Introduction

β-Thalassemia is a blood disorder that reduces the production of hemoglobin. Hemoglobin is the iron-containing protein in red blood cells that carries oxygen to cells throughout the body. In people with β-thalassemia, low levels of hemoglobin lead to a lack of oxygen in many parts of the body. Affected individuals also have a shortage of red blood cells (anemia), which can cause pale skin, weakness, fatigue, and more serious complications [1]. β-Thalassemia is a fairly common blood disorder worldwide. Thousands of infants with β-thalassemia are born each year. β-Thalassemia occurs most frequently in people from Mediterranean countries, North Africa, the Middle East, India, Central Asia, and Southeast Asia [2]. Thalassemia is caused by faulty genes that affect the production of hemoglobin. A child can only be born with the condition if they inherit these faulty genes from both parents. For example, if both parents have the faulty gene that causes β-thalassemia major, there’s a 25% chance of each child they have being born with the condition. The parents of a child with the condition are usually carriers of thalassemia. This means they only have one of the faulty genes that causes the condition [3,4]. β-Thalassemia major affects multiple organs and is associated with considerable morbidity and mortality. In β-thalassemia, a wide spectrum of skin diseases was identified, which were caused by both the hemoglobin disorder and the complications of treatment.

Background

β-Thalassemia major affects multiple organs and is associated with considerable morbidity and mortality. In β-thalassemia, a wide spectrum of skin diseases was identified, which were caused by both the hemoglobin disorder and the complications of treatment. Patients and methods

This cross-sectional study included 105 Egyptian patients (50 female individuals and 55 male individuals) with transfusion-dependent β-thalassemia major in the period spanning from June 2017 to February 2018. The study was performed on child and adult patients of β-thalassemia who presented to the hematology clinic, Menoufia University hospital. Skin examination of each patient was carried out, and any skin disease present was recorded.

Results

The main skin disorders that were noticed in decreasing order of frequency were pruritus (34.4%), xerosis (24.8%), urticaria (21.1%), freckles (17.1%), linea infections (11.6%), pityriasis alba reported in 10.5%, scars (10.5%), hypersensitivity to deferoxamine pump (9.5%), herpes simplex (9.5%), acne vulgaris (8.6%), miliaria (6.7%), contact dermatitis (4.8%).

Conclusion

Skin diseases were frequent among patients with β-thalassemia major. The most common skin lesions in our patients were pruritus, xerosis, and hyperpigmentation. Careful skin examination of thalassemia patients is required to provide early diagnosis of dermatological diseases and a better quality of life.

Keywords:

β-Thalassemia, cutaneous manifestations, iron overload, pruritus, xerosis

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transfused β-thalassemia major patients. The study was performed on child and adult patients of β-thalassemia who attended to Menoufia University hospital. All patients underwent detailed history evaluation, including age, sex, and duration of illness. All patients were examined to record any dermatological disorders. The patients did not complain about having any skin problems, but skin lesions were discovered on examination.

The work was started after obtaining approval from the department of dermatology and andrology and the research ethics committee of Menoufia Faculty of Medicine. A self-report questionnaire was given to participants after obtaining their consent. The questionnaire was designed by the investigator. Each patient was examined and asked to fill the questionnaire to ensure that all gathered information was kept confidential and the participant would be kept anonymous; each questionnaire was handed over in an envelope, and, after filling it, the participant sealed the envelope and put it in a basket containing other sealed envelopes.

All patients in the study had thalassemia for more than 1 year. This study included 105 patients aged from 2 to 60 years, as thalassemia major, which is the severe form of thalassemia, becomes apparent before 2 years of age, but thalassemia intermedia and thalassemia minor are less severe and will appear later in life. We excluded patients who were more than 60 years of age, immune-compromised patients due to other causes such as diabetes mellitus, hepatitis C virus and AIDS, and patients with other associated blood or immunological disease, to avoid other manifestations caused by aging, lowered immunity and other blood diseases.

The results were collected and entered into the computer using SPSS (statistical package for the social sciences) program for statistical analysis (version 20; Inc., Chicago, Illinois, USA).

Descriptive statistics in the form of mean, SD, number and % were applied.

### Results
The study was performed on 105 patients of β-thalassemia; female individuals comprised 52.4% while male individuals comprised 47.6% of patients. The duration of thalassemic disease ranged from 1 to 59 years (Table 2).

The main skin disorders that were noticed in decreasing order of frequency were pruritus (34.4%), xerosis (24.8%), urticaria (21.1%) freckles (17.1%), tinea infections (11.6%), pityriasis alba reported in 10.5%, scars (10.5%), hypersensitivity to deferoxamine pump (9.5%), herpes simplex (9.5%), acne vulgaris (8.6%), miliaria (6.7%), and contact dermatitis (4.8%), as shown in Table 3.

### Discussion
Thalassemia is one of the most common single-gene disorders worldwide, in which hemoglobin beta chain production is decreased. Today, the life expectancy of thalassemia patients is increased because of a variety of treatment methods; however, treatment-related complications have also increased. Profound anemia and severe hemosiderosis cause functional and physiological abnormalities in various organ systems. This study was conducted to assess the frequency of cutaneous and mucosal manifestations in patients with β-thalassemia [6].

Iron overload causes significant morbidity and mortality in patients with transfusion-dependent β-thalassemia [7]. The higher standards of care in β-thalassemia have led to a significant increase in the life expectancy in severely affected patients. Enhanced years of survival have led to the unmasking of management-related complications, which were infrequently encountered [8].

Pruritus, which occurred in 34.3% of our patients, was the most common cutaneous abnormality. Our finding is close to a Turkish study [9], which found that 37.2% of thalassemia patients had pruritus.

The pathogenesis of pruritus is unknown. It might be due to the release of histamine from tissue mast cells secondary to stimulation by iron deposits in the skin [10].

Dry skin is known as xerosis. The condition is characterized by pruritic, dry, cracked, and fissured...
The appearance of xerotic skin is like cracked porcelain. These cracks or fissures are present because of epidermal water loss. The skin splits, and cracks are deep enough to disrupt dermal capillaries, and bleeding fissures may occur. Itching or pruritus occurs, leading to secondary lesions [11].

In our study xerosis was the second most frequently observed skin disorder (24.8%). The reported frequency of xerosis among thalassemia patients ranges between 34 and 53% of the evaluated patients [12], whereas 24.8% of our patients reported this symptom. This difference may be related to the prevailing climatic conditions.

In our study, 23.9% of the patients showed pigmentary disorders. Hyperpigmentation is generalized and particularly pronounced in the sun-exposed areas of the face and hands. Most of the affected patients had dark brown hyperpigmentation. Fekri et al. have documented a prevalence rate of 28% for skin pigmentation in their patients with thalassemia [13].

Postinflammatory hypopigmentation was observed in our patients; it was 5.8%. It is close to the study by Jiquan et al., which was 6.4%. Its etiology is unknown; however, solar exposure and genetic predisposition have been hypothesized as causative factors. It is usually associated with guttate hyperkeratosis, xerosis, and lentiginosis [14].

Several immunological defects have been found in thalassemia patients [15]. Repetition of transfusions for the treatment of thalassemia major provokes the patient’s immune system and results in the production of antiepithelial antibodies (alloantibodies and/or autoantibodies) [16].

Urticaria and contact dermatitis, which were seen in our patients (21 and 4.8%, respectively), could be explained in this way, whereas urticaria and contact dermatitis were 16.7 and 13%, respectively [17].

Our study ranked ephelides as the fifth most frequently observed disorder (17.1%), whereas Taher and sheikh-Taha reported it as the most common disorder seen in their patients (70.7%) [18]. Ephelides in thalassemia patients might be explained by iron deposition in the skin [19].

Tinea infections are typically acquired directly from contact with infected humans or animals, or indirectly from exposure to contaminated soil or fomites. In our study, 11.6% of our patients complained of tinea infections, whereas 5.1% was reported by the Turkish study [20].

Eleven of our patients (10.5%) had pityriasis alba. Low levels of serum copper may account for the occurrence of pityriasis alba. Copper is indispensable to activate the tyrosinase in melanocytes, which is critical to melanin production [21].

Several studies reported reduced serum copper in thalassemia patients [22]. Pityriasis alba was reported as 6–4% by the Turkish study [23].
In this study, scars were observed in 10.5%. Scars were hypopigmented, and the abdomen was the most frequently affected area, followed by the lower limbs. Six patients had scars caused by the deferoxamine pump. A previous study in Iran reported that scars occurred in 28% of thalassemia patients [24].

In our study, hypersensitivity to deferoxamine pump was noted in 95% of the participants. Turkish study incidence of hypersensitivity to deferoxamine pump was 12.8% [25].

Reduction in serum zinc levels, as a result of deferoxamine therapy, has been described by previous studies. This might be the cause of skin disorders found in thalassemia patients receiving deferoxamine [26].

In our study, verruca vulgaris was observed in 8.6% of our patients, but, in the study by Dogram and colleagues, it was observed in 1.8% of patients. In this study, herpes simplex and miliaria were noticed in 9.5 and 6.7%, respectively, but Dogram and colleagues did not observe any cases.

In this study, acne was observed in 3.8% of our patients; we believed that this was a result of the age of the study participants, rather than being caused by thalassemia itself. Our finding is close to the Turkish study, which was 2.6% of the study group [27].

Some studies, for example, those conducted by Baccarani and colleagues and Aesspos et al. [28], have revealed that pseudoxansoma elasticum–like skin lesions are common in patients with β-thalassemia major. However, we did not observe any patient with pseudoxansoma elasticum–like skin lesions in our study. The difference may be attributed to the ethical and regional differences between the two study populations [28].

**Conclusion**

Dermatological findings are frequent in Egyptian patients with thalassemia major. The most common skin lesions in our patients were pruritus, xerosis, and hyperpigmentation. Careful skin examination of thalassemia patients is required to provide early diagnosis of dermatological diseases and a better quality of life.

Iron overload is the cause of most skin problems; hence, iron chelators are very important. The most common manifestation is pruritus; therefore, antihistamines and soothing lotions may be useful. Xerosis was the second manifestation; thus, emollient will be good treatment. Freckles were also more common; therefore, the patient should use sun screen to prevent it. Symptomatic treatment and dermatological consultation are very important.

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**Conflicts of interest**

There are no conflicts of interest.

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