UDC 616.716.1:616.211-002:616.91/.99
DOI https://doi.org/10.32782/2226-2008-2025-6-5

V. P. Polianska https://orcid.org/0000-0002-8727-9029
G. A. Loban https://orcid.org/0000-0003-0055-7696
M. I. Bezega https://orcid.org/0000-0002-1250-1190
S. V. Zachepylo https://orcid.org/0000-0001-6477-8389
I. M. Zviagolska https://orcid.org/0000-0001-7531-3966

CHARACTERISTICS OF THE MAXILLARY SINUS MICROBIOME IN ACUTE BACTERIAL RHINOSINUSITIS

Poltava State Medical University, Poltava, Ukraine

UDC 616.716.1:616.211-002:616.91/.99

V. P. Polianska, G. A. Loban, M. I. Bezega, S. V. Zachepylo, I. M. Zviagolska
CHARACTERISTICS OF THE MAXILLARY SINUS MICROBIOME IN ACUTE BACTERIAL RHINOSINUSITIS
Poltava State Medical University, Poltava, Ukraine

The onset and progression of acute bacterial rhinosinusitis are influenced by infection, genetic, and environmental factors. The application of modern microbiological methods has expanded the etiological spectrum of microorganisms capable of causing acute bacterial rhinosinusitis.

Aim of the study is to investigate the species composition and population levels of the microbiome in the maxillary sinus mucosa, assessing their adhesive potential in cases of acute bacterial rhinosinusitis.

Materials and research methods. The study involved 38 patients diagnosed with acute bacterial rhinosinusitis, from whom 45 clinical microbial strains were isolated and identified. Diagnosis was confirmed based on the presence of objective and subjective clinical signs. Microbial cultivation followed standard protocols, with final biochemical identification performed using the automated Vitek 2 bacteriological analyser. Adhesive activity of clinical strains was determined via the V.I. Brillis et al. method, calculating the mean adhesion index.

Results. Under conditions of acute bacterial rhinosinusitis, the structure of clinically significant microbial strains was dominated by S. aureus, H. influenzae, K. pneumoniae, and M. catarrhalis. Additionally, the aetiological significance of commensal bacteria such as S. epidermidis, S. warneri, and K. rizophilia was established in the development of the disease. The clinical isolates exhibited a high level of microbial colonisation in the maxillary sinuses. In 78% of patients with acute bacterial sinusitis, a mono-infection was detected, while 22% showed an association of multiple microorganisms. Among the clinical isolates colonising the mucous membranes of the maxillary sinuses in acute bacterial rhinosinusitis, 81% demonstrated high and 19% moderate adhesive activity. The findings indicate an increasing role of opportunistic microorganisms in the aetiopathogenesis of acute bacterial rhinosinusitis, driven by their virulence and significant population levels of pathogens.

Keywords: acute bacterial rhinosinusitis, microbiome, adhesion.

УДК 616.716.1:616.211-002:616.91/.99

В. П. Полянська, Г. А. Лобань, М. І. Безега, С. В. Зачепило, І. М. Звягольська
ОСОБЛИВОСТІ МІКРОБІОМУ ВЕРХНЬОЩЕЛЕПНИХ ПАЗУХ ПРИ ГОСТРОМУ БАКТЕРІАЛЬНОМУ РИНОСИНУСИТІ
Полтавський державний медичний університет, Полтава, Україна

Метою дослідження було вивчення видового складу та популяційного рівня мікробіому слизових оболонок верхньощелепних пазух з визначенням їхнього адгезивного потенціалу за умов гострого бактеріального риносинуситу. Обстежено 38 пацієнтів з діагнозом гострий бактеріальний риносинусит, від яких виділено 45 штамів мікроорганізмів. У структурі клінічно значимих ізолятів домінували *S. aureus, H. influenzae, K. pneumoniae*, *M. catarrhalis.* Також у розвитку захворювання доведена роль коменсальних бактерій *S. epidermidis, S. warneri*, *K. rizophilia*, для яких характерний високий популяційний рівень. У 78% пацієнтів виявлена моноінфекція, а у 22% – мікстінфекція. Клінічні штами, що колонізували верхньощелепні пазухи, у 81% володіли високою і у 19% середньою адгезивною активністю.

Зростання ролі опортуністичних мікроорганізмів у розвитку гострого бактеріального риносинуситу зумовлене їхньою вірулентністю та значним популяційним рівнем.

Ключові слова: гострий бактеріальний риносинусит, мікробіом, адгезія.

Introduction

The issue of acute rhinosinusitis (ARS) remains highly relevant and socially significant, both globally and in Ukraine. Each year, the incidence of rhinosinusitis among the global population reaches approximately 15%, significantly impacting quality of life, placing strain on healthcare systems, and imposing an economic burden on society [1]. In Ukraine, the overall decline in population health is primarily linked to the devastating consequences of the COVID-19 pandemic and the full-scale Russian invasion, which have substantially altered the course of infectious and respiratory diseases with pronounced microbial-inflammatory manifestations. This has led to increased disease severity and aggressive spread [2]. According to epidemiological studies in Ukraine, the prevalence of acute rhinitis, rhinosinusitis, and rhinopharyngitis reaches 489.9

cases per 10.000 population, with an incidence rate of 5–15 cases per 1.000 population depending on the season. Such patients account for 60–65% of all outpatient visits to otorhinolaryngologists [3].

Contributing factors include: anatomical abnormalities of nasal/paranasal structures; impaired mucociliary clearance; upper respiratory tract infections; immunodeficiency states; genetic and environmental factors; smoking; atopic phenotype; anxiety and depressive disorders [1; 3]. The infectious component remains pivotal in ARS pathogenesis. According to the European Position Paper on Rhinosinusitis and Nasal Polyps (EPOS 2020), ARS is classified as viral ARS (common cold), post-viral ARS, and acute bacterial rhinosinusitis (ABRS). Viral ARS demonstrates particularly high incidence rates [1; 4]. Viral invasion damages nasal epithelial cells, leading to: impaired mucociliary clearance, apoptotic and necrotic cell death, disrupted adaptive immune regulation. This compromise of the epithelial barrier's structural and functional integrity creates conditions for secondary bacterial infection. Research indicates viral rhinosinusitis progresses to bacterial infection in: 0.5–2.0% of adult cases, 5–10% of paediatric cases with the possible development of serious complications or life-threatening conditions [5–7].

It is also important to consider the etiological role of micromycetes in sinus infections. Therefore, to improve the treatment of acute rhinosinusitis of various etiologies and prevent the development of rhinogenic intracranial and orbital complications, it is essential to analyze the microbial profile of the sinuses and the sensitivity of microorganisms to antibiotics. The use of broad-spectrum antimicrobial agents targeting multiple pathogens contributes to the formation and spread of antibiotic-resistant microbial strains. For this reason, finding alternative ways to overcome microbiome resistance to antibacterial drugs remains a relevant issue today [8; 9].

In recent decades, research has confirmed that the paranasal sinuses are inhabited by microbial communities consisting of both commensal and potentially pathogenic microorganisms. However, the population levels of these microbiome representatives are typically found in low concentrations [10]. Under certain conditions, microecological imbalances occur in the normal biocenosis of the sinus mucosa. This can lead to increased microbial load from both resident and non-native microorganisms, as well as subsequent colonization of the sinus mucosa by pathogenic and opportunistic flora at high population levels – often originating from other biotopes of the upper respiratory tract [11; 12]. As a result, microbial selection occurs, driving pathogenization of the local microbiome. This process can trigger mono- or polyetiological infectious-inflammatory conditions.

Medical literature identifies several microorganisms as the most common causes of acute bacterial rhinosinusitis. These include Streptococcus pneumoniae (S. pneumoniae), Haemophilus influenzae (H. influenzae), combinations of these pathogens, β-hemolytic streptococci, non-β-hemolytic streptococci, Staphylococcus aureus (S. aureus), Moraxella catarrhalis (M. catarrhalis), and Haemophilus parainfluenzae (*H. parainfluenzae*) [1]. However, advances in diagnostic microbiological methods have expanded the range of microorganisms known to infect the paranasal sinus mucosa. Research by Miah MS et al. found that Streptococcus anginosus (*S. anginosus*) and *S. aureus* were the most frequently involved microorganisms in acute bacterial rhinosinusitis [13]. Other studies using PCR techniques have confirmed the involvement of Chlamydophila pneumoniae (*C. pneumoniae*), Streptococcus milleri *(S. milleri),* and coagulase-negative staphylococci, in addition to *H. influenzae* and *S. pneumoniae* [14].

The ability of microorganisms to colonize host biotopes depends on their biological properties. One key factor in a microorganism's virulence is its ability to adhere to surfaces. Increased adhesive potential helps bacteria establish themselves in a biotope, survive in hostile environments, and serves as the initial step in biofilm formation. Within biofilms, microbial cells become resistant to: local immune defenses of mucous membranes, antibiotics and disinfectants.

The aim is to study the species composition and population level of the microbiome of the maxillary sinus mucosa, determining their adhesive potential in cases of acute bacterial rhinosinusitis.

Materials and Methods

The microbial spectrum of the maxillary sinus mucosa was studied in patients diagnosed with acute bacterial rhinosinusitis who were treated at the otolaryngology department of the "2nd City Clinical Hospital of the Poltava City Council" between November 2024 and January 2025.

A total of 38 patients (24 women and 14 men, accounting for 63% and 37%, respectively) aged 18 to 60 years were examined. Inclusion criteria: the presence of a patient diagnosed on the basis of clinical and rhinoscopic signs of acute bacterial rhinosinusitis (according to the provisions of the Unified Clinical Protocol of Primary and Specialized Medical Care "Acute Rhinosinusitis"), the presence of the patient's informed voluntary consent to diagnostic manipulations and inclusion in the study. Exclusion criteria: patients with acute viral rhinosinusitis, acute post-viral rhinosinusitis and chronic rhinosinusitis (with or without nasal polyps), suspected or confirmed pregnancy, the presence of chronic pathology from other organs and systems in the stage of decompensation; use of various dosage forms of antimicrobial agents both systemically and locally, in particular, antiseptics during the last month, immunocompromised individuals. The diagnosis was confirmed based on: subjective symptoms (nasal congestion or difficulty breathing, nasal discharge, facial pain or pressure, reduced sense of smell); medical history (biphasic disease progression, symptom duration from 10 days to 12 weeks); objective signs (swelling and redness of the nasal mucosa, mucopurulent discharge, mainly in the middle and common nasal passages), and additional radiological tests (X-rays, computed tomography [CT], or magnetic resonance imaging [MRI] of the paranasal sinuses). The study was conducted in accordance with the Helsinki Declaration of the World Medical Association on ethical principles for medical research involving human subjects [15] and was approved by the Biomedical Ethics Committee of Poltava State Medical University (Protocol No. 292, dated 30.09.2022). Consent to the processing of personal data was granted by

the patients. In patients with acute maxillary sinusitis, biological samples were collected before treatment through a standard procedure – puncture of the maxillary sinus using a Kulikovsky needle. The material was aspirated after flushing the sinus with 0.9% sodium chloride solution using a sterile disposable syringe. Approximately 1 mL of the collected fluid was placed in a test tube containing Amies semi-solid transport medium (JS Medical Material, China). The samples were transported under controlled temperature conditions (isothermal) to the bacteriology laboratory at the Department of Microbiology, Virology, and Immunology of Poltava State Medical University (PSMU). They were processed within 2 hours for isolation, identification, and further analysis of clinical isolates.

The study examined 45 clinical strains of aerobic and facultative anaerobic bacteria, including both indigenous (autochthonous) and non-indigenous (allochthonous) species, as well as Gram-positive and Gram-negative bacteria. Samples were cultured using the sector streak method on specialized selective and differential diagnostic media. Petri dishes were incubated in a thermostat at 37°C for 24–48 hours, with daily monitoring of bacterial growth. Final biochemical identification was performed using the Vitek 2 Compact automated microbiological analyzer (BioMérieux, France). Microbial load in the maxillary sinuses was expressed as colony-forming units per milliliter (CFU/mL). Results were expressed in decimal logarithms (log CFU/mL) for statistical evaluation.

The adhesive activity of clinical strains was determined using the method by V.I. Brillis and co-authors, utilizing human blood group I(0) Rh+ erythrocytes. The following parameters were assessed: Average Adhesion Index (AAI) – mean number of bacteria attached per erythrocyte)); Erythrocyte Participation Coefficient (EPC) – percentage of erythrocytes with adhered bacteria on their surface)); Microorganism Adhesion Index (MAI). MAI was calculated using the formula: MAI = (AAI/CFU) × 100. According to V.I. Brillis and co-authors' method, microorganisms were classified as: non-adhesive (MAI ≤ 1.75), low-adhesive (MAI 1.76–2.5), moderately adhesive (MAI 2.51–4.0) and highly adhesive (MAI ≥ 4.0).

The obtained results of clinical-microbiological studies were analyzed using variation statistics methods, including arithmetic mean (M) and standard error of the mean (±m). Statistical processing was performed using Statistica for Windows 5.0 software (Statfort, USA).

Research results and their discussion

During the period from November 2024 to January 2025, 45 microbial isolates in clinically significant quantities were obtained from 38 patients with acute bacterial rhinosinusitis. The species distribution of microorganisms isolated from the maxillary sinuses of patients with ABRS is presented in Table 1.

The obtained results indicate that the microorganisms isolated from maxillary sinuses, according to Bergey's Manual, belonged to pathogens from three types and six families. The type *Firmicutes* accounted for 54% of Gram-positive cocci, including representatives of the *Staphylococcaceae* and *Streptococcaceae* families, which were isolated both in pure cultures and in microbial associations. Among coagulase-positive staphylococci, the highest percentage (26%) belonged to *S. aureus*, while coagulase-negative staphylococci (*S. epidermidis, S. warneri*) accounted for 16%. The *Streptococcaceae* family was the least numerous. α-hemolytic streptococci were detected only in microbial associations, while *S. pyogenes* (β-hemolytic streptococci) was isolated from only one patient.

With regard to the number of isolated strains, the type *Proteobacteria* – represented by three families: *Pasteurellaceae, Moraxellaceae*, and *Enterobacteriaceae* – ranked second (37%). The typical microorganisms of the *Pasteurellaceae* family identified in patients with ABRS were facultative anaerobic Gram-negative bacteria of the species

Table 1

Taxonomic characteristics of microorganisms isolated from maxillary sinuses in patients with acute bacterial rhinosinusitis

Taxonomic affiliation of the isolated strains of microorganisms			Representatives	Strain prevalence	
Type	Family	Genus		Abs.	%
Firmicutes	Staphylococcaceae	*Staphylococcus*	Coagulase positive *S. aureus*	12	26
			Coagulase negative *S. epidermidis* *S. warneri*	4 3	16
	Streptococcaceae	*Streptococcus*	α-hemolytic *S. mitis* *S.gallolyticus*	2 1	7
			б- hemolytic *S. pyogenes*	2	5
Actinobacteria	*Micrococcaceae*	*Kocuria*	*K. rizophilia*	3	7
		Rothia	*R. kristinae*	1	2
Proteobacteria	*Pasteurellaceae*	*Haemophilus*	*H. influenzae*	6	13
	Moraxellaceae	*Moraxella*	*M. catarrhalis*	4	9
		Acinetobacter	*A. junii*	1	2
	Enterobacteriaceae	*Citrobacter*	*C. freundii*	2	4
		Klebsiella	*K. pneumoniae*	4	9

H. influenzae (13%). The *Moraxellaceae* family was represented by aerobic Gram-negative diplococci of the species *M. catarrhalis* (9%), while the *Enterobacteriaceae* family included facultative anaerobic Gram-negative bacteria of the species *K. pneumoniae* (9%). Clinical isolates of *A. junii* (genus Acinetobacter) and *C. freundii* (genus Citrobacter) accounted for 6% and were detected only in microbial associations.

Representatives of the type *Actinobacteria* constituted 9% and belonged to the *Micrococcaceae* family. Clinical strains of aerobic Gram-positive cocci of the species *K. rizophilia* (genus Kocuria) made up 7%, while *R. kristinae* (genus Rothia) accounted for 2%. It was confirmed that these bacterial species participated in the development of purulent-inflammatory processes both as monoetiological agents and in microbial associations. The taxonomic classification of clinical isolates in ABRS was analyzed in accordance with microbiological studies by other researchers [16].

The overall microbial colonization of the maxillary sinus mucosa is shown in Fig. 1.

Analysis of quantitative colonization patterns reveals high colonization potential among key ABRS pathogens.

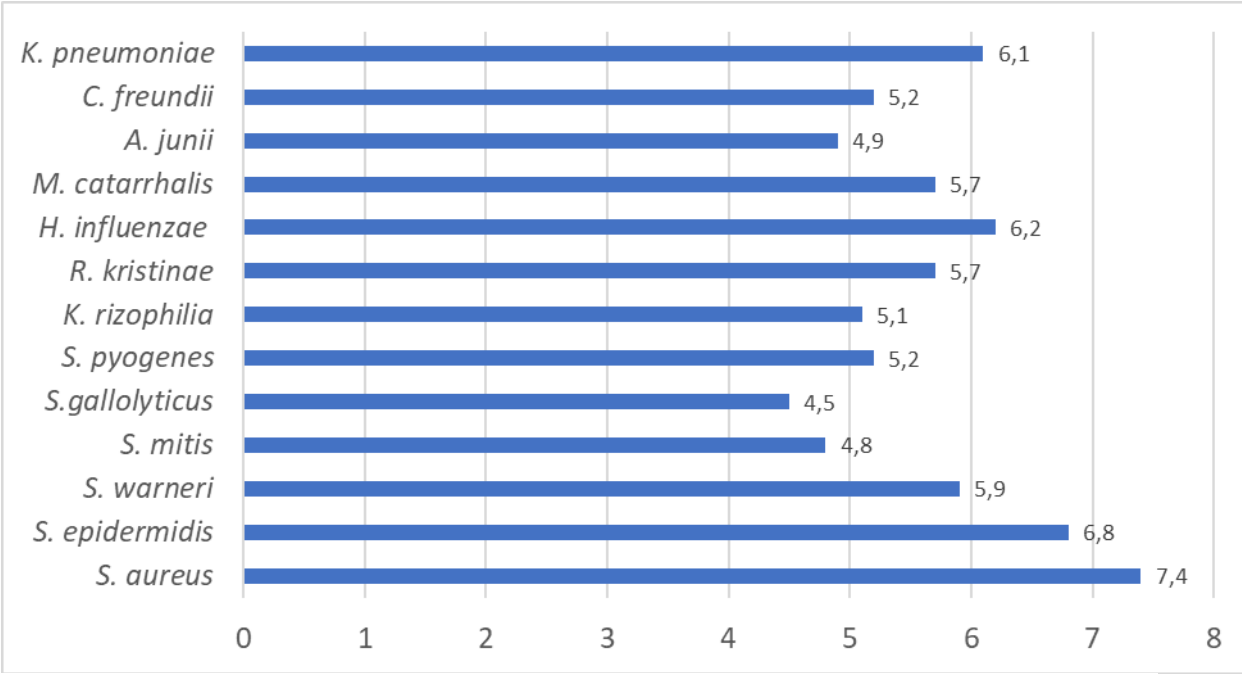

Fig. 1. Microbial population levels isolated from maxillary sinuses in patients with acute bacterial rhinosinusitis (log CFU/mL)

The highest microbial loads in maxillary sinuses were observed for Gram-positive cocci of Staphylococcus genus, particularly S. aureus clinical isolates (7.4±0.33 log CFU/mL). Other significant colonizers included S. epidermidis (6.8±0.14 log CFU/mL), S. pyogenes (5.2±0.0 log CFU/mL), H. influenzae (6.2±0.07 log CFU/mL), and K. pneumoniae (6.1±0.29 log CFU/mL). The lowest colonization levels were recorded for S. mitis (4.8±0.11 log CFU/mL), S. gallolyticus (4.5±0.0 log CFU/mL), and A. junii (4.8±0.0 log CFU/mL). Population levels of each microbial association member helped determine their etiological significance in ABRS development.

Microbial association analysis results are presented in Table 2.

In 8 (21%) patients with ABRS, mixed infections developed, where microorganisms formed microbial associations with varying qualitative and quantitative compositions in the biotope. Two-component associations were detected in samples from 6 (16%) patients, while three-component associations were found in samples from 2 (5%) patients. Our analysis revealed that bacterial associations consisted of combinations of Gram-positive microorganisms, as well as both Gram-positive and Gram-negative pathogens.

Table 2

Qualitative characteristics of microbial associations in maxillary sinuses of acute bacterial rhinosinusitis patients

No	Microorganisms forming an association	Absolute number of associations
Associations consisting of two types		
1.	S. aureus + A. junii	1
2.	S. epidermidis + Citrobacter freundii	2
3.	S. epidermidis + S. warneri	1
4.	K. rizophilia + S. gallolyticus	1
5.	*H. influenzae* + *R. kristinae*	1
Total		6
Associations consisting of three types		
1.	*S. aureus S. pyogenes, S. mitis*	1
2.	S.aureus, M.catarrhalis, S. mitis	1
Total		2

Notably, the qualitative composition of these microbial groups included opportunistic pathogens such as A. junii, C. freundii, S. gallolyticus, and S. mitis. The formation

of multi-component microbial consortia with opportunistic microbiota represents a survival strategy for associated microorganisms in symbiotic conditions. In our opinion, the interaction mechanism among these microbial associates exhibits synergistic characteristics, indicating mutual enhancement of pathogenicity among participants.

Thus, the microbiome of maxillary sinuses in ABRS demonstrated diversity across different taxonomic groups. Analysis of qualitative and quantitative composition of sinus mucosal microbiota in ABRS patients revealed that 79% of culture-positive samples were monomicrobial, while 21% were polymicrobial. The most prevalent colonizing microorganisms were Staphylococcus spp., particularly S. aureus. Our study also identified Gram-negative bacteria H. influenzae, K. pneumoniae, and M. catarrhalis as etiologically significant. Furthermore, microbiological analysis confirmed the role of commensal microorganisms (S. epidermidis, S. warneri, K. rizophilia) in ABRS development. The pathogenic potential of opportunistic bacteria is realized through high infective doses penetrating the maxillary sinus environment and reduced mucosal immunity. The etiopathogenic role of these pathogens is attributed to multiple virulence factors that disrupt mucosal barrier function, evade host immune responses, and trigger nonspecific inflammatory reactions. Recent scientific literature increasingly reports on the ability of opportunistic microorganisms to cause infectious pathology [17; 18; 19; 20].

The first crucial step in the development of an infectious process is the ability of microorganisms to adhere. The results of studying the adhesive activity of the sinus mucosal microbiome in ABRS are presented in Table 3.

Table 3

Characteristics of adhesive properties of clinical microbial strains isolated from maxillary sinuses of ABRS patients according to MAI (M±m) indicators

Microorganisms	Microorganism Adhesion Index (MAI)
S. aureus	9.63±0.29
S. epidermidis	9.89±0.28
S. warneri	7.50±0.39
S. mitis	4.09±0.12
S. gallolyticus	4.21±0.08
S. pyogenes	6.73±0.27
K. rizophilia	4.14 ± 0.13
R. kristinae	3.77± 0.12
M. catarrhalis	4.52±0.16
C. freundii	3.83±0.06
K. pneumoniae	6.22±0.18

Our research results revealed that microorganisms with the highest adhesive potential belong to the *Staphylococcus* genus. For coagulase-positive clinical isolates of *S. aureus*, the MAI was 9.63±0.29. Coagulase-negative staphylococci *S. epidermidis* and *S. warneri* also demonstrated high adhesive activity, with MAI values of 9.89±0.28 and 7.50±0.39, respectively. Other highly adhesive microorganisms included clinical isolates of: *S. pyogenes* (MAI 6.73±0.27); *K. pneumoniae* (MAI 6.22±0.18); *K. rizophilia* (MAI 4.14±0.13); *M. catarrhalis* (MAI 4.52±0.16). Moderate adhesive activity was observed in: *R. kristinae* (MAI 3.77±0.12) and *C. freundii* (MAI 3.9±0.06).

In Gram-positive clinical strains, adhesins are represented by surface proteins exhibiting hydrophobic properties that facilitate staphylococcal attachment to host cells. The presence of capsules, capsular-like polysaccharide substances, and teichoic acids further promotes bacterial adhesion to epithelium. Additionally, staphylococci and streptococci produce IgA proteases that cleave IgA, enhancing their adhesive effect. In Gram-negative bacteria, adhesins may include outer membrane proteins, fimbrial, and non-fimbrial compounds. The interaction between microbial adhesins and epithelial cell receptors in the maxillary sinuses is specific and irreversible, ensuring biotope colonization. Thus, the adhesive properties of pathogens and their high population levels constitute the initial link in the pathogenesis of ABRS.

Our research findings demonstrate the growing significance of opportunistic microbiota in the etiopathogenesis of ABRS, driven by the pathogenic potential of microorganisms and their high population levels. We suggest that the involvement of opportunistic pathogens in infectious-inflammatory processes may also be linked to reduced immunological reactivity in the population experiencing collective trauma due to Russia's full-scale invasion of Ukraine.

Conclusions

The following conclusions can be made:

1. The microbial landscape of the maxillary sinus biotope in acute bacterial rhinosinusitis is represented by the taxonomic types *Firmicutes* **(54%)**, *Actinobacteria* **(9%)**, and *Proteobacteria* **(37%)**, with *Firmicutes* being the most dominant.

2. The primary etiological agents of acute bacterial rhinosinusitis are *S. aureus (26%)*, *H. influenzae (13%)*, *M. catarrhalis* **(9%)**, and *K. pneumoniae (9%).*

3. Mixed infections were observed in **21% of cases (8 patients)**, with **two-component associations** in **15% (6 patients)** and **three-component associations** in **5% (2 patients)**.

4. Among clinical isolates colonizing the maxillary sinus mucosa, **81% exhibited high** and **19% moderate adhesive activity**. The strongest adhesive properties were found in representatives of the genus *Staphylococcus*, *Streptococcus*, *Kocuria*, and *Moraxella*.

5. Microbiological analysis confirmed the **etiologic significance** of opportunistic microorganisms such as *Kocuria spp.*, *Rothia spp.*, *Acinetobacter spp.*, and *Citrobacter spp.* in the development of acute bacterial rhinosinusitis.

BIBLIOGRAPHY

1. Fokkens WJ, Lund VJ, Hopkins C, et al. European Position Paper on Rhinosinusitis and Nasal Polyps 2020. *Rhinology*. 2020;58(Suppl S29):1–464. doi: 10.4193/Rhin20.600.

2. Loban' G, Faustova M, Dobrovolska O, Tkachenko P. War in Ukraine: incursion of antimicrobial resistance. *Ir J Med Sci*. 2023;192(6):2905–2907. PMID: 37178279. PMCID: PMC10182337. doi: 10.1007/s11845-023-03401-x.

3. Unified clinical protocol for primary and specialized medical care. Acute rhinosinusitis [Unifikovanyi klinichnyi protokol pervynnoi ta spetsializovanoi medychnoi dopomohy. Hostryi rynosynusyt]. 2023. (In Ukrainian). Available from: https://moz.gov.ua/uploads/10/50495-dn_1793_13102023_dod_1.pdf.

4. Jaume F, Valls-Mateus M, Mullol J. Common Cold and Acute Rhinosinusitis: Up-to-Date Management in 2020. *Curr Allergy Asthma Rep*. 2020;20(7):28. doi: 10.1007/s11882-020-00917-5.

5. Aring AM, Chan MM. Current Concepts in Adult Acute Rhinosinusitis. *Am Fam Physician.* 2016;94(2):97–105. PMID: 27419326.

6. Patel ZM, Hwang PH. Acute Bacterial Rhinosinusitis. *Infections of the Ears, Nose, Throat, and Sinuses*. 2018 May 4:133–143. doi: 10.1007/978-3-319-74835-1_11.

7. Khafagy Y, Moneir W, Salem MA, Ibrahim WM, Ebada HA. Increasing incidence of orbital complications of acute rhinosinusitis in the post COVID-19 era: A tertiary referral center experience. *Eur J Rhinol Allergy*. 2024;7(3):81–84. doi: 10.5152/ejra.2024150.

8. Vrynchanu NO, Dudikova DM, Hrynchuk NI, Nedashkivska VV. Biofilms. The current status and prospects of antimicrobial therapy [Bioplivky. Suchasnyi stan i perspektyvy antymikrobnoi terapii]. *Pharmacology and Drug Toxicology*. 2019;13(5):311–321. doi: 10.33250.13.05.311 (in Ukrainian).

9. Fedorchenko V, Polyanskaya V, Zachepilo S, Bobrova N, Loban G. Comprehensive study of anti-fungal effect of evgenol emulsion in polysorbat-80 on reference strain of candida albicans ATCC 885-653. *Georgian Med News*. 2018;9(282):166–170. (In Russian). PMID: 30358563.

10. Dickson R, Erb-Downward J, Martinez F, Huffnagle G. The microbiome and the respiratory tract. *HHS Public Access*. 2017;78:481–504. https://doi.org/10.1146/annurev-physiol-021115-105238.

11. Brook I. Microbiology of sinusitis. *Proc Am Thorac Soc*. 2011;8(1):90–100. doi: 10.1513/pats.201006-038RN.

12. Bezega M, Zachepylo S, Polianska V, Podovzhnii O. Current views on the functional status of the palatine tonsils in chronic tonsillitis and alternatives in treatment strategies (literature review). *Pol Otorhino Rev*. 2023;12(1):26–34. doi: 10.5604/01.3001.0016.3166.

13. Miah MS, Nix P, Koukkoullis A, Sandoe J. Microbial causes of complicated acute bacterial rhinosinusitis and implications for empirical antimicrobial therapy. *J Laryngol Otol*. 2016;130(2):169–175. doi: 10.1017/S0022215115003369.

14. Sawada S, Matsubara S. Microbiology of Acute Maxillary Sinusitis in Children. *Laryngoscope*. 2021;131(10):E2705-E2711. doi: 10.1002/lary.29564.

15. World Medical Association. World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects. *JAMA*. 2013;310(20):2191–2194. doi: 10.1001/jama.2013.281053.

16. Klymniuk SI, Savchuk MM, Andreichyn YuM, et al. Peculiarity of nose and nasopharynx microbiocenosis in people with influenza and acute respiratory viral infections [Osoblyvosti mikrobiotsenozu nosa ta nosohlotky u khvorykh na hryp ta HRVI]. *Infektsiini khvoroby*. 2014;3:38–42 (in Ukrainian).

17. Jabeen I, Islam S, Hassan AKMI, Tasnim Z, Shuvo SR. A brief insight into Citrobacter species – a growing threat to public health. *Front Antibiot*. 2023;2:1276982. doi: 10.3389/frabi.2023.1276982.

18. Ren J, Sun P, Wang M, Zhou W, Liu Z. Insights into the role of Streptococcus oralis as an opportunistic pathogen in infectious diseases. *Front Cell Infect Microbiol.* 2024;14:1480961. doi: 10.3389/fcimb.2024.1480961.

19. Ananieva MM, Faustova MO, Basarab IO, Loban' GA. Kocuria rosea, kocuria kristinae, leuconostoc mesenteroides as caries-causing representatives of oral microflora. *Wiad Lek*. 2017;70(2 pt 2):296–298. PMID: 29059646.

20. Polianska VP, Bezeha MI, Zachepylo SV, Zviaholska IM. The effect of essential oils on the viability and adhesive properties of clinical strains of candida albicans and candida glabrata obtained from patients with pharyngomycosis. *Klinichna ta profilaktychna medytsyna*. 2024;(8):77–78. https://doi.org/10.31612/2616-4868.8.2024.09 (in Ukrainian).

Надійшла до редакції 29.05.2025
Прийнята до друку 02.02.2026
Електронна адреса для листування s.v.zachepylo@gmail.com