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ORIGINAL ARTICLE

Prevalence of Dermatological Problems in Beta-Thalasemic Patients at Al-Khidmat Hospital, Peshawar

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ABSTRACT

Background: Beta-thalassemia is the world's most prevalent single-gene disease with a reduction in the synthesis of hemoglobin b-chain. A lot of skins problems occur in thalassemia patients but, no study have been conducted in Pakistan to determine their prevalence.

Objective: To determine the prevalence of dermatological problems in beta-thalasemic patients

Methodology: This was cross sectional study carried out at the department of dermatology Al-Khidmat hospital Peshawar for a period of one year from August 2020 to August 2021. All the beta-thalassemia patients were examined for dermatological problems by a single expert dermatologist. All of the data was entered and analyzed by using the SPSS version 20 software.

Results: Amongst 150 beta-thalasemic patients, 122 (81.33%) patients were observed with dermatological problems. The most frequent dermatological problem observed in our study was pruritus in 54 (36%) patients followed by xerosis in 34 (22.67%), urticaria in 30(20%), Pigmentary disorders in 33(22%) patient, freckles in 24(16%), tinea infections in 15(10%), pitriasis alba in 13 (8.67%) patients, scars in 13 (8.67%), hypersensitivity to deferoxamine pump in 12 (8%), herpes simplex in 12 (8%), Verruca vulgaris in 10 (6.67%), acne in 8 (5.33%) patients, miliaria in 8 (5.33%) while contact dermatitis was observed in 6(4%) of the patients.

Conclusion: Our study concludes that dermatological problems are highly prevalent in beta-thalassemia patients with pruritus as the most common problem followed by xerosis.

Keywords: Prevalence; Dermatological problems; Beta-thalasemia; Pruritus; Xerosis.

INTRODUCTION

There are many diseases associated with hemoglobin, including thalassemia's, that are caused by problems with synthesis of the globin polypeptides, particularly the alpha and beta-globin polypeptides chain. Due to inability to properly synthesize beta -globin chains, unpaired beta -globin chains are formed in erythroid intermediates and precipitate, causing membrane damage. In turn, this promotes inefficient erythropoiesis and erythroid apoptosis, which both contribute to anemia in the long term [1].

The most severe type, known as beta-thalassemia major, requires continuous blood transfusions in order to survive. Patients with a milder form of thalassemia called non-transfusion-dependent thalassemia generate relatively greater amounts of hemoglobin and may only need occasional blood transfusions [2]. Beta-thalassemia is the world's most prevalent single-gene disease with a reduction in the synthesis of hemoglobin beta-chain. Because of a range of treatment options, thalassemia patients' life expectancy has risen; however, therapy-related problems have also risen [3]. Multiple organs systems are affected by functional and physiological abnormalities caused by anemia and severe hemosiderosis [4]. Thalassemia is prevalent highly in Middle East, Mediterranean, Transcaucasus and central-south Asia countries [5]. Control of haemoglobinopathies, especially beta-thalassemia, is a priority for the World Health Organization (WHO) in poor countries [6]. In Pakistan, estimated 5000-9000 infants with beta-thalassemia are born each year, despite the lack of a documented record. The projected carrier percentage is 5-7%, with 9.8 million carriers in the overall population [7]. Patients with thalassemia major need frequent blood transfusions as well as intensive continuous medical treatment. RBC transfusions are required each two to three weeks to keep hemoglobin levels above 9 to 10 g/dl at all times. This helps to avoid developmental problems, organ damage, and abnormalities in the bones [8, 9]. On the other hand, repeated blood transfusions induce iron overload, which leads to a variety of consequences such as endocrinopathies [10, 11], stunted growth [12], cardiovascular issues [13], liver diseases [14], gonadal malfunction, delayed puberty [15], and an increase in the risk of infections transmitted by transfusion [16]. As a result of the combination of frequent blood transfusions and chelation treatment, individuals are now living into their fourth or fifth decade of life. It is believed that cutaneous manifestations of the illness, which include skin diseases as well as nail and hair loss, oral mucosal alterations, and lung cancer, are caused by the hemolytic process of the disease itself or are a result of the therapeutic impact of blood transfusions and an iron overload complication [8, 17, 18]. A research on the prevalence of dermatologic issues that occur in people with beta-thalassemia major has not yet been conducted in Pakistan, according to the literature. This study was thus carried out to determine the prevalence of dermatological problems in beta-thalasemic patients.

MATERIALS AND METHODS

This was cross sectional study carried out at the department of Dermatology, Al-Khidmat Hospital Peshawar, Khyber Pakhtunkhwa Pakistan. This study was carried out for a period of one year from August 2020 to August 2021. The hospitals research and ethical committee approved this study. Informed consent in written form was taken from all the included patients in our study. The inclusion criteria of our study were all the patients with diagnosis of beta-thalasemic on regular blood transfusion, patients of all age group and both gender and willing to participate in our study while the exclusion criteria were patients with beta-thalassemia intermediate, beta -thalassemia minor, sickle cell anemia and patients having other systemic problems along with skin disorders. To prevent additional manifestations caused by ageing, reduced immunity, and other blood illnesses, we omitted patients over 60 years old, immune-compromised patients owing to other reasons such as diabetes, hepatitis C virus, AIDS, and individuals with other related blood or immunologic condition. Our study's sample size comprised of all beta-thalassemia patients that have been diagnosed during the research period in patients attending the Thalassemia care unit. All patients had their medical histories thoroughly examined, including their age and gender. All of the patients were checked to see whether they had any skin problems. Although the patients did not express any concerns about their skin but examination revealed skin problems. An expert

single dermatologist completed skin examination of all the participants. All of the data was entered and analyzed by using the SPSS version 20 software. Mean and standard deviation were documented for continuous variables, while categorical variables were calculated as percentages and proportions. All the data was presented in figure and tabulated form.

RESULTS

In this study a total of 150 patients fulfilling the inclusion criteria were included. There were 95 (63.33%) male and 55 (36.67%) female in our study. (Figure 1) The mean age (SD) was 14.5 (2.82) years with minimum age of 1 month and maximum age of 37 years. According to the age wise distribution, 23 (15.33%) of the patients belong to age group (0-5) years, 40 (26.67%) patients in the age group (6-10) years, 49 (39.33%) of the patients belong to age group (11-15) years, 27 (18%) patients in the age group (16-20) years while 11 (7.33%) patients were recorded in the age group >20. (Figure 2) Amongst 150 beta-thalasemic patients, 122 (81.33%) patients were observed having dermatological problems. The most frequent dermatological problem observed in our study was pruritus 54 (36%) followed by xerosis in 34 (22.67%), urticaria in 30(20%), Pigmentary disorders in 33(22%) patient, freckles in 24(16%), tinea infections in 15(10%), pitriasis alba were observed in 13 (8.67%) patients, scars in 13 (8.67%), hypersensitivity to deferoxamine pump in 12 (8%), herpes simplex in 12 (8%), Verruca vulgaris in 10 (6.67%), acne in 8 (5.33%) patients, miliaria in 8 (5.33%) while contact dermatitis was observed in 6(4%) of the patients. (Table 1)

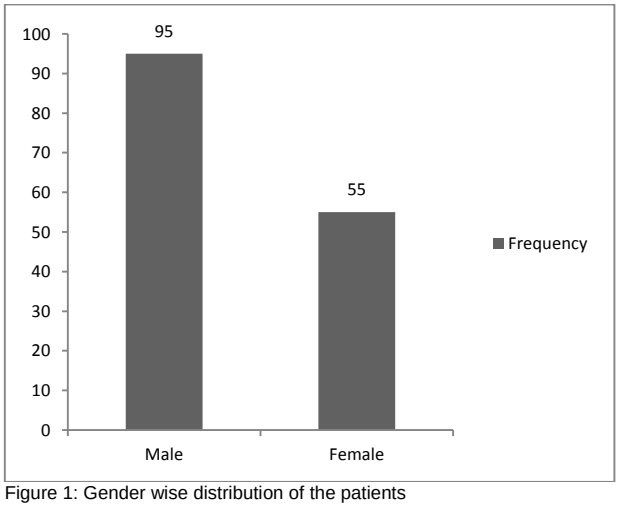

Figure 1: Gender wise distribution of the patients

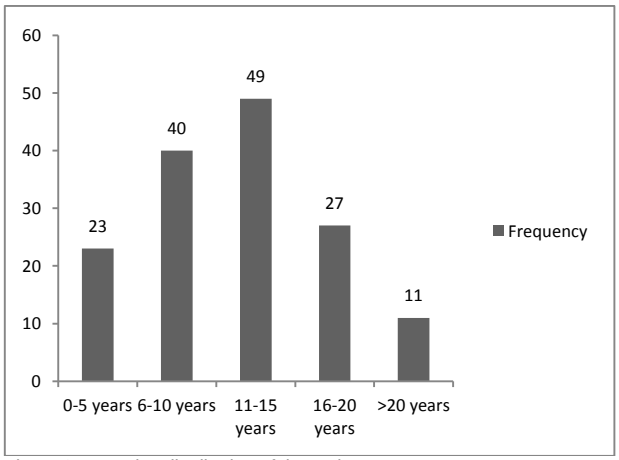

Figure 2: Age wise distribution of the patients

Table 1: Distribution of dermatological problems amongst beta-thalasemic patients enrolled in our study

Dermatological problem	Category	Frequency	Percentage
Pruritus	Yes	54	36%
	No	99	64%
Xerosis	Yes	34	22.67%
	No	116	77.33%
Urticaria	Yes	30	20%
	No	120	80%
Pigmentary disorders	Yes	33	22%
	No	117	78%
Freckles	Yes	24	16%
	No	126	84%
Tinea infections	Yes	15	10%
	No	135	90%
Pitriasis alba	Yes	13	8.67%
	No	137	91.33%
Scars	Yes	13	8.67%
	No	137	91.33%
Hypersensitivity to deferoxamine pump	Yes	12	8%
	No	138	92%
Herpes simplex	Yes	12	8%
	No	138	92%
Verruca vulgaris	Yes	10	6.67%
	No	140	93.33%
Miliaria	Yes	8	5.33%
	No	142	94.67%
Contact dermatitis	Yes	6	4%
	No	144	96%
Acne	Yes	5	3.33%
	No	145	96.67%

DISCUSSION

Beta-thalassemia is the world's most prevalent single-gene disease with a reduction in the synthesis of hemoglobin beta-chain. Because of a range of treatment options, thalassemia patients' life expectancy has risen; nevertheless, therapy-related problems have also risen [3]. Multiple organs systems are affected by functional and physiological abnormalities caused by anemia and severe hemosiderosis [4]. In individuals with transfusion-dependent thalassemia, iron excess causes substantial morbidity and death [19]. Due of improved standards of treatment in the field of thalassemia, the life expectancy of seriously affected individuals has increased by a considerable margin. Management-related problems, which were previously unknown, have been revealed as a result of increased years of survival [20].

In our study a total of 150 patients fulfilling the inclusion criteria were included. There were 95 (63.33%) male and 55 (36.67%) female in our study. Amongst 150 beta-thalasemic patients, 122 (81.33%) patients were observed having dermatological problems. These findings are consistent with the previous study who reported that skin problems were observed in all of the thalassemia patients included in their study [21]. Our findings are also in accordance with the earlier study who reported that frequency of dermatological problems was 83.3% in thalassemic patients. They also reported that skin problems were more frequent in male thalassemic patients than female [4].

The most common dermatological problem observed in our study was Pruritus in 54 (36%) patients. In accordance to our findings a previous study in turkey also reported pruritus as the most common skin problem in 37.2% of the thalassemia patients [4]. The mechanism of disease that causes pruritus is unclear. It may be related to the releasing of histamine from tissue mast cells in response to cutaneous iron deposits [22]. Xerosis was observed in 34 (22.67%) patients in our study. The reported prevalence of xerosis in our study is lower than other previous studies who reported xerosis prevalence ranging from 34-53% [4, 18]. This variation might be due to the variation in weather conditions. In our study, hypersensitivity to deferoxamine pump was observed in 8% of the thalassemic patients. These findings were in line with the previous study who reported hypersensitivity to deferoxamine pump in 12.8% of the thalassemic patients [23].

In thalassemia patients, many immunological abnormalities have been observed [24]. The patient's immune system is triggered by repeated transfusions for the therapy of thalassemia major, resulting in the formation of anti-erythrocyte antibodies [25]. This may explain urticaria and contact dermatitis, both of which were observed in our patients (20% and 4%, correspondingly).

Pigmentary disorders were found in 22% of the individuals in our research. Hyper-pigmentation is widespread, although it is more noticeable on the face and hands, which are exposed to the sun on a daily basis. Skin pigmentation was shown to be prevalent in 28 percent of thalassemia patients, according to previous study done by Fekri et al. [26].

Freckles were identified as the fifth most prevalent condition (16%) in our research. In contrast to our study a previous study done by Naderi et al. observed freckles as the most common dermatological problem in 70.7% thalassemia patients [17]. Iron deposition in the skin may be the cause of freckles in thalassemia patients.

Tinea infections was observed in 15(10%) of the thalassemia patients in our study. In contrast to our study, a previous study reported Tinea infection in 2.6% of thalassemia patients [27]. Another study also reported lower prevalence (5%) of Tinea infection in thalassemia patients than our study [4].

In our study pitriasis alba were observed in 13 (8.67%) patients. In contrast to our study high prevalence of Pitryasis alba was observed in previous study who reported 25% prevalence of pitriasis alba [27]. Another study in Turkey reported lower prevalence (6.4%) of pitriasis alba in thalassemia patients [4]. Pityriasis alba is thought to be caused by low copper levels in the blood. Copper is required for activation of tyrosinase enzyme in melanocytes, which is required for the synthesis of melanin [28]. Several investigations have shown that thalassemia patients have lower copper levels in their blood [29, 30].

In this study scars were observed in 13 (8.67%) patients. In contrast to our study a previous study done in Iran reported high prevalence (28%) of scars occurred in beta- thalassemia patients [18].

Verruca vulgaris was shown in 6.67% thalassemia patients in our study. A previous study reported low prevalence (1.8%) of verruca vulgari [4]. In our study, herpes simplex and miliaria were observed in 8% and 5.33%, respectively. An earlier study reported that none of the thalassemia patients have herpes simplex and miliaria [4]. In our research, 3.33 percent of our patients had acne, which we attributed to their age rather than to thalassemia. The prevalence of acne in thalassemia patients in our research is similar to that seen in a Turkish study [31]. The main limitation of our study is small sample size. A study having large sample size is recommended to get better results.

CONCLUSION

Our study concludes that dermatological problems are highly prevalent in b-thalassemia patients with pruritus as the most common problem followed by xerosis. In order to provide early detection of dermatological disorders and a good life quality for thalassemia patients, thorough skin examination is needed. Most skin issues are caused by an excess of iron, therefore iron chelators are essential. Pruritus is the most common complication; hence antihistamines and soothing creams may be helpful. The second condition was xerosis, which may be treated with an emollient. Freckles were also more frequent, thus the patient should be using sun protection to avoid them. Researchers must conduct more studies in order to identify the specific variables responsible for the high prevalence of various dermatologic conditions in this group.

REFERENCES

1. Sankaran VG, Nathan DG. Thalassemia: an overview of 50 years of clinical research. Hematology/Oncology Clinics. 2010;24(6):1005-20.
2. Rivella S. β-thalassemias: paradigmatic diseases for scientific discoveries and development of innovative therapies. Haematologica. 2015;100(4):418.
3. Saki N, Abroun S, Salari F, Rahim F, Shahjahani M, Javad M-A. Molecular aspects of bone resorption in β-thalassemia major. Cell Journal (Yakhteh). 2015;17(2):193.
4. Dogramaci AC, Savas N, Ozer B, Duran N. Skin diseases in patients with β-thalassemia major. Wiley Online Library; 2009.
5. Wheatherall D, Clegg J. The thalassemia syndromes. Oxford. England: Blackwell Science Ltd. 2001.
6. Angastiniotis M, Modell B. Global epidemiology of hemoglobin disorders. Annals of the New York Academy of Sciences. 1998;850(1):251-69.
7. Ahmed S, Saleem M, Modell B, Petrou M. Screening extended families for genetic hemoglobin disorders in Pakistan. New England journal of medicine. 2002;347(15):1162-8.
8. Galanello R, Origa R. Beta-thalassemia. Orphanet journal of rare diseases. 2010;5(1):1-15.
9. Zamani F, Shakeri R, Eslami S-M, RAZAVI SM, Basi A. Hydroxyurea therapy in 49 patients with major beta-thalassemia. 2009.
10. Grow K, Abrol P, Vashist M, Yadav R, Sharma S. Associated complication in beta thalassemia patients. IOSR Journal of Pharmacy. 2013;3(1):22-5.
11. Low Louis C. Growth of children with beta thalassemia major. Indian J Pediatr. 2005;72:159-64.
12. Ulger Z, Aydinok Y, Levent E, Gurses D, Ozyurek AR. Evaluation of QT dispersion in β thalassaemia major patients. American journal of hematology. 2006;81(12):901-6.
13. Aessopos A, Farmakis D, Deftereos S, Tsironi M, Tassiopoulos S, Moyssakis I, et al. Thalassemia heart disease: a comparative evaluation of thalassemia major and thalassemia intermedia. Chest. 2005;127(5):1523-30.
14. Perifanis V, Tziomalos K, Tsatra I, Karyda S, Patsiaoura K, Athanassiou-Metaxa M. Prevalence and severity of liver disease in patients with b thalassemia major. A single-institution fifteen-year experience. Haematologica. 2005;90(8):1136-8.
15. Nasr MR, Ebrahim NA, Salahedin O. Growth pattern in children with beta-thalassemia major and its relation with serum ferritin, IGF1 and IGFBP3. Journal of clinical and experimental investigations. 2012.
16. Khan FU. Frequency of complications In Beta thalassemia major in DI Khan. Biomedica. 2007;23(6):31-3.
17. Naderi M, Shamshiri H, Alizadeh S, Dorgalaleh A, Manafi R, Tabibian S. Cutaneous and mucosal manifestations in patients with beta major thalassemia. Dermatology & Cosmetic. 2013;4(1).
18. Momeni A, Adabi M, AMIN JM, HOUR FH. Skin and mucosal manifestations in patients with thalassemia major. 2001.
19. Rund D, Rachmilewitz E. β-Thalassemia. New England Journal of Medicine. 2005;353(11):1135-46.
20. Panigrahi I, Agarwal S. Thromboembolic complications in β-thalassemia: beyond the horizon. Thrombosis research. 2007;120(6):783-9.
21. Al-Rubiay K, Salem A. The pattern of skin diseases in Basrah province: Review of 9252 patients. The Medical Journal of Basrah University. 2005;13:183-95.
22. Brigant F, Hautefeuille V, Dadban A, Lok C, Nguyen-Khac E, Chaby G. Generalized pruritus in dysmetabolic hyperferritinemia treated by phlebotomy. Dermatology online journal. 2015;21(9).
23. Dubey A, Parakh A, Dublish S. Current trends in the management of beta thalassemia. The Indian Journal of Pediatrics. 2008;75(7):739-43.
24. Lombardi G, Matera R, Minervini MM, Cascavilla N, D'Arcangelo P, Carotenuto M, et al. Serum levels of cytokines and soluble antigens in polytransfused patients with beta-thalassemia major: relationship to immune status. Haematologica. 2003;79(5):406-12.
25. Sadeghian MH, Keramati MR, Badiei Z, Ravarian M, Ayatollahi H, Rafatpanah H, et al. Alloimmunization among transfusion-dependent thalassemia patients. Asian journal of transfusion science. 2009;3(2):95.
26. Fekri A, Maghsoodloonejad a. Skin and mocoos membrane lesions in major b-thalassemia. 2000.
27. Izzaddin S, Hasan KM. Cutaneous manifestation among patients with β-thalassemia major. Iraqi Journal of Hematology. 2014;3(2):98.
28. Miazek N, Michalek I, Pawlowska-Kisiel M, Olszewska M, Rudnicka L. Pityriasis Alba—Common Disease, Enigmatic Entity: Up-to-Date Review of the Literature. Pediatric dermatology. 2015;32(6):786-91.
29. Shamshirsaz AA, Bekheirnia MR, Kamgar M, Pourzahedgilani N, Bouzari N, Habibzadeh M, et al. Metabolic and endocrinologic complications in beta-thalassemia major: a multicenter study in Tehran. BMC endocrine disorders. 2003;3(1):1-6.
30. Sherief LM, El-Salam A, Sanaa M, Kamal NM, Almalky MA, Azab SF, et al. Nutritional biomarkers in children and adolescents with Beta-thalassemia-major: an Egyptian center experience. BioMed research international. 2014;2014.
31. Baccarani-Contri M, Bacchelli B, Boraldi F, Quaglino D, Taparelli F, Carnevalia E, et al. Characterization of pseudoxanthoma elasticum-like lesions in the skin of patients with β-thalassemia. Journal of the American Academy of Dermatology. 2001;44(1):33-9.