

# Clinical and Laboratory Indicators of Candido-Endocrine Syndrome in Patients with Alopecia Areata.

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## KEYWORDS

alopecia areata,  
fungi of the  
genus Candida,  
thyroid  
hormones,  
vitamin D,  
candido-  
endocrine  
syndrome.

## ABSTRACT:

Recently, the study of comorbid conditions in patients with alopecia areata (AA) has become relevant, as it directly affects the clinical course and prognosis of the disease, the choice of treatment tactics, and the quality of life of patients. The study of comorbid conditions in patients with alopecia is a priority area for determining the tactics of ongoing therapy.

**Materials and Methods:** 112 patients with alopecia areata aged from 1 to 52 years, who received inpatient treatment at the RSSPMC Dermatovenereology and Cosmetology, Ministry of Health of the Republic of Uzbekistan, were examined. Among them, 67 (59.8%) were female and 45 (40.17%) were male. Clinically, among the 112 patients, focal alopecia was diagnosed in 62 (55.4%), subtotal in 19 (16.9%), total in 18 (16.1%), and universal in 13 (11.7%). Clinical, mycological, immunological, instrumental (trichoscopy), and statistical research methods were used for all patients.

**Research Results:** Mycological studies of biological substrates in 112 patients with alopecia areata showed the presence of fungi of the genus Candida in 97 patients, accounting for 86.6% of cases. IHLA studies of thyroid hormones showed an increase in the concentration of free triiodothyronine T3 by 1.6 times, thyroxine T4 by 1.1 times, and antibodies to thyroid peroxidase (antiTPO) by 15.5 times, with an average of  $80.4 \pm 46.6$  IU/l, indicating the development of hypothyroidism in patients with alopecia areata ( $P < 0.05$ ). Vitamin D studies revealed a significant decrease in concentration by 1.6 times compared to the control group.

**Conclusion:** Patients with alopecia areata develop a component of candido-endocrine syndrome, characterized by intestinal dysbiosis caused by fungi of the genus Candida and a dysfunction of the thyroid gland - autoimmune hypothyroidism, accompanied by vitamin D deficiency.

## 1. Introduction

Alopecia areata is a chronic genetically determined inflammatory autoimmune disease that affects hair follicles, resulting in persistent or temporary non-scarring hair loss [1,4-6]. Among dermatological diseases, AA occurs with a frequency of 0.7-3.8%, and the prevalence in the population is 1:1000, with a risk of developing the disease in healthy individuals of 1.7%, equally affecting men and women, with a peak incidence at a young age of 15 to 40 years [1,2,10].

In recent times, the study of comorbid conditions in patients with alopecia areata (AA) has become relevant, as it directly influences the clinical course and prognosis of the disease, the choice of treatment tactics, and the quality of life of patients. Comorbid conditions may appear before the development of AA, during exacerbation, or remission. Patients with AA are prone to a higher incidence of immune-inflammatory pathology, which is explained by the common immunological mechanisms of these diseases [Bertolini M, McElwee K, Gilhar A, et al 2020].

In the manifestation of the disease, immunological and genetic predisposition play an important role, which at different stages of the patient's life is realized through several triggering mechanisms, such as neurological stress, metabolic disorders, and adverse environmental conditions [3,5,8].

Recently, particular attention has been drawn to the role of conditionally pathogenic microorganisms of the genus *Candida* in the clinical course of non-fungal diseases [ 2,3,5 ]. Studies have shown that the development of dysbiosis is associated with the occupation of the ecological niche of the body by pathogenic and conditionally pathogenic microorganisms, which adhere to the surface of the intestinal epithelium through special adhesion factors, proliferate, release toxins, and gradually penetrate into sections of the small intestine, leading to microbial contamination characterized by a range of pathological processes [3,4,6,11,12].

The aim of our research was to assess the state of the mycobiota of biological substrates in the body, taking into account the endocrine status of the thyroid gland and vitamin D in patients with alopecia areata.

## 2. Materials and Methods:

Under our observation were 112 patients with alopecia areata aged from 1 to 52 years, who received inpatient treatment at the clinic of the RSSPMC Dermatovenereology and Cosmetology, Ministry of Health of the Republic of Uzbekistan. Among them, 67 (59.8%) were female and 45 (40.17%) were male. Clinically, among the 112 patients, focal alopecia was diagnosed in 62 (55.4%), subtotal in 19 (16.9%), total in 18 (16.1%), and universal in 13 (11.7%).

All patients underwent clinical (trichoscopy), mycological, immunological, and statistical research methods. Mycological studies were conducted on biological substrates of the body (oral mucosa, skin, and intestines (stool) using cultural methods on Sabouraud's medium and chromogenic media. Thyroid hormones T3, T4, TSH, AntiTPO, and vitamin D were determined by immunochemiluminescent analysis (IHLA) on a closed analyzer Autolumo A1000 and reagents from Autobio (China). Blood serum from patients, obtained following sample requirements (fasting from 9 to 11 a.m.), was isolated by centrifugation at 1500 rpm

for 10 minutes, then transferred to cuvettes and placed in a special compartment for samples in the analyzer. The reaction was conducted after preliminary calibration of the reagent and construction of the curve, which is stored in the memory of the analyzer. The control group consisted of 31 healthy individuals of corresponding age.

All patients were consulted by related specialists: a therapist, an endocrinologist, and an infectious disease specialist.

Statistical studies included methods of variation analysis using the Student's t-test and the Excel-2010 software package for statistical processing. Mean values are presented as M+m (mean value and standard error). Correlation analysis was conducted using Pearson's method.

### 3. Research Results:

Mycological studies of biological substrates in 112 patients with alopecia areata showed the presence of fungi of the genus *Candida* in 97 patients, accounting for 86.6% of cases. Fungi of the genus *Candida* were most frequently found in intestinal biosubstrates, accounting for 75.3%. Among the pathogens of candidal infection, *Candida krusei* was most frequently cultivated in 64 (65.9%) patients, *Candida albicans* in 18 (18.5%), and *Candida* spp. in 15, accounting for 15.5% respectively. It should be noted that fungi of the genus *Candida* were most frequently isolated in the progressive stage (86.9%) with increased colonization of more than 103 CFU/g, indicating the development of intestinal dysbiosis caused by fungi of the genus *Candida*.

Table 1. Characteristics of virulence and degree of colonization of fungi of the genus *Candida* in biological substrates of patients with alopecia areata (CFU).

	Oral mucosa yeast-like fungi	Oral mucosa budding fungi	< 103 CFU/g	>103 CFU/g
Alopecia areata n=49				
areata n=19				
Total areata n=18				
Universal areata n=10				
n=97				

Depending on the clinical form, fungi of the genus *Candida* were most frequently isolated in patients with focal alopecia - 50.5% (49 patients), while in patients with subtotal and total

forms, the isolation frequency was 19.6% and 18.5%, and in patients with universal alopecia - 10.3% respectively.

IHLA studies of thyroid hormones showed an increase in the concentration of free triiodothyronine T3 by 1.6 times, with an average of  $17.9 \pm 0.7$  pmol/l, and the level of thyroxine also exceeded the norm by 1.1 times ( $17.9 \pm 0.7$  pmol/l). The TSH level in patients averaged  $3.1 \pm 0.4$  mIU/ml and tended to increase, but was not statistically significant ( $P > 0.05$ ). The level of antibodies to thyroid peroxidase (AntiTPO) significantly increased by 15.5 times and averaged  $80.4 \pm 46.6$  IU/l, and was statistically significant. ( $P < 0,05$ ).

Table 2. Thyroid hormones and vitamin D levels in patients with alopecia areata (M+m).

Group	Free T3 (pmol/l)	Free T4 (pmol/l)	TSH (mIU/ml)	AntiTPO (IU/l)	Vitamin D (ng/ml)
Control n=33	3,5+ 0,03	15,8+ 0,14	2,01+ 0,02	5,2+ 0,08	35,2+0,6
patients n=31	5,7+ 0,3*	17,9+ 0,7*	3,1+0,4	80,4+ 46,6*	22,1+ 1,8*

\*Note: \* Statistically significant compared to the control group.  $P < 0.05$

High concentrations of thyroid hormones indicate dysfunction and the development of hypothyroidism in patients with alopecia areata. The obtained data indicate the development of the first component of the candido-endocrine syndrome (CES), associated with a decrease in the adequacy of cellular and humoral responses, which contributes to the reduction of the barrier function of epithelial cells and suppression of the bactericidal activity of neutrophils [Karaev Z.O., Lebedeva T.N. 2006] [7].

IHLA studies of vitamin D showed a significant decrease in concentration by 1.6 times compared to the control group and averaged  $22.1 \pm 1.8$  ng/ml against  $35.2 \pm 0.6$  ng/ml ( $P < 0.05$ ), indicating a deficiency of this vitamin in patients with alopecia areata.

Correlation analysis of thyroid hormone levels showed significant positive correlations of triiodothyronine T3 with *C. albicans* ( $r=+0.8$ ), *Candida* spp. ( $r=+0.57$ ), while with *C. krusei*, it had a negative correlation ( $r=-0.34$ ) ( $P < 0.05$ ). Thyroxine (T4) and TSH levels also had statistically significant correlations with yeast-like fungi of the genus *Candida*. AntiTPO had a significant negative correlation with *C. albicans* ( $r=-0.36$ ).

Interesting data were shown by the correlation indicators of vitamin D with pathogenic fungi *C. albicans* ( $r = 0.44$ ) and *C. krusei* ( $r = -0.47$ ) ( $P < 0.05$ ). As shown in the figure, the level of vitamin D had a direct correlation with thyroid hormones T3 ( $r=+0.7$ ), T4 ( $r=+0.33$ ), TSH ( $r=+0.5$ ), and AntiTPO ( $r= +0.61$ ), and these were statistically significant ( $P < 0.05$ ).

It should be noted that vitamin D is an important regulator of phosphate and calcium metabolism and also possesses significant biological activity, modulating immune processes in

the mucosa and maintaining the integrity of the intestinal barrier [Khavkin A.I., Loshkova E.V., Doroshenko I.V. 2023].

In our opinion, the decrease in vitamin D levels contributes to reduced local immunity of the mucous membranes, increased adhesion, proliferation, and leads to an increase in the degree of colonization of yeast-like fungi in the biological substrates of the body, resulting in intestinal dysbiosis caused by fungi of the genus *Candida* - invasive candidiasis of the intestine in patients with alopecia areata.

The clinical course of alopecia with thyroid dysfunctions was characterized by drowsiness, headaches, dry skin, and constipation with alternating diarrhea, and bloating.

An analysis of the obtained results indicates a disruption in the balance of three interconnected systems - immune, endocrine, and biocenosis systems, leading to the development of the first component of the candido-endocrine syndrome (CES) in patients with alopecia areata.

#### **4. Conclusion:**

Patients with alopecia areata develop a component of candido-endocrine syndrome, characterized by intestinal dysbiosis caused by fungi of the genus *Candida* and dysfunction of the thyroid gland - autoimmune hypothyroidism, accompanied by vitamin D deficiency.

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