Original article

Cutaneous manifestation among patients with β- thalassemia major

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Abstract

Background: Dermatological manifestations among β thalassemia major patients including skin changes as well as nail, hair, oral mucosa changes and leg ulcer were reported among these patients, either due to the hemolytic process of the disease itself or as a sequel of therapeutic effect taxes of blood transfusion and iron overload complication. In Kurdistan there is no study has yet investigated the common dermatologic problems that coexist with β-thalassemia major.

Objectives: The purpose of this study was to determine the commonly seen dermatologic problems in patients with β-thalassemia major.

Patients and Method: A descriptive cross sectional study performed at Erbil Thalassemia center, the study was conducted among 176 patients over a period extended from April, 2013 to January, 2014. They were assessed for cutaneous manifestation with clinical importance of static laboratory tests.

Results: All patients enrolled in this study had at least one cutaneous manifestation. The disorders are in decreasing order of frequency was pallor, xerosis, jaundice, bronze skin, hyperpigmentation and the least frequent was vitiligo. Most of the of the findings (31.8%) were between (10-15) years age group. The mean age of patients, the mean duration of blood transfusion and the mean of serum ferritin level among patients with xerosis, pallor, hyperpigmentation and jaunduce was higher and was statistically significant ($p<0.05$) also there was a significant association between HCV positive and patients with xerosis, hyperpigmentation and jaundice ($p<0.05$).

Conclusion: The cutaneous disorders are common among beta thalasemia patients, pallor ,xerosis and jaundice were the common skin changes, while white streak (leukonychia)and gingivitis are the most common nail and oral mucoasa changes respectivly. Xerosis is common in patients recieving desferoxamine, serum ferritin level was higher in patients with xerosis,hyperpigmentation and jaundice.

Key Words: β thalassemia major, cutaneous manifestation

Introduction:

Thalassemia is the most common genetic disorders worldwide 4.83 percent of the world's populations carry globin variants, including 1.67 percent of the population who are

heterozygous for α -thalassemia and β-thalassemia.[1,2]. β thalassemia is a heterogeneous group of hereditary disorders that results from a reduced rate of production of β globin chain of haemoglobin.[2]They are autosomal recessive disorder caused by mutation in β globin gene located on chromosome 11.[3,4]

β thalassemia major is seen more frequently in the Mediterranean region, the Indian subcontinent, Middle East, Southeast Asia, and West Africa as well as countries along the North coast of Africa and South America.[3,4]

In Iraq, the total number of β thalassemia major patient was nearly 5000 according to record of ministry of health at 2003; the total number of patients registered in Erbil thalassemia center till 2013 was 650 patients.[5]

Patients with β thalassemia major requiring regular blood transfusion and extensive ongoing medical care, they need RBC transfusion every two to three weeks to maintain the hemoglobin over 9 to 10 g/dl at all times. This prevents growth impairment, organ damage and bone deformities,[3, 6] on the other hand frequent blood transfusion will lead to iron overload which cause many complications like endocrinopathies[7,8.9] growth retardation,[10] cardiovascular problems,[11,12] liver disease,[13] gonadal dysfunction, delayed puberty,[14,15] and increase the chances of transfusion transmitted infections .[9,16]The combination of regular blood transfusions and chelation therapy has dramatically increased the life expectancy of patients into 4th to 5th decades of life.

Cutaneous manifestations including skin disorders as well as nail, hair, oral mucosa changes[17, 18, 19, 20, 21], and leg ulcer[3] , either due to the hemolytic process of the disease itself or as a sequel of therapeutic effect of blood transfusion and iron overload complication.

Patients and Methods:

The study was conducted in Erbil thalassemia center over a period extended from April 2013 to January 2014; 176 patients were enrolled in this study. Patients with diagnosis of BTM on regular blood transfusion of both sex and all age groups were allocated by convenience sampling method, while patients with β-thalassemia intermediate, β -thalassemia minor and sickle cell anemia were excluded from the study. The data was collected by a direct interview of patients on blood transfusion who attended the Thalassemia center through a special designed questionnaire; at each visit ten patients were interviewed, the purpose of the study was carefully explained to each participant.

A blood sample was taken for complete blood picture, serum ferritin, virology study results for hepatitis B and C were obtained from each patient registration card.

Diagnosis of cutaneous manifestation based on history and thorough dermatological examination of the skin, nail, hair and oral mucosa under good day light .Woods lamp (ATT, ALET TIP Teknik LTD, Turkey) for clinical and skin scraping for microscopy examination. Direct microscopy (40 X, Olympus, Tokyo, Japan) was carried out in Rizgary teaching hospital/Erbil with a 20% potassium hydroxide preparation was obtained from suspected lesions.

Statistical Analysis:

Statistical package for social science (SPSS) software version (22.1) was used for data entry and analyzing, aided by Microsoft excel 2010 for calculations, plotting graphs and tables. Descriptive data were presented for continuous variables as mean ± SD, while qualitative data description done by calculating

number and percentage (n, %). t-test were used for statistical analysis and Chi-square(x^2) tests were used for significant associations, P value ≤ 0.05 considered statistically significant.

Results:

Out of 176 patients of BTM, 81 (46.0%) were female, while 95 (54.0%) were male with ratio of (1.2:1).Regarding the age group distribution ranged between 1 month and 34 years. Mean age was (10.9±5.9), 56 (31.8%) of the patients belong to age group (10-15) years, followed by 43 (24.4%) patients in the age group (5-10) years as shown in (Figure 1).
The mean (±SD) duration of blood transfusion was 9.4±5.8 years. Mean (±SD) of transfused blood units was 1.3 ± 0.60 units (Figure 2).
Cutaneous manifestation showed that all patients had at least one finding with mean 4.6 (±1.83). The disorders are in decreasing order of frequency as shown in (Table 1); pallor (75.0%), xerosis (73.9%), jaundice (61.4%), bronze skin (59.1%), hyperpigmentation (51.7%), oral mucosa changes (27.8%), Pitryasis alba (25%), coarse hair (23.3%), cutaneous infection and nail changes (21.6%), Pruritus (19.9%), post inflammatory hypopigmentation and vitiligo (0.56%).
Among 38 (21.6%) patients with skin infections, viral infection was the most common and fungal infection (tinea corporis) was the least frequent 1(2.63%) as shown in (Figure 3).
Regarding oral findings gingivitis was the most common disorder had been seen in 25(14.2%) patients as shown in (Table 2).The prevalence of nail changes was (21.6%) and white streak (39.5%) was the most common nail disorder (Figure 4).
The mean age of patients with xerosis, pallor, hyperpigmentation and junduce was higher than those without these skin changes and the difference was statistically significant ($p<0.05$) as shown in (Table 3).
Mean duration of blood transfusion of paients with xerosis, pallor, hyperpigmentation and junduce was higher and it was statistically significant ($p<0.05$) as shown in (Table 4) .

Mean of serum ferritin level was higher in patients with xerosis, pallor, hyperpigmentation and juandice than in patients with no skin findings ($p\leq 0.05$) as shown in (Table 5).
The viral study for HCV was positive in 53 (30%) patients, the association between HCV and xerosis, hyperpigmentation and jaundice was significant ($p<0.05$) (Table 6).

Discussion

In this study pallor observed in 75% of the patients and close to result of study done in India[22] 64% but was higher than the study done in Iran[20] 1% probably due to irregular or inadequate blood transfusion.
Xerosis was observed in 74% and close to result of a study done by Nadri M *et al* 70.3% in Iran[20] but was higher than results of other studies done in Basrah[17], Iran[18] and Turkey[19] 64%, 53% and 34.6%, respectively and this is may be related to the time the study conducted in winter season. Jaundice reported in 61.4% patients and was higher than the findings of a study done in Basrah[17] 7.2%.
Bronzy skin reported 59% and was close to the result observed in Basrah[17] 54.9% but this rate was higher than a study done in Iran[20] 0.7%.
Hyperpigmentation commonly observed 51.7% and it is close to the results found in Basrah[17] and Iran[21] 49% and 53% respectivly.
Freckles reported 67% and is close to the findings of a study done by Naderi M *et al* in Iran[20] 71% but was higher than the result of studies done in Basrah[17],

Iran[18]and Turkey[19] 31%, 33% and 23% respectivly.

Gingivitis observed 14.2% and was lower than result of studies done in Iran[20]and Sulaimanya[23] 21.7% and 55.6%, respectivly, hard palate pigmentation observed in 1.7% and was lower than studies done by Momeni A *etal*[18] and Fekri A *etal*[21] in Iran , 30% and41%, respectivly.

Pitryasis alba observed in 25% and was higher than the findings of Turkey[19] and Iran[20] 6.4% and18% respectivly and lower than results of Basrah[17] 38.5% .

Coarse hair seen in 23.3% and it is close to findings Fekri A *etal*[21] in Iran 20.7% .

Cutaneous infection seen in 21.8% and the result was consistent with the result of a community based study done in rural Erbil[24]; bacterial infection observed in 7 (4%) and was lower than findings of Basrah[17] 21(11%). Tinea infection observed in 2.6% and was lower than the result that found in a research in Turkey[19] 5%.

Postinflamtuary hyperpigmentation was obsorved in 16% among patients taking deferoaxmine at site of injection and it was lower than result of a study done by Momenia A *et al* in Iran[18] 30% but, was higher than findings of a study done by Naderi M *et al* in Iran[20]1.7%.

Xerosis found to be significantly higher in patients on deferoxamine than patients using deferasirox and consistent with a study done in Turkey.[19]

The mean of serum ferritin was significantly higher in patients with Xerosis, Pallor, Hyperpigmentation and Jaundice and correlates with the result of a study done in Turkey[19] and this is may be due to iron accumulation in tissue and skin. In this study HCV infectin observed in 30% which is close to the findings of North America[16] 35% and Pakistan[25] 37.5%, and lower than findings of studies done in Southwest Iran[26] 95% and Egypt[27] 49%. In the current study Xerosis, Hyperpigmentation, and Juandice were significantly more common among patients with HCV, while pruritis had no association with hepatitis C and inconsistent with the findings of the studies done in Pakistan.[28]

Conclusion

The cutaneous disorders are common among BTM patients, Pallor ,xerosis and juandice were the common skin changes obsorved among our patients, White streak and gingivitis are the most common nail and oral mucoasa changes. Xerosis is common in patients recieving deferoxamine. Serum ferritin level was higher in patients with xerosis,hyperpigmentation and juandice also we conclude that transfusion related hepatitis C is still common among BTM patients.

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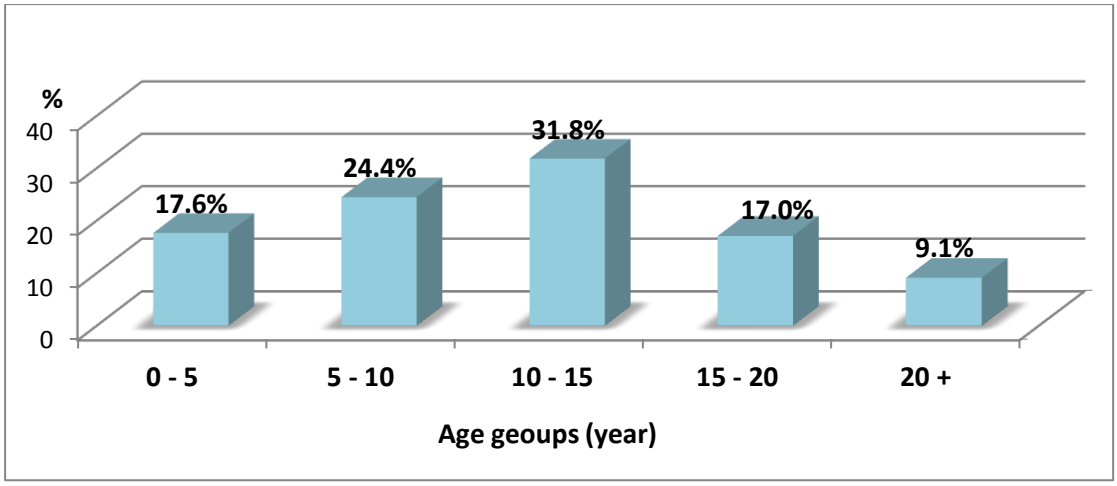


Figure 1: Distribution of BTM patients by age groups.

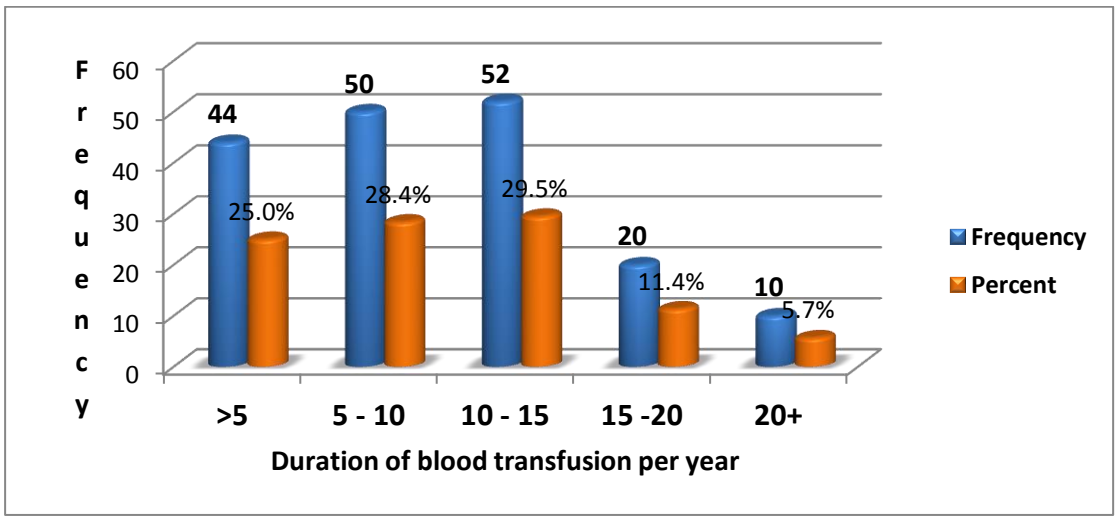
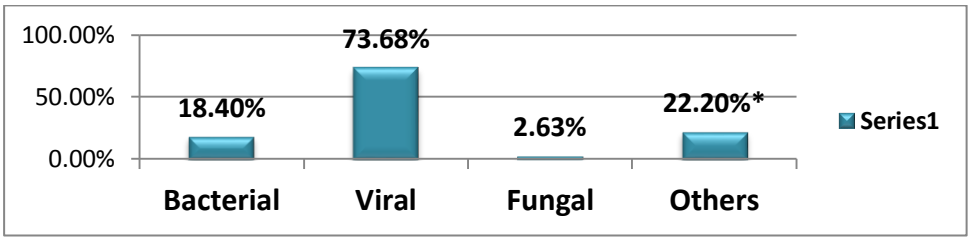


Figure 2: Duration of blood transfusion in BTM patients.



*__Others__ = Burn infections, secondary infection of dermatitis.

Figure 3: Distribution of cutaneous infection among BTM patients.

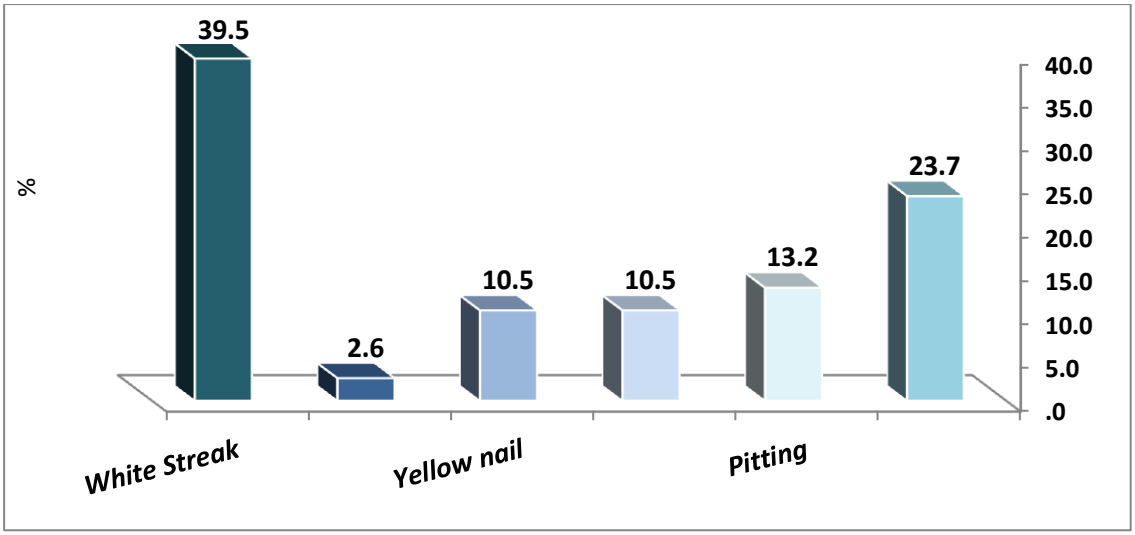


Figure 4: Distribution of types of nail changes among BTM patients.

Table 1: Frequency of cutaneous disorders among BTM patients.

Cutaneous disorder	Frequency	Percent (%)
Pallor	132	75.0
Xerosis	130	73.9
Jaundice	108	61.4
Bronze skin	104	59.1
Hyperpigmentation	91	51.7
Oral mucosa changes	49	27.8
Pitryasis alba	44	25
Coarse hair	41	23.3
Cutaneous infection	38	21.6
Nail changes	38	21.6
Pruritus	35	19.9
Post inflammatory hypopigmentation	1	0.56
Vitiligo	1	0.56

Table 2: Distribution of oral mucosa changes among BTM patients.

Description	Frequency	Percent (%)
Gingivitis	25	14.2
Hyperpigmentation of Gingiva	21	11.9
Pigmentation of Hard Palate	3	1.7
Total	49	27.8

Table 3: Mean age of patients and presence or absence of skin changes.

Skin changes		Age (year) Mean ±SD	P- Value
Xerosis	No(46) Yes(130)	8.4±4.96 11.9±6.02	<.000
Pruritus	No(141) Yes(35)	10.6±5.95 12.49±5.86	.095
Pallor	No(44) Yes(132)	13.33±6.16 10.20±5.71	.002
Hyperpigmentation	No(85) Yes(91)	8.07±5.41 13.7±5.13	<.000
Hypopigmentation	No(130) Yes(46)	10,83±6.49 11.41±4.14	.483
Bronze skin	No(72) Yes(104)	10.9±5.99 11.03±5.97	.892
Jaundice	No(68) Yes(108)	8.54±5.28 12.51±5.88	<.000
Cutaneous infection	No(138) Yes(38)	11.01±6.02 10.88±5.82	.922

Table 4:Mean duration of blood transfution with presence or absence of skin changes.

Cutanous disorder	Duration of BT (Month) Mean ± SD	P-Value
Xerosis	No (6.5±4.89) Yes (10.5±5.87)	<.000
Pruritus	No (9±5.83) Yes (11±5.89)	.094
Pallor	No (11 .7±5.81) Yes (8.7±5.72)	.003
Hyperpigmentation	No (6.5±5.24) Yes (12.2±5.03)	<.000
Hypopigmentation	No (9.2±6.42) Yes(10.1±3.92)	.242
Bronze skin	No (9.2±5.75) Yes (9.6±5.97)	.688
Jaundice	No (7.1±5.107) Yes (10.9±5.86)	<.000
Cutaneous infection	No (9.4±6.08) Yes(9.6±5.11)	.812

Table 5: Mean of serum ferritin with presence or absence of skin changes.

Cutaneous disorder		S.ferritin (Mean ±SD)ng/ml	P- Value
Xerosis	No (44) Yes (128)	3689.37±3076.03 4975.23±3065.92	.02
Pruritis	No (137) Yes (35)	4417.333±2995.2391 5542.494±3427.3266	.06
Pallor	No (43) Yes (129)	5560.349±3690.1299 4341.604±2843.5452	.05
Hyperpigmentation	No (81) Yes (91)	3566.827±2834.9741 5607.131±3043.0820	<.00
Hypopigmentation	No (126) Yes (46)	4499.267±3271.2523 5049.004±2611.8291	.31
Bronze skin	No (71) Yes (101)	4825.137±3089.0992 4520.566±3135.2030	.53
Juandice	No (66) Yes (106)	3747.874±3182.1424 5205.681±2944.1812	<.00

Table 6: Assocation between Hepatits C and skin changes.

Cutaneous Disorder	HCV positive (n=53)	HCV negative (n=123)	P-Value
Xerosis	47(88.7%)	83(67.5%)	.003
Pruritus	11(20.8%)	24(19.5%)	.850
Hyperpigmentation	39(73.6%)	52(42.3%)	<.000
Jaundice	44(83.0%)	64(52.0%)	<.000