

Density of *Demodex folliculorum* in facial dermatosis.

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ABSTRACT :

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Background : *Demodex folliculorum* (DF) is found in human pilosebaceous units. Various clinical forms have been defined. As the *Demodex* mite is also present in many healthy individuals, it has been suggested that the mite may have a pathogenic role when it is present in high densities. Moreover, some authors have proposed that a mite density above 5/cm² may be a criterion for the diagnosis of demodicidosis.

Objective : To compare the DF density in facial dermatosis patients and healthy subjects.

Methods : Cross sectional study. One hundred fifty patients with facial dermatosis and 150 age and sex matched healthy subjects were enrolled to this study. Standardized skin surface biopsies (SSSB) were performed from three regions (forehead, cheek and nasal dorsum) and suspected lesions. We determined the mite positivities, the mean mite counts in both groups, the mean mite density at each facial site and in the facial dermatosis subgroups, and the mite densities above 5/cm². Non parametric statistical tests were used in the study.

Results DF was found in 59 (39.3%) of the 150 facial dermatosis patients and in 45 (30%) of 150 controls. A mean mite density in the facial dermatosis group (1.46±3.78; range 0-27.33) was significantly higher than that in controls (0.55±1.70; range 0-16.67). The cheek was the most frequently and heavily infested facial region. Our study demonstrates a high density of DF in 1 case with facial eczematous eruptions (27.33/ cm²), 1 case with acne vulgaris (26.33/ cm²) and

1 case from healthy subject ($16.67/\text{cm}^2$). When the various clinical types of facial dermatosis were considered separately, Demodex density was statistically higher than in controls in the patients presented with facial eczematous eruptions (mean = $1.9/\text{cm}^2$; $p=0.001$) and folliculitis (mean = $3.6/\text{cm}^2$; $p=0.002$).

Conclusions The density of DF was significantly higher in facial dermatosis patients than controls, especially those with eczematous eruptions and folliculitis.

Key words: Demodex mite, Demodex density, facial dermatosis

บทคัดย่อ :

อรพิน พุทธานุกาพันธ์, เวสรัช เวสสโกวิท, รัตนี อัครพันธ์, สุทธิรัตน์ เรียงชัยนาม ความหนาแน่นของ DEMODEX FOLLICULORUM ในผู้ป่วยที่มีผื่นผิวหนังบนใบหน้า วารสารโรคผิวหนัง 2555; 28: 251-261.

สถาบันโรคผิวหนัง กรมการแพทย์

เดโมเด็กซ์เป็นไรที่พบในต่อมขนของมนุษย์ ในคนปกติสามารถตรวจพบได้ แต่ก็มีรายงานว่าไรชนิดนี้สัมพันธ์กับผื่นผิวหนังบางชนิด โดยเฉพาะเมื่อมีความหนาแน่นของตัวไรที่มากกว่า $5/\text{cm}^2$

วัตถุประสงค์: เพื่อเปรียบเทียบความหนาแน่นของไรเดโมเด็กซ์ในผู้ป่วยที่มีผื่นบนหน้ากับผู้ป่วยที่มีผื่นหน้าปกติ

วิธีการศึกษา: สุ่มตัวอย่างผู้ป่วยที่มีผื่นบริเวณใบหน้า 150 ราย และผู้ป่วยที่มีผื่นหน้าปกติ 150 ราย โดยมีอายุและเพศใกล้เคียงกัน ตรวจหาไรเดโมเด็กซ์ด้วยวิธี Standardized skin surface biopsies 3 ตำแหน่ง (หน้าผาก แก้ม และจมูก) รวมทั้งรอยโรคที่สงสัย คำนวณหาความหนาแน่น ความถี่ ค่าเฉลี่ยในการตรวจพบไรเดโมเด็กซ์

ผลการศึกษา: ตรวจพบไรเดโมเด็กซ์ 59 คน (39.3 %) จาก 150 คน ในกลุ่มผู้ป่วยที่มีผื่นบนหน้า และ 45 คน (30 %) จาก 150 คนในกลุ่มปกติ ค่าเฉลี่ยความหนาแน่นของไรเดโมเด็กซ์ของกลุ่มผู้ป่วยที่มีผื่นบนหน้า สูงกว่ากลุ่มปกติอย่างมีนัยสำคัญทางสถิติ แก้มเป็นบริเวณที่มีโอกาสพบและมีความหนาแน่นของไรเดโมเด็กซ์มากที่สุด เมื่อวิเคราะห์ความสัมพันธ์ของผื่นผิวหนังพบว่า ผู้มีผื่นผิวหนังอักเสบ และรูขุมขนอักเสบมีความหนาแน่นของตัวไรชนิดนี้มากกว่ากลุ่มปกติอย่างมีนัยสำคัญทางสถิติ

สรุปผล: ความหนาแน่นของไรเดโมเด็กซ์ในผู้ป่วยที่มีผื่นผิวหนังบนหน้ามีมากกว่ากลุ่มปกติอย่างมีนัยสำคัญทางสถิติ โดยเฉพาะผู้ที่มีผื่นผิวหนังอักเสบ และรูขุมขนอักเสบ

คำสำคัญ: เดโมเด็กซ์, ไรรูขุมขน, ความหนาแน่น, ใบหน้า

Introduction

Demodex mite is hair follicle parasite. There are two species which live in human pilosebaceous duct.

Demodex folliculorum (DF) is a 0.3 mm long, oblique, hair follicle parasite which lives in clusters and found in greater number on face than Demodex brevis. Only DF

were found by standardized skin surface biopsies (SSSB).^{1,2} These mites can occur anywhere on the face but are mostly found on the forehead, malar areas of cheeks, nose and nasolabial folds.³ Most people are only carriers of *Demodex* mite and do not develop any symptoms and skin lesions. The prevalence of these mites in healthy individuals varies between 23.5% and 100%.⁴⁻⁷ To date, it is thought to have a pathogenic role in various dermatological conditions such as rosacea, perioral dermatitis, eosinophilic folliculitis.⁸ Some authors consider the mite may have a pathogenic role when it is present in high density. In a recent study, it has been reported that a diagnosis could be regarded as positive when the mite density is over 5/cm².^{9,10}

The principle aim of the present study was to determine the pathogenic relevance of DF in facial dermatosis by comparing the DF density in healthy subjects with that in patients suffering from facial dermatosis. We considered the various clinical types of facial dermatosis separately.

Materials and Methods

Study design

This was a cross-sectional study.

Selection of patients and controls

Patients who attended the outpatient clinic of the Institute of Dermatology, Bangkok, Thailand, during 1 April 2009 to 30 April 2010, with facial itching, burning or stinging, with or without clinical signs of flushing, telangiectasia, erythema, tiny follicular papule, tiny follicular pustule, inflammatory papule, plaque, pustule, nodule, scaling, and abscess were recruited. Controls were selected from patients without facial lesions during the same period. The exclusion criteria for both groups were as follows: the use of topical benzoyl peroxide and topical or systemic antibiotic therapy within the last 4 weeks before entry to this study. Informed consent was obtained before examination of all subjects. All patients and controls were examined by the same dermatologist.



Figure 1 Standardized skin surface biopsy. **A** Sampling method, **B** Direct microscopic examination (x100) DF in cluster obtained

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Sampling method

A standardized skin surface biopsy (SSSB) (Fig.1) was taken from three different facial anatomic sites (forehead, cheek and nasal dorsum) and suspected lesions. A drop of cyanoacrylate glue was placed on a microscopic slide at the middle of the circle (11.5mm in diameter), applying the adhesive bearing surface of the slide to the skin, and removing it after it had been allowed to dry (about 1 min). After removal from the skin, each sample was clarified with two drops of immersion oil, and then covered with a coverslip. The samples were studied microscopically at standard magnifications ($\times 40$, $\times 100$). All measurements in this study were performed by the same investigator in a standard environment to minimize errors.

Statistical analysis

Due to the data that was not normally distributed, non parametric statistical tests should be used to

compare the frequencies and counts of the mites. We used chi-square test and Mann-Whitney U test, respectively.

Results

One hundred and fifty patients with facial dermatosis (118 women, 32 men, age range 15-80 years, mean 34.3 ± 12.71 years) and 150 age and sex matched healthy controls were enrolled in this study. DF was positive in 59 facial dermatosis patients (39.3%) and in 45 subjects (30%) of the control group. The difference between the two groups was not statistically significant ($\chi^2=2.89$, $p=0.08$). The mean mite counts were 1.46 ± 3.78 (range 0-27.33, median 0, mode 0) in facial dermatosis patients and 0.55 ± 1.70 (range 0-16.67, median 0, mode 0) in controls. The difference was found to be statistically significant ($z=-2.07$, $p=0.03$) (Table 1).

Table 1 Mite positivities and mean mite counts in the facial dermatosis and control groups

	Facial dermatosis (n= 150)	Controls (n= 150)	p Values
Mite positivities	59 (39.3%)	45 (30%)	0.08
Mean mite counts	1.46 ± 3.78	0.55 ± 1.70	0.01
Median	0 (0-27.33)	0 (0-16.67)	0.03

The most frequently and heavily infested facial region was the cheek. Mite positivity on the cheeks of patients with facial dermatosis was found to be 40.6% (in 39 patients), not significantly higher than that in controls (46.2% in 30 patients) ($\chi^2=1.53$, $p=0.22$). The

mean mite densities on the cheeks were $1.71/\text{cm}^2$ in the facial dermatosis and $0.80/\text{cm}^2$ in the control groups, the difference was not significant ($z=-2.57$, $p=0.08$). The differences between the two groups were not statistically significant in terms of the mite positivity

and mean mite density at the other facial regions (Table 2).

Our study demonstrated a high density of DF in 1 case with facial eczematous eruptions (27.33/ cm²), 1 case with acne vulgaris (26.33/ cm²) and 1 case from healthy subject (16.67/ cm²). The clinical subgroups of

patients with facial dermatosis were classified in Table

3. DF density in the patients with eczematous eruptions (mean 1.9/cm²; median 0.3/cm²) and folliculitis (mean 3.6/cm²; median 3.3/cm²) were significantly higher than in controls (mean 0.6/cm²; median 0/cm²) (Fig. 2).

Table 2 DF frequencies and mean mite density at facial sites

Site	DF frequencies			Median mite densities		
	case	controls	p Values	case	controls	p Values *
Cheek	39 (40.6%)	30 (46.2%)	0.22	0 (0-76)	0 (0-38)	0.08
Forehead	38 (39.6%)	27 (41.5%)	0.12	0 (0-19)	0 (0-19)	0.12
Nose	19 (19.8%)	8 (12.3%)	0.03	0 (0-39)	0 (0-7)	0.02

* P value after Bonferroni correction < 0.017 is significant

Table 3 DF density in groups studied

Clinical pattern	N	DF density (demodex/cm ²)	
		Mean ±SD	p value *
Controls	150	0.55±1.70	-
Facial dermatoses (all)	150		
Acne vulgaris	64	1.25±3.80	0.54
Perioral dermatitis	1	-	-
Folliculitis **	7	3.57±3.48	0.002
Seborrheic dermatitis	24	0.49±1.33	0.15
Eczematous eruptions +	51	1.88±4.51	0.001
Dermatomyositis	1	-	-
SLE	1	-	-
PMLE	1	-	-

N, number of subjects; -, no computable value.

* Mann-Whitney U-test, p value after Bonferroni correction < 0.005 is significant and < 0.001 is highly significant

** Folliculitis = Ofuji's folliculitis, suppurative folliculitis + Eczematous eruption, not compatible with seborrheic dermatitis

In facial dermatosis group, 14 patients (9.33%) had a mite density higher than $5/\text{cm}^2$, whereas 3 of control subjects (2%) had a mite density over $5/\text{cm}^2$. The difference was statistically significant ($\chi^2=7.55$,

$p=0.006$). The sensitivity was found to be 9 % in all of facial dermatosis cases, the specificity was 98%, the positive predictive value was 82 % and the negative predictive value was 48 % (Table 4).

Table 4 Value of the criterion density of DF $>5/\text{cm}^2$ to confirm a clinical diagnosis of patients with facial dermatosis

Density of DF/ cm^2	Cases	Controls	Total
>5	14	3	17
≤ 5	136	147	283
Total	150	150	300

Diagnostic value: Specificity $147/150 \times 100 = 98\%$

Sensitivity $14/150 \times 100 = 9\%$

Positive predictive value $14/17 \times 100 = 82\%$

Negative predictive value $136/283 \times 100 = 48\%$

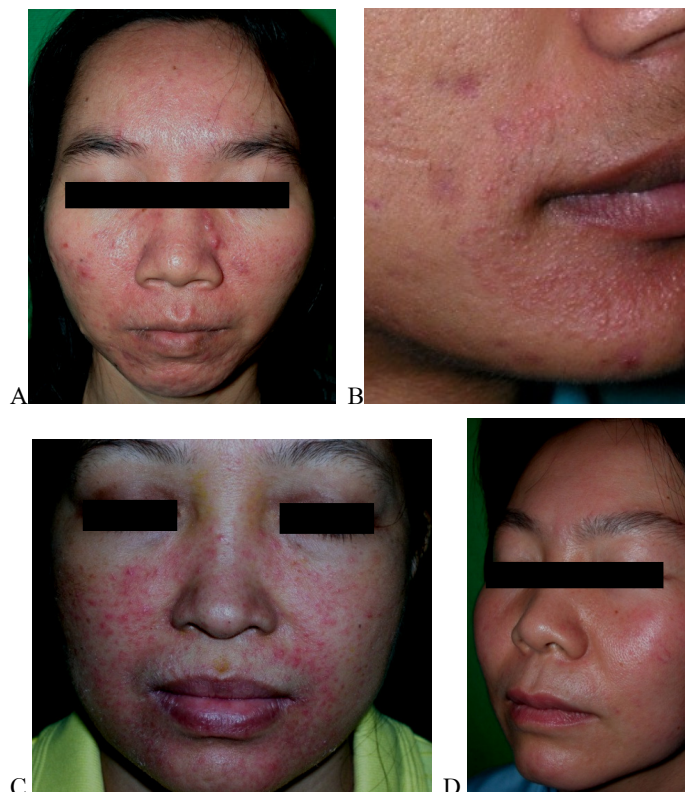


Figure 2 Clinical manifestations of some facial dermatosis patients with DF density $>5/\text{cm}^2$.

A, Acne vulgaris with mean mite density $26.33/\text{cm}^2$.

B, Perioral dermatitis with mean mite density $5.67/\text{cm}^2$.

C, Folliculitis with mean mite density $9.3/\text{cm}^2$.

D, Eczematous eruption with mean mite density $18.7/\text{cm}^2$.

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Discussion

Various techniques have been used to demonstrate the Demodex mite such as skin scraping, skin impression, adhesive band, skin surface biopsy and punch biopsy. With noninvasive techniques, DF can be detected more easily because they are alive, intact and movable. In addition, the whole follicular content where DF are found in clusters can be obtained with the SSSB technique. *D. brevis* cannot be detected with this method.¹¹⁻¹³

The reported counts of mites are variable according to the techniques used and facial sites examined. With the SSSB technique, most published studies have shown that the most frequently and heavily infested facial region was the cheek.¹⁴ This is similar to the results in our study. We did not find a statistically significant difference in the mite positivity and the mean DF density between patients and controls in all anatomic regions studied which is similar to those reported by Erbagci et al. and Mustafa et al.^{15,16}

Demodex mite feeds on sebum and cellular proteins obtained by epithelial and glandular cell destruction through its own enzymatic activity. Consequently, it causes splitting of the follicular epithelium and may elicit perifollicular inflammation. Some investigations support the hypothesis that Demodex mite induces the formation of a perifollicular lymphohistiocytic infiltrate and the cell mediated immune response plays an important role in the pathogenesis of rosacea. Akilov

and Mumcuoglu et al. found a significant decreased in the percentage of CD3+, CD4+, CD8+ and CD16+ cells, the ratio of CD3+/CD20+ and the functional activity of leucocytes in individuals infested with Demodex mites. In addition the absolute number of CD95+ was higher in patients with demodicidosis. This could be the result of local immuno suppression caused by the mites, which allows them to survive in the host skin. Thus colonization of the skin with Demodex mites could be a reflection of the host's immune response in the pathogenesis of the skin condition.¹⁷⁻¹⁹

In previous studies (Table 5) the prevalence of DF were found in various skin conditions, mostly in rosacea and demonstrated in large numbers.²⁰ Erbagci et al. found that the mean DF count in rosacea patients (mean 6.7) was significantly higher than that in controls (mean 2.9).¹⁵ Clinical presentations of DF infestation resembling pustular folliculitis, pityriasis folliculorum, perioral dermatitis, facial follicular spinulosis, eosinophilic folliculitis and blepharitis have been described in the literature.²¹⁻²⁹ Pityriasis folliculorum occurs predominantly in women as diffuse but faint facial erythema with itching and burning sensations as well as fine follicular plugs and scales that give the skin a sandpaper- like appearance. In the study of Yelda et al., DF infestation can also present with non-specific features such as facial itching with or without erythema, pityriasisiform squamous or acneiform lesions.³⁰

Table 5 Clinical presentations of DF infestations in previous reports

Study	Clinical	Time	Study design	N
Erbagci et al.	Rosacea	1998	Cross-sectional	38
Forton F		1993		33
Georgala et al.		2001		92
Forton F	Pityriasis folliculorum	2005	Prospective	115
Dolenc et al.	Perioral dermatitis	2005	Cross-sectional	82
Purcell et al.	Pustular folliculitis	1986	Case report	1
Karincaoglu	Seborrheic dermatitis	2009	Cross-sectional	38
Schaller et al.	Demodex abscess	2003	Case report	1
Ecker et al.	Granuloma	1979	Cross-sectional	30
Yelda et al.	Non specific facial dermatitis	2004	Cross-sectional	32
Joseph et al.	Erythema, dry, scale, rough	2009	Retrospective	63

In our study, we found that the mite density in the facial dermatosis group ($1.46/\text{cm}^2$) was significantly greater than in controls ($0.55/\text{cm}^2$). We also found that DF can present in various skin conditions but only facial eczematous eruptions and folliculitis show DF density significantly higher than controls. The significance of this finding is still not completely understood, because many people who have no facial lesions may also have mites and some of them have mite density more than $5/\text{cm}^2$. In addition, some patients with facial dermatosis may have partial treatment with topical corticosteroid which predisposed to the increased density of DF. Lubbe et al. postulated that a local immunosuppressive effect contributes to more favorable conditions for the proliferation of demodex mites.³¹ Due to the low incidence of rosacea in Thailand, we did not find any case with this disease.

In practice, to be able to confirm the pathogenic relevance of DF in facial dermatosis, it is important to know the abnormally high density of Demodex mite. Forton et al. found a density of DF $>5/\text{cm}^2$ to be very specific for papulopustular rosacea with a 98% specificity, a 95% positive predictive value, a 55% sensitivity, and a 75% negative predictive value. Erbagci and Ozgoztasi showed similar results¹⁵. Therefore we chose a threshold of $5 \text{ DF}/\text{cm}^2$ to determine the abnormal density of the mite in facial dermatosis and we also found a same specificity (98%) but a very lower sensitivity than in the previous studies.

This study did not clearly support the pathogenic role of DF because we did not compare DF density before and after treatment and surface area studied is limited due to small volume of material asses.

Conclusions

The density of DF was significantly higher in facial dermatosis patients than in controls. The pathogenic relevance of this mite is still unknown. Further study should be carried out.

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