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ATROPHIC RHINITIS: CURRENT CONCEPTS AND CLINICAL FEATURES IN THE CONTEXT OF TYPE 2 DIABETES MELLITUS

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Abstract*: The article provides an overview of modern data on the pathogenesis, clinical manifestations, and diagnosis of atrophic rhinitis, as well as an analysis of the features of the disease course against the background of diabetes mellitus. Special attention is paid to microbiological and immunological risk factors, methods of endoscopic and laboratory diagnostics, as well as modern approaches to treatment and their optimization. Based on literature sources, the need for a comprehensive interdisciplinary approach and further research, taking into account regional characteristics, including in the context of Uzbekistan, has been shown.*

Key words: *atrophic rhinitis, type 2 diabetes mellitus, mucosillar clearance, diagnosis, treatment, literature review.*

The urgency of problem: ATrophic rhinitis is considered a chronic degenerative-inflammatory process of the nasal mucosa, characterized by gradual atrophy of the epithelium, glands, and elements of nervous regulation with an increased tendency towards dryness and cortical formation. In the literature, it is often described as the "pre-stage" (or phenotype) of atrophic rhinitis, while clinical attention is traditionally shifted to already formed atrophic conditions (ozene) [4,16]. This creates a "blind zone": patients with atrophic phenotype remain out of focus for a long time, despite the risk of progression and quality of life deterioration.

The etiology of atrophic changes is multi-component: from nutritional deficiencies (iron, vitamins A/D) and hormonal influences to infectious factors. In Bist et al. (2012), as well as Friedel et al. (2011) notes a connection between primary atrophic rhinitis and Klebsiella ozaenae; at the same time, other possible microbial associations (diphtheroids, Proteus, Escherichia coli) are also reported, which fits into the polyetiological concept of the disease) [10,5,6]. (For a clinician, this is important: the atrophic phenotype can be maintained by the infectious component even in the absence of a pronounced foul odor and classic signs of ozene.

Type 2 diabetes mellitus radically alters the "ecology" of the mucous membrane: it disrupts mucociliary clearance, shifts the pH of secretions to an alkaline side, and increases the risk of persistent colonization by potentially pathogenic flora. Even classic clinical and physiological studies have shown that in diabetic patients, the time of nasal mucociliary clearance increases by approximately 2-3 times, and the pH of secretions is higher than in healthy individuals) [13,14,17]. These observations are also confirmed in Russian-language reviews of mucociliary transport) [15,2]. For atrophic rhinitis, this means a decrease in natural protection and greater vulnerability to chronic inflammation.

The infectious vulnerability in patients with type 2 diabetes is manifested, in particular, by an increased frequency of Staphylococcus aureus carriage. Meta- and cross-sectional studies in diabetic patients often reveal nasal carriage of S. aureus and/or MRSA; according to Anafo et al. (2021), the presence of diabetes was associated with a nearly fourfold increase in the chance of S. aureus carriage (OR≈3.9), and a number of cohort studies also noted an increased prevalence of colonization) [9,16]. From a practical standpoint, this increases the risk of persistent inflammation and a prolonged course in patients with atrophic changes in the mucous membrane.

Against this background, interest in the atrophic phenotype is natural: it is here that one can maximize the benefits of early diagnosis and correction of risk factors (glycemic control, restoration of mucociliary clearance, nasal cavity sanitation, local anti-inflammatory/barrier therapy). Updated reviews of atrophic rhinitis emphasize the multifactorial nature of the pathogenesis and the need for personalized treatment regimens, including modern approaches to local therapy and regenerative methods (Sumaily, 2023), however, targeted data specifically for subtrophic rhinitis against the background of DM2 are significantly lower. This forms a clear gap in knowledge and poses a practical task: optimizing the diagnosis and treatment of atrophic rhinitis in the context of diabetes mellitus.

The aim of the study Study modern data on atrophic rhinitis and its clinical features.

Research methods and methodology:

To prepare the review, publications dedicated to the problem of atrophic and atrophic rhinitis, as well as the features of the course of inflammatory diseases of the nasal cavity in patients with type 2 diabetes mellitus, were used. The search for sources was carried out in international scientific databases PubMed, Scopus, as well as in national electronic resources - eLibrary.ru and CyberLeninka.

The selection criteria for publications were:

- publication period - mainly for the last 10 years (2013-2023), including earlier fundamental research;
- availability of clinical or experimental data on the pathogenesis, diagnosis, or treatment of atrophic rhinitis;
- studies examining the effects of diabetes on the function of the upper respiratory tract mucosa.

The analysis included articles in Russian and English. Additionally, reviews, clinical recommendations, and individual dissertation studies available in open scientific libraries were taken into account.

Results of the research: General information about atrophic rhinitis.

Atrophic rhinitis refers to chronic diseases of the nasal mucosa in which progressive thinning of the epithelium, decreased activity of the glandular apparatus, and disruption of local neurovegetative regulation are observed. Clinically, this manifests as a feeling of dryness in the nasal cavity, the formation of crusts, periodic nosebleeds, and a decrease in the sense of smell. Unlike pronounced atrophic rhinitis (ozenas), the subatrophic form is not always accompanied by a foul odor and gross destructive changes, but without treatment, it can progress) [16].

Etiology and Pathogenesis. Modern studies confirm the polyetiological nature of atrophic rhinitis. Among the possible causes are hereditary predisposition, hormonal imbalances, iron and vitamin (A, D) deficiencies, chronic viral infections, and autoimmune processes [4]. The infectious factor also plays a role: Klebsiella ozaenae, diphtheroids, Proteus, and Escherichia coli can participate in maintaining inflammation[3,6].

Classification.

Primary atrophic rhinitis, which develops against the background of genetic and metabolic factors, and secondary rhinitis, which develops after previous infections, injuries, surgical interventions, or systemic diseases, are distinguished [5]. The secondary variant is especially relevant for patients with endocrine pathology, including diabetes mellitus, when local disorders are combined with systemic metabolic changes.

Clinical features. The patients' main complaints include a dry and burning sensation in the nose, the formation of dense crusts, periodic nosebleeds, difficulty breathing, and decreased sense of smell. Endoscopic examination reveals a thin, pale mucous membrane with areas of cortical formation and widened nasal passages [15]. The chronic course of the disease leads to a significant decrease in quality of life, sleep disturbance, increased fatigue, and social discomfort.

Epidemiological data. Accurate indicators of subatrophic rhinitis prevalence are limited, as in several studies, it is combined with atrophic rhinitis. However, according to systematic reviews, the frequency of atrophic forms of chronic rhinitis varies from 0.5 to 1% in the general population, while in endemic regions it can reach 2-3% [16]. In Central Asian and Eastern European countries, the incidence is traditionally higher, which is attributed to climatic factors, infectious load, and limited access to medical care [4].

Diabetes mellitus and nasal mucosa pathology: Disruption of mucociliary clearance.

One of the main protective mechanisms of the respiratory tract is mucociliary clearance. Its role is to remove mucus along with microorganisms and allergens from the respiratory tract. In diabetes mellitus, this process is significantly impaired. Also in the research of Sachdeva et al. (1993) showed that in patients with diabetes, the time for cleansing the nasal mucosa is on average 2-3 times longer than in healthy individuals. Selimoğlu et al. (1999) confirmed these data and noted an increase in nasal secretion pH, which makes the mucus less bactericidal and facilitates the reproduction of conditionally pathogenic flora. These changes are associated with both hyperglycemia and diabetic neuropathy affecting the functions of the glandular apparatus and ciliated epithelium. Disruption of mucociliary transport in diabetics is considered an important pathophysiological risk factor for chronic rhinitis.

A propensity for infections. Chronic hyperglycemia is accompanied by a decrease in the activity of innate and adaptive immunity. In the works of Russian authors (Shishkova et al., 2015), it has been shown that patients with diabetes mellitus often develop chronic inflammatory processes in the nasal mucosa and paranasal sinuses. Decreased local production of antimicrobial peptides, impaired phagocytosis, and a deficiency of secretory immunoglobulin A make the mucous membrane more susceptible to bacterial and fungal infections. This explains the high percentage of diabetes combined with chronic sinusitis, rhinosinusitis, and atrophic changes in the mucous membrane.

Nasal carriage of Staphylococcus aureus. The problem of nasal carriage of Staphylococcus aureus deserves special attention. According to Lin et al. (2016), the prevalence of S. aureus carriage in patients with diabetes mellitus is almost twice as high as in healthy individuals. Hart et al. (2015) in a large cohort study confirmed that diabetes is an independent risk factor for S. aureus carriage. In the study, Anafo et al. (2021) showed that in patients with diabetes, the probability of carrying methicillin-resistant strains (MRSA) increases almost fourfold. These data indicate the importance of microbiological control in patients with diabetes mellitus, especially in the chronic forms of rhinitis, including atrophic rhinitis. [7].

Final Provisions. Thus, diabetes mellitus creates an unfavorable background for the nasal mucosa: it disrupts mucociliary transport, alters the composition of secretions, reduces local immunity, and increases the likelihood of chronic carriage of pathogenic flora. All of this makes the course of chronic nasal inflammatory diseases, including atrophic rhinitis, more severe and prone to progression.

Atrophic rhinitis and its clinical course against the background of diabetes mellitus. Features of the course. The combination of atrophic rhinitis with type 2 diabetes mellitus leads to the formation of more pronounced and persistent clinical manifestations. Patients often complain of constant dryness in the nasal cavity, the formation of dense crusts, a burning sensation, and a feeling of congestion. Often, difficulty breathing through the nose, recurrent nosebleeds, and decreased or distorted sense of smell (hypo- and cacosmia) occur. These symptoms are more pronounced than in patients without endocrine pathology, which is associated with a combination of local atrophic processes and systemic metabolic disorders.

Foreign research data. Foreign studies confirm that in patients with diabetes, the nasal mucosa is more vulnerable to degenerative changes. In the study Selimoğlu et al. (1999) noted that increased secretion pH and slowed mucociliary clearance create conditions for chronic inflammation. Lin et al. (2016) showed that the prevalence of S. aureus carriage in diabetic patients is higher than in healthy

individuals, which is directly related to an increased risk of chronic rhinosinusitis and atrophic changes in the mucous membrane. Hart et al. (2015) also identified that diabetes is an independent risk factor for the persistence of pathogenic flora in the nasal cavity. These data indicate that atrophic rhinitis is more severe in patients with DM2 and tends to recur.

Local studies and regional characteristics. Publications by Russian and Uzbek authors also note a high frequency of atrophic rhinitis combined with endocrine pathology. Thus, in the review by Shishkova et al. (2015) emphasize that in diabetic patients, the chronic inflammatory processes in the nasal cavity proceed more aggressively, with pronounced trophic disorders. Clinical observations published in domestic sources indicate that subatrophic changes in such patients are accompanied by earlier formation of crusts and persistent loss of olfactory sensation. The importance of climatic factors is further emphasized: the dry and hot air of Central Asia contributes to the worsening of symptoms in patients with diabetes.

Risk factors and progress. The main factors affecting the severity of atrophic rhinitis in patients with diabetes are:

- degree of disease compensation (with unsatisfactory glycemic control, symptoms are significantly more pronounced);
- the presence of diabetic neuropathy affecting the secretory functions of the mucous membrane;
- concomitant infections (S. aureus, Klebsiella ozaenae, etc.), supporting chronic inflammation;
- environmental and climatic factors contributing to mucosal dryness;
- vitamin and microelement deficiency, which further exacerbates trophic disorders.

Together, these factors explain why the course of atrophic rhinitis in patients with type 2 diabetes mellitus is characterized by greater resistance to standard therapy and a higher risk of transitioning to atrophic form.

Diagnostic methods. Endoscopy and clinical examination

Endoscopy is considered the "gold standard" in diagnosing chronic forms of rhinitis. In the works of Dolgov and Pankova (2024), it is noted that it is endoscopic examination that allows for reliable detection of mucosal thinning, crust formation, and nasal dilation, which is especially important in patients with metabolic disorders. Uzbek researchers (Nasretdinova, 2021) also emphasize the importance of endoscopic control in the management of patients with c subatrophic and atrophic rhinitis, linking it to the earlier detection of complications.

Functional methods. Mucociliary clearance is one of the key indicators of mucosal function. Also Sachdeva et al. (1993) showed its elongation in patients with diabetes mellitus. Selimoğlu et al. (1999) supplemented these data by also identifying an increase in the pH of the secretion, which reduces its antimicrobial properties. Uzbek studies (Hamroyeva et al., 2019) indicate that functional tests for mucociliary transport should be included in the standard examination of patients with chronic rhinitis in endemic regions of Central Asia.

Microbiological diagnostics. Microbiological studies allow for the identification of pathogenic flora that supports inflammation. In the research of Ghallab et al. (2020) confirm the significance of Klebsiella ozaenae and other conditionally pathogenic microorganisms in atrophic forms of rhinitis. Lin et al. (2016) showed that patients with diabetes mellitus have a significantly higher probability of carrying S. aureus, which is also confirmed by data from Hart et al. (2015). Uzbek authors' publications (Saidov et al., 2020) emphasize that bacteriological examination of nasal smears is necessary for selecting targeted antibacterial therapy.

Radiological methods. Computer tomography and MSCT allow for an objective assessment of the paranasal sinuses. According to Friedel et al. (2011), it is CT that allows for the detection of bone structure changes and the prevalence of the atrophic process. Publications in Russian and Uzbek

(Karimov et al., 2022) note that using CT in diabetic patients allows for the elimination of secondary processes (sinusitis, osteomyelitis) that often complicate the course of rhinitis.

New trends. Modern works emphasize the importance of molecular methods - PCR diagnostics for detecting S. aureus and Klebsiella spp.) [1]. In domestic publications (Nasretdinova, 2021; Saidov et al., 2020) indicates the prospects for including immunological studies (IgA, cytokines) to assess the barrier function of the mucous membrane.

Treatment and its optimization. Standard approaches

Traditionally, atrophic rhinitis therapy is aimed at moisturizing the mucous membrane, improving mucociliary clearance, and preventing infections. In the works of Sumaily et al. (2023) note that isotonic and hypertonic solutions, oil drops, and topical medications that improve mucosal regeneration remain the basis of treatment. Dolgov and Pankova (2024) emphasize that using local preparations with dexpanthenol and antioxidants promotes epithelial regeneration and reduces dryness symptoms.

Features in patients with diabetes mellitus

In patients with type 2 diabetes, treatment is complicated by tissue regeneration disorders and a tendency towards infections. Lin et al. (2016) showed that it is S. aureus carriage that requires more careful selection of antibacterial therapy. Hart et al. (2015) recommend including microbiological control in the standard for managing diabetics with chronic rhinitis. In Uzbek studies (Saidov et al., 2020), it is emphasized that diabetic patients require a combination of antibacterial and immunomodulatory agents, which reduces the risk of recurrence.

Local and systemic drugs

In domestic practice (Nasretdinova, 2021), a positive effect has been noted when using complex schemes including salt irrigation, oil solutions (for example, based on sea buckthorn oil), as well as physiotherapeutic methods. Hamroeva et al. (2019) emphasize the need for regular moisturization of the mucous membrane and the use of mucolytics to dilute secretions in the arid climate of Uzbekistan.

New directions

Current trends include the use of topical immunomodulators, hyaluronic acid preparations, and regenerative technologies. In the publications of Russian authors (Shishkova et al., 2015), it is indicated that the addition of immunocorrecting agents increases the effectiveness of therapy. In international studies (Ghallab et al., 2020), the possibility of targeted antibacterial therapy, taking into account the resistance of the flora, is being studied.

Treatment optimization

In summary, this literature data allows us to identify several areas for optimizing the treatment of subatrophic rhinitis in patients with diabetes:

- correction of glycemia as a mandatory element of patient management;
- regular endoscopic and microbiological assessment of the mucosal state;
- combined use of local moisturizing, antibacterial, and immunomodulatory drugs;
- taking into account the climatic features of the region, which is especially important for Uzbekistan;
- implementation of regenerative technologies (hyaluronic acid, peptide complexes).

Conclusions:

Atrophic rhinitis is a multifactorial disease in which degenerative and inflammatory changes in the nasal mucosa are combined. In the literature, it is emphasized that the disease has a complex pathogenesis and can develop both primarily (against the background of hereditary, hormonal, and infectious factors) and secondarily - after past infections or systemic disorders (Bist et al., 2012; Dolgov & Pankova, 2024).

The presence of type 2 diabetes mellitus significantly aggravates the clinical course of atrophic rhinitis. As shown by the research of Sachdeva et al. (1993), Selimoğlu et al. (1999), in patients with diabetes, mucociliary clearance is disrupted, and the physicochemical properties of secretions change,

making the mucous membrane vulnerable to infections. Works by Lin et al. (2016), Hart et al. (2015) demonstrated a high frequency of S. aureus carriage in patients with diabetes, and studies by Uzbek authors (Saidov et al., 2020; Khamroeva et al., 2019) confirmed that in endemic regions, the clinical manifestations of rhinitis in diabetics are more persistent and difficult to tolerate with standard therapy.

Optimizing the diagnosis and treatment of atrophic rhinitis against the background of diabetes requires a comprehensive approach. By Sumaily et al. (2023), Dolgov and Pankova (2024) emphasize that standard methods (irrigation, oil drops) should be combined with antibacterial and immunomodulatory therapy, as well as correction of systemic factors, primarily glycemic control. Uzbek studies (Nasretdinova, 2021; Saidov et al., 2020) show that it is combined regimens, including local and systemic medications, physiotherapy, and endocrine status control, that yield the best results.

Thus, a literature review allows us to draw several key conclusions:

Atrophic rhinitis remains a poorly understood form of chronic rhinitis, especially in the context of its combination with diabetes mellitus.

Diabetes significantly worsens the course of the disease due to impaired mucociliary clearance, altered secretions, and increased carriage of pathogenic flora.

Effective treatment requires an interdisciplinary approach that combines otorhinolaryngologists, endocrinologists, and immunologists.

Further clinical research is needed, including in Uzbekistan, to develop local diagnostic and treatment protocols that take into account the region's climatic and epidemiological characteristics.

REFERENCES

1.B. Anafo, E. A. Tagoe, and I. G. Ampomah (2021). Methycillin-resistant Staphylococcus aureus (MRSA) nasal carriage among patients attending a tertiary hospital in Ghana. African Journal of Laboratory Medicine, 10 (1), a1232. https://doi.org/10.4102/ajlm.v10i1.1232

2.Birykova, E. V. (2012). [Review of the influence of diabetes mellitus on the state of ENT mucous membranes]. Diabetes mellitus, (3). (Cited from the summary review; access to the network is restricted)

3.Bist, S. S., Bisht, M., Purohit, J. P., Singhal, A., & Saxena, R. K. (2012). Primary atrophic rhinitis: Clinical profile, microbiological and radiological study. ISRN Otolaryngology, 2012, 404075. https://doi.org/10.5402/2012/404075

4.Dolgov, O. I., & Pankova, O. V. (2024). Changes in nasal mucosa in atrophic rhinitis: Literature review. Russian Otorhinolaryngology (Rossijskaya otorinolaryngologiya). https://doi.org/10.17816/otorhinolaryngology638131

5.Friedel, M. E., Nelson, B. L., & Vuitch, F. (2011). Skull base defect in a patient with ozene undergoing endoscopic sinus surgery. Allergy & Rhinology, 2 (3), e121-e124. https://doi.org/10.2500/ar.2011.2.0021

6.Ghallab, A. F., El Sayed, A. A., & Abou El Fadl, A. (2020). Microbiological profile and AmpC β-lactamase among isolates in primary atrophic rhinitis. Egyptian Journal of Medical Microbiology, 29 (3), 1-9.

7.Hart, J., et al. (2015). Prevalence and risk factors for nasal colonization of Staphylococcus aureus in a community-based sample: The Fremantle Diabetes Study Phase II. Journal of Diabetes and Its Complications, 29 (8), 1092-1097. https://doi.org/10.1016/j.jdiacomp.2015.06.004

8.Hart, J., et al. (2015). Prevalence, risk factors, and consequences of Staphylococcus aureus carriage in diabetes: The Fremantle Diabetes Study Phase II. Journal of Diabetes and Its Complications, 29 (8), 1092-1097. https://doi.org/10.1016/j.jdiacomp.2015.06.005

9.Hart, J., Hamilton, E. J., Makepeace, A., Davis, W. A., Latkovic, E., Lim, E. M., Dyer, J. R., & Davis, T. M. E. (2015). Prevalence, risk factors, and consequences of Staphylococcus aureus carriage in diabetes: The Fremantle Diabetes Study Phase II. Journal of Diabetes and Its Complications, 29 (8), 1092-1097. https://doi.org/10.1016/j.jdiacomp.2015.06.005

10.Ist, S. S., Bisht, M., Purohit, J. P., Singhal, A., & Saxena, R. K. (2012). Primary atrophic rhinitis: Clinical profile, microbiological and radiological study. ISRN Otolaryngology, 2012, 404075. https://doi.org/10.5402/2012/404075

11.Lin, J., et al. (2016). Prevalence and characteristics of nasal carriage of Staphylococcus aureus in patients with diabetes mellitus. Journal of Laboratory Physicians, 8 (3), 176-180.

12.Lin, J., Peng, Y., Bai, C., Zhang, T., Zheng, H., Wang, X.,... Yao, Z. (2016). Prevalence and characteristics of nasal carriage of Staphylococcus aureus in patients with diabetes mellitus. Journal of Laboratory Physicians, 8 (3), 176-180. (Free full text).

13.Sachdeva, A., Sachdeva, O. P., Gulati, S. P., & Kakkar, V. (1993). Nasal mucociliary clearance and mucus pH in patients with diabetes mellitus. The Indian Journal of Medical Research, 98, 265-268. PMID: 8132227.

14.Selimoğlu, M. A., Selimoğlu, E., & Kurt, A. (1999). Nasal and oral pH and mucociliary clearance in patients with insulin-dependent diabetes mellitus. Ear, Nose & Throat Journal, 78 (8), 585-590, 590. https://doi.org/10.1177/014556139907800814

15.Shishkova, V. N., et al. (2015). Features of the development of acute and chronic inflammation of the nasal mucosa. *Consilium Medicum*, 17 (4), 29-36. (review fragments on mucociliary clearance)

16.Sumaily, I. A., Zakzouk, S., & AlMomen, A. (2023). An updated review on atrophic rhinitis and empty nose syndrome. Ear, nose & throat journal. https://doi.org/10.1177/01455613231185022

17.Yue, W. L. (1989). Nasal mucociliary clearance in patients with diabetes mellitus. Journal of Laryngology & Otology, 103 (9), 853-855. https://doi.org/10.1017/S0022215100110291

18.Nasretdinova, M. (2021). A comprehensive treatment method for patients with atrophic rhinitis and hyposiderosis. Oral Medicine (Uzbekistan).

19.Saidov, B. R., et al. (2020). Microbiological characteristics of chronic rhinitis in patients with endocrine pathology. Bulletin of Science and Education, 5 (77), 44-49.

20.Hamroeva, G. Sh., et al. (2019). Functional state of the nasal mucosa in patients with chronic rhinitis in arid climates. Eurasian Journal of Academic Research, 9 (2), 112-118.

21.Shishkova, V. N., et al. (2015). Features of the development of acute and chronic inflammation of the nasal mucosa. *Consilium Medicum*, 17 (4), 29-36.

22.Shishkova, V. N., et al. (2015/updated review see: 2024). Features of the microbiota of the nasal cavity and its connection with the inflammatory processes of the upper respiratory tract. Consilium Medicum (an overview publication on ENT microbiota). A modern overview is available: https://consilium.orscience.ru/2075-1753/article/view/625571