7.59, body mass index was 21.23±18.13, and most (53.3%) were females. Dual Energy X-Ray Absorptiometry results showed that 53.3% of the patients had osteopenia, 21.3% had osteoporosis, 36.7% had average bone mineral density, and 6.7% had low bone mineral density for age. In addition, there was a significant difference between the frequencies of bone density disorders in patients who used one chelating agent (46.4%) versus two chelating agents (85%) (P≥0.001). Also, there was a significant difference between the incidence of bone density disorders with low and average body mass index (78%) in comparison with overweight and obese patients (8%) (P≥0.001).

Conclusions: There is a high prevalence of osteoporosis and osteopenia in transfusion-dependent thalassemia patients, which are more prone to trauma and bone fracture.

Keywords: Osteopenia, Osteoporosis, Retrospective study, Transfusion dependent thalassemia

Introduction

Thalassemia is a diverse set of hereditary hemolytic anaemias distinguished by a defect in production of one or more globin polypeptide chains.[1] The beta-globin gene has more than 200 known mutations that cause thalassemia, which accounts for the disease's extreme genotypic and phenotypic diversity.[2]

Thalassemia is long-lasting pathology; if not managed well, the side effects of the treatments will cause problems by affecting many body organs.

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Among the most crucial side effects of thalassemia are osteoporosis and osteopenia, and there have been limited studies on this issue in the geographical region of Iraq. So, it is necessary to conduct this study to address the prevalence of osteoporosis and osteopenia in transfusion-dependent thalassemia (TDT) in Sulaimaniyah, Iraq. Clinical and laboratory results differentiate the different types of thalassemia Beta-thalassemia (minor, intermedia, and major)and alfa thalassemia are among the common subtypes of thalassemia in our locality that require blood transfusion every 2-4 weeks.[3]

Clinically, beta-thalassemia (thalassemia major and some of thalassemia intermedia), alfa-thalassemia major (hydrops fetalis) and some haemoglobin H (HbH) diseases are characterized by transfusion dependency.[4] Regular blood transfusion treatment causes iron overload problems and organ deposition.[5] Accordingly, transfusion-dependent thalassemia patients are more susceptible to infections related to blood transfusion due to their weak immune systems.[6] The highest prevalence rates for thalassemia mutations may be found worldwide in the Mediterranean, Middle East, Southeast Asia, and Central Asia. Beta-thalassemia affects 68000 newborns globally, and around the world, there are 80–90 million carriers.[7] A total number of registered symptomatic hemoglobinopathy patients in the Kurdistan region of Iraq is more than 3200, which constitutes around one-fourth of the registered patients in the country.[8, 9]

One of the thalassemia's most debilitating complication is decreased bone mass density (BMD), which makes patients prone to skeletal pain and pathological fractures.[10] Despite receiving the best treatments, 40–50% of thalassemia major patients see a decline in BMD.[11] There are several accurate and trustworthy ways to measure BMD. The DEXA method, which assesses BD in the lumbar spine, femoral neck, and forearm region, is one method used to quantify BMD.[12]

The World Health Organization (WHO) states that the T-score for BMD, measured at the lumbar spine or the femoral neck, is used to diagnose osteoporosis. A BMD that is 2.5 standard deviations (SD) or more below the mean value for a young adult female (T-score ≤ -2.5 SD) is considered osteoporosis, while BMD between 1 and 2.5 SD below the mean is osteopenia. The Z-score indicates how many SDs an individual's BMD deviates from the median value anticipated for their age and sex.[13]

The aim of this study was to determine prevalence rates of osteoporosis/osteopenia using Dual Energy X-Ray Absorptiometry in transfusion-dependent thalassemia patients and its relationship with chelation agents and body mass index.

Patients and methods

This retrospective analytical study was conducted between December 01, 2021, to July 31, 2022, at the Thalassemia and Congenital Blood Disorders Center, Sulaimaniyah, Kurdistan Region of Iraq, on 150 transfusion-dependent thalassemia (TDT) patients. All registered patients with a definitive diagnosis of thalassemia regardless of age and gender were included, while patients with bone marrow transplants and those with secondary causes of low bone density (BD) due to factors that may not be related to thalassemia and transfusion, such as prolonged steroid management, and chronic bone/joint disorders were excluded from the study. The necessary legal permits were taken from the scientific and ethical committees of the College of Medicine, University of Sulaimani. The study procedure and its aims were discussed with patients and their guardians, and written informed consent was obtained. Patients are allowed unrestricted to leave the study at any time without giving a reason.

The patients' sociodemographic data such as age, gender, height, weight (to determine body mass index (BMI)) and bone mineral density (BMD) were collected from the patient's files and Thalassemia and Congenital Blood Disorders Centers database using a special validated questionnaire that was prepared for that purpose. First, the BMD in the spine and femoral neck were selected. Then, the Dual Energy X-Ray Absorptiometry (DEXA) scan was used to check the BMD according to WHO guidelines. Then, DEXA report details were interpreted and analyzed by expert colleagues from the research team, and the presence or absence of osteopenia or osteoporosis was reported. Data analysis was done using Statistical Package for Social Science (SPSS, version 23) software (IBM, Chicago, USA). Statistical significance was reported using a t-test or chi-square test with a p value of less than 0.05.

Results

The mean age of patients was 19.59±7.59, of which 70 (46.7%) were males, and 80 (53.3%) were females. The patients' mean weight was 46.75±14.05 kg, while the mean height was 151.06±17.20 cm. Thus; the mean BMI was 21.23±18.13 kg/cm^2. In the interpretation of the patient BMI, the results showed that 50 (33.3%) patients had low weight, 89 (59.3%) had average weight, 10 (6.7%) were overweight, and only 1 (0.7%) patient was obese. The results of DEXA showed that 53 (35.5%) patients had osteopenia, 32 (21.3%) had osteoporosis, 55 (36.7%) had normal BD, and 10 (6.7%) had low BD for age. Regarding the use of chelating agents, 110 (73.3%) patients used one and 40 (26.7%) used two chelating agents, as shown in Table (1).

Table (1): Sociodemographic variables, DEXA interpretation findings, and history of chelating agent usage in the studied participant.

Variable		No. (%)
Gender	Male	70 (46.7)
	Female	80 (53.3)
Body weight	Low weight	50 (33.3)
	Normal weight	89 (59.3)
	Overweight	10 (6.7)
	Obese	1 (0.7)
DEXA finding	Osteopenia	53 (35.5)
	Osteoporosis	32 (21.3)
	Normal	55 (36.7)
	Low bone density for age	10 (6.7)
History of using a chelating agent	One chelating agent	110 (73.3)
	Two chelating agents	40 (26.7)

Regarding the relationship and association of BD disorders to the gender of the patients, the results showed that out of 70 male participants, 20 (28.6%) had osteopenia, 19 (27.1%) had osteoporosis, 5 (7.1%) had low BMD for age, and 26 (37.1%) had normal BD. Also, out of the 80 females, 33 (41.3% had osteopenia, 13 (16.3%) had osteoporosis, 5 (6.3%) had low BMD for age, and 29 (36.3%) had normal BD. There is no significant difference between gender in terms of the prevalence of BD disorders (P=0.34), as shown in Table (2).

Table (2): DEXA-scan findings according to patients' gender.

Gender	DEXA-scan finding (Number, %)				Total	p value
	Osteopenia	Osteoporosis	Normal	Low BMD for age		
Male	20 (28.6)	19 (27.1)	26 (37.1)	5 (7.1)	70	0.34
Female	33 (41.3)	13 (16.3)	29 (36.3)	5 (6.3)	80	
Total	53 (35.3)	32 (21.3)	55 (36.7)	10 (6.7)	150	

DEXA: Dual Energy X-Ray Absorptiometry, BMD: Bone Mineral Density

In this study, using chelating agents in managing iron overload was investigated with differences in the frequencies of BD disorders in both groups. The prevalence of BD disorders among 110 patients who had a history of using one chelating agent revealed osteopenia in 33 patients (30%), osteoporosis in 18 patients (16.14%), low BMD for age in 10 patients (9.1%) and normal status BD in 49 patients (44.5%). While amongst the remaining 40 patients who have used two chelating agents, there was osteopenia in 20 patients (50%), osteoporosis in 14 patients (35%), normal BD in 6 patients (15%), with no low BMD for age (0.0%). There was a highly significant difference between the frequencies of BD disorders in patients who used one or two chelating agents (P≤0.001), as shown in Table (3).

Table (3): Comparison between the number of used chelating agents and the bone density disorders among the studied participants.

Chelating agent	DEXA-scan finding (Number, %)				Total	p value
	Osteopenia	Osteoporosis	Normal	Low BD for age		
One	33 (30.0)	18 (16.4)	49 (44.5)	10 (9.1)	110	0.001*≤
Two	20 (50.0)	14 (35.0)	6 (15.0)	0 (0.0)	40	
Total	53 (35.3)	32 (21.3)	55 (36.7)	10 (6.7)	150	

*: Highly significant difference using Chi-square test, DEXA: Dual Energy X-Ray Absorptiometry, BD: Bone Density

The results of comparing the frequency of BD disorders in different BMI categories showed that low-weight patients with osteopenia were 11 (22%), those with osteoporosis were 5 (10%), and low BMD for age were 4 (8%). Those with the normal BD were 30 (60%) with a highly significant difference (P<0.001). In people with normal BMI, the frequency of osteopenia was shown in 36 patients (40.4%), osteoporosis in 26 patients (29.2%), the low BMD for age was demonstrated in 5 patients (5.6%) and average bone density in 22 patients (24.7%), with highly significant difference (P<0.001). In overweight patients, the frequency of osteopenia was 5 (50%), osteoporosis/low BMD for age was one patient (10%) each and normal was 3 (30%) with no significant difference (P=0.66). In obese people, the frequency of osteopenia was 1 (100%) with no significant difference (P=0.61), as shown in Table (4).

Table (4): Comparison between the frequency of bone density disorders amongst the BMI class categories.

BMI	DEXA-scan finding (Number, %)				Total	p value
	Osteopenia	Osteoporosis	Normal	Low BMD for age		
Low	11 (22.0)	5 (10.0)	30 (60.0)	4 (8.0)	50	0.001*≤
Normal	36 (40.4)	26 (29.2)	22 (24.7)	5 (5.6)	89	0.001*≤
High	5 (50.0)	1 (10.0)	3 (30.0)	1 (10.0)	10	0.66
Obese	1 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)	1	0.61
Total	53 (35.3)	32 (21.3)	55 (36.7)	10 (6.7)	150	

*: Highly significant difference using Chi-square test, DEXA: Dual Energy X-Ray Absorptiometry, BMD: Bone Marrow Density, BMI: Body Mass Index

Discussion

This study investigated the prevalence of osteoporosis and osteopenia in TDT patients. The DEXA results showed that 35.3% of the patients had osteopenia, 21.3% had osteoporosis, 36.7% had normal BD, and 6.7% had low BMD for age. The delay in bone formation due to the expansion of the bone marrow space in these patients causes thinning of the cortical part of the bone, increasing the weakness and fragility of the bones. The continuous need to produce blood cells is an important factor in osteoporosis. Hemochromatosis is the main complication of treating the disease with blood transfusion, which is usually associated with hypogonadism, diabetes, hypothyroidism, and other hormonal disorders and all of these are risk factors for osteoporosis and osteopenia, risk factors for osteoporosis. Iron also prevents the maturation of the organic bone matrix and its mineralization. Iron binding to hydroxyapatite crystals affects their growth and increases the organic matrix in bone tissue. The prevalence of osteopenia and osteoporosis in thalassemic patients is 30-50%, and related fractures are reported in >20% of adult patients with thalassemia.[14, 15]

The study participants' mean age was 19.59±7.59 years, similar to Shawkat et al. study,[16] while other studies reported a lower/higher mean age than this study.[17-19] Most of the patients in this study were females, which is consistent with the study conducted in Iran by Bordbar et al.[20] but it is not agreed with another study conducted in Iraq.[21, 22]

Regarding the BMI, the results showed that the obtained mean within the normal range. Most of the patients had a normal BMI, and 7.4% of the patients had a BMI higher than normal, which is consistent with the results of other studies that investigated the prevalence of osteopenia and osteoporosis.[23, 24]

DEXA findings showed that the most common bone disorder among thalassemic patients was osteopenia, osteoporosis and low BMD for age. Osteopenia was more common than the other two disorders in the studied patients. Meanwhile, 55% of the surveyed people had no specific bone problems. These outcomes are consistent with that found by Abbassy et al., who showed that most β-thalassemia patients suffered from bone problems, especially osteopenia and osteoporosis.[25] Also, our findings are consistent with the study of Al-Samkari et al., who showed that osteopenia, osteoporosis, and low BMD for age were the most common skeletal disorders in thalassemia patients.[26] Additionally, Noormohammadi et al. found osteoporosis in 69.9% of the patients, followed by hypogonadism (35.5%), hypothyroidism (9.7%), heart failure (5.4%), and hepatitis C (2.2%), while liver failure had the lowest incidence rates.[27] Whereas Hashemieh et al. found osteoporosis in 65.6% of the patients, of which 10.7% was in the lumbar spine alone, 11% was in the femoral neck alone,

and 43.9% was in both sites. Only 15.7% of the remaining patients were normal, while 18.7% had osteopenia.[10]

Moreover, most patients in this study used one chelating agent to manage iron overload in TDT, and cheating agents have a significant difference in osteoporosis, osteopenia, and normal BD. These results are consistent with the that of Lal et al.[28] and Ghanavat et al.,[29] who found that most patients used at least one chelating agent, while Gaudio et al. showed a difference in using one or two chelating agents.[30] Other studies have shown that thalassemia patients differ in the use of one or two chelating agents.[31, 32]

Studies have shown that, in normal circumstances, women start losing BD faster than men at a young age. Until the sixth decade of life, the rate of osteoporosis and osteopenia in women is 4 and 2 times higher than in men.[33] In this study, based on the findings of DEXA, it was shown that patients did not have significant differences in terms of gender concerning osteoporosis, osteopenia, BD and normal bone density. While a study in Italy showed that thalassemia patients had a significant difference in bone disorder according to gender.[34] Also, Modagan et al. showed a significant difference in the rate of osteoporosis and osteopenia between males and females.[35] Moreover, in this study, osteopenia in patients with normal BMI was 40.4%, while osteoporosis 29.2%. Whereas, in overweight patients, the osteopenia was found in 50%, and osteoporosis in10%, while in obese people, the frequency of osteopenia was 1 (100%). The time limit of the entire research work and the non-availability of serum iron, serum ferritin, vitamin D level, and calcium levels in all TDT cases force us to discuss only DEXA technology and the BMI index.

Conclusions

Our transfusion dependent thalassemia patients have a high rate of osteopenia and osteoporosis. As a result, implementing methods better to detect low BMD status in its early stages are necessary. In addition, low BMI and use of more than one chelating agent among TDT cases may indicate the developed low BMD status. For such reasons, we recommend using the available resources to detect better the adverse effects of thalassemia and chelating agents on bone integrity and decrease the suffering of TDT cases.

Conflict of interest:

The authors recorded no conflict of interest.

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