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Relationship between demodex infestation and clinical parameters in polycystic ovary syndrome: A prospective observational study

Polikistik over sendromunda demodex enfestasyonu ile klinik parametreler arasındaki ilişki: Prospektif gözlemsel çalışma

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ABSTRACT

Aim: Polycystic ovary syndrome (PCOS) is frequently accompanied by dermatologic findings and metabolic disturbances. Because Demodex mites thrive in sebaceous areas and have been linked to several inflammatory and metabolic conditions, we explored whether Demodex positivity is associated with clinical and laboratory features in women with PCOS.

Material and Methods: In this prospective observational study, 63 women aged 18–40 years with a confirmed diagnosis of PCOS based on the Rotterdam criteria were enrolled. The presence of Demodex spp. was assessed using the standardized superficial skin biopsy technique. Sociodemographic data, anthropometric measurements, ovarian volume, oral glucose tolerance test results, and a panel of hormonal parameters were collected.

Results: Demodex-positive patients had significantly higher body mass index, waist and abdominal circumference, ovarian volume, and fasting glucose levels, while their waist-to- abdominal ratio was lower compared to Demodex-negative patients ($p < 0.05$). In contrast, multivariate logistic regression analysis revealed that none of these parameters remained independently significant ($p > 0.05$).

Conclusion: The findings suggest that Demodex spp. infestation in women with PCOS may reflect both dermatological and metabolic alterations. Although univariate analyses indicated significant associations, these did not persist in multivariate models, underscoring the need for larger, prospective studies. Screening for Demodex may provide additional insight into the comprehensive management of PCOS, particularly in patients presenting with dermatological complaints.

Keywords: Polycystic ovary syndrome, demodex spp., fasting glucose, insulin resistance, hormonal profile, ovarian volume

ÖZ

Amaç: Polikistik over sendromu (PKOS), ovulatuvar disfonksiyon, hiperandrojenizm ve polikistik over morfolojisi ile karakterize, sıklıkla metabolik bozukluklarla birlikte görülen yaygın bir endokrin hastalıktır. PKOS'ta akne ve sebore gibi cilt belirtileri sık görülür ve cildin yağ bakımından zengin bölgelerinde yaşayan Demodex türleri çeşitli dermatolojik ve metabolik rahatsızlıklarla ilişkilendirilmiştir. Bu çalışmanın amacı, PKOS'lu kadınlarda Demodex türleri enfestasyonu yaygınlığını belirlemek ve antropometrik, hormonal ve glisemik parametrelerle ilişkisini değerlendirmektir.

Gereç ve Yöntemler: Bu prospektif gözlemsel çalışmaya, Rotterdam kriterlerine göre doğrulanmış PKOS tanısı almış 18-40 yaş arası 63 kadın dahil edildi. Demodex türlerinin varlığı, standart yüzeyel deri biyopsisi tekniği kullanılarak değerlendirildi. Sosyodemografik veriler, antropometrik ölçümler, over hacmi, oral glukoz tolerans testi sonuçları ve bir dizi hormonal parametre toplandı.

Bulgular: Demodex pozitif hastaların vücut kütle indeksi (VKİ), bel ve abdominal çevresi, over hacmi ve açlık kan şekeri düzeyleri anlamlı derecede daha yüksekken, bel-abdominal oranları Demodex negatif hastalara kıyasla daha düşüktü ($p<0,05$). Buna karşılık, çok değişkenli lojistik regresyon analizi bu parametrelerin hiçbirinin bağımsız olarak anlamlı olmadığını ortaya koydu ($p>0,05$).

Sonuç: Bulgular, PKOS'lu kadınlarda Demodex spp. enfestasyonunun hem dermatolojik hem de metabolik değişiklikleri yansıtabileceğini düşündürmektedir. Tek değişkenli analizler anlamlı ilişkiler gösterse de bunlar çok değişkenli modellerde kalıcı olmamıştır ve bu da daha büyük, prospektif çalışmalara duyulan ihtiyacı vurgulamaktadır. Demodex taraması, özellikle dermatolojik şikayetlerle başvuran hastalarda PKOS'un kapsamlı yönetimine ilişkin ek bilgi sağlayabilir.

Anahtar Kelimeler: Polikistik over sendromu, demodex türleri, açlık glikozu, insülin direnci, hormonal profil, over hacmi

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Highlights

- The prevalence of Demodex spp. was evaluated in women with polycystic ovary syndrome using a standardized superficial skin biopsy method.
- Demodex-positive patients had higher BMI, waist and abdominal circumference, ovarian volume, and fasting glucose levels.
- Waist-to-abdominal ratio was significantly lower in Demodex-positive individuals.
- No independent predictors of Demodex positivity were identified in multivariate logistic regression analysis.
- The findings suggest a possible association between metabolic alterations and Demodex infestation in PCOS.

INTRODUCTION

Polycystic ovary syndrome (PCOS) is a common endocrine disorder in reproductive-aged women, defined by ovulatory dysfunction (anovulation or oligo-ovulation), clinical and/or biochemical hyperandrogenism, and polycystic ovarian morphology. Its estimated prevalence in the general population is approximately 10%, and although its etiology is thought to be multifactorial, it has not yet been fully elucidated (1-5). PCOS presents with a wide clinical spectrum; hirsutism, obesity, acne, and alopecia are among the most common manifestations. Although acne is not included in the diagnostic criteria, it is a frequent complaint that can significantly impair quality of life. While the role of androgens in acne development has long been recognized, androgen levels may remain within the normal range in some PCOS patients with acne. This observation suggests that, in addition to systemic hormone levels, factors such as increased peripheral tissue sensitivity to androgens may contribute to acne pathogenesis (3,5).

Demodex species (particularly Demodex folliculorum and Demodex brevis) are saprophytic or opportunistic ectoparasites that reside in areas of the human face with high sebaceous gland density. While they may exist in limited numbers as part of the normal skin flora, they have also been associated with increased sebum production, aging, immunosuppression, rosacea, blepharitis, acne, and diabetes (6-14). Recent studies have suggested that disturbances in glucose metabolism may increase Demodex density, pointing to a possible association with insulin resistance or hyperglycemia (10-13). Since PCOS is frequently accompanied by metabolic disturbances such as glucose intolerance, hyperinsulinemia, and insulin resistance, the potential relationship between Demodex infestation and PCOS gains clinical significance. Therefore, in the etiopathogenesis of acne observed in PCOS patients, not only hormonal factors but also parasitic infestations should be considered.

Nevertheless, studies directly examining the relationship between Demodex infestation and impaired glucose metabolism in PCOS are quite limited, and current data remain insufficient (11,12). Given the complex endocrine and metabolic profile of PCOS, the role of parasitic factors such as Demodex has not been well defined. Accordingly, the present study aimed to determine the prevalence of Demodex infestation in women with PCOS and to investigate its associations with glucose regulation, hormonal profiles, and anthropometric parameters in detail.

MATERIAL and METHODS

The study was designed prospectively and carried out between November 1, 2020, and April 30, 2021, at the Department of Obstetrics and Gynecology of Adıyaman University Faculty of Medicine. Women aged 18–40 years presenting with menstrual irregularities and signs of hyperandrogenism, who were diagnosed with PCOS based on the Rotterdam criteria, were invited to participate. All participants provided written informed consent. The study protocol was approved by the Non-Interventional Clinical Research Ethics Committee of Adıyaman University (approval date: 17 November 2020; decision number: 2020/10-10). This study was conducted with the utmost ethical sensitivity in accordance with the Principles of the Declaration of Helsinki.

A total of 63 women diagnosed with PCOS and reporting acne complaints were included, provided they were not morbidly obese (body mass index [BMI]>40 kg/m^2), had no known systemic diseases, and met the inclusion criteria. For each participant, demographic data (age, BMI, obstetric history, smoking status, anthropometric measurements), laboratory results, and ultrasonographic findings were recorded. Abdominal circumference was preferred over hip circumference to better reflect central adiposity, which is more closely associated with metabolic activity in PCOS.

Exclusion criteria were: incomplete follow-up or insufficient data, systemic diseases associated with immunosuppression, a history of hormonal therapy within the past year, allergic diseases, previously diagnosed dermatological conditions (e.g., rosacea, seborrheic dermatitis, blepharitis, allergic dermatitis), and antibiotic use within the last month.

The presence of Demodex spp. was determined using the standard superficial skin biopsy (SSSB) method, performed on the nasolabial and chin regions as previously described. A 1 cm² area was marked on a microscope slide with a ruler, and the remaining surface was cleaned with ether. A drop of cyanoacrylate-based adhesive was applied to the marked area, and the slide was gently pressed onto the skin surface. After approximately one minute, the slide was carefully removed and examined within one hour. Two to three drops of immersion oil were applied to the sampled area, covered with a coverslip, and examined microscopically. An initial survey was performed under 4x magnification, followed by scanning at 10x and 40x magnification with a partially closed diaphragm. The density of Demodex spp. per cm² was evaluated by an experienced parasitologist (TÇ), who was blinded to the clinical and laboratory data of participants. A positive diagnosis was defined as the presence of five or more Demodex spp. per cm² (9,10).

Statistical Analysis

Statistical evaluation was performed using SPSS version 21 (IBM Corp., Armonk, NY, USA). A p value of less than 0.05 was considered significant. Continuous variables were reported as mean ± standard deviation, while categorical variables were expressed as percentages. Categorical comparisons were made with Pearson's chi-square test. The Shapiro-Wilk test was used to assess normality. According to the distribution pattern, continuous variables were compared using either the independent samples t-test or the Mann-Whitney U test.

To identify factors associated with Demodex positivity, a multivariate logistic regression analysis was performed using the backward stepwise (Wald) method. In the initial step, body mass index, waist circumference, abdominal circumference, total ovarian volume, fasting glucose level, and waist-to-abdominal ratio were entered into the model. At each subsequent step, variables with the highest p-values were sequentially removed according to the Wald statistic.

RESULTS

A total of 63 women diagnosed with PCOS were included in the study. Of these, 38 (60.3%) were identified as Demodex-positive, while 25 (39.7%) were Demodex-negative (Table 1).

When sociodemographic and anthropometric characteristics were compared, BMI (26.2 ± 5.9 vs. 23.3 ± 2.5; p = 0.026), waist circumference (79.3 ± 11.8 cm vs. 71.2 ± 6.9 cm; p = 0.003), and abdominal circumference (86.2 ± 12.9 cm vs. 75.3 ± 10.3 cm; p = 0.001) were significantly higher in the Demodex-positive group compared to the Demodex-negative group. However, the waist-to-abdominal ratio was lower in the Demodex positive group (0.92 ± 0.05 vs. 0.95 ± 0.05; p = 0.013). No significant differences were observed between the groups with respect to other demographic variables such as age, age at menarche, body weight, height, gravida, parity, or marital status (p > 0.05).

Laboratory data of the participants are presented in Table 2. Comparisons of laboratory findings showed that the mean fasting glucose level was significantly higher in the Demo-

Table 1: Sociodemographic data of participants according to Demodex positivity.

		Demodex Negative	Demodex Positive	p-value
	n	25	38	
Age (years, mean ± SD)		23.5±4.3	22.8±4.9	0.561*
Age of first menstruation (years, mean ± SD)		12.9±1.4	13.0±1.1	0.707*
Marital status (n (%))	Married	6 (24.0)	16 (42.1)	0.140
	Single	19 (76.0)	22 (57.9)	
Gravida (mean ± SD)		0.4±0.9	0.4±0.9	0.804**
Parita (mean ± SD)		0.4±0.9	0.3±0.8	0.932**
Abortus (mean ± SD)		0.00±0.00	0.03±0.16	0.422**
Height (cm, mean ± SD)		164.7±6.6	161.8±7.5	0.119*
Weight (kg, mean ± SD)		63.4±8.4	68.5±15.2	0.325**
BMI (kg/m², mean ± SD)		23.3±2.5	26.2±5.9	0.026*
Waist circumference (cm, mean ± SD)		71.2±6.9	79.3±11.8	0.003*
Abdominal circumference (cm, mean ± SD)		74.9±10.3	86.2±12.9	<0.001*
Waist-to-abdominal ratio (mean ± SD)		0.95±0.05	0.92±0.05	0.013*
Acanthosis (n, (%))		2 (8.0)	3 (7.9)	0.988

BMI: Body mass index, **SD:** Standard deviation. *Independent samples t-test, **Mann-Whitney U test

Table 2: Laboratory findings of participants according to Demodex positivity.

		Demodex Negative	Demodex Positive	p-value
	n	**25**	**38**	
HbA1c (%, mean ± SD)		5.3±0.4	5.3±0.5	0.719**
75 gr OGTT (mg/dl, mean ± SD)	Fasting Glucose	91.6+9.9	98.3±8.5	0.036**
	T1 (60 min)	123.0±34.3	135.0±47.1	0.428*
	T2 (120 min)	114.6±28.2	105.5±23.8	0.887**
Free T3 (pg/ml, mean ± SD)		3.7±1.1	3.4±0.4	0.486**
Free T4 (ng/dl, mean ± SD)		0.92±0.14	0.87±0.18	0.290**
TSH (IU/mL, mean ± SD)		1.86±1.15	2.17±1.87	0.459**
AMH (ng/ml, mean ± SD)		6.2±3.8	6.9±3.3	0.356*
DHEA-S (μg/dl, mean ± SD)		270.3±105.3	305.4±91.7	0.167**
FSH (IU/mL, mean ± SD)		7.6±2.5	8.4±5.1	0.447**
LH (IU/mL, mean ± SD)		8.0±3.7	8.2±3.5	0.905**
Vitamin D (ng/mL, mean ± SD)		12.0±5.1	12.7±5.5	0.621*
Hemoglobin (gr/dl, mean ± SD)		13.8±1.4	13.8±1.5	0.898*
Hematocrit (%, mean ± SD)		40.7±3.3	40.3±3.6	0.647*
Platelet (x10^3/μl, mean ± SD)		267.2±62.7	273.3±71.4	0.730*
Total antral follicle (mean ± SD)		20.3±13.6	22.8±12.2	0.455**
Total Ovarian Volume (cm^3, mean ± SD)		12.9±3.5	16.3±4.9	0.005*

SD: Standard deviation; **HbA1c:** Glycated hemoglobin; **TSH:** Thyroid-stimulating hormone; **AMH:** Anti-Müllerian hormone; **DHEA-S:** Dehydroepiandrosterone sulfate; **FSH:** Follicle-stimulating hormone; **LH:** Luteinizing hormone, *Independent samples t-test, **Mann-Whitney U test.

dex-positive group (98.3 ± 8.5 mg/dL vs. 91.6 ± 9.9 mg/dL; p = 0.036). In addition, the total ovarian volume was also significantly greater in this group (16.3 ± 4.9 mL vs. 12.9 ± 3.5 mL; p = 0.005). No statistically significant differences were observed between the groups regarding other hormonal, metabolic, or hematological parameters (p > 0.05).

In the multivariate logistic regression analysis using the backward stepwise (Wald) method, none of the included variables remained statistically significant in the final model (all p > 0.05), indicating that no parameter independently predicted Demodex positivity.

DISCUSSION

This study aimed to contribute to the limited literature by examining the association between Demodex spp. infestation and anthropometric, hormonal, and glycemic parameters in women with PCOS. Our findings demonstrated that body mass index, waist and abdominal circumference, ovarian volume, and fasting glucose levels were significantly higher in Demodex-positive individuals in univariate analyses. However, none of these parameters remained statistically significant as independent predictors in the multivariate logistic regression model. This finding may reflect the complex and interrelated metabolic-endocrine characteristics of PCOS, in which factors such as insulin resistance, obesity, and hyperandrogenism are closely intertwined. Consequently, the associations observed in univariate analyses may be attributable to collinearity among variables or the influence of shared underlying metabolic pathways rather than independent effects.

Previous studies have reported positive correlations between impaired glucose metabolism and increased Demodex density (11,12). In contrast, although fasting glucose levels were higher in the Demodex-positive group in our study, this variable did not remain an independent predictor. This finding indicates that the unique metabolic profile of PCOS—particularly hyperinsulinemia and insulin resistance, which are independent of glucose levels—may directly influence Demodex proliferation. Similarly, previous studies reported that even after glycemic control was achieved in women with gestational diabetes, elevated Demodex density persisted (10). These observations suggest that not only systemic glucose levels but also local skin microenvironmental factors and sebaceous gland activity play important roles (15,16).

From an anthropometric perspective, BMI, waist circumference, and abdominal circumference were significantly higher in the Demodex-positive group. However, these effects also disappeared in multivariate analyses. This may imply that increased adiposity indirectly promotes sebum produc-

tion and thereby creates a more favorable environment for Demodex, but the relationship is not necessarily direct.

Although no distinct hormonal differences were found, total ovarian volume was significantly greater in the Demodex-positive group. This common feature of PCOS may elevate local androgen levels and sebum secretion, thereby facilitating Demodex infestation. Nevertheless, the absence of independent significance in regression analysis suggests that this relationship is also likely indirect or mediated by glucose-related mechanisms.

The therapeutic implications of these findings are noteworthy. Metformin, commonly used in the management of PCOS, not only improves insulin sensitivity but may also reduce sebum production, potentially limiting Demodex proliferation. Likewise, combined oral contraceptives suppress androgen activity and reduce sebaceous gland secretion, which could lower parasite density. Therefore, integrating systemic metabolic approaches with dermatological interventions may be beneficial in managing PCOS patients (16). All these speculative findings deserve investigation through randomized controlled trials.

The discrepancies between our results and those of previous studies may stem from methodological differences, such as sample size, diagnostic methods for Demodex, sampling sites, and the homogeneity of the study population. The restriction of this study to women with PCOS limits the generalizability of the findings to the broader population. Nevertheless, considering the unique hormonal and metabolic characteristics of PCOS, such focused analyses provide valuable insights.

This study has some limitations. The relatively small sample size may have limited statistical power. As this was designed as a pilot study, no power analysis was conducted, and the results should be considered hypothesis-generating rather than confirmatory. This may be the reason for the discrepancy between univariate and multivariate analyses. Furthermore, Demodex assessment was restricted to two facial regions (nasal wings and chin), which may not reflect the overall infestation level across the entire facial surface. The fact that only PCOS patients with acne complaints were included in the study may create a selection bias. Hormonal and metabolic parameters were measured at a single time point, which may have overlooked circadian or cyclic variations. Lastly, given the cross-sectional design, the observed associations should not be interpreted as causal.

Conclusion

This study demonstrated that Demodex spp. infestation in women with PCOS may be associated with certain anthropometric and metabolic parameters. However, the absence of independent predictors in multivariate analyses suggests that these relationships may not be direct but rather mediated through indirect mechanisms. The results highlight a potential interaction between the complex hormonal and metabolic profile of PCOS and the cutaneous microecology.

The evaluation of Demodex infestation may contribute to a better understanding and management of dermatological symptoms in women with PCOS. In particular, in PCOS patients presenting with persistent acne or other dermatological manifestations, a simple Demodex screening could guide the inclusion of topical antiparasitic agents (e.g., metronidazole, ivermectin) in treatment plans. Such an approach may improve the dermatological management of PCOS and support the development of multidisciplinary treatment strategies.

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Author Contributions

Study conception and design: **Mehmet Bülbül, Mustafa Kaplanoğlu, Tuncay Çelik;** data collection: **Mehmet Bülbül, Mustafa Kaplanoğlu, İpek Çakılkaya, Emel Dündar;** analysis and interpretation of results: **Mehmet Bülbül, Mustafa Kaplanoğlu, Tuncay Çelik;** draft manuscript preparation: **Mehmet Bülbül, Mustafa Kaplanoğlu, Tuncay Çelik, İpek Çakılkaya, Emel Dündar.** The authors reviewed the results and approved the final version of the article.

Conflicts of Interest

The authors declare that they have no conflict of interest relevant to this study.

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Ethical Approval

This study was approved by the Non-Interventional Clinical Research Ethics Committee of Adıyaman University (Approval Date: 17.11.2020, Decision No: 2020/10-10). All participants provided written informed consent prior to enrollment.

Data Availability Statement

The datasets generated and analyzed during the current study are available from the corresponding author on reasonable request.

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