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Mucocutaneous manifestations in patients with rheumatoid arthritis: A cross sectional study

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Abstract
Aim: The purpose of this research was to determine the various dermatosis patterns among a cohort of patients with rheumatoid arthritis.
Methodology: Patients who met the 1987 revised criteria for the classification of rheumatoid arthritis as established by the American Rheumatism Association and presented with various dermatoses were recruited to participate in this cross-sectional study. A comprehensive clinical assessment and relevant laboratory examinations were conducted as required. The data were entered into a predetermined schedule, and the corresponding statistical analysis was conducted.
Results: Total 100 patients were recruited for the study. The prominent cutaneous manifestation in our study was Xerosis 27 (27%) followed by Pigmented purpuric dermatoses 15 (15%), Dermatophytosis 14 (14%), Leg ulcer 10 (10%), Periungual telangiectasia 10 (10%), Candidiasis 9 (9%), Rheumatoid-nodules 8 (8%), Purpura and ecchymoses 7 (7%), Small vessel vasculitis 7 (7%), Corn and callosity 6 (6%), Onychomycosis 6 (6%), Palmar erythema 4 (4%), Neutrophilic dermatosis 4 (4%), Skin atrophy 4 (4%), Panniculitis 3 (3%), Pyoderma 3 (3%), Raynaud's phenomenon 3(3%), Chronic urticarial 2(2%), Erythema multiforme 2 (2%), Steroid-induced acneform 2(2%), eruption 2(2%), Granuloma telangiectaticum 1 (1%), Hemorrhagic vesicle 1 (1%), Livedoid vasculopathy 1 (1%). Methotrexate-induced mucositis 1 (1%), Hyperpigmentation 1 (1%), Herpes zoster 1 (1%), Digital gangrene 1 (1%).
Conclusion: Although certain aspects of this study exhibited similarities to data from the West, there were also discrepancies in other aspects that could potentially be attributed to ethnic variations among the patients diagnosed with rheumatoid arthritis.

Keywords: Rheumatoid arthritis, Mucocutaneous manifestations, sectional study

Introduction

Rheumatoid arthritis (RA) is an autoimmune disease that affects multiple systems and has a multifaceted and intricate etiopathogenesis. Systemic manifestations may include inflammatory ocular diseases, serositis, peripheral neuropathy, systemic vasculitis, and mucocutaneous arthritis; this can lead to chronic, disabling arthropathy [1, 2]. A delayed diagnosis is possible due to the fact that mild articular and systemic symptoms precede the commencement of the disease [3]. In 1987, the American Rheumatism Association revised its criteria for the diagnosis of rheumatoid arthritis (RA). These criteria included the following: morning stiffness, arthritis affecting three or more joint areas, arthritis affecting the hand joint, symmetric arthrtitis, rheumatoid nodules, serum rheumatoid factor positivity, and radiographic changes such as erosions and bone decalcifications [4].

Extra-articular manifestations such as rheumatoid nodules were the only ones that met the criteria for classification. In contrast, the 2010 criteria established by the American College of Rheumatology/European League against Rheumatism exclusively incorporated symptoms associated with the joints and serology. Extra-articular manifestations, which contribute to increased morbidity and mortality, may be observed in as many as 40% of cases across various phases of the disease [5]. The interaction between articular and extra-articular symptoms results in substantial morbidity, reduced quality of life, and a decreased lifespan. The severity of these symptoms is predominantly observed in patients with advanced disease. Before further disease progression, the identification of extra-articular cutaneous conditions can assist dermatologists in developing a clinical suspicion of rheumatoid arthritis [6]. Skin disease and other extra-articular manifestations of rheumatoid arthritis are comparatively frequent, affecting nearly 40% of patients with the condition over the course

of their lifetime [7, 8]. RA is characterised by an extensive array of both specific and nonspecific mucocutaneous manifestations [6, 9]. Similar to other extra-articular manifestations, patients with more severe rheumatoid arthritis (RA) often experience dermatologic involvement. Understanding the cutaneous manifestations of rheumatoid arthritis may result in earlier detection, more timely intervention, and consequently reduced morbidity and mortality among those affected [10].

There is an abundance of data on RA from high-income and developed nations in the scientific literature. Nevertheless, in light of the escalating disease burden observed in low- and middle-income nations [5], it is critical to investigate the extra-articular cutaneous presentations of rheumatoid arthritis (RA) in a developing economy such as India.

Therefore, the purpose of the current investigation was to assess the prevalence of various dermatological manifestations among individuals diagnosed with rheumatoid arthritis.

Materials & Method

The research was a cross sectional study conducted within the departments of tertiary care dermatology and rheumatology at an academic institution. One hundred individuals were enrolled in the study throughout its duration. Mucocutaneous features were evaluated in all individuals of either gender, aged 21 to 70 years, who visited the outpatient department (OPD) during the study period and were diagnosed with rheumatoid arthritis (RA) according to the ARA 1987 revised criteria [4].

Inclusion criteria

- Patients of RA with mucocutaneous findings
- Willing to participate and be photograph

Exclusion criteria

- Pregnant women.
- Patients with other autoimmune diseases and psychiatric comorbidities.
- Rheumatic diseases other than RA.
- Juvenile RA.
- Arthritis that was not unambiguously classifiable.
- Concomitant medical problems which would confound the interpretation of the information gathered by this protocol.
- Those not consenting to the study.
- Written informed consent was obtained from every participant in the study. A consent was obtained for the publication of clinical data with the assurance that anonymity would be maintained. In a pretested, predesigned, semi-structured questionnaire, epidemiological data, clinical history (including symptoms, duration of disease), family history, and comorbidities were documented.
- The skin examination results of every patient were assessed by a minimum of two dermatologists. All patients underwent testing for anticyclic citrullinated peptides (CCP) and rheumatoid factor (RF) antibodies. Additional laboratory investigations, such as radiological examination and histopathology, were performed as required. Descriptive statistics were employed to enumerate the data.

Statistical Analysis

The chi-squared test and the Student's t-test are employed to analyse comparative data. The statistical analysis was conducted utilizing Microsoft Excel and GraphPad Prism version 5.

Results

One hundred evaluable patients were examined. The study participants ranged in age from 21 to 70 years, with an average age of 42.05 ± 11.8 standard deviations (SD). 87% of the patients (n = 87) were female, constituting the plurality. The average age in years for females was 38.7 ± 12.0 SD, while for males it was 54 ± 11.7 SD. The average duration of RA symptoms (in years) was 7.1 ± 38.

The average duration of the disease (in years) was 5.1 ± 2.3 SD for males and 6.9 ± 4.9 for females. One patient was the only one with a familial predisposition to RA.

Table 1: Profile of different patterns of dermatoses in patients with rheumatoid arthritis

Cutaneous manifestations	n (%)
Xerosis	27 (27%)
Pigmented purpuric dermatoses	15 (15%)
Dermatophytosis	14 (14%)
Leg ulcer	10 (10%)
Periungual telangiectasia	10 (10%)
Candidiasis	9 (9%)
Rheumatoid-nodules	8 (8%)
Purpura and ecchymoses	7 (7%)
Small vessel vasculitis	7 (7%)
Corn and callosity	6 (6%)
Onychomycosis	6 (6%)
Palmar erythema	4 (4%)
Neutrophilic dermatosis	4 (4%)
Skin atrophy	4 (4%)
Panniculitis	3 (3%)
Pyoderma	3 (3%)
Raynaud's phenomenon	3 (3%)
Chronic urticaria	2 (2%)
Erythema multiforme	2 (2%)
Steroid-induced acneform	2 (2%)
Eruption	2 (2%)
Granuloma telangiectaticum	1 (1%)
Hemorrhagic vesicle	1 (1%)
Livedoid vasculopathy	1 (1%)
Methotrexate-induced mucositis	1 (1%)
Hyperpigmentation	1 (1%)
Herpes zoster	1 (1%)
Digital gangrene	1 (1%)

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Discussion

Rheumatoid arthritis (RA) is a systemic inflammatory disorder that predominantly impacts the joints, although it

often manifests in other areas, including the skin.

A significant burden of cutaneous disease may indicate the onset of rheumatoid arthritis and necessitates a more aggressive treatment approach. A multitude of cutaneous manifestations are possible in RA [6]. Activation of inflammatory cells (including macrophages, lymphocytes, and neutrophils), vasculopathy, vasculitis, acral deformity, and medications are all mechanisms underlying cutaneous affection [11]. Rheumatoid vasculitis, granulomatous and neutrophilic dermatitis in the context of immune complex disorders, and specific skin lesions are all associated with RA. Granulomatous and neutrophilic dermatitis in immune complex diseases may be drug-induced, co-occurring with systemic autoimmune diseases or lymphoproliferative disorders, whereas RNs are almost exclusively observed in patients with RA [12].

Similarly, rheumatoid vasculitis exhibits no discernible clinical or histological distinctions when compared to alternative types of vasculitis. In rheumatoid arthritis patients, a multitude of additional nonspecific lesions, including iatrogenic lesions, have been documented [13]. There are ethnic and geographic variations among RA patients. The mean age and disease duration in a prior Turkish study of rheumatoid arthritis with cutaneous manifestations were 55.3 years and 138.1 months, respectively. Ziemer *et al*. [12] found in a separate study that the average age and duration of the disease were, respectively, 62.81 and 15.54 years.

In contrast, the current series exhibited significantly lower mean age of presentation (42.05 years) and mean disease duration (6.9 years). However, similar to previous research [9, 12], the current series exhibited a preponderance of female participants. The average age at which females presented was significantly lower (38.7 years) than that of males (54 years). Rare is the familial occurrence of RA; in the present series, only one patient possessed a positive family history for the disease.

The most prevalent specific cutaneous manifestation observed in patients with RA is RNs [14]. Classic RNs manifest as movable, subcutaneous nodules that are firm or hard, persistent, and typically asymptomatic. They commonly originate on the extensor surface of the elbow, olecranon, extensor tendons of the forearms, proximal ulna, sacrum, occipital region, and sole. It is worth mentioning that each of these regions is susceptible to friction. Anatomically, they can also manifest internally in the gastrointestinal tract, lung, cardiac valve, and spine. The exact mechanism by which RN is formed is still unknown. Typically, palisades of histiocytes encircling a zone of necrosis are observed histopathologically [15]. The prevalence of RN has been observed to vary, reaching 53% among 127 hospitalised patients, 34% among outpatients with RA, and 75% among those with Felty syndrome. Yamamoto *et al*. [11] further documented an exceptionally low frequency (less than 2%) among patients from Japan. A comparatively lesser incidence rate of 8% was also identified in the current investigation. 7.5% of patients in another Indian series conducted by Prakash B *et al*. [16] had RN. RF positivity was detected in 5% of the RN patients.

Rheumatoid papules are an additional cutaneous manifestation that is characteristic of the disease. In contrast to RNs, the histological characteristics of these papules indicate palisading granuloma accompanied by collagen degeneration and leukocytoclastic vasculitis in the dermis's most superficial layer. Infrequently do rheumatoid papules vanish spontaneously following crusting as a result of transepidermal elimination.

In fact, the incidence of RV has decreased over the past two decades, possibly due to the more aggressive treatment of RA that is presently in practice. It remains a significant complication of rheumatoid arthritis that requires immediate diagnosis and treatment [17, 18]. The exact cause of clinical rheumatoid vasculitis remains unknown. Nevertheless, the pathological findings, elevated levels of RF and cryoglobulins, reduced circulating complement, and a heightened prevalence of HLA-DR4 all indicate an immune aetiology. A previous investigation conducted by Prakash B *et al*. [16] identified RV in 5.8% of the patients. A comparatively elevated incidence rate of 7% was observed in the current investigation.

Chronic limb ulcers, with or without edema, are frequently observed in individuals diagnosed with rheumatoid arthritis. Multiple factors contribute to the development of leg ulceration in rheumatoid arthritis. Chronic venous insufficiency is the primary aetiology, with peripheral artery disease, hypertension (specifically Martorell's ulcer), diabetes mellitus, or a combination thereof, occurring infrequently. In the context of rheumatoid arthritis, vasculitic limb ulcers are uncommon, which is noteworthy. Vasculopathy is an additional cause of leg ulcers [12]. Leg ulcers affected approximately 2.7% of patients in a prior study by Ziemer M, *et al*. [12]. This issue was prevalent in a comparatively greater proportion (10%) of the patients in the present series.

We suggest that the palmar erythema was less noticeable in the patients of the present series due to the fact that they all had skin types IV and V. Weedon D *et al*. [15] found that prevalence estimates of Raynaud's phenomenon in rheumatoid arthritis range from 2.7% to 17.2%. 3% of patients in the current series had a medical history that was suggestive of Raynaud's phenomenon.

A previous study encompassing the German population found that atrophic epidermis affected 1.9% of the participants, while xerosis affected 3.2%. A greater proportion of the participants in our study exhibited cutaneous atrophy (4%), while xerosis was present in 27%. A similar proportion of the patients in the current series tested positive for RF. In the current series, however, there was no statistically significant difference between the RF positive and negative groups regarding the incidence of leg ulcers, palpable purpura, RN, or Raynaud's phenomenon.

Conclusion

The present study elucidated the patterns of mucocutaneous manifestations among patients with rheumatoid arthritis. This may or may not align with the prevailing norms regarding the incidence and prevalence of diseases across various ethnic groups. For rheumatologists and dermatologists to treat cutaneous and extracutaneous afflictions in a coordinated manner, it is critical that they both comprehend and identify the mucocutaneous changes that occur in rheumatoid arthritis.

Conflict of Interest

Not available

Financial Support

Not available

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