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STUDY OF THE MICROFLORA AND PH OF THE SKIN ENVIRONMENT IN PATIENTS WITH ZOOANTHROPONOTIC TRICHOPHYTOSIS OF THE PUBIC REGION.

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Abstract:
The article describes the Study of the microflora and pH of the skin environment in patients with zooanthroponotic trichophytosis.

Keywords: Zoo anthroponotic trichophytes and features of microbiology.

THE RELEVANCE OF THE WORK. Serious ecological changes taking place on the planet in recent decades could not but affect the state of microecology and immunoreactivity of modern man. This is one of the global reasons for the increase in the number of fungal diseases. In addition, outbreaks of zooanthroponotic dermatomycosis are also caused by a change in the properties of the pathogens themselves - the emergence of new strains of fungi, an increase in their pathogenicity and contagiousness, a violation of the structure and boundaries of nosoareals. It should be noted that today in Uzbekistan, favus has been eliminated almost everywhere, and the incidence of anthroponotic dermatomycosis has been sharply reduced. At the same time, zooanthroponotic trichophytosis has a wide and widespread distribution throughout the territory of the Republic.

Zooanthroponotic trichophytosis is a natural focal infection, the epidemic features and the frequency of outbreaks of which depend on geographical, environmental and a number of other factors **[1].** In modern conditions, trichophytosis in the Republic of Uzbekistan has a number of characteristic features: the species composition of pathogens has changed (the main pathogen is trichophyton faviform, whose share in the total structure of trichophytosis pathogens is 80-85%). The age composition of patients also changed (at the end of the 90s, 86% of patients with trichophytosis were children of preschool and primary school age, and by 2003, 61% of patients were over 15 years old), atypical localizations of trichophytosis lesions appeared, including the pubic area, genitals, buttocks **[1,3].**

Since 2002, registration of patients with zooanthroponotic trichophytosis with localization of the process in the genital area has begun. In all regions of the Republic, cases of registration of zooanthroponotic trichophytosis among the adult population with a predominant lesion of the pubic and inguinal region have become more frequent, and the vast majority of patients indicate the sexual route of infection. There is a direct relationship between the frequency of infection with sexually transmitted infections (STIs) and the occurrence of pubic trichophytosis. Given the steady increase in the number of STIs and the complications they cause, we should expect an outbreak of morbidity and pubic trichophytosis.

In this connection, knowledge of the distribution features, conditions of clinical manifestation and characteristics of the pathogen, the development of adequate methods of treatment will allow influencing the main links of the epidemic process.

The degree of knowledge of the problem. Despite ongoing measures to prevent fungal diseases of the skin around the world, there is an increase in infection with this infection. Thus, in the Republic of Kazakhstan, the incidence of fungal infections of the skin in recent years has increased from 3756 cases in 1999 to 5401 cases in 2003 with a predominant lesion of the urban (2412 people) and male (3310 people) population **[1].** The study of the incidence of zooanthroponotic trichophytosis in different regions of the CIS made it possible to find out that against the background of a significant decrease in the total number of patients with fungal diseases, it remains at a fairly high level, amounting to 95% in rural areas. **[1,2]**

In the Republic of Uzbekistan, there is also a widespread increase in the incidence of zooanthroponotic trichophytosis. Since a dry, hot climate prevails on the territory of Uzbekistan, the highest incidence of trichophytosis occurs in the summer period of the year. This is due to the fact that skin moist from excess sweat, often macerated stratum corneum of the epidermis, a shift in the pH of the skin and sweat towards an alkaline reaction contributes to the penetration of pathogens into the

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skin and the development of fungal infections in it **[1,5].**

Currently, zooanthroponotic trichophytosis is characterized by a pronounced clinical diversity. The pathogenesis of the development of clinical forms of mycosis can be influenced by the characteristics of the nature and intensity of the body's immune response to the introduction of the pathogen, the degree of their virulence and pathogenicity, as well as disorders of the immunogenesis system. Numerous clinical studies have shown that at the present stage of development of mycology, a change in the spectrum of mycosis pathogens, the development of fungal-bacterial associations entail not only a change in the characteristic clinical manifestations of diseases, but also, importantly, the development of resistance to the antifungal agents used **[1,2].** However, a comprehensive study of the most significant factors influencing the development of pubic trichophytosis, the state of the body's immune reactivity, the study of the nature of the accompanying microflora and skin pH in combination with various clinical forms of trichophytosis in Uzbekistan was not carried out.

It is known that against the background of an imbalance in the immune system and a decrease in nonspecific protective factors of the body, the microbial landscape of the body as a whole, and in particular on the skin, changes. In the foci of zooanthroponotic trichophytosis, often associated microflora complicates the mycotic process, which changes the clinical course of dermatosis. Moreover, the role of secondary microflora in the foci of trichophytosis and the mechanism of its influence on the clinic of the disease have not been studied enough. In addition, the pH environment of the skin plays an important role in the development of this pathology, which contributes to the creation of favorable or unfavorable conditions for the development of various microorganisms and the development of their dysbiosis.

PURPOSE OF THE STUDY. To study the state of the accompanying microflora and the pH of the skin environment in the lesions in patients with pubic trichophytosis.

MATERIAL AND METHODS. The state of the microflora and pH of the skin environment with zooanthroponotic trichophytosis of the pubic area was studied by us in 84 patients in comparison with the data of 20 practically healthy individuals (control group). Among the examined patients with zooanthroponotic trichophytosis of the pubic region, 20 patients had a superficial-spotted form, 22 had an infiltrative form, and 42 had an infiltrative-suppurative form of the disease.

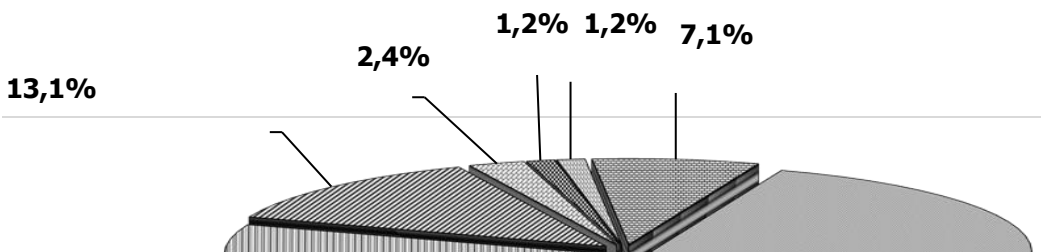
In the study of skin washings from the pubic area in the control group, the content of microbes ranged from 2.0 to 5.0 CFU/cm². In this group, microbiological detection of various microbes was observed in 4 out of 20 individuals. As can be seen from Table 1, the microbial landscape of the skin of the pubic region in apparently healthy individuals includes Staphylococcus epidermidis, aureus, and Candida.

Table 1.

The state of the microflora of the pubic area in the control group (n=20).

Type of microflora	ber of microbes per 1 cm ² of skin (CFU / cm ²)
Staphylococcus epidermidis	5,0 ± 0,3
Staphylococcus aureus	2,0 ± 0,2
Streptococcus haemolyticus	-
Clostridium perfringens	-
Candida	3,0± 0,5
Klebsiella	-
Enterococcus	-

The study of the state of the microflora of the skin of the pubic region in 84 patients with zooanthroponotic trichophytosis showed that the cultural study of skin washings revealed different microflora from the lesion (Fig. 1).



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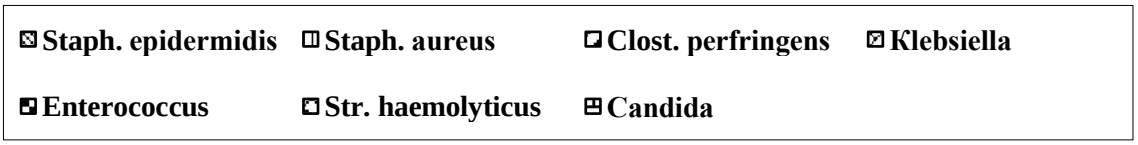

Fig. 1. The state of skin microflora in patients with zooanthroponotic trichophytosis of the pubic area

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Among the identified microorganisms from the lesions of trichophytosis, Staphylococcus epidermidis was sown in 36 (42.9%), Staphylococcus aureus - in 27 (32.1%), Clostridium perfringens - in 11 (13.1%), Candida - in 6 (7, 1%), Klebsiella - in 2 (2.4%) cases, and Enterococcus and Streptococcus haemolyticu - in 1 (2.4%) case.

Table 2.

The state of the microflora of the pubic area in the control group (n=84).

Type of microflora	Total number of microbes per 1 cm2 of skin (CFU/cm2)
Staphylococcus epidermidis	109,0 ± 5,2
Staphylococcus aureus	97,0 ± 4,3
Streptococcus haemolyticus	14,0 ± 1,2
Clostridium perfringens	22,3 ± 2,3
Candida	4,0 ± 0,2
Klebsiella	10,7 ± 4,2
Enterococcus	8,1 ± 0,4

Along with this, when examining the microflora in the lesions of patients with trichophytosis of the pubic region, changes were observed both in qualitative and quantitative characteristics in relation to the control group (Table 2). As can be seen from the table, in the focus of trichophytosis of the pubic region, there is a qualitative predominance of microflora (Streptococcus haemolyticus, Clostridium perfringens, Klebsiella, Enterococcus), which is not a normoflora in the microbial landscape of the skin of healthy individuals. In a place with this, their number increases, for example; St. epidermidis in the control group was 5.0 ± 0.3 CFU/cm², and in the focus of trichophytosis of the pubic region, this figure increased to 109.0 ± 5.2 CFU/cm² ($p<0.001$), an analogous picture was observed with St. aureus 2.0 ± 0.2 and 97.0 ± 4.3 CFU/cm², respectively ($p<0.001$). In the quantitative indicator of fungi of the genus Candida, there was a slight upward trend (3.0 ± 0.5 and 4.0 ± 0.2 CFU / cm², respectively), perhaps small quantitative fluctuations are associated with the antagonistic properties of fungi of the genus Candida and Trichophyton, manifested in growth suppression fungi of the genus Candida last **[3].**

Considering the revealed imbalance in the microbiological landscape of the skin of the pubic area in case of trichophyton damage, it seemed very interesting to study the state of the microflora in the lesions depending on the clinical forms of zooanthroponotic trichophytosis of the pubic area. Studies conducted in 20 patients with a superficially spotty form of zooanthroponous trichophytosis of the pubic region showed that when sowing skin washings of Staphylococcus epidermidis was sown in 9 (45.0%) cases, Staphylococcus aureus - in 4 (20.0%), Clostridium perfringens - in 2 (10.0%) and Candida - in 5 (25.0%) cases (Fig. 2).

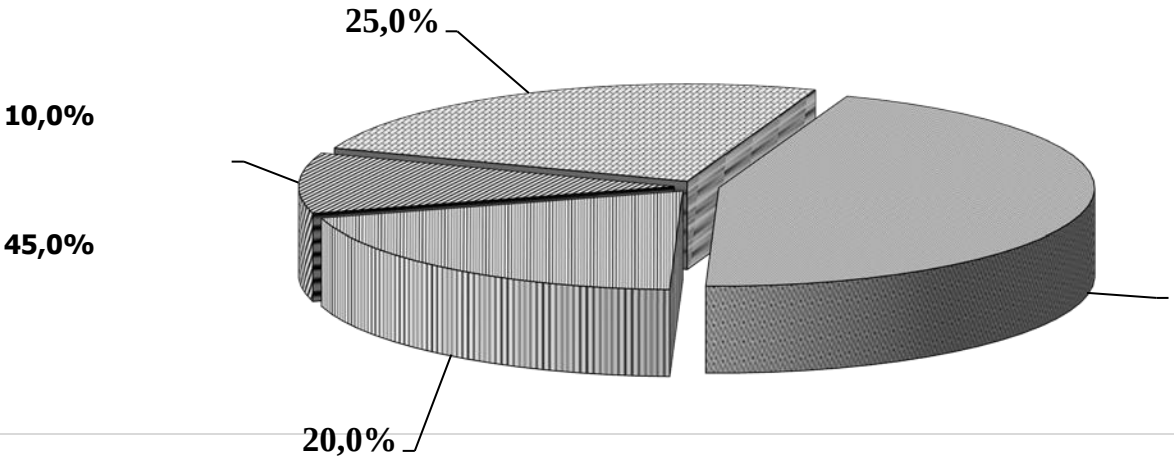

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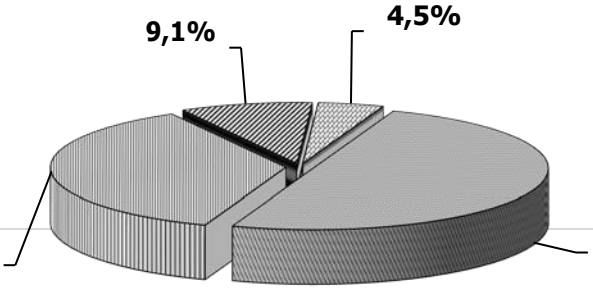
Fig. 2. The state of microflora in patients with superficially spotted form of zooanthroponous trichophytosis of the pubic region

The study of the microbiological landscape in case of damage to the surface-spotted form of zooanthroponous trichophytosis of the pubic region showed a quantitative increase in St. epidermidis compared with the control group 5.0 ± 0.3 CFU/cm² versus 19.0 ± 4.8 CFU/cm², St. aureus 2.0 ± 0.2 CFU/cm² and 14.0 ± 6.4 CFU/cm², respectively (Table 3).

Table 3. **The state of the microflora in the focus of zooanthroponotic trichophytosis of the pubic region depending on the clinical forms of the disease**

Type of microflora	The number of microbes per 1 cm ² of skin (CFU / cm ²)		
	Superficial spotted form (n=20)	ltrative form (n=22)	Infiltrative suppurative form (n=42)
Staphylococcus epidermidis	19,0 ± 4,8	35,4± 7,1	54,6 ± 3,5
Staphylococcus aureus	14,0 ± 6,4	32,0 ± 9,2	51,0 ± 6,0
Streptococcus haemolyticus	-	-	14,0
Clostridium perfringens	4,3 ± 3,0	6,4 ± 4,4	11,6 ± 3,7
Candida	2,0 ± 0,8	2,0	-
Klebsiella	-	-	6,0
Enterococcus	-	-	8,1 ± 5,7

The study of microflora inoculation in patients with infiltrative form of zooanthroponous trichophytosis showed that among patients with this clinical form of the disease, Staphylococcus epidermidis was found in 11 (50.0%), Staphylococcus aureus - in 8 (36.4%), Clostridium perfringens - in 2 (9 .1%) and Candida - in 1 (4.5%) cases (Fig. 3.).



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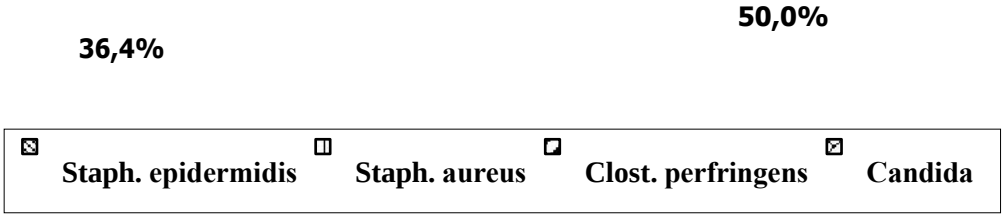

Fig.3. State of microflora in patients with infiltrative form of zooanthroponic trichophytosis of the pubic area

The study of the microbiological landscape with the defeat of the infiltrative form of zooanthroponous trichophytosis of the pubic region revealed both a qualitative and quantitative increase in various types of microorganisms. In quantitative terms, St. epidermidis in the infiltrative form of the disease was 35.4± 7.1 CFU/cm², which prevailed in comparison with the control group 5.0 ± 0.3 CFU / cm ², and in relation (19.0 ± 4.8 CFU / cm ²) to indicators for the surface-spotted form of zooanthroponotic trichophytosis. A similar pattern of quantitative increase was observed for Staphylococcus aureus, which amounted to 32.0 ± 9.2 CFU/cm². On the contrary, in the infiltrative form of the disease, a decrease in the inoculation of fungi of the genus Candida was noted, which was detected in this group only in one case. It is especially important to note that with a change in the form of zooanthroponotic trichophytosis of the pubic region, there is a qualitative change in the composition of microbes in the lesion, which is expressed by the detection of such a microorganism as Clostridium perfringens, which was identified in our studies. As is known, these microorganisms are extremely sensitive to drying and do not multiply on healthy skin, however, according to the scientific literature, a person can be its carrier on the skin in 40% of cases **[4].** This microorganism is able to infect wound surfaces and cause a destructive abscess, where the products of its metabolism can cause toxemia, which is probably what characterizes the violations of the general condition of patients (weakness, fever, etc.) with deep infiltrative-suppurative forms of the disease.

Next, we studied the microbiological state of the skin of the pubic region with a deep (infiltrative-suppurative) form of zooanthroponotic trichophytosis. The results of cultural studies showed an increase in the qualitative indicator with the seeding of lesions with new types of microbes such as Klebsiella in 2 (4.8%) cases, as well as Enterococcus and Streptococcus haemolyticus in 1 (4.8%) case (Fig. 3.9).

Along with them, the quantitative ratio of Staphylococcus epidermidis increased - 54.6 ± 3.5 CFU / cm ², Staphylococcus aureus - 51.0 ± 6.0 CFU / cm ², Clostridium perfringens - 11.6 ± 3.7 CFU / cm ² in the lesion, compared with the superficial - spotted and infiltrative forms of the disease.

The study of microflora inoculation in patients with infiltrative-suppurative form of zooanthroponous trichophytosis of the pubic region showed that among patients Staphylococcus epidermidis was found in 16 (38.0%), Staphylococcus aureus - in 15 (35.7%), Clostridium perfringens - in 7 (16, 7%), Klebsiella - in 2 (4.8%) cases, and Enterococcus and Streptococcus haemolyticus in 1 (2.4%) case (Fig. 4). And fungi of the genus Candida were not detected in this group of patients, which is consistent with the latest literature data on antagonistic properties with fungi of the genus Trichophyton, which, in quantitative terms, becomes larger in the lesions of the infiltrative and infiltrative-suppurative form of zooanthroponic trichophytosis of the pubic region.

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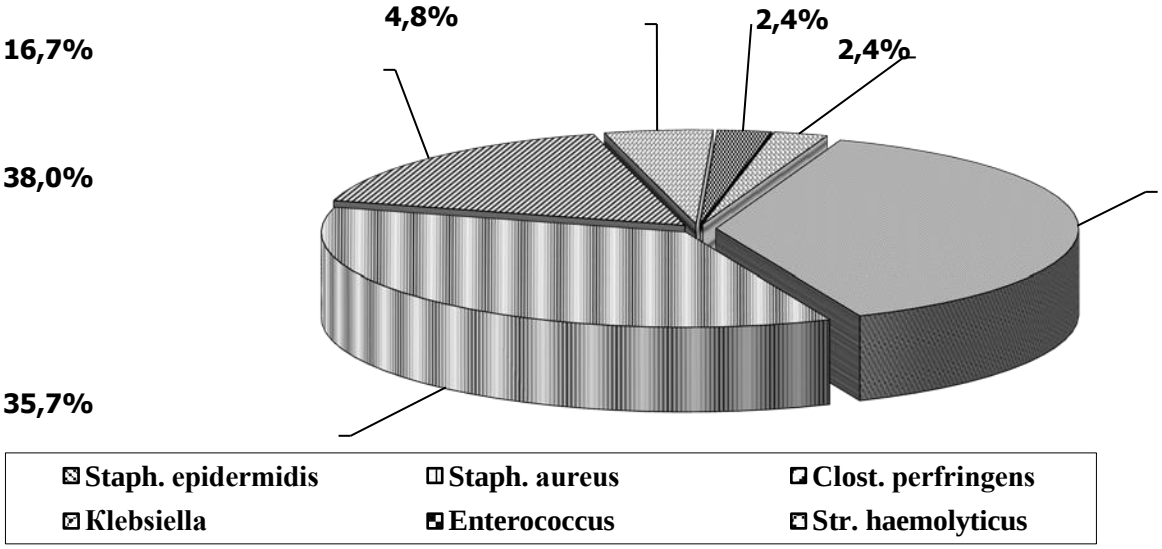

Fig. 4. The state of the microflora in patients with infiltrative-suppurative form of zooanthroponotic trichophytosis of the pubic region

The results of the study showed that in all clinical forms of pubic trichophytosis, there is a combination of concomitant microflora with the causative agent of the underlying disease, which is characterized by both a qualitative and quantitative increase in it in the lesion in direct proportion to the clinical forms of the disease.

It is especially important to note that with the transition to more severe forms of the disease, there is a large contamination of the lesions with various types of microorganisms, especially the detection of anaerobic species such as Clostridium, Klebsiella, which are unsuitable for reproduction on the surface of the skin. However, given the fact that the dermis actively metabolizes oxygen diffusing through the epidermis and taking into account the characteristics of the pubic and perigenital zones, such as relative humidity (over 90%) and the effect of occlusion, which leads to an increase in the pH of the environment in these areas of the skin, various microorganisms (aerobes and anaerobes) find favorable conditions for survival and generation. Identical conditions (humidity 97%) are favorable for growth and reproduction of trichophyton dermatomycetes **[4,5].** Optimal conditions, the symbiosis of these microorganisms, violations of the functions of the immune system, which cannot adequately control and fight secondary infections, are probably the main factors contributing to the development of atypical localization of trichophytosis and aggravation of the course of mycotic dermatosis with a deeper lesion of the skin and the development of an infiltrative-purulent process with trichophytosis of the pubic region.

In this connection, in further studies, we studied the pH level of the skin environment in patients with zooanthroponotic trichophytosis of the pubic region.

A comparative study of the pH of the environment of the affected area of the skin of the pubic area in patients with trichophytosis was carried out in 84 patients, depending on the clinical forms of the disease, in comparison with the data of 20 practically healthy individuals (control group). As is known from the scientific literature, the pH environment of the pubic region, perineum and perigenital zones has a neutral pH environment, while in other parts of the skin, these values average 5.4 **[4,5].**

The results of our studies of the pH of the medium in the control group are consistent with the scientific literature and average 6.98 ± 0.10. Studies of the pH of the environment in patients with zooanthroponotic trichophytosis of the pubic area in the lesion, significantly increase compared with the data of the control group ($p<0.001$) and average 7.52 ± 0.07 with 6.98 ± 0.10 in the control (table 4).

Table 4.

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pH index of the skin environment in patients with various clinical forms of trichophytosis of the pubic area (M±m)

Clinical forms	The number of examined persons	f the skin nt
Control	20	6,98 ± 0,10
In the lesion focus of patients with trichophytosis	84	7,52 ± 0,07*
Superficial spotty	20	7,50 ± 0,11*
Infiltrative	22	7,56 ± 0,09*
Infiltrative suppurative	42	7,50 ± 0,13*

Note: p is the reliability of the data in relation to the control. * - p<0.001

Analysis of changes in the pH value of the skin environment in patients with zooanthroponotic trichophytosis, depending on the clinical forms, revealed that in all the examined groups of patients with various clinical forms of the disease, the same statistically significant increase in the pH of the skin environment in the lesions was observed in relation to the indicators of healthy individuals (p<0.001) . This indicates that in this pathology there is a violation of the pH value of the skin environment with its shift to the alkaline side. The indicators themselves did not differ significantly in different clinical forms of the disease.

Based on the research results and scientific literature data, it should be noted that the increase in the number of cases of zooanthroponotic trichophytosis of the pubic area, along with the above factors, is characterized by an increase in the pH values of the skin environment of the pubic area to the alkaline side, which also increases by 1.5 units in hyperhidrosis, which is often created by a greenhouse zone effect. **[5,6].** In addition, the alkaline environment, being favorable for the generation of secondary microflora, promotes loosening of the epidermis and facilitates a deeper penetration of trichophyton and secondary microflora into the skin, creating favorable soil for the development of deep forms (infiltrative and infiltrative-suppurative) of the disease with the development of an infiltrative-purulent process. with zooanthroponotic trichophytosis of the pubic region.

Thus, the studies showed an abundance of microbial landscape in the foci of zooanthroponotic trichophytosis of the pubic region with the detection of Staphylococcus epidermidis - in 42.9%, Staphylococcus aureus - 32.1%, Clostridium perfringens - 13.1%, Candida - in 7.1%, Klebsiella- 2.4%, Enterococcus and Streptococcus haemolyticus - in 2.4% of cases. Which were characterized by both qualitative and quantitative increase in the lesion in direct proportion to the clinical forms of the disease. In patients with zooanthroponotic trichophytosis of the pubic region, the disease occurs against the background of a violation of the pH value of the skin environment with a shift to the alkaline side, which contributes to the creation of favorable conditions for the reproduction of various microorganisms with the development of their dysbiosis and complicates the clinical course of the mycotic process.

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INVESTIGATING THE ROLE OF KLOTHO IN DIABETIC NEPHROPATHY: CORRELATION WITH GLYCEMIC STATUS

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Abstract:

Diabetic nephropathy (DN) is a prevalent and severe complication of diabetes mellitus that leads to progressive kidney damage, often culminating in end-stage renal disease (ESRD). The pathogenesis of DN is multifactorial, involving chronic hyperglycemia, oxidative stress, inflammation, and fibrosis. Despite advances in therapeutic strategies, DN remains a significant cause of morbidity and mortality in diabetic patients. Therefore, identifying novel biomarkers and therapeutic targets is crucial to improve the management of DN.
One such promising target is Klotho, a protein that has garnered attention due to its potential anti-aging, anti-inflammatory, and renal protective properties.

Keywords: Cystatin C, glycated hemoglobin, diabetic nephropathy, glomerular filtration rate, kidney dysfunction.

What is Klotho? Klotho is a transmembrane protein that primarily functions in the kidneys, although it also exists in a soluble form in the blood. It was first identified as an anti-aging gene, and subsequent studies have revealed its broader role in maintaining kidney function, regulating phosphate metabolism, and modulating oxidative stress and inflammation.[1,3]
Klotho exerts its protective effects by:
- Regulating phosphate and calcium homeostasis: Klotho works alongside fibroblast growth factor-23 (FGF-23) to regulate phosphate excretion by the kidneys.
- Inhibiting fibrosis: Klotho downregulates pathways involved in kidney fibrosis, such as the TGF-β pathway, which is highly active in DN.
- Reducing oxidative stress: It acts as an antioxidant, helping to mitigate oxidative damage—a key contributor to DN progression.
- Modulating insulin signaling and glucose metabolism: Emerging evidence suggests that Klotho may also influence glucose metabolism and insulin sensitivity, which is particularly relevant in diabetes.

The Role of Klotho in Diabetic Nephropathy
In DN, the expression of Klotho is significantly reduced, both in the kidneys and in circulation, which may contribute to the progression of kidney damage. Low Klotho levels have been associated with worse outcomes in kidney disease and may serve as a potential biomarker for early detection of renal dysfunction in diabetic patients.[4,5]
Recent research has focused on understanding the correlation between blood Klotho levels and glycemic control in patients with DN. The hypothesis is that reduced Klotho levels may be linked to poor glycemic status, thus contributing to the worsening of kidney function in diabetic patients.[2,6]

Study Objective

This study aimed to investigate:
1. The correlation between blood Klotho levels and glycemic control (as measured by glycated hemoglobin, HbA1c) in patients with diabetic nephropathy.
2. The relationship between Klotho levels and kidney function, including markers like estimated glomerular filtration rate (eGFR) and albuminuria.
3. The potential role of Klotho as a biomarker for early detection of DN and its utility in monitoring disease progression.

Methodology

- Study Population: The study included patients diagnosed with diabetic nephropathy, along with a control group of diabetic patients without nephropathy and healthy individuals for comparison. The severity of DN was classified based on albuminuria levels and eGFR.
- Blood Klotho Measurement: Serum levels of soluble Klotho were measured using enzyme-linked immunosorbent assay (ELISA).
- Glycemic Control: Glycated hemoglobin (HbA1c) was used as a marker of long-term glycemic control. Fasting blood sugar (FBS) and postprandial glucose (PPG) levels were also recorded.
- Kidney Function Assessment: eGFR was calculated using the CKD-EPI formula, and albuminuria was measured to assess kidney damage.

Key Findings

1. Klotho Levels and Glycemic Control:
   - Patients with poor glycemic control (high HbA1c) exhibited significantly lower levels of circulating Klotho compared to those with better glycemic control.
   - A negative correlation was observed between Klotho levels and HbA1c, indicating that as glycemic control worsens, Klotho levels decrease.
2. Klotho Levels and Kidney Function: