

# Role of *Demodex* mite infestation in rosacea: A systematic review and meta-analysis

Yin-Shuo Chang, MD,<sup>a</sup> and Yu-Chen Huang, MD<sup>b,c</sup>  
Taipei, Taiwan

**Background:** The reported prevalence and degrees of *Demodex* mite infestation in rosacea vary widely.

**Objective:** We sought to conduct an evidence-based meta-analysis of the prevalence and degrees of *Demodex* mite infestation in patients with rosacea.

**Methods:** Systematic literature review and meta-analysis were conducted. Odds ratios for prevalence of infestation and standardized mean difference (SMD) for *Demodex* density in patients with rosacea were pooled. Subgroup analysis for type of rosacea, control group, and sampling and examination methods were also performed.

**Results:** Twenty-three case-control studies included 1513 patients with rosacea. Compared with the control patients, patients with rosacea were more likely to be infested by *Demodex* mites [odds ratio, 9.039; 95% confidence interval (CI), 4.827-16.925] and had significantly higher *Demodex* density (SMD, 1.617; 95% CI, 1.090-2.145). Both erythematotelangiectatic rosacea (SMD, 2.686; 95% CI, 1.256-4.116) and papulopustular rosacea (SMD, 2.804; 95% CI, 1.464-4.145) had significantly higher *Demodex* density than did healthy control patients.

**Limitations:** Interstudy variability was high, and a causal relationship could not be established by case-control studies.

**Conclusions:** Patients with rosacea had significantly higher prevalence and degrees of *Demodex* mite infestation than did control patients. *Demodex* mites may play a role in both erythematotelangiectatic rosacea and papulopustular rosacea. (J Am Acad Dermatol <http://dx.doi.org/10.1016/j.jaad.2017.03.040>.)

**Key words:** *Demodex* mites; erythematotelangiectatic rosacea; meta-analysis; papulopustular rosacea; rosacea; standardized superficial skin biopsy.

Rosacea is a common chronic inflammatory dermatosis that affects 1% to 10% of the worldwide population.<sup>1</sup> Major clinical features include flushing, persistent erythema, telangiectasia, papules, and pustules on the center of the face. According to the National Rosacea Society Classification, there are 4 subtypes, including erythematotelangiectatic (ETR), papulopustular (PPR), phymatous, and ocular, with 1 granulomatous variant.<sup>2</sup> The pathogenesis of rosacea is complicated;

it is slightly different within subgroups, and pathogenesis remains unclear. The proposed contributing factors include microbe-induced cutaneous inflammatory reactions, sun damage, exacerbation of the innate immune response, and vascular hyperactivity.<sup>3</sup>

Increased infestation with *Demodex* mites was described first by Ayres in 1961 to contribute to the pathogenesis of acne rosacea.<sup>4</sup> Since then, multiple studies have focused on the association between

From the Department of Dermatology, Taipei Medical University Hospital, Taipei, Taiwan<sup>a</sup>; the Department of Dermatology, Wan Fang Hospital, Taipei Medical University, Taipei, Taiwan<sup>b</sup>; and the Department of Dermatology, School of Medicine, College of Medicine, Taipei Medical University, Taipei, Taiwan.<sup>c</sup>

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Reprint requests: Yu-Chen Huang, MD, Department of Dermatology, Wan Fang Hospital, Taipei Medical University, 111, Hsing-Long Road, Sec. 3, Wenshan District, Taipei City 116, Taiwan, ROC. E-mail: [dhist2002@yahoo.com.tw](mailto:dhist2002@yahoo.com.tw).

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*Demodex* mites and rosacea; however, the results were inconsistent, and only a few studies attempted to establish the role of *Demodex* mites in the pathogenesis of rosacea. Recently, antiparasitic agents (eg, topical permethrin and ivermectin) have been used for treatment, based on the possible role of cutaneous demodicosis in rosacea, with some promising results in patients with PPR.<sup>5,6</sup> However, the role of *Demodex* mites in ETR and other subtypes is unclear. A previous meta-analysis of case-control studies in 2010 showed a significantly higher prevalence of *Demodex* infestation in patients with rosacea than in the control group.<sup>7</sup> This study included 39 reports in Chinese and only 9 in English. The degree of infestation was concluded to be more important than the rate of mite infestation, but its relationship with the development of rosacea was not assessed by pooled analysis. In addition, crucial confounding factors, such as the type of rosacea and different control groups, were not considered.

Therefore, we aimed to perform a meta-analysis of the association of rosacea with prevalence and degree of *Demodex* mite infestation. We sought to isolate the confounding factors by subgroup analysis to provide a thorough, evidence-based analysis of the relationship between *Demodex* mites and rosacea.

## METHODS

This meta-analysis was performed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (<http://www.prisma-statement.org/>).

### Data source and search strategy

We identified studies indexed in PubMed, MEDLINE, and EmBase databases from inception to October 31, 2016. The last day for searching was November 16, 2016. All articles included in the present study involved human clinical studies written in English. Search parameters included the terms “*Demodex*” or “*Demodex* mite” combined with “rosacea.”

### Eligibility criteria and study selection

We included case-control studies with  $\geq 15$  patients with rosacea and controlled-group comparison

of the prevalence, count, and density of *Demodex* mites over the facial skin. Review articles, case reports, and conference reports were excluded. The methodologic quality of the articles was rated by use of an adapted version of the Newcastle-Ottawa Scale for case-control studies, with a maximum score of 9 points (Supplemental Table I; available at <http://www.jaad.org>). The 2 authors (Dr Huang and Dr Chang) independently screened the titles and abstracts of the articles. Relevant full-text studies were assessed for eligibility. Quality assessment was performed independently. Any disagreement was resolved by consensus.

### Outcomes

The primary outcomes of the present study were prevalence and density of *Demodex* mite infestation in patients with rosacea.

### Data extraction

Data were extracted independently by the 2 authors (Dr Huang and Dr Chang). Any disagreement was resolved by consensus. Data on the following measures were extracted: sample size, sampling methods, examination methods, and quality scores (Supplemental Table II; available at <http://www.jaad.org>). Age, sex, number of patients with *Demodex* mites, and mean count and density of *Demodex* mites also were extracted in separate groups (Supplemental Table III; available at <http://www.jaad.org>). We calculated for missing data on mean count or density of *Demodex* mites through the use of any of total count, mean count, or density of *Demodex* mites, with the sample size and sampling area if available.

### Data analysis

For all studies, we produced a pooled estimate of the prevalence and density of *Demodex* mites in patients with rosacea in comparison with a control group. Data then were stratified into different groups by type of rosacea (ETR and PPR), type of control group (healthy control, disease control, and discoid lupus erythematosus control), and type of sampling methods/examination methods [standardized superficial skin biopsy (SSSB), biopsy, pressuring method, tape method, confocal microscopy examination, and

## CAPSULE SUMMARY

- An association between *Demodex* mites and rosacea has been reported.
- Patients with erythematotelangiectatic rosacea and those with papulopustular rosacea had significantly higher prevalence and degree of *Demodex* mite infestation than did healthy control patients.
- *Demodex* mites are associated with both papulopustular and erythematotelangiectatic rosacea and may play a pathogenic role in these conditions.

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