The histopathological pattern of benign and non-neoplastic skin diseases at King Fahad Hospital, Madinah, Saudi Arabia

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ABSTRACT

Objectives: To characterize and compare the histopathological pattern of benign skin diseases in patients from Madinah region of Saudi Arabia.

Methods: This retrospective study was conducted at the Department of Pathology, King Fahad Hospital, Madinah, Saudi Arabia, and contained cases of benign skin diseases for 11 years (from January 2006 to December 2017). The findings were tabulated in Microsoft Excel sheet and classified based on histopathological diagnosis.

Results: Of 1,125 skin tissues reviewed, 579 (51.5%) specimens were from male patients and 546 (48.5%) specimens were from females giving a male: female ratio of 1.1:1. The ages ranged from 1 to 101 years with a mean age of 36.9±9.8 years. Most of the skin diseases (n=639; 57%) were seen in the age group 20-49 years. The most common skin diseases observed were disorders of skin appendages (29.6%) followed by benign tumors (18.3%), disorders of pigmentation (11.9%), papulosquamous lesions (11.4%), and dermatitis/eczema (10%). In the group of skin appendages disorders, epidermal inclusion cyst was the most common disease entity representing 20.4% of cases, followed by trichilemmal cyst accounting for 9.2% of the total cases. Mean ages of the patients were 35±8.5 years and 36.7±9.7 years respectively.

Conclusion: A variety of benign skin lesions were seen in the present study in a wide age distribution range. The most common skin diseases observed in this study were skin appendage disorders, benign skin and adnexal tumors, pigmentation disorders, and papulosquamous lesions.

Saudi Med J 2019; Vol. 40 (6): 548-554
doi: 10.15537/smj.2019.6.24205

Disclosure. Authors have no conflict of interests, and the work was not supported or funded by any drug company.
The skin or integument is the largest organ in the human body, and it performs many functions, including protection from microbial infections, body temperature regulation, and the perception of various sensations. Although it is a complex organ, the 3 main histological components of the skin can be classified as the epidermis and adnexae, the melanocytic system and dermis, and the subcutis. An imbalance in the skin functions can affect skin cell homeostasis, which results in various skin diseases. Skin diseases occur quite frequently, and there are thousands of specific skin diseases ranging from benign acne, eczema, and blisters to extremely fatal malignancies, including melanoma. Benign skin diseases are extremely common, with a wide array of lesions and various pathological processes ranging from inflammatory to infectious to autoimmune mechanisms. Every individual encounters some kind of benign skin disease at some point in his or her lifetime. Interestingly, most benign skin diseases are not notifiable, and they are not regarded as significant health problems, although their effects on the quality of life can be undesirable. The skin disease prevalence depends on various factors, including individual genetic and racial constitutions, customs, hygiene, nutritional statuses, and climatic conditions, and it varies from one country to another and in different regions of the same country. The histopathological patterns of benign skin diseases vary, and they constitute a wide range of morphologies; however, the clinical presentations are limited to only a few changes, such as pigmentation variations (hypo or hyperpigmentation), macules, papules, nodules, vesicles, and ulcers. These clinical presentations may be common to different diagnoses; therefore, a histopathological examination is required for a definitive diagnosis. It has been observed that most benign skin disorders are diagnosed on the basis of the patient’s history and clinical examination alone, while a histopathological diagnosis is used mainly in the management of unresponsive lesions. Therefore, clinicopathological corroboration between the treating dermatologist and the diagnosing pathologist is crucial, and it plays a vital role in the management of skin diseases. Most of the data available on benign skin diseases in the current English literature is based mainly on the clinical findings rather than the histopathological evaluations, and these studies have been conducted principally by dermatologists. Very few studies have been carried out by pathologists or dermatopathologists. Moreover, there is a lack of histopathologically-based data on benign skin diseases in Saudi Arabia.

Therefore, the main objective of the present study was to provide comprehensive data on the histopathological patterns of benign skin diseases in the histopathology laboratory of King Fahad Hospital in Al-Madinah Al-Munawwarah, Saudi Arabia.

**Methods.** This retrospective study included 1,125 skin biopsy specimens received from January 2006 to December 2017 at the Department of Pathology, King Fahad Hospital, Madinah, Saudi Arabia. This hospital is the key referral and tertiary care hospital in the Madinah region with more than 500 bed capacity. The specimens were preserved in 10% buffered formalin as a fixative, and a team of consulting histopathologists provided reports on the skin biopsies after routine slide staining with hematoxylin and eosin. In addition, special staining, such as periodic acid-Schiff, Ziehl-Neelsen, and Fite-Faraco staining, and immunohistochemistry were performed in selected cases. The dermatological diagnosis, gender, and age were recorded for each patient. We excluded all the records that did not include any of the above variables. As the main aim of the study was to address the basic demographic and histopathological information, and no comparison was indicated between the parameters, hence no statistical analysis was performed and the findings were tabulated in Microsoft Excel sheet and classified based on histopathological diagnosis, male to female ratio and age distribution. The histopathological diagnoses were further subclassified according to the 10th revision of the International Statistical Classification of Diseases and Related Health Problems (ICD-10).

**Results.** During the study period, 1,125 patients with skin pathologies were identified. More than one half (n=579; 51.5%) of the patients were males, and 546 (48.5%) of the patients were females, with a male to female ratio of 1.1:1. The ages ranged from 1 to 101 years, with a mean age of 36.9±9.8 years. The majority of the skin diseases (n=639, 57%) were seen in the 20 to 49-years age group. The young age group (<10 years) contained 4.6% and the elderly age group (≥70 years) contained 5.2%.

The frequencies, percentage and the ICD-10 code of the total 1,125 benign skin diseases samples are summarized in the Table 1.

Tables 2 - 6 show the numbers, percentages, gender distributions, and mean ages of the patients with regard to the specific skin disease groups. In the skin appendage disorder group, epidermal inclusion cysts were the most common disease entity, representing 20.4% of the cases, followed by trichilemmal cysts. The mean ages of these patients were presented in Table 2.
Seborrheic keratosis, fibroepithelial polyps, and dermatomyofibromas were the most commonly seen benign tumors. The mean ages of these patients were presented in Table 3. Melanocytic nevi constituted the majority of the pigmentary disorders, accounting for 11.8% of the cases, with a mean age of 32.6±8 years. Psoriasis and lichen planus were the most commonly seen papulosquamous diseases. In the dermatitis/eczema group, atopic dermatitis was seen most commonly, at a rate of 4.7% and a mean age of 26±6.3 years.

Seborrheic dermatitis, nummular dermatitis, and lichen simplex chronicus were less common (Table 4). In the infectious disease group, viral infections were most common (4.4%), followed by bacterial (0.6%), parasitic (1%), and fungal (0.08%) infections. Viral warts were the most commonly seen infectious disease, making up 4.1% of the total cases, with a mean patient age of 33.9±8.7 years (Table 5). Dermatoses due to discoid lupus erythematosus, leukocytoclastic vasculitis, and bullous pemphigoid were presented in Tables 4 & 6.

**Discussion.** The histopathologically-based literature on benign skin diseases in Saudi Arabia is scant. Rather, most of the associated articles published in the recent literature were written by dermatologists, and they were predominantly related to the clinical practices and differential diagnoses.

**Table 1** - ICD code groups, frequencies and percentages of 1,125 benign skin diseases.

| ICD Codes | Official name of ICD Group | n  | (%) |
|-----------|---------------------------|----|-----|
| L00-L08   | Infections of the skin and subcutaneous tissue | 68 | (6.1) |
| L10-L14   | Bullous disorders | 28 | (2.5) |
| L20-L30   | Dermatitis and eczema | 114 | (10.0) |
| L40-L45   | Papulosquamous disorders | 128 | (11.4) |
| L50-L54   | Urticaria and erythema | 19 | (1.6) |
| L60-L75   | Disorders of skin appendages | 334 | (29.6) |
| L80-L99   | Other disorders of the skin and subcutaneous tissue | 62 | (5.5) |
| M35.1, M35.9 | Connective tissue diseases | 32 | (2.8) |
| L81.1, D22 | Disorders of pigmentation | 134 | (11.9) |
| D10-D36   | Benign tumors | 206 | (18.3) |

**Table 2** - Details of numbers, percentages, mean age and sex ratios of disorders of skin appendages.

| Disorders of skin appendages | n  | (%) | Mean age (years) | M/F |
|-----------------------------|----|-----|------------------|-----|
| Epidermal inclusion cyst     | 230| (20.4) | 35.0 | 152/78 |
| Trichilemmal cyst            | 104| (9.2)  | 36.7 | 48/56  |
| Total                        | 334| (100) |                  |      |

**Table 3** - Details of numbers, percentages, mean age and gender ratios of benign tumors.

| Tumors                      | n  | (%) | Mean age (years) | M/F |
|-----------------------------|----|-----|------------------|-----|
| **Adnexal tumors**          |    |     |                  |     |
| Chondroidysyringoma         | 2  | (0.16) | 58.5 | 2/0 |
| Eccrineporoma               | 2  | (0.16) | 62.5 | 2/0 |
| Eccrinepiradomenoma         | 2  | (0.16) | 71   | 2/0 |
| Hidradenoma                 | 2  | (0.16) | 43   | 1/1 |
| Syringocystadenomapapilliferum | 2 | (0.16) | 42   | 1/1 |
| Keratocanthoma              | 5  | (0.4)  | 49.5 | 2/3 |
| Pilomatricoma               | 5  | (0.4)  | 18.5 | 5/0 |
| Eccrinecylindroma           | 3  | (0.2)  | 37.7 | 3/0 |
| Trichoepithelioma           | 4  | (0.3)  | 57.3 | 2/2 |
| Trichofofolliculoma         | 2  | (0.16) | 33.5 | 1/1 |
| Sebaceous adenoma           | 1  | (0.08) | 70   | 1/0 |
| Nevus sebaceous             | 4  | (0.3)  | 15.3 | 2/2 |
| **Total**                   | 34 |     |                  |     |

| **Epidermal tumors**        |    |     |                  |     |
| Fibroepithelial polyp       | 57 | (5.1) | 46   | 32/25 |
| Seborrheic keratosis        | 67 | (5.9) | 47.7 | 42/25 |
| Dermoid cyst                | 17 | (1.5) | 9.6  | 9/8  |
| **Total**                   | 141|     |                  |     |
| **Dermal tumors**           |    |     |                  |     |
| Dermatomyofibroma           | 31 | (2.8) | 32.5 | 15/16 |
In this study, a total of 1,125 patients were diagnosed with various benign skin diseases. Of these, 579 (51.5%) of the patients were males, 546 (48.5%) of the patients were females, and the male to female ratio was 1.1:1. This finding indicates a slight preponderance of males when compared to females in our sample of benign skin disease patients. This gender distribution corresponds to those of previous studies conducted in Saudi Arabia by Al Shobaili (58.5% in males and 41.5% in females), Hofny et al (58.9% in males and 41.1% in females) and from India by Celine et al,1 Singh et al (58.8% in males and 41.12% in females, 60.8% in males, 39.2% in females and 63.41% in males and 36.59% in females respectively). Contrary to our observation of male preponderance, there are many previous data from Saudi Arabia by Alghanmi et al from King Abdulaziz University Hospital, Jeddah, Al-Zoman and Al-Asmari from Riyadh Military Hospital, and Alshammrie et al from King Khalid Hospital, Hail reported a female preponderance. Studies from other parts of the world also reported higher skin disease incidences in females. For example, Symvoulakis et al from a Mediterranean island, El-Khateeb et al from Egypt, Bilgili et al from Turkey, and Sevensson et al from Europe all reported higher female skin disease rates. They claimed that the female predominance was mainly attributed to the higher awareness of women with regard to skin problems for the obvious cosmetic reasons, as well as a greater sensitivity that women have in general regarding health-related issues.

In our study, the maximum number of cases (n=639, 57%) was seen in the 20 to 49-year-old age group, with a mean age of 36.9 years old. Similar observations were made by Symvoulakis et al from a Mediterranean
island, Hofny et al\textsuperscript{11} from Egypt, Narang et al\textsuperscript{20} from India, Alshobaili et al\textsuperscript{2} from Saudi Arabia, and Bilgili et al\textsuperscript{18} from Turkey, who reported the maximum number of cases in adult patients (21-40 years old, 18-39 years old, 21-30 years old, 15-34 years old, and 20-29 years old, respectively). In the present study, the rate of skin diseases in children was 4.6%; however, Celine et al\textsuperscript{1} from India and Memon et al\textsuperscript{22} from Pakistan have documented the maximum number of cases in populations that were less than 15 years old. In the present study, only 5.2% of the cases were in the elderly age group; however, Alghanmi et al\textsuperscript{7} from Saudi Arabia and Singh et al\textsuperscript{13} from India reported the maximum number of cases in elderly patients.

In this study, we encountered a large variety of benign skin diseases, and for ease of discussion, we classified them based on internationally recognized criteria, grouping them into 10 categories according to the ICD-10. The most frequently occurring benign skin diseases in our study were skin appendage disorders (29.6%), benign skin and adnexal tumors (18.3%), pigmentation disorders (11.9%), papulosquamous lesions (11.4%), and dermatitis/eczema (10%). Skin infections and nonspecific disorders of the skin (6.1%) and subcutaneous tissue occurred less frequently (5.5%), while connective tissue disorders affecting the skin (2.8%), bullous disorders (2.5%), and urticaria and erythema (1.6%) were the least frequently encountered diseases. We compared our findings with those of previous studies of a similar nature from other regions in Saudi Arabia and other parts of the world. As mentioned earlier, little histopathologically-based data is available on benign skin diseases; therefore, our comparison included both clinical and pathologically-based studies.

In our study, skin appendage disorders were the most commonly encountered diseases, and this group included epidermal inclusion cysts and trichilemmal cysts. Our results were similar to the results of studies conducted in Turkey\textsuperscript{2} and Iran.\textsuperscript{23} Benign skin and adnexal tumors were the next frequently encountered skin diseases in our study. According to a recent study conducted in India by Bezbaruah et al,\textsuperscript{2} benign skin and adnexal tumors were the most common lesions encountered in their cohort, at a rate of 61.1%. The melanocytic lesions were seen in 11.9% of the cases,
and these consisted mainly of benign melanocytic nevi. Alghanmi et al from western Saudi Arabia observed benign melanocytic neoplasms in 19% of the cases, which was higher than our observed rate of 11.9%. The papulosquamous lesions were the fourth most commonly occurring lesions in our study, and this included psoriasis, pityriasis lichenoides et varioliformis acuta, and pityriasis rosea. Biligili et al from Turkey also observed these lesions as the fourth most commonly seen lesions in 9.2% of the cases; psoriasis was the most common diagnosis, followed by lichen planus, and pityriasis rosea. Gulia et al from India and Ogun et al from Nigeria reported papulosquamous lesions as some of the most common benign skin lesions in their study. In this study, eczema and dermatitis were the fifth most commonly seen benign skin diseases, making up 10% of the total cases. Contrary to our observation, eczema and dermatitis were the most frequently encountered benign skin diseases in previous studies from the other regions of Saudi Arabia and other nations, this could be attributed to the diagnosis of eczema and dermatitis is mainly done on history and clinical examinations and biopsy is rarely performed for the diagnostic purpose. Histopathological examinations are usually indicated in doubtful cases of eczema and dermatitis.

A detailed comparison of our findings with the previously published literature from Saudi Arabia and other parts of the world is depicted in Table 7. The comparison of our observations revealed that most of the benign skin diseases seen in the previous literature were eczema and dermatitis, infections and infestations, and benign skin and adnexal tumors. As highlighted previously, limited histopathologically-based data is available in the recent literature on the benign skin disease pattern, and the majority of the studies that we compared were dermatology clinic-based studies. Therefore, the clinical diagnoses of eczema and dermatitis were the most common benign skin diseases observed in most of the literature. However, it has also been observed that the geographical and racial distributions and environmental and socioeconomic factors of the affected population also affect the skin disease occurrence rates. Thus, eczema and dermatitis were the more prevalent benign skin diseases documented in developed and industrialized countries, whereas infections and infestations were the most frequently encountered diseases from the nations with poorer socioeconomic indices.

**Study limitations.** This study has a few limitations, First the sample was restricted to one tertiary care government hospital, which might limit the extension of results to the general population and provide a rough estimate of benign skin disease in the Madinah region. Second, the data were obtained from the histopathology department and not from the dermatology clinic, hence the chances of underreporting cannot be ruled out as most of the benign skin diseases are diagnosed and treated based on history and clinical examination, biopsy is done only in doubtful cases. Last, the occupational history, type of residence, exposure to sun and irritants are not included in the patients history.

In conclusion, a variety of benign skin lesions were seen in the present study in a wide age distribution range. The most common skin diseases observed in this study were skin appendage disorders, benign skin and adnexal tumors, pigmentation disorders, and papulosquamous lesions. Various regional factors, including the geographic distribution, genetic influence, socioeconomic status, cultural differences, and personal hygiene, affect the skin disease prevalence. However, there is a significant lack of histopathologically-based studies on benign skin lesions in the world, and no such studies from the Madinah region of Saudi Arabia were found. Our histopathologically-based retrospective study provides a baseline tool for future population-targeted studies on benign skin diseases. We strongly recommend further histopathology-based studies of the larger cohort at national and international levels.

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**Ethical Consent**

All manuscripts reporting the results of experimental investigations involving human subjects should include a statement confirming that informed consent was obtained from each subject or subject's guardian, after receiving approval of the experimental protocol by a local human ethics committee, or institutional review board. When reporting experiments on animals, authors should indicate whether the institutional and national guide for the care and use of laboratory animals was followed.