History of Medicine, 2022, 8(2): 29–34
DOI: 10.17720/2409-5834.v8.2.2022.004

Prevalence of skin manifestations in patients with β-thalassemia and its association with serum hemoglobin and serum ferritin in Diyala province

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Received: 14 December 2021 **Accepted:** 23 July 2022

Citation: Alzuhairi ZN, Hasan IA, Fadhel TA (2022) Prevalence of skin manifestations in patients with β-thalassemia and its association with serum hemoglobin and serum ferritin in Diyala province. History of Medicine 8(2): 29–34. https://doi.org/10.17720/2409-5834.v8.2.2022.004

Abstract

Introduction: β-Thalassemia is a blood disease that associated with decrease in hemoglobin (Hb) production. Hemoglobin is the iron-containing protein located inside red blood cells (RBC), their function is transport oxygen to all cells in the body. The aim of study is to identify the prevalence of skin manifestations in patients with β-thalassemia and its association with serum hemoglobin and serum ferritin. **Method:** cross sectional design for 367 patients with thalassemia, the data collected from Hematological word in Baqubah teaching hospital. The period of study from April 2021 to February 2022. Study population: Diagnosed cases of Beta thalassemia major and intermedia patients between 2 to 38 years' age already diagnosed Hb electrophoresis by hemoglobinelectrophoresis attended to Hematological word in Baqubah teaching hospital. **Results:** study of 367 patients with thalassemia, (60.2%) of patients at age group 1-3 years, (58%) of patients are males and (42%) of them are females. (71.9%) of patents have received regular blood transfusion. (80.9%) of patients have paler, (71.7%) of patients have xerosis, (50.4%) of them have jaundice, (76%) of patients have bronze skin, (55%) of patient's have hyperpigmentation, (40.1%) of patients have pruritus. **Conclusion:** most thalassemia patients are males at age group 1-3 years they received regular blood transfusion. The most prevalence skin manifestations of thalassemia are pallor, xerosis, bronze skin, yellowish discoloration of skin (jaundice), also most patients had pruritus and hyperpigmentation.

Keywords
Prevalence, skin manifestations, β-thalassemia, serum hemoglobin, serum ferritin

β-Thalassemia is a blood disease that associated with decrease in hemoglobin (Hb) production. Hemoglobin is the iron-containing protein located inside red blood cells (RBC), their function is transport oxygen to all cells in the body (Sayani & Kwiatkowski, 2015). In thalassemia patients the low Hb level cause reduction of oxygen supply in many parts of the body cells [1]. Affected persons have a deficiency of red blood cells (RBC) lead to anemia, cause pallor, weakness, fatigability (Sayani & Kwiatkowski, 2015). β-Thalassemia is an impartially public blood illness international. Many of infants with β-thalassemia are born each year (Canatan, 2014), it is commonly occurring in Middle East countries (Canatan, 2014). Thalassemia is produced by defective genes that affect the creation of hemoglobin. From both parent affected by thalassemia their baby has this abnormal gene and born with 25% chance to have thalassemia (Pande & Kharkar, 2014; Traeger-Synodinos, Vrettou, & Kanavakis, 2019). β-Thalassemia major affects numerous organs and is related with significant illness and death (Wolff et al., 2008). In β-thalassemia, an extensive range of skin illnesses was recognized, which lead to hemoglobin illness and the problems of management (Wolff et al., 2008). Many articles and studies written in β-thalassemia, but there is a small data about the cutaneous appearance of this illness. So the aim of study is to identify the prevalence of skin manifestations in patients with β-

thalassemia and its association with serum hemoglobin and serum ferritin.

Method

Descriptive observational type with cross sectional design for 367 patients with thalassemia, the data collected from Hematological word in Baqubah teaching hospital. The period of study from April 2021 to February 2022. Study population: Diagnosed cases of Beta thalassemia major and intermedia patients between 2 to 38 years' age already diagnosed Hb electrophoresis by hemoglobin electrophoresis attended to Hematological word in Baqubah teaching hospital. Age groups, gender and blood transfusion. Hematological study consists of hemoglobin and serum ferritin, dermatological signs consist of polar, xerosis, jaundice, bronze skin, hyperpigmentation, pruritus, vitiligo and hypersensitivity and urticaria. Also assessment if patients have tinea infection, herpes infection, perteriasis alba, contact dermatitis and acne. Inclusion criteria all patients with thalassemia. No excluded criteria. Statistical analysis done by SPSS 22, categorical data used frequency and percentage, continuous data used mean, median and SD. T test and ANOVA test used for assessment differences between mean and median of continues variables. P-value less or equal to 0.05 is consider significant.

Results

Cross sectional study of 367 patients with thalassemia, (60.2%) of patients at age group 1-3 years, (58%) of patients are males and (42%) of them are females. (71.9%) of patents have received regular blood transfusion. As show in table 1.

Table (1): distribution of age groups, gender and blood transfusion.

variables		frequency	percentage
	<1	132	36.0
Age groups (y)	***1-3***	221	60.2
	3-6	10	2.7
	>6	4	1.1
Gender	***female***	213	58.0
	male	154	42.0
Blood transfusion	***irregular***	103	28.1
	regular	264	71.9

In table 2, (80.9%) of patients have polar, (71.7%) of patients have xerosis, (50.4%) of them have jaundice, (76%) of patients have bronze skin, (55%) of patient's have hyperpigmentation, (40.1%) of patients have pruritus, but just (1.4% and 1.9%) of patients have vitiligo and hypersensitivity. (10.9%) of patients have urticarial.

Table (2): distribution of symptoms.

variables		frequency	percentage
paler	***no***	70	19.1
	yes	297	80.9
xerosis	***no***	104	28.3
	yes	263	71.7
jaundice	***no***	182	49.6
	yes	185	50.4
Bronze skin	***no***	88	24.0
	yes	279	76.0
hyperpigmentation	***no***	165	45.0
	yes	202	55.0
Vitiligo	***no***	362	98.6
	yes	5	1.4
pruritus	***no***	220	59.9
	yes	147	40.1
hypersensitivity	***no***	360	98.1
	yes	7	1.9
urticarial	***no***	327	89.1
	yes	40	10.9

In table 3, just (4.4%, 18.3%, 10.9%, 21%, 1.6%, 1.4) of thalassemia patients have tinea infection, herpes infection, perteriasis alba, contact dermatitis and acne respectively.

Table 3: distribution of tinea infection, herpes infection, perteriasis alba, contact dermatitis and acne.

variables		frequency	percentage
Tinea infection	***no***	351	95.6
	yes	16	4.4
Herpes infection	***no***	300	81.7
	yes	67	18.3
Pityriasis alba	***no***	290	79.0
	yes	77	21.0
Contact dermatitis	***no***	361	98.4
	yes	6	1.6
Acne	***no***	362	98.6
	yes	5	1.4

In table 4, there is significant difference between the mean of ferritin level according to gender, male with thalassemia have more ferritin level than female. there is no significant difference between the mean of Hb according to gender.

Table 4: difference between the mean of Hb, ferritin according to gender.

Variables	Gender	N	Mean	SD	P-value
Hb (mg/dl)	***Female***	213	6.53	1.68	0.9
	Male	154	6.55	1.59	
Ferritin (mg/dl)	***Female***	213	1354.44	864.31	**0.039**
	Male	154	1555.47	955.54	

P-value ≤0.05 (significant).

In table 5, there is significant difference between the mean of ferritin level according to blood transfusion, patients with thalassemia they have regular transfusion have more ferritin level. there is no significant difference between the mean of Hb according to blood transfusion.

Table 4: difference between the mean of Hb, ferritin according to blood transfusion.

Variables	Blood transfusion	N	Mean	SD	P-value
Hb (mg/dl)	***Irregular***	103	6.46	1.64	0.6
	Regular	264	6.57	1.64	
Ferritin (mg/dl)	***Irregular***	103	820.86	587.72	**0.0001**
	Regular	264	1679.89	897.34	

P-value ≤0.05 (significant).

In table 6, there is significant difference between the mean of ferritin level according to age groups, patients with thalassemia at age group 1-3 years have more ferritin level and then age group 3-6 years. there is no significant difference between the mean of Hb according to age groups.

Table 6: difference between the mean of Hb, ferritin according to age groups.

Variables	Age groups	N	Mean	SD	P-value
Hb (mg/dl)	***<1***	132	6.43	1.54	
	1-3	221	6.55	1.66	0.6
	3-6	10	7.27	1.98	
	>6	4	7.70	2.27	
Ferritin (mg/dl)	***<1***	132	1146.50	678.16	
	1-3	221	1616.20	981.25	**0.0001**
	3-6	10	1425.50	984.43	
	>6	4	1316.50	928.93	

P-value ≤0.05 (significant).

In table 7, there is significant difference between the mean of ferritin level according to jaundice, patients with thalassemia they have jaundice have high ferritin level. there is no significant difference between the mean of Hb according to jaundice.

Table 7: difference between the mean of Hb, ferritin according to jaundice.

Variables	Jaundice	N	Mean	SD	P-value
Hb (mg/dl)	***No***	182	6.56	1.6	0.8
	Yes	185	6.51	1.6	
Ferritin (mg/dl)	***Yes***	182	1626.39	899.67	**0.0001**
	No	185	1254.25	879.94	

P-value ≤0.05 (significant).

In table 8, there is significant difference between the mean of ferritin level according to hyperpigmentation, patients with thalassemia they have hyperpigmentation have high ferritin level. there is no significant difference between the mean of Hb according to hyperpigmentation.

Table 8: difference between the mean of Hb, ferritin according to hyperpigmentation.

Variables	hyperpigmentation	N	Mean	SD	P-value
Hb (mg/dl)	***No***	165	6.55	1.60	0.9
	Yes	202	6.53	1.67	
Ferritin (mg/dl)	***Yes***	165	1645.12	901.39	**0.0001**
	No	202	1270.27	880.04	

P-value ≤0.05 (significant).

In table 9, there is significant difference between the mean of ferritin according to Pruritic, patients with thalassemia they have Pruritic have high ferritin level. there is no significant difference between the mean of Hb according to Pruritic.

Table 9: difference between the mean of Hb, ferritin according to Pruritic.

Variables	Pruritic	N	Mean	SD	P-value
Hb (mg/dl)	***No***	220	6.56	1.65	0.7
	Yes	147	6.50	1.63	
Ferritin (mg/dl)	***Yes***	220	1527.15	885.79	**0.024**
	No	147	1306.57	927.36	

P-value ≤0.05 (significant).

In table 10, there is significant difference between the mean of ferritin according to Piteriasis alba, patients with thalassemia they have jaundice have high ferritin level. there is no significant difference between the mean of Hb according to Piteriasis alba.

Table 10: difference between the mean of Hb, ferritin according to Pityriasis alba.

Variables	Pityriasis alba	N	Mean	SD	P-value
Hb (mg/dl)	***No***	290	6.52	1.61	0.7
	Yes	77	6.61	1.77	
Ferritin (mg/dl)	***Yes***	290	1510.65	915.60	**0.002**
	No	77	1168.16	829.27	

P-value ≤0.05 (significant).

Discussion

Skin manifestations are common in hematologic illnesses, including thalassemia, assumed the great variability of hematological illnesses, counting thalassemia (El-Dash & Adel, 2018). A varied skin sicknesses related with hemoglobin illness, hemosiderosis, and problems of management was recognized. Xerosis (dehydrated skin) is more occurring disorder that associated with pruritus blistering skin, cracking, and erythema (Croom, Barlow, & Landers, 2019). In current study (60.2%) of patients at age group 1-3 years, (58%) of patients are males and (42%) of them are females. (71.9%) of patents have received regular blood transfusion, this is agreed with other study stated that patients with beta-thalassemia major aged (8.3 ± 3.7) years attending the Paediatric Department of Fayoum University Hospital (61 [61%] male, 39 [39%] female) most of them received regular blood transfusion (El-Dash & Adel, 2018). Also in current study most of patients have polar, xerosis, bronze skin, jaundice, pruritus, this is similar to other study that stated xerosis was the utmost common skin appearance, then pruritus (El-Dash & Adel, 2018). Asena and colleagues stated pruritus in 37.2% of persons with thalassemia and xerosis in 34.6% (Dogramaci et al., 2009). Also Fahmey et al. (2018) stated that pruritus in 37% of persons have thalassemia. So long period of disease lead to xerosis and accumulation high level of iron inside organ this occur due to frequent blood transfusion (Dogramaci et al., 2009). Urticaria also detected by other study in thalassemia patients due to the occurrence of many immunologic faults in patients with thalassemia. This finding was reliable with Fahmey et al. (2018) who stated urticaria in occur in 16.7% of persons with thalassemia. Recurrent blood transfusions and continuous immune stimulus may aggravate immune dysfunction (Dogramaci et al., 2009). Scars were hypopigmented that occur in patients have minor

trauma due to deferoxamine pump, it is occur mostly in lower limbs then abdomen (El-Dash & Adel, 2018). Also hyperpigmentation and dark skin occur in thalassemia found ephelides (flat, light brown or red freckles that fade in winter) (Croom et al., 2019; Dogramaci et al., 2009; El-Dash & Adel, 2018). Recurrent blood transfusions can lead to endocrine abnormal function as a consequence of iron overload that is placed in vigorous organs such as the heart, pituitary, thyroid, and gonads (De Sanctis et al., 2019; Yassin et al., 2019). High ferritin levels were significantly associated with xerosis, pruritus, and ephelides, as found in other studies (Dogramaci et al., 2009; El-Dash & Adel, 2018; Fahmey et al., 2018). Bronzy colored skin was the 2nd utmost common dermatological variation well-known in their study, similar to another study also found the bronze skin (Roy et al., 2018). Urticaria was found only in those patient who had serum ferritin level more than 2000 mcg/dl and the correlation was found to be statistically significant ($p<0.05$). Dogramaci A.C et al also found urticaria among 3.8% study population (Croom et al., 2019; Dogramaci et al., 2009; El-Dash & Adel, 2018). In current study also patients have tinea infection, herpes infection, perteriasis alba, contact dermatitis and acne other study stated that tinea infections are classically attained straight from contact with infected humans or animals, or indirectly from contact to dirty soil or fomites, 11.6% of patients have tenia infections (López-Martínez et al., 2010). (10.5%) had pityriasis alba. Low levels of serum copper may account for the incidence of pityriasis alba (Miazek et al., 2015). Pityriasis alba was reported as 6–4% by the Turkish study (Gupta & Gupta, 2004). When there is increase in no. of blood transfusion and also age of patients this lead to increase serum ferritin level. Serum ferritin level in men was 2900 ng/ml and it is analogous in women 2591 ng/ml (Mishra & Tiwari, 2013). Pallor occur in patients due to anemia and jaundice occur due to hyperbilirubinemia subsequent from intravascular hemolysis these lead to skin manifestations appear. Fatigue occur due to anemia. Extremities checkup can demonstration ulcerations. Chronic iron deposition occur due to numerous transfusions can consequence in bronze color of skin (Bajwa & Basit, 2022).

Conclusion

In current study we conclude that most thalassemia patients are males at age group 1-3 years they received regular blood transfusion. The most prevalence skin manifestations of thalassemia are pallor, xerosis, bronze skin, yellowish discoloration of skin (jaundice), also most patients had pruritus and hyperpigmentation. In thalassemia patient's serum ferritin associated with male gender, age group 1-3 years, regular blood transfusion, jaundice, hyperpigmentation, pruritus and petriasis alba it is become high level.

References

Bajwa H, & Basit H (2022) Thalassemia. In StatPearls. Treasure Island (FL): StatPearls Publishing. URL: http://www.ncbi.nlm.nih.gov/books/nbk545151/

Canatan D (2014) Thalassemias and hemoglobinopathies in Turkey. Hemoglobin 38 (5): 305-307. DOI: https://doi.org/10.3109/03630269.2014.938163

Croom D, Barlow T, & Landers JT (2019) Pruritic rash on chest and back. J Fam Pract 68 (2): 113-116. URL: https://pubmed.ncbi.nlm.nih.gov/30870537/

De Sanctis V, Soliman AT, Canatan D, Yassin MA, Daar S et al. (2019) Thyroid Disorders in Homozygous β-Thalassemia: Current Knowledge, Emerging Issues and Open Problems. Mediterr J Hematol Infect Dis 11 (1): e2019029. DOI: https://doi.org/10.4084/mjhid.2019.029

Dogramaci AC, Savas N, Ozer B, & Duran N (2009) Skin diseases in patients with beta-thalassemia major. Int J Dermatol 48 (10): 1057-1061. DOI: https://doi.org/10.1111/j.1365-4632.2009.04176.x

El-Dash H, & Adel S (2018) Cutaneous manifestations in Egyptian children with beta-thalassemia major: Relationship with serum ferritin, thyroid profile, and treatment modalities. Pediatr Dermatol 35 (5): 639-643. DOI: https://doi.org/10.1111/pde.13570

Fahmey SS, Taha G, El-Refaey A, & Adly S (2018) Skin Disorders in Egyptian Children with β-Thalassemia Major. J Trop Pediatr 64 (2): 104-109. DOI: https://doi.org/10.1093/tropej/fmx035

Gupta MA, & Gupta AK (2004) Stressful major life events are associated with a higher frequency of cutaneous sensory symptoms: an empirical study of non-clinical subjects. J Eur Acad Dermatol Venereol 18 (5): 560-565. DOI: https://doi.org/10.1111/j.1468-3083.2004.00931.x

López-Martínez R, Manzano-Gayosso P, Hernández-Hernández F, Bazán-Mora E, & Méndez-Tovar LJ (2010) Dynamics of dermatophytosis frequency in Mexico: an analysis of 2084 cases. Med Mycol 48 (3): 476-479. DOI: https://doi.org/10.3109/13693780903219006

Miazek N, Michalek I, Pawlowska-Kisiel M, Olszewska M, & Rudnicka L (2015) Pityriasis Alba--Common Disease, Enigmatic Entity: Up-to-Date Review of the Literature. Pediatr Dermatol 32 (6): 786-791. DOI: https://doi.org/10.1111/pde.12683

Mishra AK, & Tiwari A (2013) Iron overload in Beta thalassaemia major and intermedia patients. Maedica (Bucur) 8 (4): 328-332. URL: http://www.ncbi.nlm.nih.gov/pmc/articles/pmc3968466/

Pande SY, & Kharkar V (2014) Clinical profile of cutaneous manifestations with and without hematologic disease: A comparative study. Indian Dermatol Online J 5 (2): 138-143. DOI: https://doi.org/10.4103/2229-5178.131081

Roy K, Das SK, Dutta A, & Mandal RK (2018) Dermatological manifestations in beta thalassemia major patients between 2 to 12 years and their relation with serum ferritine level. Journal of the Pediatrics Association of India 7 (3): 149-157. URL: https://www.jpai.in/temp/JPediatrAssocIndia73149-4708302_130443.pdf

Sayani FA, & Kwiatkowski JL (2015) Increasing prevalence of thalassemia in America: Implications for primary care. Ann Med 47 (7): 592-604. DOI: https://doi.org/10.3109/07853890.2015.1091942

Traeger-Synodinos J, Vrettou C, & Kanavakis E (2019) Rapid Detection of Fetal Mendelian Disorders: Thalassemia and Sickle Cell Syndromes. Methods Mol Biol 1885: 207-219. DOI: https://doi.org/10.1007/978-1-4939-8889-1_14

Wolff K, Goldsmith L, Katz S, Gilchrest B, Paller AS et al. (2008) Fitzpatrick's dermatology in general medicine (7th ed.). McGraw-Hill. URL: https://www.scholars.northwestern.edu/en/publications/fitzpatricks-dermatology-in-general-medicine-7th-edition-2

Yassin MA, Soliman AT, De Sanctis V, Yassin KS, & Abdulla MA (2019) Final Height and Endocrine Complications in Patients with β-Thalassemia Intermedia: Our Experience in Non-Transfused Versus Infrequently Transfused Patients and Correlations with Liver Iron Content. Mediterr J Hematol Infect Dis 11 (1): e2019026. DOI: https://doi.org/10.4084/mjhid.2019.026