

## Original Article

## Association of Rosacea with Demodicosis

Hamideh Moravvej MD\*, Mohammad Dehghan-Mangabadi MD\*,  
 Mohammad-Reza Abbasian MD\*, Gita Meshkat-Razavi MD\*

**Background:** There are controversial reports about the role of *Demodex mites* in pathogenesis of acne rosacea. The aim of this study was to examine the relationship between the presence and number of *Demodex mites* and the pathogenesis of rosacea.

**Methods:** In this case-control study, the prevalence of *Demodex mites* was studied in facial biopsy of 75 patients with acne rosacea as case group, and in 75 patients with discoid lupus erythematosus and 75 patients with actinic lichen planus as control groups.

**Results:** The prevalence of *Demodex mites* in patients with acne rosacea (38.6%) was significantly higher than the patients with discoid lupus erythematosus (21.3%) and actinic lichen planus patients (10.6%) ( $P < 0.001$ ).

**Conclusion:** This study suggests that *Demodex mites* may play a role in pathogenesis of rosacea but it is not clear whether rosacea merely provides a suitable environment for multiplication of mites, or the mites play a role in the pathological changes.

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**Keywords:** Acne rosacea • actinic lichen planus • *Demodex mites* • discoid lupus erythematosus

## Introduction

Rosacea is a chronic inflammatory disease of skin in young to middle-aged adults, but can occur occasionally in children. Females are more affected than males. Although the complication of rhinophyma is not common in females who generally experience less severe disease than males.<sup>1</sup>

Although the etiology of rosacea remains a mystery, various factors contribute to this condition.

Its increased prevalence in lighter-skinned races and the histological findings of elastotic degeneration suggest a role for solar irradiation.<sup>2</sup> The occurrence of rosacea-like lesions in carcinoid syndrome and the presence of elevated

substance P levels in some patients with rosacea increase the possibility that inflammatory mediators may be involved in the pathogenesis of the disease.<sup>3, 4</sup> Gastrointestinal disturbance (e.g., *Helicobacter pylori* infection), psychogenic stress, hormonal imbalance, sebaceous gland abnormalities, and infections may play roles; however, clinical studies have not approved it.<sup>5-12</sup> Histological examination shows dilatation of small dermal blood vessels with thickened walls.<sup>13</sup> Although it can explain the mechanism of flushing, but it does not explain how the papules and pustules in most cases can occur.

It has been proposed that occurrence of papules and pustules are related to the presence of the mite, *Demodex folliculorum* because this is a normal follicular inhabitant. But the etiologic importance of this parasite in the disease process is doubtful because the topical application of sulfur ointment will improve rosacea without affecting the mite populations.<sup>14</sup>

*Demodex mites* (*D.mites*) are saprophytic mites, which asymptotically parasitize the human pilosebaceous follicles.<sup>15-18</sup> The prevalence of *Demodex* carriers increases with

**Authors' affiliation:** \*Skin Research Center, Department of Dermatology, Shaheed Beheshti University of Medical Sciences, Tehran, Iran.

**Corresponding author and reprints:** Hamideh Moravvej MD, Skin Research Center, Shohada Hospital, Tehran 1989934148, Iran.

Telefax: +98-212-274-4392-5,

E-mail: hamideh\_moravvej@yahoo.com; hmoravej@dermrc.ac.ir.

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age.<sup>15, 19 - 23</sup> A variety of prevalence rates in different age groups have been reported in various studies.<sup>19, 21, 24, 25</sup>

## Materials and Methods

We designed a case-control study and examined existing slides at the Pathology Wards of Lohman and Bou-Ali Hospitals in Tehran, Iran. Cases were selected from the patients whose diagnoses had been confirmed by pathologist.

Because *D.mites* are found in normal facial skins,<sup>26</sup> control subjects were selected from patients with discoid lupus erythematosus (DLE) and actinic lichen planus (ALP) whose pathological diagnoses had been confirmed and the role of *D.mites* in their pathogenesis were conclusively ruled out.

The presence of *D.mites*, *D.folliculorum*, and *D.brevis* was assessed in 75 patients with rosacea, and in 150 age- and sex-matched control subjects. For age matching, we classified the patients in three groups with five-year intervals.

To evaluate *D.mites* colonization, standard skin biopsies were taken from the face in patients and controls, then we coded the slides and a pathologist examined them in four sections (the thickness of the sections was 5  $\mu$ m). Each sample was counted by light microscopy at standard magnifications ( $\times 4$ ,  $\times 10$ ,  $\times 40$ ) and each specimen was examined at least three times.

In this study, we considered no difference between two species of *D.mites* and we examined each slide for presence of mite positivity and total count of mites. Slides without follicle excluded from the study and none of the cases and controls had received treatment at least two months before the skin biopsy.

Data regarding the age at presentation, sex, and previous treatments were obtained from the notes.

Three groups of patients were analyzed:

1- Seventy-five controls who were diagnosed as having DLE (mean age 45 years, range: 20 – 72). Of them 44 (59.7%) were women.

2- Seventy-five controls who were diagnosed as having ALP (mean age 44.7 years, range: 26 – 78). Of them 48 (62.8%) were women.

3- Seventy-five patients who had rosacea (mean age 43 years, range: 21 – 93) and 49 (65.4%) of them were women.

Comparability of control and study groups for sex, age, mite positivity and mite counts was

assessed by mean of the Chi-square test and odds ratio.

## Results

Pathological findings in skin biopsy of the patients with rosacea were degeneration of collagen fibers due to sun exposure, vascular dilatation, and a nonspecific perivascular and perifollicular lymphocytic infiltration or granulomatous inflammation around hair follicles with no evidence of epidermal changes.

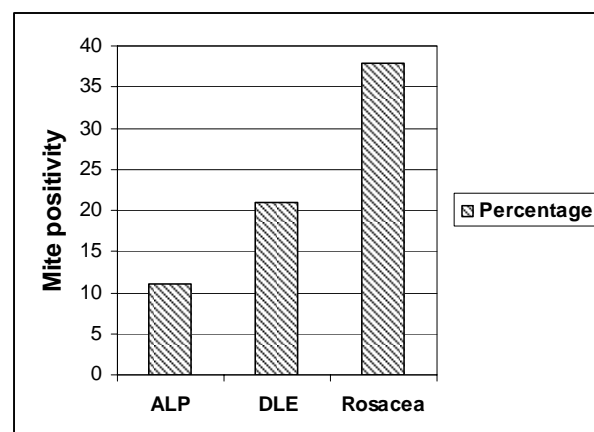
Pathological findings in the DLE patients were hyperkeratosis and well-developed follicular plugging, vacuolar alternation along the dermoepidermal junction and smudged appearance of the dermoepidermal junction, edema of dermis, perivascular infiltration of lymphocytes, and perifolliculitis.

In patients who were diagnosed as having ALP pathological findings were thinned epidermis, liquefaction degeneration of the basement membrane and basal cells, and band-like infiltration of lymphocytes across a thickened papillary dermis obscuring dermoepidermal junction.

Twenty-nine (38.6%) out of the 75 patients with rosacea were infested by *D.mites* compared to 16 patients in DLE (21.3%) group and 8 patients in ALP group (10.6%) (Figure 1).

The prevalence of *D. mites* (mite positivity) in the group of rosacea patients was significantly higher than controls ( $P < 0.001$ ).

Mite positivity in females with rosacea (20 cases, 40.8%) was higher than males (9 cases, 34.6%). *D.mites* in DLE patients were higher in females (22.7%) than males (19.3%). In ALP



**Figure 1.** The prevalence of *D.mites* in sections with rosacea compared with DLE and ALP.

patients, mite positivity was 10.7% in males vs. 10.63% in females. None of these differences was significant ( $P > 0.01$ ).

Total mite count was 106 in rosacea patients, 51 in DLE patients, and 15 in patients with ALP.

The mean mite count in patients with rosacea was 1.4 (range: 1 to 13), 0.66 (range: 1 to 8) in DLE patients and 0.2 (range: 1 to 3) in patients with ALP. This difference was statistically significant ( $P < 0.01$ ) (Figure 2).

Odds ratio between rosacea and DLE group was 2.3. Odds ratio between rosacea and ALP groups was 5.2 and between DLE and ALP groups was 2.27.

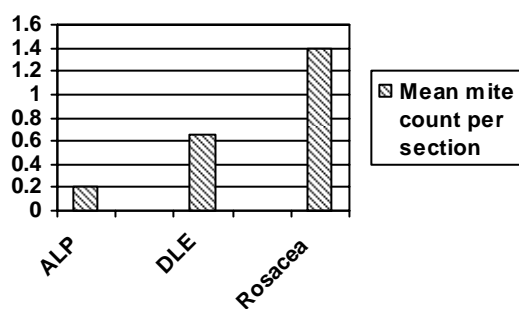
### Discussion

Despite its frequency, the etiology of rosacea is unclear. Rosacea is a chronic disorder of the face, which is more common in females. The development of rosacea is often but not invariably multiphasic.<sup>27</sup>

Several studies have demonstrated that rosacea is mainly a vascular disorder of the skin.<sup>28 - 29</sup> It frequently starts with flushing and redness of the skin, which leads to an increase in the skin blood flow and accumulation of extracellular fluid in the dermis. Edema and elastotic degeneration are because of sun exposure that cause damage to lymphatic vessels. Inflammatory lesions, papules, pustules, and nodules will happen then.

The most severe stage of the disease is rhinophyma, which is due to hypertrophy of nose and proliferation of sebaceous glands, connective tissues, and vessels.

In skin biopsy telangiectasia, edema in upper dermis, dilatation of hair follicles, and perifollicular lymphocytic infiltration are present.



**Figure 2.** The mean mite count per section in rosacea compared with DLE and ALP

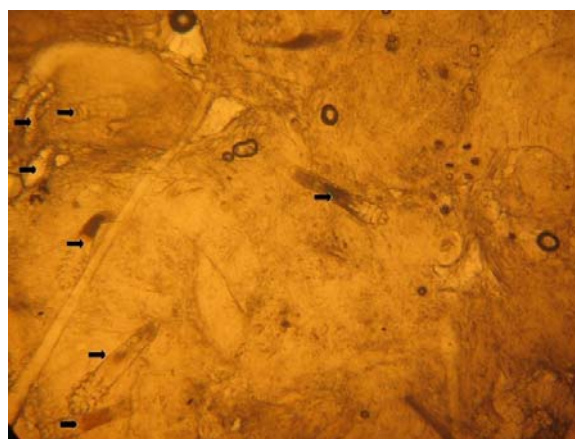
Granulomatous type inflammatory infiltration may be seen.<sup>14</sup> *D.mites* are considered to be involved in the pathogenesis of acne rosacea. They include *D.folliculorum* and *D.brevis*, which are saprophytic mites in human pilosebaceous follicles. For the first time in 1841 Berger and Henle discovered them, but differentiation between them was propounded by Akbulatova.<sup>14-37</sup>

*D.folliculorum* is a transparent and worm-like mite, 0.3 mm long, which occupies the hair follicles, upper the sebaceous glands level. *D.brevis* is smaller than the former and exists solely in depth of sebaceous and meibomian glands.

*D.folliculorum* is more common than *D.brevis* in human skin. *D.mites* can be found in any age groups except the newborns who are presumably infested soon after birth by direct contact.<sup>24, 30 - 31</sup> The mite population varies with age. It is the lowest in children and adolescents and the highest in the middle age and elderly.<sup>17</sup> No sexual difference in prevalence has been found.<sup>24, 30</sup> *D.mites* have been retrieved from almost every area of human skin but have a predilection for face.

There are different methods for skin sampling to examine *D.mites* such as: adhesive tape, skin scraping, skin impression, hair epilation, comedo extraction, skin surface biopsy, and skin biopsy.<sup>26, 32, 34</sup> Skin surface biopsy and skin biopsy have more commonly been used.

In skin surface biopsy, the mites are intact, alive, mobile, and are easy to detect (Figure 3). It is not a method to study the mite prevalence in the population but to estimate *Demodex* density — or more precisely, *D.folliculorum* density — in each

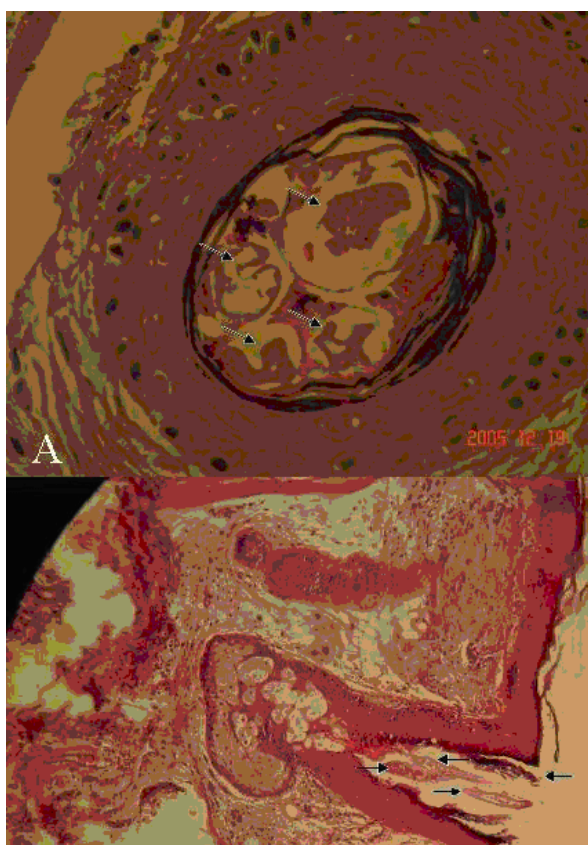


**Figure 3.** *Demodex mites* in superficial skin biopsy (×40).

subject. The method collects the superficial part of the horny layer and the whole follicle contents, therefore detects the few mites present on the skin surface and the more numerous mites in the pilosebaceous duct.<sup>26</sup> *D.folliculorum* and *D.brevis*, which are principally found in the sebaceous glands and occasionally penetrated in to the dermis, are not detected by this method.<sup>16–35</sup>

It is difficult to find *D.mites* in standard skin biopsy because in histological preparations the mite shrinks rapidly and transforms into a translucent “ghost” sac of chitin.<sup>26</sup>

Our findings showed that the *Demodex* population of the face was increased significantly in patients with rosacea compared to age- and sex-matched control subjects. Whether this increase is opportunistic or contributes to the disease is still to be determined. Because the difference is statistically significant, the possibility of a pathogenic role for *Demodex* must be considered (Figure 4). This finding is in agreement with Roihu and Kariniemi’s findings,<sup>33</sup> but is against



**Figure 4.** A) *Demodex mites* in histopathological section of a patient with rosacea ( $\times 40$ ). B) Telangiectasia and *Demodex mites* are seen in the histopathological section of a patient with rosacea ( $\times 10$ ).

the reports from Marks and Harcourt-Webster, and Varotti et al.<sup>36, 27</sup> Most published studies have shown that the prevalence of *Demodex* increases with age.<sup>15, 19–23</sup>

Sengbusch and Hauswirth found a pronounced increase in the prevalence of *D.brevis* with increasing age. Whereas the prevalence of *D.folliculorum* tended to remain more constant.<sup>38</sup> In our study, we did not observe an increase in the mites prevalence in patients older than 40 years.

Mite count in each slide in the rosacea patients (1.4) was significantly higher than the control group (0.66 in DLE group and 0.2 in ALP group), which was against the findings of Roihu and Kariniemi.<sup>33</sup> This discrepancy between our study and Roihu and Kariniemi can be explained by the different methods employed.

Regardless of calculated odds ratios between different groups, we found that possibility of *D.mites* detection in skin biopsy of a patient with rosacea is 2.3 folds higher than a DLE patient and 5.2 folds higher than a patient with ALP.

Considering the results of this study, we can conclude that the prevalence and the number of *D.mites* in rosacea patients are higher than the control subjects. This finding supports the pathogenic role of *D.mites* in rosacea, but whether these mites play a role in initiating rosacea or simply find the lesions of rosacea as a convenient home is still uncertain. However, it is possible that *D.mites* can stimulate an inflammatory reaction that ultimately results in connective tissue damage and telangiectasia. The findings of the present study should be confirmed in a larger patient group.

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