

Investigation of *Demodex folliculorum* frequency in patients with polycystic ovary syndrome*

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Abstract: BACKGROUND: Background: Demodex mites are acari that reside in the pilosebaceous unit of the skin and have been associated with skin disorders.

OBJECTIVE: The objective of this study was to investigate the prevalence of *Demodex folliculorum* (*D. folliculorum*) mites in polycystic ovary syndrome patients as well as to examine the relationship between Demodex infestation and the presence of acne and oily or dry skin types in polycystic ovary syndrome patients.

METHODS: 41 polycystic ovary syndrome patients and 47 non-polycystic ovary syndrome control subjects were enrolled in the study. polycystic ovary syndrome was diagnosed according to the revised 2003 ESHRE/ASRM polycystic ovary syndrome Consensus Workshop Group diagnostic criteria. Microscopic examination of *D. folliculorum* mites was carried out by standardized skin surface biopsy. The result was considered positive when there were more than 5 mites per cm².

RESULTS: *D. folliculorum* was positive in 53.7% of the polycystic ovary syndrome patients and 31.9% of the non-polycystic ovary syndrome group (p=0.052). Demodex positivity was significantly associated with acne (p=0.003) and oily skin (p=0.005) in the polycystic ovary syndrome patients but not in the controls.

STUDY LIMITATION: Our study is limited by the relatively small number of subjects and the observational nature of the study design.

CONCLUSION: Demodex mites might have a role in acne pathogenesis in patients with polycystic ovary syndrome. Anti-Demodex treatment may increase the response to treatment of acne. Further studies are indicated.

Keywords: Acaridae; Acne vulgaris; Polycystic ovary syndrome

INTRODUCTION

Demodex species are microscopic, obligate, elongated mites of the Demodicidae family, Acari order, and Arachnida class. Both *Demodex folliculorum* (*D. folliculorum*) and *Demodex brevis* (*D. brevis*) are common colonisers of human skin, particularly the face, and occupy the pilosebaceous unit, including hair follicles and sebaceous glands. *D. folliculorum* is more prevalent, but *D. brevis* has a wider bodily distribution.^{1,2} Normal rates of colonisation have been estimated between 20% and 80%, increasing with age, and they are considered part of the normal dermatological flora of the skin.¹⁻³ Their potential connection to skin diseases is controversial, with many considering them to be coincidentally present in diseased skin, or to be temporarily and opportunistically parasitic in the diseased state.^{2,4} However, some evidence points to a contribution of *Demodex* to the pathogenesis of multiple skin disorders, including rosacea,

blepharitis, and pustular folliculitis.⁴⁻⁷ Oily or mixed skin appears to increase the risk of *Demodex* infestation.⁸ It is also well-known that *Demodex* mites are pathogenic in the context of immunosuppression.^{1,2} A potential link to acne, a disorder of the pilosebaceous unit, in humans is controversial.^{4,9} However, a recent meta-analysis of case control studies supported an association between *Demodex* infestation and acne vulgaris.¹⁰

Polycystic ovary syndrome (PCOS) is a common endocrine disorder that affects 5-10% of women of reproductive age and commonly features chronic anovulation and hyperandrogenism.¹¹⁻¹³ Hyperandrogenism is typically associated with systemic effects, including acne, hirsutism, and central obesity. In women with PCOS, acne is predominantly distributed as inflammatory lesions on the lower face, neck, chest, and upper aspect of the back.¹³ Women with PCOS

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are also at high risk of depression and anxiety, which has a negative impact on their health-related quality of life. Acne has been identified as one of the factors potentially contributing to the risk of affective disorders and a reduced quality of life in women with PCOS.^{14,15}

Given the association between PCOS and acne, as well as the proposed association of *Demodex* infestation with acne, we hypothesised that *Demodex* infestation may be more prevalent in women with PCOS and that there may be a link between *Demodex* and the presence of acne and/or oily skin in PCOS patients. One recent study on 30 PCOS patients and 30 matched healthy control subjects has shown that *D. folliculorum* infestation is increased in women with PCOS.¹⁶ The objectives of this study were, therefore, to determine whether or not the prevalence of *Demodex* mites was increased in a larger group of women with PCOS and to examine the relationship between *Demodex* infestation and the presence of acne, as well as with oily or dry skin types in PCOS patients.

METHODS

The study was carried out at the Department of Obstetrics and Gynecology, and at the Dermatology Department, between May 2013 and August 2014. This study was approved by Turgut Ozal University Ethical Committee and complied with the Helsinki Declaration of 1975, as revised in 1983. All participants gave their written informed consent. The study was designed as a case-control study, with 41 PCOS patients and 47 non-PCOS control subjects, matched for age, weight, and body mass index (BMI), enrolled in the study. Physical examination and transvaginal ultrasound were performed on all women by same gynecologist. PCOS was diagnosed according to revised 2003 Rotterdam European Society for Human Reproduction and Embryology (ESHRE) / American Society for Reproductive Medicine (ASRM) PCOS Consensus Workshop Group diagnostic criteria.¹² The healthy control group was composed of 47 females with regular menses, normal medical history, physical and pelvic examination, pelvic ultrasound, and blood chemistry. None of the PCOS or control patients had been on any medication for at least 3 months prior to the study, including oral contraceptives, glucocorticoids, ovulation induction agents, or anti-diabetic and anti-obesity drugs. All subjects were examined for dermatological lesions. The diagnosis of acne vulgaris was made based on the presence of comedons, papules, pustules, and/or cysts. Three samples for mite examination were taken from the inflammatory lesions of the acne on the forehead, cheeks, and jaw. Microscopic examination of mites was performed by cyanoacrylate glue standardized skin surface biopsy (SSSB) in both the patient and control groups. A slide covered with cyanoacrylate glue and a marked square was pressed against the skin surface. After 30sec, the slide was removed and the samples were collected. The preparation was inspected with the use of a light microscope at 40x and 100x magnification. The result was considered positive when there were more than 5 *D. folliculorum* mites in a 1-cm² area by SSSB.

Facial skin types of the PCOS and control groups were classified as dry or oily. There is no standardized quantitative method to reliably measure cutaneous sebum levels; therefore, qualitative distinction between dry skin and oily skin is commonly made in clinical practice through the interpretation of clinical signs, such as

texture, hydration, sebaceous follicle dilatation, tendency to wrinkles and pigmentation, shine, and oiliness.¹⁷

STATISTICAL ANALYSIS

Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS) version 16.0 for Windows XP (SPSS Inc., Chicago, IL, USA). Normal distribution of measurement values was examined graphically and with the Shapiro-Wilk test. The data were presented as mean \pm Standard Deviation (SD) and analysed using the Student's t-test to determine whether differences between PCOS and control groups and between subgroups were significant. $P \leq 0.05$ was considered statistically significant.

RESULTS

There was no significant difference between the PCOS and control groups in terms of BMI, weight and median age (Table 1).

Significantly more PCOS than control patients had acne (70.7% v 42.6% respectively; $p=0.01$); 36 of 41 PCOS patients (87.8%), as compared to none of the control subjects complained of hirsutism ($p<0.001$). The rate of oily skin was similar for the two groups, at 70.7% of PCOS patients and 74.5% for controls ($p=0.811$); 53.7% of the PCOS group were *D. folliculorum* positive, while 31.9% of the control group were *D. folliculorum* positive, determined to be statistically significant at the limit ($p=0.052$) (Table 2).

Both the control and PCOS groups were separated into two subgroups each according to whether or not acne was diagnosed by dermatological examination. When these four subgroups were assessed separately, in the control group no significant association was found between *D. folliculorum* positivity and having acne or not (Table 3; $p=0.553$). By contrast, in the PCOS group, there was a significant association between being *Demodex* positive and having acne vulgaris versus not having acne vulgaris ($p=0.003$) (Table 3). A significant difference was also found in terms of *D. folliculorum* positivity between those in the PCOS group who have acne versus both subgroups of the control group ($p=0.007$ and $p=0.001$, respectively), but no significant difference was found between those who did not have acne in the PCOS group and both subgroups of the control group ($p=1.000$ and $p=0.559$, respectively) (Table 3 and Figure 1)

D. folliculorum positivity was also assessed according to skin type in all cases. While 69% *Demodex* positive patients in the PCOS group had oily skin, significantly fewer (16.7%) had dry skin ($p=0.005$). In the control group, while 40% of *Demodex* positive patients had oily skin, 8.3% had dry skin ($p=0.071$; Table 4). When patients with an oily skin type from both the PCOS and the control groups were compared for *Demodex* positivity, the difference between them was statistically significant (Table 4; $p=0.026$). In patients with dry skin types, there was no significant difference between the control and the PCOS groups in terms of *Demodex* positivity (Table 4; $p=1.000$, Figure 2).

DISCUSSION

In this study, we aimed to determine whether the prevalence of *D. folliculorum* mites was increased in women with PCOS, and to examine the relationship between *Demodex* infestation and the presence of acne, as well as with oily or dry skin types, in PCOS

TABLE 1: Distribution of demographic data of patients according to groups

	PCOS	Control	p
Age (y)	24 (19-40)	24 (19-42)	0.470
Weight (Kg)	70 (42-116)	68 (45-110)	0.558
BMI	27.3±5.7	26.9±5.7	0.347

BMI: Body Mass Index; PCOS: Polycystic Ovary Syndrome
p≤0.05 considered statistically significant

TABLE 2: Distribution of *Demodex* positivity results according to the groups

		<i>Demodex</i>		
Group		negative	positive	p
Control	Count	32	15	0.052
	% group	68.1	31.9	
	% <i>Demodex</i>	62.7	40.5	
PCOS	Count	19	22	
	% group	46.3	53.7	
	% <i>Demodex</i>	37.3	59.5	

PCOS: Polycystic Ovary Syndrome
p≤0.05 considered statistically significant.

TABLE 3: Distribution of *Demodex* positivity by subgroups

		<i>Demodex</i>		
Group		negative	positive	p
Control-acne negative	Count	19	7	0.003
	% group	73.1	26.9	
	% <i>Demodex</i>	37.3	18.9	
Control-acne positive	Count	13	8	
	% group	61.9	38.1	
	% <i>Demodex</i>	25.5	21.6	
PCOS - acne negative	Count	17	10	
	% group	63.0	37.0	
	% <i>Demodex</i>	33.3	27.0	
PCOS -acne positive	Count	2	12	
	% group	14.3	85.7	
	% <i>Demodex</i>	3.9	32.4	

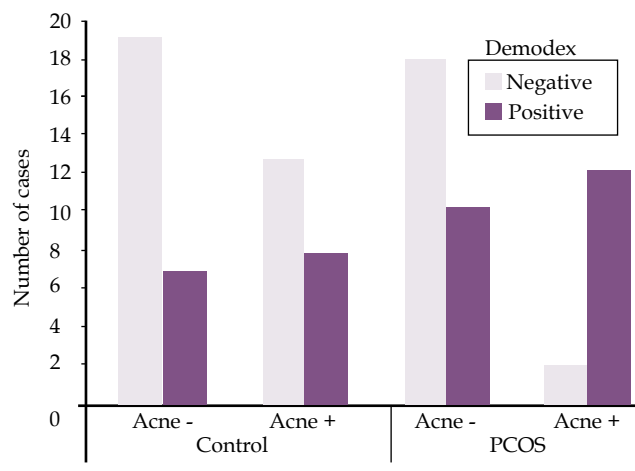
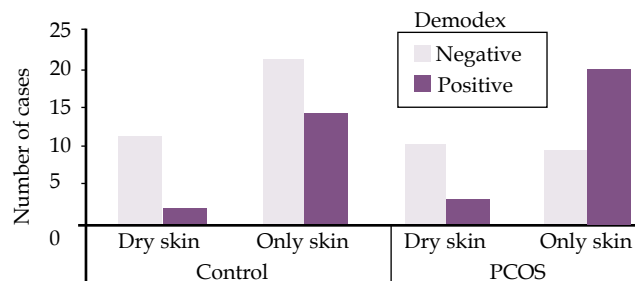
PCOS: Polycystic Ovary Syndrome; P≤0.05 was considered statistically significant.

TABLE 4: *Demodex* positivity distribution according to skin types

Skin type		Control		p	PCOS		p	p*
		negative	positive		negative	positive		
Oily	Count	21	14	0.071	9	20	0.005	0.026
	% skin type	60.0	40.0		31.0	69.0		
	% <i>Demodex</i>	65.6	93.3		47.4	90.9		
Dry	Count	11	1		10	2		1.000
	% skin type	91.7	8.3		83.3	16.7		
	% <i>Demodex</i>	34.4	6.7		52.6	9.1		

PCOS: Polycystic Ovary Syndrome; P≤0.05 was considered statistically significant.

patients. The results showed that a significantly higher prevalence of *D. folliculorum* infestation was found in women with PCOS than in a control group matched for age, weight, and BMI. Prevalence of acne was also higher in the PCOS group and *Demodex* positivity was positively associated with the presence of acne in the PCOS group but not in the control group. Prevalence of oily skin was comparable in the two groups, but in the PCOS group, oily skin was significantly more likely to be associated with *Demodex* positivity. To the best of

**FIGURE 1: *D. folliculorum* positivity according to the presence or absence of acne****FIGURE 2: *D. folliculorum* positivity according to the dry or oily skin type**

our knowledge, this is the first study to show differential association of *Demodex* positivity and acne, as well as with the oily skin type, in women with PCOS, as compared to the controls.

Any proposed association between acne and *Demodex* in the general population is controversial. Some studies have found no evidence of increased *Demodex* prevalence and acne vulgaris, and many consider *Demodex* mites to be opportunistic rather than causative pathogens in skin diseases in general.^{2,4,9,18} However, others

have proposed that there is an association between *Demodex* and acne.¹⁹ Recent meta-analysis of case control studies indicated that there was a positive association between the amount of *Demodex* infestation and the presence of acne vulgaris.¹⁰ While this does not prove a causative association, it does suggest that in cases where standard acne treatment is unsuccessful, consideration should be given to the presence of *Demodex* mites and the possible efficacy of acaricidal therapies. One double-blind, controlled clinical trial of acaricidal medications showed the efficacy of these medications in the treatment of 100 acne-like demodicidosis cases.²⁰ However, there is a lack of studies in English on the potential effectiveness of anti-*Demodex* medications in acne treatment or even of the potential pathogenic role of *Demodex* mites in acne.

The results of our study suggest that there is a differential association of *D. folliculorum* infestation with acne in PCOS patients as compared to the controls. PCOS is frequently associated with acne, which is thought to contribute to affective disorders and a reduced quality of life in women with PCOS (14,15). One recent study on 30 PCOS patients and 30 matched healthy control subjects showed an increased prevalence of *D. folliculorum* infestation in women with PCOS.¹⁶ Our study confirmed that *D. folliculorum* infestation is more prevalent in PCOS patients as compared to the controls. We also showed that there is an association between the occurrence of acne in women with PCOS and the presence of *Demodex* mites, which

was not present in the controls, which in turn suggests that in these patients the *Demodex* infestation could be contributory to the pathogenesis of acne. Oily or mixed skin appears to increase the risk of *Demodex* infestation.⁸ In our study, there was no significant difference between PCOS and the control groups for the prevalence of the dry skin type. However, the PCOS group presented a significantly higher association between oily skin and the presence of *Demodex* mites than did the control group. This again suggests that some aspect of the hormonal, metabolic, or inflammatory changes in PCOS patients increases the likelihood of *Demodex* infestation over and above other risk factors, such as the oily skin type.

CONCLUSION

The present study has shown an association between PCOS and *D. folliculorum* positivity and, more importantly, a further association of *D. folliculorum* positivity and the presence of acne in PCOS but not in control patients. The literature in general is limited and divided on the possible connections between *Demodex* and acne. The results of our study suggest that PCOS is a condition in which this connection may have pathological significance. This study is limited by the relatively small number of subjects and the observational nature of the study design. Larger observational studies on the prevalence of *Demodex* in women with PCOS are warranted, especially as regards its association with acne, in order to determine if acaricidal therapies can be effective in the treatment of acne in PCOS. □

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