

# Keloid in Iraqi Patients: A Clinicohistopathologic Study

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**BACKGROUND.** Keloid is a benign, well-demarcated area of fibrous tissue overgrowth that extends beyond the original defect. It is not an uncommon problem and is encountered frequently in daily practice.

**OBJECTIVE.** To evaluate the different clinical and histopathologic aspects of this disease in Iraqi people.

**METHODS.** Eighty-eight patients with keloid were clinically assessed. Histopathologic examination was performed in 16 patients. Giemsa stain was used in eight patients to assess the presence of mast cells.

**RESULTS.** There were 47 females and 41 males. The disease started in the second and third decades of life in 62 patients (70.5%). Itching was present in 46 patients (52.2%) and was more predominant in those with early lesions. Darier sign was elicited in 22 patients (25%); all of them had itching. The

duration of the disease ranged from 0.33 to 20 years, with a mean of 5.4 years. Spontaneous keloid was found in 30 patients (34%). The lesions were mainly single (63.4%). All of these patients had lesions on the face and upper trunk in addition to involvement of extremities in five of them (16.7%). BCG keloid was observed in females only, and it showed downward gravitational extension in three of seven patients (43%). The histopathologic examination of keloid in 16 patients showed many interesting findings, such as the presence of hyperplastic epidermis in six specimens (37.5%), Grenz zone in 11 patients (68.75%), telangiectasia in 12 patients (75%), and pseudopodia extension of the growth to the adjacent tissues in half of the patients. Giemsa stain of eight specimens demonstrated the presence of mast cells in four patients (50%), more in biopsies that were taken from early lesions.

K. E. SHARQUIE, MBChB, PhD, AND M. A. AL-DHALIMI, MBChB, FICMS HAVE INDICATED NO SIGNIFICANT INTEREST WITH COMMERCIAL SUPPORTERS.

KELOIDS ARE benign proliferative lesions of dermal connective tissue that usually result from an excessive tissue response to cutaneous trauma in predisposed individuals. Keloids expand beyond the boundaries of the original wounds, develop for many months to years, and persist for years or even for life.<sup>1</sup> Keloids can occur from infancy to old age. They affect males and females equally. The highest incidence is in Blacks and dark-skinned individuals.<sup>2</sup> The etiology of keloid is debated, although trauma seems to play a key role.<sup>3</sup>

Histopathologically, keloids are characterized by thick glassy collagen bundles, an abundance of mucinous ground substance, minimal to no foreign body reaction, and few fibroblasts.<sup>4</sup> Hypertrophic scars have frequent foreign body reactions and numerous fibroblasts but few glassy collagen bundles and scanty mucinous ground substance. In ordinary and hypertrophic scars, collagen fibers are oriented parallel to the long axis of the scar, whereas in keloid, collagen is arranged in a haphazard pattern.<sup>1,5,6</sup>

This work was designed to evaluate the different clinical and histopathologic aspects of this problem in Iraqi patients.

## Methods

Eighty-eight patients with keloid were studied in the outpatient department of dermatology and venereology in Baghdad Teaching Hospital (Baghdad, Iraq) during the period from October 1995 to August 1997.

The diagnosis was mainly clinical, and the scar was accepted as keloid when one or more of the following criteria were present: (1) extension of the growth beyond the boundaries of the original lesion or injury, (2) growth in mounds over mounds in a pseudotumor fashion with distortion of the lesion, and (3) continuation of the growth for more than 6 months.

Black patients were not included in this study because of their small number in our population and to avoid bias and confusion regarding the relationship between the disease and skin color of the patients.

For each patient admitted to the study, a detailed history was taken, including name, age, gender, chief complaint (cosmetic disfigurement; symptomatic complaint such as itching, pain, and tenderness; or both), duration of the disease, the presence or absence of a

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definite history of trauma or lesion that initiates the disease, and their types if present like burn, surgical operation, accidental trauma, infection, BCG vaccination, or ear piercing. Also, the presence of a family history of the same condition in the close relatives was recorded.

The physical examination included the following: (1) color of the skin of the patient: white, light brown, dark brown, or black; (2) site of the lesion; (3) sizes of the lesion, which were divided into three groups: (a) small, a surface area of less than 5 cm<sup>2</sup>, (b) medium, a surface area of between 5 and 25 cm<sup>2</sup>, and (c) large, a surface area of more than 25 cm<sup>2</sup>; (4) number of the lesions; (5) the shape of the lesion; and (6) a single lesion from each patient, which was rubbed with a blunt object to demonstrate swelling and itching of the lesion within 3 to 5 minutes, "Darier-sign-like response." The same procedure had done on the adjacent normal skin as a control.

A sample of 100 age- and gender-matched individuals without keloid was examined for their skin color as a control group. There were 60 females and 40 males; their ages ranged between 5 and 75 years with a mean of 24.6 years. Black persons were not included.

Skin biopsies were obtained from 16 patients, 8 with early lesions and 8 with old lesions, from unmodified, untreated lesions and sent for hematoxylin and eosin histopathologic processing and examination. Giemsa stain was done in eight specimens to demonstrate the presence of mast cells.

The lesions were divided into two groups: early, which was less than 2 years in duration, or old, which was 2 years or more. Statistical analysis had been done using chi-square test at  $\alpha = 0.05$ .

## Results

Eighty-eight patients, 47 females and 41 males, were enrolled in this study. Their ages ranged between 3 and 70 years, with a median of 23 years (Figure 1). Sixty-two patients (70.5%) had their disease started in the 2nd and 3rd decades of life, whereas only in 15 patients (17%), the disease started after the age of 30.

Cosmetic disfigurement was the chief complaint in 64 patients (72.7%) either alone in 42 patients (47.7%) or in combination with other symptoms in 22 patients (25%). The symptomatic presentation alone was found in 24 (27.3%). Itching was the main symptom and was found in 46 patients (52.3%). This itching was more commonly seen in early lesions (30 patients, 65.25%) than old lesions (16 patients, 34.75%). Itching was mostly intermittent and was more severe in those with early lesions.

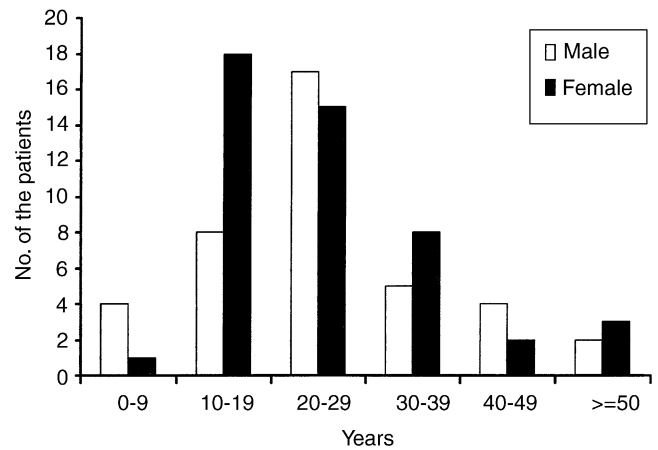


Figure 1. Age distribution of the patients.

Table 1. Initiating Factors of the Disease in 88 Patients

Type of Trauma	Female	Male	Total	Percentage
Burn	14	10	24	27.27
Infections	4	8	12	13.63
External trauma	4	6	10	11.36
Surgical incision	6	2	8	9.09
BCG vaccination	7	0	7	7.95
Ear piercing	3	0	3	3.4
No definite trauma	13	17	30	34.09

Some patients had more than one type of initiating factors.

The duration of keloid ranged between 0.33 and 20 years, with an average of 5.4 years. Early lesions were noticed in 46 patients (52.3%) and old lesions in 42 patients (47.7%).

Regarding the initiating etiologic factors, it was found that 30 patients (34%) had no definite history of a preceding trauma while burns precede keloid in 24 patients (27.27%) (Table 1).

In the group of patients without a definite history of trauma (30 patients), there were 13 females and 17 males. Their ages ranged from 7 to 32 years, with a mean of 20.25 years. The upper trunk and the face were affected in all of them; in addition, five patients (16.7%) had involvement of the extremities. Chest, including the presternal area, was affected in 20 patients (66.6%). Single lesions were noticed in 19 patients (63.4%).

BCG-induced keloid was seen in seven patients (7.95%), all of which were females. They were located on the left deltoid area at the site of BCG vaccination. Three of these patients (43%) had downward extension of the lesion in a form of a linear band from the deltoid region to the middle of the upper arm. The



**Figure 2.** Gravitational extension of BCG keloid.

**Table 2.** Site of the Lesions in 88 Patients

Site	Female	Male	Total	Percentage
Central face	0	2	2	2.27
Lateral face	3	8	11	12.5
Ears	3	0	3	3.4
Nape of the neck	0	8	8	9.09
Rest of the neck	3	4	7	7.95
Chest including the presternal area	13	15	28	31.81
Abdominal wall	6	4	10	11.37
Upper limbs	15	6	21	23.85
Deltoid region	8	3	11	12.5
Back	4	5	9	10.22
Lower limbs	8	7	15	17.03
External genitalia	1	0	1	1.13

Some patients had more than one site of involvement.

lesions were thicker upward with a teardrop-like appearance (Figure 2). Family history of keloid was positive in 14 patients (16%).

The skin color of the patients was dark brown in 43 patients (48.8%), light brown in 30 patients (34%), white in 13 patients (14.7%), and black in 2 patients (2.3%), whereas that of the control group was light brown in 52 individuals (52%), dark brown in 31 individuals (31%), white in 16 individuals (16%), and black in 1 individual (1%). Thus, the disease occurs significantly more in pigmented people ( $P < 0.05$ ).

The chest, including the presternal area, was involved in 28 patients (31.8%). The distribution of the lesions among different body areas is shown in Table 2.

The size of the lesions was variable: 40 patients (45.5%) had small lesions; 41 patients (46.6%) had medium size lesions, and 14 patients (15.9%) had large lesions.

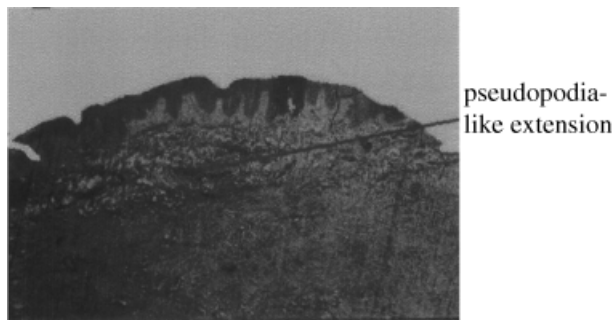
**Table 3.** The histopathologic Findings in 16 Patients, 8 With Early Lesions and 8 With Old Lesions

Histopathologic Feature	Early, Less Than 2 Years Old	2 Years Old or More	Total	Percentage
Epidermis				
Normal	4	6	10	62.5
Hyperplastic	4	2	6	37.5
Rete ridges				
Normal	7	4	11	68.75
Flattened	1	4	5	31.25
Grenz zone	7	4	11	68.75
Homogenous eosinophilic collagen bundles	8	8	16	100
Arrangement				
Haphazard	8	8	16	100
Nodules or whorls	5	6	11	68.75
Telangiectasia	7	5	12	75
Site				
Papillary dermis	7	5	12	100
Reticular dermis	2	0	2	16.6
Fibroblasts				
Scanty	4	6	10	62.5
Abundant	4	2	6	37.5
Arrangement				
Haphazard	8	8	16	100
Inflammatory Infiltrate				
Mild	3	6	9	56.25
Severe	5	2	7	43.75
Foreign body reaction	0	0	0	0
Mast cells "by Giemsa stain"	3/4	1/4	4/8	50

A single lesion was present in 35 patients (39.8%); 30 patients had two to four lesions (34.09%), whereas 23 patients had five lesions or more (26%).

Darier sign was demonstrated in 22 patients (25%). All patients with positive Darier sign had itching. It was more common among patients with early lesions (15 patients, 68.2%). This sign was appeared within 30 to 90 seconds after rubbing of the lesion with a blunt object. None of the patients with positive Darier sign had positive reaction in the adjacent normal skin.

The histopathologic findings are summarized in Table 3. The main findings included the presence of epidermal hyperplasia in 6 specimens (37.5%). Grenz zone was present in 11 specimens (68.75%). The characteristic whorl appearance was found in 11 specimens (68.75%). The margin of the lesion intermingled with the surrounding tissue-forming pseudopodia-like pattern in half of the lesions (Figure 3). Telangiectasia was a prominent feature that present in



**Figure 3.** Epidermal hyperplasia, Grenz zone, and the characteristic whorl appearance of keloid tissue (hematoxylin and eosin stain, original power,  $\times 40$ ).

12 (75%) patients and was found mainly in the papillary dermis.

Mast cells were seen in four patients (50%). These cells were more plenty in early lesions and were admixed among inflammatory cells and collagen bundles.

## Discussion

The good number of patients collected in this study reflected that keloid is not an uncommon disease in our country. The great cosmetic and symptomatic impacts on the patients necessitate good study of its different aspects.

This work showed that the disease had a universal distribution of age incidence with predilection for young people. The disease started mainly in the second and third decades of life. These facts were almost consistent with literature.<sup>7-10</sup>

In the group of patients with no definite history of trauma—so-called spontaneous keloid—the disease started mainly around or shortly after puberty (mean age of 20.25 years). We cannot explain why this type of keloid was a disease of young people, but we can speculate that this age group had more hormonal changes, especially in the level and metabolism of androgen hormones, and that young people have tenses skin when compared with children and older people.<sup>9</sup>

The gender distribution of patients was almost equal, which is in agreement with literature,<sup>2,9</sup> although some authors<sup>3,8</sup> describes female predominance. An interesting finding in this work was the occurrence of BCG keloid only among females, a finding that cannot be explained.

The disease had a great cosmetic impact on the affected patients of both genders, and it complained of by 72.7% of patients in this study. This complaint is increasing when they know that the disease cannot be

corrected well and with no possibility of spontaneous recovery.<sup>8,9,11</sup>

Itching was the most common symptom among studied patients, and it was more severe and more predominant in early lesions. This might be related to the presence of mast cells and other inflammatory cells more in the early lesions as shown in this study. This might also explain the positive Darier sign that was noticed in this work. This sign was not reported before.

Most literature express the importance of trauma as an initiating factor for the disease, and it is reported to precede the lesions in about 98% of the patients;<sup>8,9</sup> however, a study done in the white population stated that keloid is usually not preceded by an overt injury.<sup>11</sup> A known initiating factor before the lesion was found in 66% of Iraqi patients, which is relatively less than what has been reported, and this may be related to racial factors or because some patients had forgotten the trauma that could be in the form of small folliculitis or acneform rash, especially in the seborrhoeic area that had passed unnoticed or regarded as unimportant by the patient. The list of major types of trauma that may be followed by keloid in this study was almost similar to what have been published.<sup>3,9,10</sup>

Family history had been reported in patients with keloid in a range between 5% and 10% in a white population,<sup>12</sup> whereas it was positive in 16% of the patients in this study.

The distribution of the sites of the lesions in this work was almost similar to what had been reported,<sup>3,9</sup> apart from higher involvement of extremities in our patients, which is probably due to the fact that these sites are more exposed to trauma.

The disease occurs more in pigmented people in this work ( $P < 0.05$ ); this was similar to what had been reported elsewhere.<sup>2</sup>

In the group of patients with no definite history of trauma, the upper trunk and the face were involved in all of them. This is probably related to hormonal factors, that is, more androgen receptor binding,<sup>13</sup> or increased rate of dihydrotestosterone metabolism in these areas,<sup>4</sup> or because these are a common sites of acne. Shaving and tension may be factors also.

The downward extension of BCG keloid in 43% of patients with a teardrop-like appearance is a new observation that may be related to the gravitational extension of the newly formed collagen.<sup>14</sup>

The histopathologic evaluation had revealed many interesting findings. Most studies had described a normal or flattened epidermis overlying the keloid tissue,<sup>6,8,10,15</sup> but we found hyperplastic epidermis in six specimens (37.5%), which may reflect the effect of keloid tissue on the epidermis through certain growth factor and cytokines that lead to increase epidermal

turnover.<sup>16</sup> Grenz zone was present in 68% of present specimens with more preponderance in early lesions. This finding is not well appreciated before, which probably indicated that keloid lesions originate in the deep dermis and enlarge gradually until they encroach on the epidermis. Telangiectasia was a more remarkable feature in this study in comparison with other reports.<sup>6,8,10,15</sup> The keloid tissue moves peripherally with pseudopodia-like extensions and gradually intermingled with the surrounding tissue. This feature had not been mentioned in previous studies.<sup>6,8,10,15</sup>

Mast cells were demonstrated in 50% of the specimens stained with Giemsa stain. They were found more in early lesions, and this is comparable with the published literature.<sup>3,8,10,15</sup>

## Conclusion

Keloid is a disease that is not encountered uncommonly among Iraqi people. These findings were considered new, as they were not reported in literature: (1) BCG keloid was seen only in female patients. (2) Keloid lesions may show gravitational extension of the newly formed collagen, especially in BCG keloid. (3) Keloid should be regarded as an important cause of Darier sign. (4) Most of the spontaneous keloid were single and lie mainly in the upper part of the body. (5) Many histopathologic features should be considered in the diagnosis of keloid-like hyperplastic epidermis, prominent Grenz zone, pseudopodia-like extension of the collagen fibers to the surrounding tissue, and the presence of mast cells especially in early lesions.

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