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## INFLUENCE OF MITES GENUS DEMODEX ON CLINICAL PICTURE OF THE DISEASE AT PATIENTS WITH ACNE AND ROSACEA

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### Introduction

In modern medicine, it is always important to identify the etiologic factors and pathogenic mechanisms of the disease in order to establish an accurate diagnosis and selection of appropriate therapies. The topical issue of dermatology is to clarify the development of pathogenic mechanisms of the most common dermatoses – acne and rosacea, associated with opportunistic skin flora. In particular, mites genus Demodex, capable of parasitizing, are the most frequently reported microbial agents in this pathology [1]. There are no demodex mites on the skin of newborns. However, dissemination occurs in childhood and to middle age 80-100% of population become carriers of mites, thus the infection happens through direct contact or through everyday when using general hygiene means; mites live on a damp surface and do not survive without the owner, parasite everywhere at all races and are found at all geographical zones [2]. Mites of genus Demodex are the most common human ectoparasites, living in hair follicles and in excretory ducts of sebaceous glands [1].

In spite of the fact that there are known more than 100 species of Demodex mites (class Arachnida, subclass Acarina) only two types of mites parasite on human's skin - Demodex folliculorum longus and Demodex folliculorum brevis [2, 3]. Demodex folliculorum brevis is detected less, than Demodex folliculorum longus, in the ratio 1:4 at men and 1:10 at women accordingly [4]. These types differ in the preferential localization and morphological characteristics. Consequently, the study of the influence of mites genus Demodex on the clinical picture of the disease is on the one hand of great theoretical interest, on the other - has undeniable practical importance defining new therapy directions of these diseases.

The goal of the present research is to determine the influence of Demodex mites (*Demodex folliculorum longus* and *Demodex folliculorum brevis*) on clinical picture and the development of the diseases at patients with acne and rosacea.

## **Materials and methods**

There were surveyed total 128 patients with symptoms of acne and rosacea on the face and 30 healthy volunteers. During the examination the direct diagnoses were established to the patients on the basis of clinical picture of the diseases. For the diagnosis of acne, the classification of the European guidelines for the treatment of acne was used (EU Guidelines group, 2012) [5]:

- comedonal acne,
- mild and moderate papulopustules acne,
- severe papulopustules acne, moderate nodular acne,
- severe nodular acne, acne conglobate.

At establishing diagnose of rosacea, the classification of the American National Rosacea Society (2002) was used:

Subtypes of rosacea:

Subtype I – erythematotelangiectatic,

Subtype II – papulopustules,

Subtype III – phymatous,

Subtype IV – ocular [6].

The following clinical aspects of the disease were highlighted; these aspects included primary as well as secondary morphological features: papules, pustules, open comedones, milium, telangiectasia, perifocal erythema, excoriation, pigmentation, greasy luster.

The study group included patients with the following criteria:

1. Men and women with acne and rosacea;
2. Age 18 years or older;
3. Informed consent of patients to participate in the study.

Exclusion criteria from the study:

1. Existence of concurrent somatic diseases of a heavy current or neoplastic character;
2. Existence of hyperandrogenism;

3. Alcohol or drug addiction;
4. Lack of desire at the patient to continue the study;
5. The occurrence of allergic reactions and the development of significant side effects during treatment;
6. Pregnancy and lactation.

By means of questions in the questionnaire, duration of the disease was assessed on three periods: <1 year, 1-5 years and 5-10 years.

All patients were conducted scraping for the detection of Demodex mites with the definition of their species - Demodex folliculorum longus or Demodex folliculorum brevis. The study included patients who have a positive test with the presence of mites more than 5 individuals per 1cm<sup>2</sup>. Two days before the study, patients discontinued the use of any topical medications, as well as decorative cosmetics. On the day of the study patients did not wash.

Material for the analysis was taken with a sterile scalpel from facial zones with the greatest concentration of sebaceous glands (nose, chin, glabellar area). The received material was placed on a glass slide in a drop of 10% KOH solution (potassium hydroxide) for 24 hours, and then the light microscopy was carried out with the magnification x10 and x40.

As part of the study, patients were divided into two equal groups: group I – patients with Demodex mites (N=64) and group II – patients who have not been detected Demodex mites (N=64). The first group included 64 patients with acne (N=38; 59.37%) and rosacea (N=26; 40.62%), complicated with demodecosis; the second group consisted of 64 patients with acne (N=34; 53.13%) and rosacea (N=30; 46.87%) uncomplicated with demodecosis.

The control group included 30 healthy volunteers: 15 men and 14 women at the age of 18-40 years old. The distribution by sex, age and diagnosis is shown in Table 1.

**Table1. The distribution by sex, age and diagnosis of respondents included in the study.**

I group (with Demodex mites)					Total
Gender	Men (N =18; 28.13%)		Women (N=46; 71.88%)		64 (100%)
Diagnosis	Acne	Rosacea	Acne	Rosacea	
Age	23±5.5	44±10.4	29±6.4	51±17.6	
II group (without Demodex mites)					64 (100%)
	(N =20; 31.25%)		(N =44; 68.75%)		
Age	24±2.2	41±6.3	33±2.9	50±5.4	

III group (healthy volunteers)			30 (100%)
	(N =15; 50%)	(N =15; 50%)	
Age	26±1.4	31±3.1	

Evaluation of morphofunctional skin properties was carried out on a digital video camera “Aramo SG” with the use of Skin XR Pro 2.0 program. Before the study, the skin was cleared. The camera was strictly in upright position, in order to avoid additional tension of the skin in the evaluation of its relief. Light-emitting diodes of blue, orange and red colors were applied. We used the lens with increasing x10 and x60. Dermatoscopy on digital camera “Aramo SG” allows making photos with further processing of the received image and interpretation of the results.

The digital video camera “Aramo SG” allows conducting the following studies:

1. Moisture test.
2. Oiliness test with the definition of skin type. The skin oiliness was measured in two zones: U-zone (chicks) and T-zone (forehead, nose and chin).
3. Elasticity test.
4. Definition of pore size.
5. Pigmentation test.
6. Sensitivity test.
7. Smoothness test (skin relief).
8. Test to determine the depth of wrinkles.

After the study with the use of digital video camera “Aramo SG”, the program Skin XP Pro 2.0 gives the result, which we can simultaneously compare with norm parameters. The results are presented in graphical and entered in the patients’ cards automatically. To determine the PH of skin, litmus test-strips were used. The test-strip was soaked under running water at indoor temperature, and then it was applied to previously cleaned skin for 10 seconds. Each level of PH corresponds to a certain color.

When comparing the change in color of litmus test-strips and scale color, we defined the corresponding pH level of the patient. Statistical methods: Statistical analysis was performed using the software Statistica 7.0. To assess the accuracy of differences Mann-Whitney test criteria were used. To assess the reliability of quality indicators, the two-sided Fisher’s exact test was used. Statistically accurate were differences when  $p < 0.05$ . In addition, the correlation analysis was performed using Spearman's rank-order correlation coefficient.

**Results of the research**

In the analysis of the age of patients, some statistical differences were revealed. In both groups, with a diagnosis of acne, younger persons prevailed ( $p < 0.0001$ ), which corresponds to the age of the manifestations of nosology. However, in age ration among patients with acne, age of men is statistically significantly lower ( $p=0.045$ ) than age of women (tab.1). Statistical differences in the diagnosis of rosacea among the sexes were not revealed. Distribution of diagnoses among sexes is shown it table 2.

**Table 2. The distribution of patients by sex and diagnoses.**

	Men		Women		Total
	Acne	Rosacea	Acne	Rosacea	
Group I	17	10	21	16	64
Number of people (%)	13.28%	7.8%	16.4%	12.52%	50%
Group II	15	8	19	22	64
Number of people (%)	11.7%	6.25%	14.8%	17.25%	50%
TOTAL	32	18	40	38	128
	24.98%	14.05	31.2%	29.77%	100%

The general structure of diagnoses among women revealed an approximately equal number of cases of acne and rosacea (40 and 38 respectively), in structure of male population incidence, acne significantly predominates over rosacea (32 and 8 of cases) (Table 2).

When analyzing the frequency of diagnoses of acne and rosacea at patients of groups I and II, the diagnosis of acne was registered more often - in 72 cases (56.25%), the diagnosis of rosacea was established in 56 cases (43.75%), but statistically accurate difference was not found (Table 2).

In determining the species of Demodex mites some of the features were ascertained (Table 3):

**Table 3. The distribution of Demodex mites according to diagnosis.**

	Demodex folliculorum longus		Demodex folliculorum brevis		Combined cases		Total
	Acne	Rosacea	Acne	Rosacea	Acne	Rosacea	
Number of people (%)	30	22	4	4	4	-	64
	46.87%	34.38%	6.25%	6.25%	6.25%		100%

As the table shows, statistically accurate that Demodex folliculorum longus accompanied acne and rosacea in most clinical cases ( $p < 0.0001$ ). Demodex folliculorum longus was detected in 30 out of 38 cases at the diagnosis of acne, and in 22 cases out of 26 at the diagnosis of rosacea. Demodex folliculorum brevis was detected equally at patients with acne and rosacea (total 8 clinical cases). In four cases, there was the combined parasitizing by two species of mites at patients with acne. There were no cases of combined mites' parasitizing at patients with the diagnosis of rosacea.

According to the objectives of the study, patients were assigned depending on the availability of mites and severity of the disease (Table 4, 5). As a result of the analysis, the connection between the severity of the diseases of acne and rosacea and the presence of mites was established.

**Table 4. Distribution of patients of group I and II according to the severity of acne.**

Severity of disease	Group I	Group II	Total
I degree Comedonal acne	2* 2.6%	20* 25.6%	22 28.2%
II degree Mild and moderate papulopustules acne	8* 10.3%	16* 20.5%	24 30.8%
III degree Severe papulopustules acne, moderate nodular acne	18* 23%	4* 5.2%	10 12.8%
IV degree Severe nodular acne, acne conglobate	10* 12.8%	-	78 100%
Total	38 48.7%	40 51.3%	78 100%

Note: \* -  $p < 0.0001$

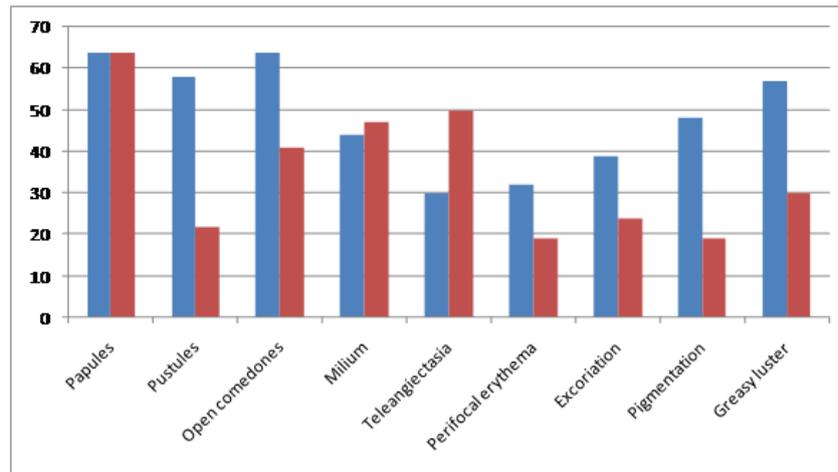
**Table 5. Distribution of patients of group I and II according to the severity of rosacea.**

Severity of disease	Group I	Group II	Total
I degree Erythematotelangiectatic subtype	6* 12%	11* 22%	17 34%
II degree Papulopustules subtype	10 20%	10 20%	20 40%
III degree Phymatous subtype	6* 12%	3* 6%	9 18%
IV degree Ocular subtype	4* 8%	-	4 8%
Total	26 52%	24 48%	50 100%

Note: \* -  $p = 0.005$

As seen from the table 4 and 5 Demodex mites were more often found in patients with more severe clinical forms of acne (papulopustules, nodular moderate, severe nodular acne, acne conglobate) and rosacea (phymatous subtype).

For the objectivity of the study, patients were assigned according to clinical manifestations of primary and secondary elements (papules, pustules, open comedones, milium, telangiectasia, perifocal erythema, excoriation, pigmentation, greasy luster). Degree of incidence of various primary and secondary morphological elements is presented on the histogram 1 (the group I – blue color, the group II – red).



**Picture 1. Degree of incidence of primary and secondary morphological elements at patients of groups I and II (group I – blue color, group II – red).**

Histogram once again clearly confirms that more severe cases with presence of deep papulopustules elements, nodules, total skin erythema, greasy luster prevailed at patients from group I ( $p < 0.0045$ ) having Demodex mites. Patients from group II had papules, pustules, a small amount of telangiectasia and pigmentation. Thus, with high degree of confidence it is possible to claim that mites of genus Demodex complicate the course of papulopustules rashes on face with prevalence of the acute inflammatory and productive elements.

Further study allowed to establish the dependence of clinical disease on the type of a mite. For this purpose, the patients were divided according to the type of a mite and clinical forms of the disease (Table 6).

**Table 6. Distribution of patients according to the type of Demodex mite and the severity of the disease.**

Severity of disease (acne, rosacea)	D.f.longus	D.f.brevis	Combination D.f.longus and D.f.brevis	Total
I degree comedonal acne, erythematotelangiectatic subtype rosacea	6* 9.4%	2 3.1%	-	8 12.5%
II degree mild and moderate papulopustules	12* 18.6%	6 9.4%	-	18 28.0%

acne, papulopustules subtype rosacea				
III degree severe papulopustules acne, moderate nodular acne, phymatous subtype rosacea	20* 31.3%	-	4 6.3%	24 37.6%
IV degree severe nodular acne, acne conglobate, ocular subtype rosacea	14* 21.9%	-	-	14 21.9%
Total	52 81.2%	8 12.5%	4 6.3	64 100%

Note: \* - p=0.0045

As seen from the presented table (table 6), mites *Demodex folliculorum longus* were often detected in more severe forms of the disease (II-IV degree) (p = 0.005). *Demodex folliculorum brevis* was detected in the milder forms (I-II degree). Parasitizing of two species of mites was found in the third degree of acne (severe papulopustules acne, moderate nodular acne) (p = 0.0001).

This fact can be explained most likely by the fact that *Demodex folliculorum longus* presents in hair follicles mostly in groups. *Demodex folliculorum brevis* parasites in sebaceous and meibomian glands and is found in the singular, making it difficult to diagnose, since it dwells in the deeper parts of the glands. [7] Besides, *Demodex folliculorum longus* is a larger mite (≈0.3-0.4 mm) in comparison with *Demodex folliculorum brevis* (≈0.186 mm), which facilitates diagnostics.

Further research consisted in the evaluation of morphofunctional characteristics of facial skin obtained with the use of digital video camera “Aramo SG”. The data obtained in the survey, presented in Table 7.

**Table 7. Morphofunctional characteristics of skin obtained with the use of digital video camera “Aramo SG”**

	Group I	Group II	Group III
pH	7.5±0.82 ↑	6.0±0.9 ↑	5.5±0.7
moisture	32.7±7.84 ↓	34.5±4.2 ↓	45.6±5.1
oiliness U-zone	18.2±18.7 ↑	15.3±18.0 ↑	8.8±10.4
oiliness T-zone	38.25±26.1 ↑	27.5±21.7 ↑	22.9±16.5
pigmentation	44.6±29.07 ↑	41.7±23.8 ↑	29.5±22.6
pore size	27.4±16.0 ↑	24.0±17.4 ↑	20.7±9.4
elasticity	59.5±16.3 ↓	63.7±16.3 ↓	69.3±13.9
smoothness	46.8±9.1 ↑	45.2±8.4 ↑	38.7±7.1
depth of wrinkles	34.7±16.1 ↑	34.7±13.1 ↑	19.4±6.4

From the table it is visible that healthy volunteers of group III in comparison with groups I and II have a reliable difference between indicators of skin oiliness in U and T-zones (p=0.0001). Thus, patients with acne and rosacea have more oily skin, than healthy people.

The shift in pH in patients of group I to the alkaline side suggests reducing the protective properties of the skin that is most likely a favorable condition for infection with Demodex mites.

Further analysis revealed that patients of groups I and II have significantly higher parameters of skin oiliness in U- and T-zones (p=0.0001), pigmentation (p=0.0005), depth of wrinkles (p=0.0045), pore size (p=0.0045) and lower skin moisture (p=0.0001) in comparison with healthy people. When comparing indicators of groups I and II, the difference is set statistically significant towards deterioration of moisture index, oiliness, pigmentation, pore size and skin elasticity (p=0.0045) at patients from group I. Therefore, subject to the existence of mites, patients have statistically significant change of functional characteristics of skin. The explanation of this fact is that patients in this group are dominated by more severe forms of the disease, which is undoubtedly related to the functions of facial skin.

The duration of acne and rosacea diseases at patients of groups I and II was evaluated at three periods: <1 year, 1-5 years, 5-10 years (Table 8). To study the impact of the mite on the disease, we carried out a comparative assessment of the disease duration at patients from groups I and II (tab. 8).

**Table 8. Duration of the disease at patients with acne and rosacea depending on the presence of Demodex mites.**

	Disease duration			Total
	<1 year	1-5 years	5-10 years	
Group I 64 (50%)	9 (7%)	24 (18.75%)	31* (24.2%)	64 (50%)
Group II 64 (50%)	32 (25%)	21 (16.4%)	11* (8.6%)	64 (50%)
Total	41 (32%)	45 (35.2%)	42 (32.8%)	128 (100%)

Note: \* - p=0.0045

As it can be seen from table 8, at patients with acne and rosacea the presence of Demodex mites significantly increases the duration of the pathological process. Among the people of the first group, there were patients with the predominant disease duration of more than 5 years, in the second group there were patients with disease duration of 5 years or less.

In addition, morphofunctional skin characteristics depending on the duration of the disease were evaluated (Table 9).

**Table 9. Morphofunctional characteristics of patients with acne and rosacea depending on the duration of the disease.**

Index	Disease duration					
	I group			II group		
	<1 year	1-5 years	5-10 years	<1 year	1-5 years	5-10 years
pH	7.2±0.3	7.4±0.43	7.5±0.82	5.7±0.7	6.2±0.7	7.0±0.9
moisture	33±5.93	32.7±5.97	32.7±7.84	37±2.6	35±3.9	34.5±4.2
oiliness U-zone	13.7±7.9	15.4±10.4	18.2±18.7	14.7±11.7	15.3±14.3	15.3±18.0
oiliness T-zone	36.3±18.4	38.0±21.3	38.25±26.1	27.5±16.8	27.3±17.6	27.5±21.7
pigmentation	37.3±20.09	40.1±24.3	44.6±29.07	36.8±16.4	42.0±15.9	41.7±23.8
pore size	25.5±14.3	25.9±15.8	26.4±16.0	19.8±11.9	24.0±13.2	24.0±17.4
elasticity	64.0±13.9	60.2±14.1	59.5±16.3	65.8±12.3	62.4±14.8	63.7±16.3
smoothness	46.0±7.8	46.0±8.7	46.8±9.1	41.8±5.9	42.0±6.3	45.2±8.4
depth of wrinkles	33.9±14.8	34.5±15.7	34.7±16.1	30.4±7.9	31.2±10.2	34.7±13.1

Although reliable distinctions of the received indicators were not found, but as it can be seen from table 8, indicators of morphofunctional skin characteristics gradually change for the worse, depending on the presence of Demodex mites and disease duration.

### Argument and conclusions

As a result of our research, it is possible to note that in the structure of diagnoses of acne and rosacea, acne is registered more often. Appealability of women concerning diseases of acne and rosacea is approximately equal; at men the diagnosis of acne prevails.

Demodex folliculorum longus is found at patients with acnes and rosacea more often, thus causing severe forms of diseases. This fact can be explained most likely by the fact that Demodex folliculorum longus presents in hair follicles mostly in groups. Demodex folliculorum brevis parasites in sebaceous and meibomian glands and is found in the singular, making it difficult to diagnose, since it dwells in the deeper parts of the glands [7]. Besides, Demodex folliculorum longus is a larger mite in comparison with Demodex folliculorum brevis, which facilitates diagnostics.

When comparing the primary and secondary morphological elements the statistical difference between groups I and II was obtained. Such abnormal formations as deep papulopustules elements, nodules, total facial skin erythema, greasy

luster are more pronounced at patients from group I, which once again confirms that the presence of Demodex mites is a persistent development of inflammatory elements and the maintenance of the pathological process on the facial skin. A significant increase in the duration of the pathological process at patients with acne and rosacea with the presence of Demodex mites is further evidence that the mites can cause resistant forms of the disease.

When comparing morphofunctional characteristics of facial skin, obtained with the help of digital video camera "Aramo SG", statistical differences were revealed. The shift in pH in patients of group I to the alkaline side suggests reducing the protective properties of the skin that is most likely a favorable condition for infection with Demodex mites. Having mites in patients, there is a statistically significant change in morphofunctional characteristics of skin to deterioration of moisture index, oiliness, pigmentation, pore size and skin elasticity in comparison with patients uninfected with mites and healthy people. The explanation of this fact is that patients in this group are dominated by more severe forms of the disease, which is undoubtedly related to the functions of skin. In the course of the research, it was noted that morphofunctional characteristics of skin become worse with the increase of the disease duration.

Thus, the presence of Demodex mites complicates the course of such diseases as acne and rosacea, favours the development of inflammatory process, which confirms the need for timely and compulsory diagnostics. Changes of morphofunctional characteristics of facial skin in patients with acne and rosacea, complicated with demodicosis suggests the correlation of severe clinical forms of acne and rosacea with changes in functional characteristics of the skin.

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