

Original Article

A Cross-Sectional Survey of the Relationship between Rosacea and *Demodex* Mite Infestation in Patients Referred to the Medical Centers of Tabriz University of Medical Sciences

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Abstract

Background: Rosacea is a common chronic and recurrent skin disease whose etiology is not precisely clear. This study aimed to investigate the relationship between rosacea and *Demodex* mite infestation in patients referred to the medical centers of Tabriz University of Medical Sciences during 2023.

Methods: Patients' information, including age, gender, and clinical symptoms of rosacea diagnosis, was recorded. 60 out of 71 patients underwent standard superficial skin biopsy with a thickness of 5 µm from their faces, with a drop of immersion oil, and were examined under a light microscope.

Results: The mean *Demodex* density was 19.20 mites/cm². Of these 60 rosacea patients, 47 (78.3%) were female and 13 (21.7%) were male. The highest *Demodex* mite infestation was in the 31–40 age group (38%). Out of 50 patients with positive *Demodex* (83.3%), 41 (68.3%) were related to *D. folliculorum* and 9 (15%) were related to *D. brevis*. Of the 41 patients infected with *Demodex*, 31 (out of 47, 66.0%) were women and 10 (out of 13, 76.9%) were men. The p-values for the relationships between age, gender, and mite species with mite count were all greater than 0.05. This indicates no statistically significant evidence of a direct relationship.

Conclusion: *Demodex* mite density was higher in rosacea than the normal benchmark of <5 mites/ cm². This strong association suggests *Demodex* overpopulation plays a key role in the disease. Therefore, treatment strategies for rosacea should include acaricidal therapy targeting the mites.

Keywords: Rosacea; *Demodex*; Mite; Demodicosis; Iran

Introduction

Rosacea is a common chronic and recurrent skin disease whose etiology is not precisely known (1). In other words, rosacea is a skin disorder with multiple symptoms (2). The origin of rosacea and its prevalence in the community are not precisely known, with a reported prevalence of 0.9 to 22% (3). Rosacea can present with various skin symptoms, including redness, flushing, telangiectasia, edema, papules, pustules, rhinophyma and ocular manifestations. Rosacea is classified into subtypes or subgroups

of Erythematotelangiectasia, Papulopustular, Phymatous and Ocular (4-6).

Genetic studies suggest the involvement of gene combinations in the development of rosacea, but the gene that causes rosacea has not yet been identified. Studies based on the molecular method, Real-Time PCR, have also shown that rosacea subtypes differ from each other and from healthy skin (7, 8). In rosacea, blood vessels and hair follicle units called pilosebaceous are affected, which include hair

follicles, sebaceous glands and arrector pili muscle (9, 10).

The diagnosis of this disease is made by a dermatologist after a physical examination of the skin, assessment of family history and exclusion of other diseases such as lupus, acne, and scalp eczema. For treatment, in the first line, after educating the patient about skin care, topical creams and gels such as metronidazole 1%, permethrin 5%, tea tree cream and azelaic acid 15% are used and in the later stages, oral medications such as metronidazole and tetracyclines, laser and light therapy are also used (11). In treatment, if the redness is normal, anti-allergic and sunscreen gels and creams with at least Sun Protection Factor (SPF) 30 are used, but if it is ulcerated, metronidazole and azelaic acid will be used. Thickening of the skin around the nose, which is caused by enlarged sebaceous glands, makes the nose look large and eye symptoms of rosacea are treated with topical cyclosporine, as well as eyelid hygiene and the use of antibiotics locally and systemically (12–14).

Today, researchers have identified factors such as an increased density of *Demodex* mites on the face as being involved in the occurrence and exacerbation of rosacea (15). Regarding the relationship between rosacea and *Demodex* mite infestation, several studies have been conducted in different parts of the world, most of which have reported a high prevalence of *Demodex*. In a study in Iran, this prevalence has been reported to be 38%, but it is not clear whether rosacea provides the basis for the activity and increase in the population of mites or whether the increase in the population of mites leads to rosacea (16). In another study in Hungary, it was estimated at 17.7% (17). Therefore, the pathogenic role of *Demodex* mites in rosacea has been demonstrated by original research and systematic reviews (14, 16).

Demodex mites are from the phylum Arthropoda and the order Arachnida and have different types, of which more than 100 species have been identified so far (17). *Demodex* has a striped abdomen and is generally not similar

to other mites. It is relatively similar to a tapeworm and has a thorax and four pairs of very small, fat legs with 5 segments. *Demodex folliculorum* and *D. brevis* were first identified by Henle and Berger in 1841 and were distinguished from each other by Akbulatova in 1963. *Demodex folliculorum* is larger than *D. brevis* and its tip is rounded; its size is 300–400 microns, while *D. brevis* has a pointed tip, short legs and a size of 100–200 microns (18–26). Under normal conditions, these mites are the natural fauna of human skin, especially in the facial area, and there are usually fewer than 5 mites per centimeter of skin (27). If their number increases and they penetrate the skin, they cause acne, folliculitis, especially rosacea and the higher the mite population, the more severe the dermatitis becomes (28–30). Moravvej et al. (16), Roihu and Kariniemi (24) and Cengiz et al. (31) have proven a relationship between rosacea and *Demodex* mite infestation.

We hypothesized that *Demodex* mite density would be significantly higher in rosacea patients compared to established normal thresholds. Therefore, this study was conducted to investigate the relationship between rosacea and *Demodex* mite infestation in patients referred to the medical centers of Tabriz University of Medical Sciences during 2023.

Materials and Methods

Study population and data collection

This study was conducted over one year at the dermatology department of Sina Hospital, Tabriz. Patients presenting with skin disorders were evaluated and those with a definitive diagnosis of rosacea were included. A total of 60 rosacea patients were enrolled. Patient data, including age, gender and clinical symptoms, were recorded. The primary symptoms assessed were flushing, transient and permanent erythema, papules, pustules and telangiectasia. Secondary symptoms included skin

burning or tingling, edema, dryness, and ocular or phymatous manifestations.

Sample collection and microscopic examination

Following diagnosis, a standardized skin surface biopsy (SSSB) was performed on the facial skin. A cyanoacrylate glue strip was applied to the skin and gently removed after a minute, collecting the superficial portion of the stratum corneum and the contents of the pilosebaceous follicles. The sample was placed on a microscope slide with a drop of immersion oil, covered with a coverslip, and examined under a light microscope.

Parasite identification and quantification

Samples were examined for the presence of *Demodex* mites. Each sample was examined in its entirety and the process was repeated for three non-consecutive areas per patient, with the results averaged to determine the mite density (mites/cm²). The two main species, *Demodex folliculorum* and *Demodex brevis*, were differentiated based on their distinct morphology: *D. folliculorum* possesses a longer, sharper capitulum (gnathosoma) and is often found in clusters, while *D. brevis* has a spindle-shaped body and is typically found singly. An infestation was considered positive based on a density of >5 mites/cm².

Statistical analyses

The results of descriptive statistics were determined for qualitative variables as frequency and percentage and for quantitative variables as mean and standard deviation, using SPSS software. Chi-square test and independent t-test were used to examine the relationship between qualitative variables. Linear regression was also used to examine the relationship between the number of parasites and other variables.

Results

Of the 71 patients referred to the dermatology department for facial skin disorders, 60 were

diagnosed with rosacea and 11 were excluded from the study. Of these 60 rosacea patients, 47 (78.3%) were female and 13 (21.7%) were male. The average age of the patients was 35 years, with the lowest being 17 and the highest being 55 years. The prevalence of *Demodex* mite infestation across age groups was as follows: 10–20 years: 12% (6/50), 21–30 years: 22% (11/50), 31–40 years: 38% (19/50), 41–50 years: 18% (9/50) and 50+ years: 10% (5/50) (Fig. 1). The number of mites in each sample was also counted and the average severity of infestation of individuals with mites was 19.20 (Average number of parasites per patient).

Out of 50 rosacea patients with positive *Demodex* infestation, 41 were related to *D. folliculorum* and 9 were related to *D. brevis*. Of the 41 patients infected with *D. folliculorum*, 31 were women and 10 were men. This means that the percentage of *Demodex* mite infestation in the male population is higher than that in the female population in this study. To investigate the relationship between the variables of gender, age groups, *D. folliculorum* and *D. brevis* with the number of *Demodex* species (*D. folliculorum* and *D. brevis*) parasites, a linear regression model was used, according to the results. Linear regression showed that gender was not a significant predictor of mite density ($p > 0.05$). This suggests that the density of *Demodex* mites was consistently high across different patient demographics and parasite species. Furthermore, standardized skin surface biopsy revealed a high *Demodex* density (>5 mites/cm²) across the cohort, confirming a diagnosis of demodicosis. In other words, these results demonstrate a strong relationship between *Demodex* mite overpopulation and rosacea, independent of the specific patient demographics or *Demodex* species investigated.

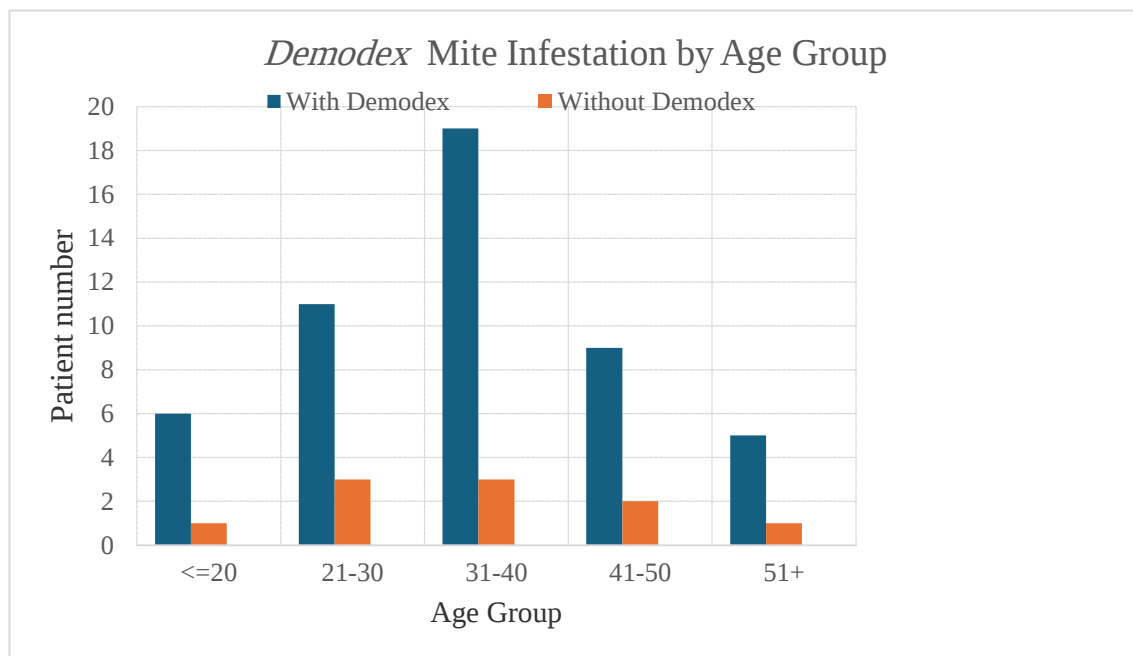


Fig. 1. *Demodex* mite infestation by age group in patients referred to the medical centers of Tabriz University of Medical Sciences during 2023



Fig. 2. Representative clinical photograph of a female patient with papulopustular rosacea. The image shows centrofacial erythema, telangiectasia, and several inflammatory papules and pustules. The patient was part of the cohort referred to the medical centers of Tabriz University of Medical Sciences during 2023. Informed consent for publication was obtained

Discussion

This study aimed to investigate the relationship between rosacea and *Demodex* mite infestation in patients referred to the medical centers of Tabriz University of Medical Sciences. Our findings demonstrate a high prevalence of demodicosis, with 83.3% (50/60) of rosacea patients presenting with a *Demodex* mite density above the clinical threshold of 5 mites/cm². The mean mite density across the cohort was 19.20 mites/cm², clearly confirming demodicosis in this patient population. Out of 60 patients, 47 (78.3%) were female and 13 (21.7%) were male. The average age of patients was 35±10.5 years. These results strongly support a significant association between *Demodex* mite overpopulation and rosacea.

A linear regression analysis was performed to determine if mite density was influenced by gender, age group, or *Demodex* species (*D. folliculorum* vs. *D. brevis*). The analysis revealed that none of these variables had a statistically significant relationship with the mite count ($P>0.05$). This indicates that the high mite density observed in this rosacea cohort was a consistent finding, independent of the patient's demographic background or the predominant *Demodex* species. *Demodex folliculorum* was the most frequently identified species (68.3% of infested patients), which aligns with its common predominance in the facial skin microenvironment.

Our results are consistent with a body of international research linking *Demodex* mites to rosacea. For instance, Moravvej et al. (2007) in Tehran reported a significantly higher prevalence of *Demodex* in rosacea patients (38.6%) compared to those with other dermatoses like actinic lichen planus (10.6%) and discoid lupus erythematosus (21.3%) (16). Similarly, Roihi and Kariniemi (1998) in Finland found a *Demodex* prevalence of 51% in their rosacea group, significantly higher than in control groups with lupus or eczema (24). The prevalence of 83.3% in our study is notably high, which may be

attributed to the use of the highly sensitive standardized skin surface biopsy (SSSB) technique for mite quantification, a method not always employed in earlier histological studies.

Rosacea has a progressive course but is not always seen as multiphasic (33). Numerous studies have shown that rosacea is a vascular skin disorder. Rosacea often begins with flushing and redness of the skin, leading to increased blood flow in the skin vessels, which causes the accumulation of intercellular fluid in the skin. Edema and cellular changes also damage the lymphatic vessels, which are followed by inflammatory lesions in the form of papules, pustules, telangiectasias and sometimes nodules. The acute form of rosacea is rhinophyma, which causes an enlarged nose.

The German dermatologist Simon Gustav first reported the presence of *D. folliculorum* and *D. brevis* in the human body about 170 years ago. The difference between these two species was also stated by Akbulatova (34–36).

The pathogenic role of *Demodex* in rosacea remains a subject of discussion. It is hypothesized that the mites may act as triggers for an inflammatory response, or conversely, that the altered skin environment of rosacea patients facilitates mite overpopulation (16). Our study, showing a universal high mite density regardless of specific demographic factors, lends weight to the idea of a fundamental host-skin environment interaction in rosacea that permits *Demodex* proliferation. This is further supported by the low mite densities (<5 mites/cm²) typically reported on healthy skin, a stark contrast to our findings (16).

While some studies, such as one by Horvath et al. (2011), report a much lower *Demodex* prevalence in healthy populations (17.7%), others, like the study by Taş Cengiz et al. in Türkiye, report rates closer to 48% in their sample, also noting an increase with age (31). This variability underscores the influence of geographical, methodological and population-

specific factors.

In general, studies in Iran and other parts of the world have shown that there is a significant relationship between *Demodex* density and rosacea. The results of the present study are in line with the studies conducted and suggest simultaneous treatment of rosacea and demodicosis.

The strengths of the study were the diagnosis of patients by a dermatologist. Time limitation, lack of coverage of a larger population, and the lack of a control group were the weaknesses of this study.

Conclusion

In summary, the results of the present study provide compelling evidence of a strong association between *Demodex* mite overpopulation and rosacea in the studied population. The consistently high mite density, independent of age or gender, highlights the importance of assessing *Demodex* infestation in rosacea patients. Therefore, we suggest that the evaluation for and concomitant treatment of demodicosis should be considered an integral component of the management strategy for patients presenting with rosacea.

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Ethical Considerations

This study was approved by the ethical committee of Tabriz University of Medical Sciences and followed the Helsinki Declaration (approval number: IR.TBZMED.REC.1402.970). Informed consent was obtained from all participants.

Conflict of interest statement

The authors declare that there is no conflict of interest.

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