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Increased Density of *Demodex folliculorum* Mites in Pregnancies with Gestational Diabetes

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Key Words
Demodex folliculorum · Gestational diabetes · Pregnancy

Abstract
Objective: To investigate the presence of *Demodex* in patients with gestational diabetes and the impact of glucose regulation on *Demodex* density in gestational diabetes. ***Subjects and Methods:*** The study population consisted of 33 patients with gestational diabetes and 30 pregnant women without gestational diabetes (control group). The age, parity, gestational age, and BMI of the study group were recorded and the patients were divided into 2 groups, i.e. those with regulated and unregulated glucose levels, according to their postprandial 1st- and 2nd-hour glucose values. A standardized skin surface biopsy method was used to determine if patients had *Demodex folliculorum* infestation (>5 mites/cm^2 of skin). ***Results:*** Patients with gestational diabetes had a statistically significantly higher *Demodex* density compared to the control group (24.2 vs. 3.3%; $p < 0.001$). Furthermore, a significantly higher proportion of gestational diabetes patients with unregulated glucose levels had a higher *Demodex* density compared to those in the regulated subgroup (6/19 vs. 2/14; $p = 0.001$). ***Conclusion:*** Our study revealed that the *Demodex* density was increased in gestational diabetes patients. Further, poor glucose regulation could be the mechanism responsible for the increased *Demodex* density in gestational diabetes patients with unregulated glucose levels compared to those with regulated glucose levels.

Introduction

Demodex folliculorum and *D. brevis* are presumed saprophytic parasites living in the pilosebaceous glands and hair follicles of humans [1]. *D. folliculorum* can be found anywhere in the body where there are hair follicles, but it is particularly located in the cheeks, eyelids, nose, forehead, and chin, which are rich in sebaceous glands [2]. Although it is colonized in many individuals, it does not have clinical symptoms. Therefore, some do not regard this parasite as a pathogen. The density of the parasite had been shown to be <5 parasites/cm^2 in asymptomatic individuals [3]. However, an increased *Demodex* density in skin disorders such as rosacea and blepharitis suggests that this parasite may be a pathogen. Furthermore, the *Demodex* density had been reported to be high in immunosuppressive conditions such as leukemia, HIV(+), and cancer [4–6]. It has also been shown that the *Demodex* density does not change in pregnancy [7].

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Gestational diabetes, seen in 6–7% of pregnancies, is a carbohydrate intolerance which starts or is recognized in pregnancy [8]. Gestational diabetes increases the risk of preeclampsia, macrosomia, and cesarean section in pregnancy. Furthermore, 50% of women with gestational diabetes become diabetic in 22–28 years [9].

Studies have shown an increased incidence of *D. folliculorum* in diabetic patients [10, 11]. There is as yet no study investigating the *Demodex* parasite in gestational diabetes. Therefore, the aim of this study was to investigate the presence of *Demodex* in patients with gestational diabetes and the impact of glucose regulation on *Demodex* density in gestational diabetes.

Table 1. Baseline clinical characteristics of the study population

	Gestational diabetes (n = 33)	Control (n = 30)	p value
Mean age ± SD, years	29.4±5.6	30.3±3.2	0.30
Mean parity ± SD	3.4±2.1	3.3±2.6	0.72
Mean gestational age ± SD, weeks	28.5±2.1	30.2±2.1	0.56
Mean BMI ± SD	28±4.4	27±3.1	0.32
Participants with an increased *Demodex* density, n			
Skin	8	1	<0.001
Eyelashes	9	1	<0.001

Subjects and Methods

Thirty-three patients with gestational diabetes and 30 pregnant women without gestational diabetes (control group) attending the Obstetrics and Gynecology Outpatient Clinic of Mustafa Kemal University Hospital for pregnancy control from August 2013 to November 2013 were included in this study. The patients' age, gestational age, parity, and BMI were recorded. The BMI was calculated as weight in kilograms divided by the square of the height in meters. At 24–28 weeks of gestational age, all pregnant women underwent an initial screening with a 1-hour 50-gram glucose challenge test. Subjects with a normal glucose tolerance test were considered the control group. If a patient's glucose was higher than the threshold of 130 mg/dl, a 3-hour 100-gram glucose tolerance test was performed after an 8- to 12-hour fasting period. Gestational diabetes was diagnosed if 2 out of 4 blood glucose measurements were higher than the Carpenter and Coustan criteria's cut-off level [12]. A postprandial 1st-hour glucose level below 140 mg/dl and a 2nd-hour glucose level below 120 mg/dl in pregnant women are accepted as good glucose controls [13]. Patients with gestational diabetes had their fasting and 1st- and 2nd-hour postprandial glucose levels checked each week. The patients were divided into 2 groups, i.e. those with regulated and unregulated glucose levels according to the postprandial 1st- and 2nd-hour glucose values. Exclusion criteria were: patients diagnosed with diabetes before pregnancy, those with systemic diseases such as chronic liver and renal failure, systemic lupus erythematosus, and cancer, and those with dermatologic disorders such as facial seborrheic dermatitis and rosacea and blepharitis. All of the patients underwent detailed dermatological and eye examinations and no one in the study population had a manifestation of demodicosis, rosacea, or ocular rosacea. Our study was approved by the Ethics Committee of Mustafa Kemal University, and written informed consent was obtained from all participants.

After an 8-hour fasting period, 5-ml venous blood samples were collected from gestational diabetic patients; postprandial 1st- and 2nd-hour blood glucose levels were measured via the glucose oxidase method.

Eyelash and skin samples taken via the noninvasive standardized skin surface biopsy technique from the cheek, chin, forehead, and nose were collected from the participants [14]. The presence of *D. folliculorum* mites was investigated to measure the density of *Demodex* mites. To standardize the standardized skin surface biopsy technique, a 1-cm^2 area of a cyanoacrylate glue-containing slide was marked and applied to the patients' face for 1 min after wiping the patients' face with alcohol. The density of *D. folliculorum* mites was determined using a light microscope (Olympus CH20; Olympus Optical, Tokyo, Japan) at ×40 and ×100 magnifications. The identification of >5 mites/cm^2 of skin was defined as *D. folliculorum* mite infestation. For *D. folliculorum* evaluation, overall 4 eyelashes (from the upper and lower eyelashes of each eye) were taken from all individuals, placed between a slide and coverslip with a drop of glycerin, and evaluated under a light microscope at ×40 and ×100 magnifications.

Statistical Analysis

Data analysis was performed using SPSS 17 for Windows statistical software (SPSS Inc., Chicago, Ill., USA). Normal and continuous variables were described as means ± SD, whereas categorical variables were summarized as numbers of patients and percentages. $p < 0.05$ was considered statistically significant. To determine the relation between 2 variables, Pearson's or Spearman's correlation analysis was used. Student's t test and the Mann-Whitney U test were used to compare differences between continuous variables. The χ^2 test was used to compare differences between categorical variables.

Results

The mean age of the patients with gestational diabetes was 29.4 ± 5.6 years (range 18–36) and that of the control group was 30.3 ± 3.2 years (range 20–35); the difference in age was not statistically significant ($p = 0.30$). The mean BMI values of the gestational diabetes and control groups were similar (28 ± 4.4 and 27 ± 3.1; $p = 0.32$). The mean gestational age was similar in both groups (28.5 ± 2.1 and 30.2 ± 2.1 weeks). Nineteen patients with gestational diabetes had unregulated glucose levels, and 14 had regulated blood glucose levels. *Demodex* was noted in the skin biopsies of 8 patients with gestational diabetes

Table 2. Subgroup analysis of gestational diabetic pregnancies according to glucose regulation

	Good glucose control (n = 14)	Poor glucose control (n = 19)	p value
Mean fasting glucose ± SD, mg/dl	93±16.5	112±14.2	0.03
Mean 1st-hour postprandial glucose ± SD, mg/dl	131±18.9	159±22.5	0.004
Mean 2nd-hour postprandial glucose ± SD, mg/dl	112±14.9	135±12.5	0.02
Participants with an increased *Demodex* density, n			
Skin	2	6	0.001
Eyelashes	2	7	0.001

(24.2%) and only in 1 patient (3.3 %) in the control group, which was statistically significant ($p < 0.001$) (table 1). *Demodex* was seen more in the eyelashes of patients with gestational diabetes compared to the control group (27.2 vs. 3.3%; $p < 0.001$). The *Demodex* frequency in eyelash follicles was significantly higher in patients with gestational diabetes compared to the control group (27.2 vs. 3.3%; $p < 0.001$). When a subgroup analysis was carried out in gestational diabetes, the results revealed that the *Demodex* density was higher in patients with unregulated glucose levels (6/19 vs. 2/14; $p = 0.001$) (table 2).

Discussion

The results of this study revealed an increased *Demodex* density in gestational diabetes. Moreover, the *Demodex* density increased in gestational diabetic patients with unregulated glucose levels compared to those with regulated glucose levels. Hence, the increased *Demodex* infestation might have been related to a poor glucose metabolism since papulopustular rosacea, granular rosacea, and blepharitis were excluded in the present study. *D. folliculorum* are found more commonly in the face, cheeks, nose, forehead, external ear, and hair follicles of the eyes, where sebaceous secretion is abundant. Because *Demodex* mites are found in the skin following birth, they are considered normal skin flora. Their number increases in puberty with the activation of sebaceous glands. *D. folliculorum* can be seen in 20–80% of humans in normal skin, with a density below 5 mites/cm^2 [15–17]. For that reason, in the present study we accepted densities above 5 mites/cm^2 as *Demodex* infestation. Our study results were concordant with other research in diabetic populations. Karincaoglu et al. [18] found the *Demodex* density to be greater in patients with end-stage renal failure and greatest (44%) in those with renal failure related to diabetes mellitus. Although the immune system is impaired in chronic renal failure, a higher incidence of *Demodex* in chronic diabetic renal failure suggests that diabetes itself and an impaired glucose tolerance might influence the *Demodex* density. Similarly, in our study, the *Demodex* incidence was increased in gestational diabetes without immune suppression. Akdeniz et al. [19] compared skin samples obtained from diabetics and healthy individuals and found an increased *Demodex* density and volume in diabetics. Clifford and Fulk [20] examined the eyelashes of 256 individuals and reported *Demodex* with a higher incidence in elderly and diabetic patients [20]. Our study results revealed for the first time in the literature that patients with gestational diabetes had increased *Demodex* infestation in their eyelashes.

The prevalence of *Demodex* mites has been reported to increase with age [21]. Regarding age, no significant differences were found between the groups in the present study. There is no consensus about whether or not *Demodex* is pathogenous. As *Demodex* does not produce infestation in many hosts, some authors consider *Demodex* an opportunistic agent [21]. The presence of *Demodex* in immunosuppressed conditions such as chronic renal disease, cancers, and malnutrition suggests that it can be an opportunistic pathogen [6, 22, 23]. On the contrary, *Demodex* densities were similar in a study comparing immunocompromised patients with a control group, and it was stated that *Demodex* could not be an opportunistic pathogen [24].

Although Aydingoz et al. [7] reported that the *Demodex* incidence did not increase in pregnancy, we found an increased *Demodex* incidence of 24.4% in gestational diabetes similar to the 24% reported by Gokce et al. [11]. Since gestational diabetes is not a chronic disease and has no direct effect on the immune system, the high *Demodex* incidence in our study may have arisen from an impaired glucose metabolism, as is the case with high glu-

cose levels in gestational diabetic patients with unregulated glucose levels compared to controls with regulated glucose levels.

The major limitation of this study was the relatively low patient number. Another limitation is the absence of a repeat oral glucose tolerance test in the 8th postpartum month in gestational diabetes patients.

Conclusion

The results showed an increased *Demodex* density in pregnant women with gestational diabetes. Furthermore, in patients with gestational diabetes with unregulated glucose levels the *Demodex* density was found to be higher than in patients with regulated glucose levels.

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