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Sensitivity profile to antibacterial drugs of *Streptococcus pyogenes* isolated from patients with infections of various biotopes

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Streptococcus pyogenes is a Gram-positive, facultatively anaerobic, β-hemolytic bacterium, a typical human pathogen that causes pathological processes in various biotopes of the human body.The prevalence of the phenomenon of antibiotic resistance among bacteria requires the study of the sensitivity profile of pathogen strains to antibacterial drugs to develop a rational antibiotic therapy regimen. The biomaterial was inoculated on Columbia agar with 5% sheep blood, incubated at a temperature of +37 ± 1 ^{0}C for 18–24 hours in an atmosphere of 5% CO_2. Colonies whose morphotype corresponded to *S. pyogenes* were further identified using the bacitracin S test, PYR test, HIPPURAT test .A pure culture was isolated, and identification was performed using a GP card on a VITEK 2 Compact 15 bacteriological analyzer. The sensitivity of the isolated strains to antibacterial drugs was determined by the disk diffusion method in accordance with the requirements of the recommendations of the European Committee on Antimicrobial Susceptibility Testing. During the period 2021–2023, 50 strains of *S. pyogenes* isolated from the oropharynx of pediatric and adult patients with suspected upper respiratory tract infection and 21 strains isolated from wounds of adult patients were studied. It was found that the percentage of *S. pyogenes* strains isolated from the oropharynx of adults sensitive to benzylpenicillin was 100.0%, norfloxacin – 69.7%, erythromycin – 63.6%, clindamycin – 87.9%, tetracycline – 54.5%. The percentage of *S. pyogenes* strains isolated from the oropharynx of children sensitive to benzylpenicillin was 100.0%, norfloxacin – 82.4%, erythromycin – 70.6%, clindamycin – 94.1%, tetracycline – 64.7%. β-lactam antibiotics can be used in 100% of cases for the treatment of infections caused by *S. pyogenes* in children and adults. The increase in the number of *S. pyogenes* strains isolated from the oropharynx of children occurs in the autumn-winter-spring period of the year, and in adults – in the winter-spring-summer period. The aim of this study was to establish the level of susceptibility profile to antibacterial drugs of isolated *S. pyogenes* strains from pediatric and adult patients with infections of different biotopes.

Keywords: group A *Streptococcus*; antibiotic; children; wound; antibiotic resistance; oropharynx; Ukraine.

Introduction

Streptococcus pyogenes or Group A *Streptococcus* (GAS) is one of the common etiological causes of invasive and non-invasive bacterial infections of various biotopes in children and adults. Noninvasive infection caused by GAS can manifest as pharyngitis, tonsillitis, scarlet fever, erysipelas, and contagious impetigo, while invasive infection has clinical manifestations of necrotizing fasciitis, septic shock, and meningitis. Some of the more serious poststreptococcal complications or immunogenic sequelae include acute rheumatic fever, poststreptococcal glomerulonephritis, rheumatic heart disease, and toxic shock syndrome. Infections caused by *S. pyogenes* are most common in children and adolescents (Burckhardt et al., 2024; Keller et al., 2024; Gashaw et al., 2025).

GAS is a Gram-positive, facultatively anaerobic, β-hemolytic, chain-forming bacterium and is a typical human pathogen. Oropharyngeal carriage is approximately 3% for adults and 8% for school-age children, however, these rates show seasonal peaks in the fall-winter-spring period. According to statistics, one in three children experiences a sore throat each year, and pharyngotonsillitis or streptococcal tonsillitis is the cause of one in four of these cases. *S. pyogenes* accounts for 4–10% of cases of pharyngitis in adults (Bergsten et al., 2024; Biała et al., 2024; Tyrrell et al., 2024).

Acute sore throat or pharyngotonsillitis is a common reason for patients to seek primary care, often resulting in the prescription of antibiotics. Although acute sore throat is usually benign and resolves on its own, regardless of the causative agent of the infectious inflammation, it can sometimes lead to complications. Healthy individuals can become carriers of GAS in the oropharynx after recovery from an illness caused by the same pathogen, or without any previous illness, potentially through contact with other patients who have been infected with *S. pyogenes*, or asymptomatic carriers. Asymptomatic carriage of GAS is more common among children and adolescents than among adults. Human skin and mucous membranes are the only natural reservoirs of this organism, and it initially colonizes the oropharynx and skin, from where it can progress to severe disease. Misdiagnosis of carriers of *S. pyogenes* with a viral condition as a streptococcal infection may lead to unnecessary antibiotic exposure, which will not provide treatment benefits for patients and may catalyze the development of antibacterial drug (ABD) resistance in both *S. pyogenes* itself and other members of the human microbiome (Boutin et al., 2024; Marco et al., 2024; Woldan-Gradalska et al., 2024).

Streptococcus pyogenes is the most common cause of pharyngitis among school-aged children. It is responsible for 616 and 111 million cases of pharyngitis and pyoderma in children, respectively. Approximately 18 million people worldwide suffer from severe disease associated with this organism, with 1.78 million new cases and at least 517,000 deaths each year. More than 660,000 people suffer from invasive GAS infections, which result in more than 160,000 deaths worldwide each year. Pharyngitis caused by *S. pyogenes* is responsible for approximately 5.2 million outpatient visits and 2.8 million antibiotic prescriptions each year in the United States, accounting for 5.9% of all outpatient antibiotic prescriptions for children aged 3–9 years. According to the Centers for Disease Control and Prevention, GAS accounts for 20–30% of cases of pharyngitis in children and 5–15% of cases of pharyngitis in adults (Biała et al., 2024; Kline et al., 2024; Su et al., 2024). According to research by Australian scientists, the annual incidence of scarlet fever in the state of Victoria, Australia,

from 2007 to 2017 was generally stable, ranging from 1.9 cases per 100,000 in 2012 and 2014 to 3.1 cases per 100,000 in 2016 (mean 2.5 per 100,000). The researchers found no significant trend in annual incidence over the study period, adjusted for sex and age group (aIRR, 0.99, 95% CI 0.98–1.01) (Phakey et al., 2024).

Quick antibiotic treatment of GAS infections in children after microbiological confirmation is essential to prevent complications, further disease transmission, and death. Untreated GAS infections can progress to poststreptococcal complications, and inappropriate antibiotic prescribing based on inaccurate data can lead to the emergence and spread of antibiotic-resistant bacteria. Factors contributing to resistance include misuse, overuse, and poor infection prevention practices and empirical treatment practices. Diseases caused by *S. pyogenes* and their post-infectious sequelae, which predominantly affect children, have a significant public health and economic impact (Di Pietro et al., 2024; Su et al., 2024; Gashaw et al., 2025).

The human skin and mucous membranes are the first line of defense against *S. pyogenes* attachment to cells and subsequent invasion into the human body. They form a barrier immune system that is recognized as part of the innate immune system. Furthermore, in addition to the physical barriers that prevent pathogen entry, chemical barriers in the dermis also enhance the effectiveness of this barrier immune system. GAS has a high pathogenic potential due to its ability to carry multiple virulence factors, including the surface protein M, which is encoded by the emm gene. Several lineages of hypervirulent GAS strains have been identified to date, including emm 1 (global clone M1), as well as emm 3, emm 12, emm 28, emm 59, and emm 89. Today, there are over 250 registered serotypes of *S. pyogenes,* which exhibit a wide range of pathogenic effects in the blood, skin and soft tissues, the lymphatic system, and on immune cells and neurons (Bazhar et al., 2024; Mills et al., 2024; Sitkiewicz et al., 2024).

Clinical aspects are visualized alongside an example of a virulence factor with this property and, in some cases, a specific host cell receptor. This organism is spread by airborne droplets from asymptomatic oropharyngeal carriers, often school-aged children. In the blood, *S. pyogenes* causes hemolysis, multiplies, is able to dissolve thrombi, evade phagocytes, hyperactivate T cells, and disrupt B cell responses. It masquerades as host tissue elements, penetrates through pore-forming toxins, causes inflammation, pain, skin necrosis, and spreads through lymphatic vessels (Bergsten et al., 2024; Ramírez de Arellano et al., 2024; Su et al., 2024).

The pathogenesis of GAS consists of several steps. *S. pyogenes* overcomes physical barriers in the epidermis, bypasses chemical barriers and immune attacks by host leukocytes in the dermis, and spreads into deeper tissues. The initial attachment of the microorganism to the extracellular matrices of human skin and mucous membranes is due to strong adhesion to them through the interaction of the adhesins of the encapsulated GAS (M protein, F1 protein, and *S. pyogenes* fibronectin-binding protein) with host cell surface receptors (fibronectin, laminin, and collagen). When there is skin/mucosal damage, GAS or complement-opsonized GAS enters and aggressively infects host cells. Opsonization by *S. pyogenes* involves mannose-IgG-recognizing C1 interactions as well as a mannose-binding lectin related to the lectinserine protease family that binds mannan. GAS has various virulence factors – M protein, complement evasion factor, streptococcal pyrogenic exotoxin B, streptococcal C5a peptidase, hemolysins or streptolysins O and S, hyaluronic acid capsule, streptokinase, hyaluronidase, streptodornase or deoxyribonuclease, and other biologically active substances that affect human immune functions. GAS has always been considered an extracellular bacterium. However, there is growing evidence that this organism is capable of entering human cells by internalization, a mechanism that helps it evade antibiotics and phagocytosis, which increases antibiotic treatment failure, the development of biofilms, and the rise of antibacterial resistance (Cinicola et al., 2024; Martín-Delgado et al., 2024; Mills et al., 2024).

The M protein is one of the main factors in the pathogenicity of GAS, as it acts as an adhesion factor to the host epithelium and has anti-opsonin activity against the host immune system. The type of M protein determines the tropism of the strain to certain organs and tissues that are likely to be affected, in particular strains with M1 and M12 proteins are tropic to cells of the oropharyngeal mucosa, while the preferred tissue site for strain M81 is the skin. The tissue preference for strain M89 is unknown. Invasive infections caused by *S. pyogenes* are most commonly found in strains with proteins of the M1, M3, M6, M12, M18 and M28 types (Karapati et al., 2024; Matsui et al., 2024; Leśnik et al., 2025).

Effective empirical treatment of most infections caused by *S. pyogenes* is crucial for the prevention of poststreptococcal complications. β-lactam antibiotics, particularly penicillin, are considered the standard choice for empirical treatment of infections caused by this organism. Despite this, treatment failure remains a significant problem, possibly due to intracellular persistence of *S. pyogenes*, biofilm formation, protection by β-lactamase-producing bacteria, alteration of the commensal microbiota, or insufficient penetration of penicillin into tissues. Penicillin resistance remains a rare phenotype for *S. pyogenes*, but alarming rates of resistance to alternative treatments such as macrolides, lincosamides, and even third- and fourth-generation cephalosporins are causing public concern. Penicillin acts on penicillin-binding proteins (PBPs), limiting peptidoglycan synthesis, ultimately leading to streptococcal cell death. To date, rare strains of GAS have been identified that possess an altered penicillin-binding protein 2X (PBP2X) with a recombinant segment of *Streptococcus dysgalactiae* subspecies *equisimilis*, which contributes to a decrease in their sensitivity to penicillin. This led to the emergence of a new strain characterized by high fitness, virulence and reduced susceptibility to penicillin. Two clonally related strains of the rare type emm 43.4 have been recorded, which demonstrate lower susceptibility to various antibiotics. These two strains had identical non-synonymous mutations in the pbp2x gene, which encodes PBP2X. This mutation involves a threonine to lysine substitution at amino acid 553 (Thr553Lys), which was not found in susceptible strains of the emm 43.4 type. This discovery was perceived as the basis for the development of β-lactam resistance, which became a major cause of concern in the medical community (Lapthorne et al., 2024; Thacharodi et al., 2024; Geteneh et al., 2025).

Macrolides are antibiotics with a distinct macrocyclic lactone ring attached to deoxysugars. Some of the widely used macrolides include erythromycin, azithromycin, and telithromycin. They exhibit a broader spectrum of activity and are often prescribed to patients with penicillin allergies. Clindamycin is often prescribed as an adjunct to penicillin because it binds to 23S ribosomal RNA and *in vitro* immediately reduces GAS toxin production, providing an antitoxin effect. It is estimated that one in five invasive infections caused by *S. pyogenes* are caused by strains resistant to erythromycin and clindamycin, limiting clinicians' ability to prescribe antibacterial therapy. Recent reports show that the rate of resistance to macrolides is 32.8% in Spain, 40.0% in Turkey and Belgium, 98.4% in China, and 22.8% in Greece. Macrolide resistance in GAS is influenced by several mechanisms: ribosomal post-transcriptional and pre-transcriptional modification (methylation), active expulsion by efflux pumps, and target protection. Transcriptional modifications are determined by erythromycin-resistant proteins, which provide point mutation in the ribosomal system by methylating an adenyl residue on the 23S rRNA chain of *S. pyogenes* strains. The major genes conferring macrolide resistance include ermB, ermT, and ermTR. The US Centers for Disease Control and Prevention (CDC) Active Bacterial Surveillance Program reported an increase from 11.9% to 24.7% and from 8.9% to 23.8% of erythromycin- and clindamycin-resistant *S. pyogenes* strains, respectively, due to the expression of emm 77, emm 58, emm 11, emm 83, and emm 92. Another major mechanism of resistance involves the use of macrolide efflux pumps controlled by the mef(A) gene. Initially, mef(A) was thought to be the gene responsible for conferring macrolide resistance in GAS, but a new gene, namely msr(D), was discovered along with mef(A), which also helped confer macrolide resistance in *S. pyogenes* strains (Thacharodi et al., 2024; Geteneh et al., 2025; Ünübol et al., 2025).

Tetracycline is an oral antibiotic derived from *Streptomyces* bacteria that acts on bacterial cells by inhibiting protein translation. Several well-known tetracycline antibiotics include doxycycline and eravacycline. Tetracycline resistance was not a prominent phenomenon

in *S. pyogenes* until the early 21st century. Tetracycline resistance has been shown to be due to the presence of the tetO, tetM, and tetK genes. Studies of several tetracycline-resistant GAS strains carrying the tetM gene have shown that the prtF1 gene, which is used to synthesize the fibronectin-binding protein F1 for cell adhesion, was found in 60% of tetracycline-resistant strains compared to 28% of tetracycline-susceptible strains. Efflux pumps also constitute an important part of tetracycline resistance in *S. pyogenes* strains, as these pumps are membrane-bound and are mainly controlled by the plasmid-encoded tetK and tetL genes. These genes actively work together to pump excess tetracycline out of the cytoplasm and slow its accumulation, thereby conferring tetracycline resistance. Fluoroquinolones have high antibiotic activity and are rarely prescribed as empiric antibacterial therapy due to adverse side effects such as gastrointestinal and central nervous system toxicity. In most cases, they are used as a last resort in the treatment of invasive infections caused by GAS. Fluoroquinolones act by inhibiting two type II DNA topoisomerases, DNA gyrase and topoisomerase IV, which leads to the arrest of DNA replication and, consequently, cell death. In recent years, there has been an increase in fluoroquinolone-resistant GAS strains, which has led to the need for a deeper understanding of the mechanism involved in the development of fluoroquinolone resistance. Resistance to fluoroquinolones is due to mutations in the amino acid sequences of ParC, ParE, and GyrA, with all isolates having at least one mutation in their ParC sequence. Sulfamethoxazole and trimethoprim are bacteriostatic antimicrobials commonly prescribed for respiratory diseases. They work by inhibiting dihydrofolate production, stopping the production of folic acid in GAS bacterial cells. Folate plays a key role in DNA replication, and inhibition of the folate cycle inevitably leads to cell death. The genes that contribute to this resistance are variants of the Dyr sequences, namely DfrF, DfrA, and DrfG, which are dihydrofolate reductases (Thacharodi et al., 2024).

The aim of this study was to establish the level of susceptibility profile to antibacterial drugs of isolated *S. pyogenes* strains from pediatric and adult patients with infections of various biotopes who received medical care at the Municipal Non-Commercial Enterprise "City Clinical Hospital No. 6" of the Dnipro City Council.

Materials and methods

Study area and data collection. Informed Consent Statement: Patients gave their informed consent in accordance with the primary accounting documentation No. 003-6/o "Informed voluntary consent of the patient for diagnosis, treatment and surgery and anesthesia and for the presence or participation of participants in the educational process". This study was conducted during 2021–2023 by bacteriological culture of oropharyngeal and wound samples from patients. Oropharyngeal samples from children and adults were collected before the administration of ABD. The procedure was performed on an empty stomach with sterile disposable applicators and delivered to the bacteriological laboratory within 2 hours of collection. When using a transport medium, the delivery time was increased to 72 hours. Samples of wound discharge from children and adults were also collected before the administration of ABD, using sterile disposable applicators and delivered to the bacteriological laboratory within 2 hours of collection. When using a transport medium, the delivery time was increased to 72 hours. The biomaterial was transferred to Columbia agar with 5% sheep blood (Graso, Poland), incubated at a temperature of +37 ± 1 C for 18–24 hours in an atmosphere of 5% CO_2. Colonies, the morphotype of which corresponded to *S. pyogenes*, were further identified using the bacitracin S test (Erba Lachema, Czech Republic), PYR test (Erba Lachema, Czech Republic), Hippurat test (Erba Lachema, Czech Republic). A pure culture was isolated, identification was carried out using a GP card (BioMeriuex, France) on a Vitek 2 Compact 15 bacteriological analyzer (BioMeriuex, France). The susceptibility of the isolated strains to ABD was determined by the disk diffusion method in accordance with the requirements of the recommendations of the European Committee on Antimicrobial Susceptibility Testing (Eucast). The following ABD discs were used: benzylpenicillin (1 U) (Liofilchem, Italy), norfloxacin (10 μg) (Farmaktiv, Ukraine), erythromycin (15 μg) (Farmaktiv, Ukraine), clindamycin (2 μg) (Farmaktiv, Ukraine), tetracycline (30 μg) (Farmaktiv, Ukraine). For determination of sensitivity by disk diffusion method according to EUCAST recommendations, Mueller-Hinton agar + 5% defibrinated horse blood and 20 mg/L β-NAD (Graso, Poland) were used. Cultures were incubated at +35 ± 1 ^{0}C for 18 ± 2 hours in an atmosphere of 5% CO_2. The diameters of growth inhibition zones around the ABD disks were measured with a calibrated ruler. Quality control of the studies was performed in accordance with the approved internal laboratory quality control program and EUCAST recommendations.

Statistical data processing was carried out using ANOVA analysis of variance to find the dependence in the obtained data by examining the significance of differences in mean values and correlation. The one-way analysis of variance (ANOVA) test was applied for the diameters of growth retardation zones (mm), considering $P < 0.05$ as statistically significant.

Results

During the period 2021–2023, we studied 50 strains of *S. pyogenes* isolated from the oropharynx of patients with suspected upper respiratory tract infection who sought medical help at the Municipal non-commercial enterprise "City Clinical Hospital No. 6" of the Dnipro City Council (Dnipro, Ukraine), including 17 strains (34.0%) obtained from children, 33 strains (66.0%) from adults.

The number of *S. pyogenes* strains isolated from the oropharynx of children and adults depending on the period of the year for 2021–2023 is shown in Figure 1.

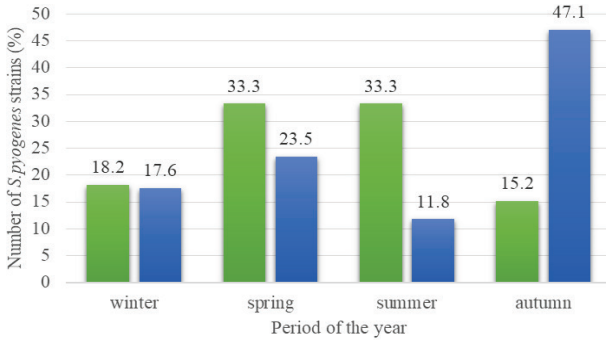

Fig. 1. Distribution of the number of *S. pyogenes* strains isolated from the oropharynx of children and adults depending on the period of the year for 2021–2023 ($\chi^2 = 8.121$, $P < 0.05$), green columns – adults (n = 33), blue columns – children (n = 17)

It was found that in 2021–2023, the number of *S. pyogenes* strains isolated from the oropharynx of adults in the winter period was 18.2%, in spring – 33.3%, in summer – 33.3%, in autumn – 15.2% (correlation coefficient is –0.12; $P < 0.05$). Among children, the distribution rate of GAS strains isolated from the oropharynx in 2021–2023 in the winter period was 17.6%, in spring – 23.5%, in summer – 11.8%, in autumn – 47.1% (correlation coefficient is 0.64; $P < 0.05$).

The number of *S. pyogenes* strains isolated from the oropharynx of children and adults depending on the type of medical care provided for 2021–2023 is given in Table 1.

It was found that in 2021–2023, the number of GAS strains isolated from the oropharynx of adults was 51.5% for outpatient diseases and 48.5% for inpatient diseases, this distribution among children was 58.8% for outpatient diseases and 41.2% for inpatient diseases.

The number of *S. pyogenes* strains isolated from the oropharynx of children and adults, depending on age, for 2021–2023 is given in Table 2. It was found that in 2021–2023, 57.6% of *S. pyogenes* strains were isolated from the oropharynx of adults aged 18 to 30 years, 42.4% – 30 years and older. Among children under 5 years of age, the number of *S. pyogenes* strains isolated from the oropharynx was 52.9%, from 5 years to 17 years – 47.1%. The number of *S. pyogenes* strains isolated from the oropharynx of children and adults, depending on gender, for 2021–2023 is given in Table 3.

Table 1
Distribution of the number of *S. pyogenes* strains isolated from the oropharynx of children and adults depending on the type of medical care provided in 2021–2023

Type of medical care provided	Age category of patients			
	adults (n = 33) (χ^2 = 3.975, P < 0.05)		children (n = 17) (χ^2 = 4.121, P < 0.05)	
	number of strains	%	number of strains	%
Outpatient	17	51.5	10	58.8
Inpatient	16	48.5	7	41.2

Table 2
Distribution of the number of *S. pyogenes* strains isolated from the oropharynx of children and adults in relation to age for 2021–2023

Age of adult patients	Number of strains *GAS* (n = 33) (χ^2 = 4.294, P < 0.05)		Age of children	Number of strains *GAS* (n = 17) (χ^2 = 4.356, P < 0.05)	
	absolute number	%		absolute number	%
18–30 years old	19	57.6	< 5 years	9	52.9
≥ 30 years	14	42.4	5–17 years old	8	47.1

Note: GAS – group A *Streptococcus*.

Table 3
Distribution of the number of *S. pyogenes* strains isolated from the oropharynx of children and adults in relation to gender for 2021–2023

Gender of adult patients	Number of strains *GAS* (n = 33) (χ^2 = 3.912, P < 0.05)		Gender of children	Number of strains *GAS* (n = 17) (χ^2 = 4.012, P < 0.05)	
	absolute number	%		absolute number	%
Female	27	81.8	Female	11	64.7
Male	6	18.2	Male	6	35.3

Note: GAS – group A *Streptococcus*.

It was found that in 2021–2023, 81.8% of *S. pyogenes* strains were isolated from the oropharynx of adult women, 18.2% from adult men. Among children, the number of *S. pyogenes* strains isolated from the oropharynx was 64.7% for girls, 35.3% for boys.

The antibacterial susceptibility profile of *S. pyogenes* strains isolated from the oropharynx of children and adults for 2021–2023 is shown in Figure 2.

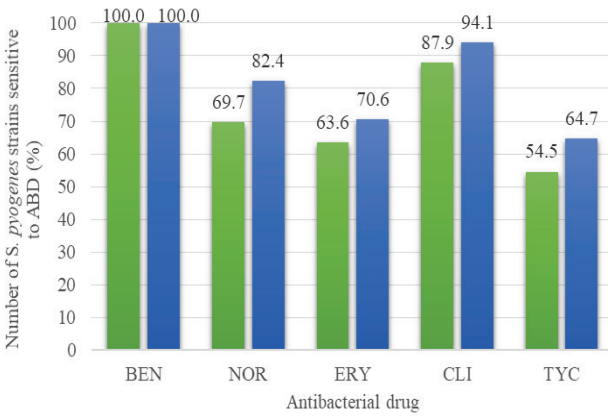

Fig. 2. Number of ABD-sensitive *S. pyogenes* strains isolated from the oropharynx of children and adults in 2021–2023 (χ^2 = 3.978, P < 0.05), green columns – adults (n = 33), blue columns – children (n = 17), BEN – benzylpenicillin, NOR – norfloxacin, ERY – erythromycin, CLI – clindamycin, TYC – tetracycline

It was found that in 2021–2023, the percentage of GAS strains isolated from the oropharynx of adults (n = 33) sensitive to benzylpenicillin was 100.0%, norfloxacin – 69.7%, erythromycin – 63.6%, clindamycin – 87.9%, tetracycline – 54.5%. The percentage of *S. pyogenes* strains isolated from the oropharynx of children (n = 17) sensitive to benzylpenicillin was 100.0%, norfloxacin – 82.4%, erythromycin – 70.6%, clindamycin – 94.1%, tetracycline – 64.7%.

The antibacterial drug resistance profile of *S. pyogenes* strains isolated from the oropharynx of children and adults for 2021–2023 is shown in Figure 3. It was found that in 2021–2023, the percentage of *S. pyogenes* strains isolated from the oropharynx of adults (n = 33) resistant to benzylpenicillin was 0.0%, norfloxacin – 30.3%, erythromycin – 36.4%, clindamycin – 12.1%, tetracycline – 45.5%. The precentage of GAS strains isolated from the oropharynx of children (n = 17) resistant to benzylpenicillin was 0.0%, norfloxacin – 17.6%, erythromycin – 29.4%, clindamycin – 5.9%, tetracycline – 35.3%.

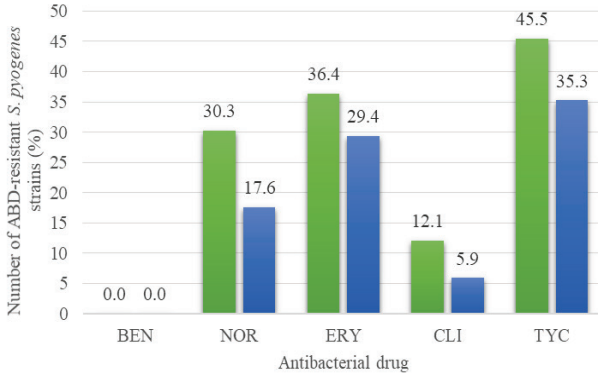

Fig. 3. Number of ABD-resistant *S. pyogenes* strains isolated from the oropharynx of children and adults in 2021–2023 (χ^2 = 3.865, P < 0.05), green columns – adults (n = 33), blue columns – children (n = 17), BEN – benzylpenicillin, NOR – norfloxacin, ERY – erythromycin, CLI – clindamycin, TYC – tetracycline

During the period 2021–2023, we studied 21 strains of *S. pyogenes* isolated from wounds of adult patients. The number of GAS strains isolated from wounds of adult patients depending on the type of medical care provided for 2021–2023 is given in Table 4.

Table 4
Distribution of the number of *S. pyogenes* strains isolated from wounds of adult patients depending on the type of medical care provided in 2021–2023

Type of medical care provided	Number of strains *GAS* (n = 21) (χ^2 = 3.914, P < 0.05)	
	absolute number	%
Outpatient	10	47.6
Inpatient	11	52.4

Note: GAS – group A *Streptococcus*.

It was found that for the years 2021–2023, the number of *S. pyogenes* strains isolated from wounds of adult patients was 47.6% for outpatients and 52.4% for inpatients. The number of GAS strains isolated from wounds of adult patients depending on age for the years 2021–2023 is given in Table 5. It was found that in 2021–2023, 23.8% of *S. pyogenes* strains were isolated from wounds of adult patients aged 18 to 30 years, 76.2% – 30 years and older. The number of *S. pyogenes* strains isolated from wounds of adult patients depending on the period of the year for 2021–2023 is shown in Figure 4.

Table 5
Distribution of the number of *S. pyogenes* strains isolated from wounds of adult patients depending on age for 2021–2023

Age of adult patients	Number of strains *GAS* (n = 21) (χ^2 = 4.454, P < 0.05)	
	absolute number	%
18–30 years old	5	23.8
≥ 30 years	16	76.2

Note: GAS – group A *Streptococcus*.

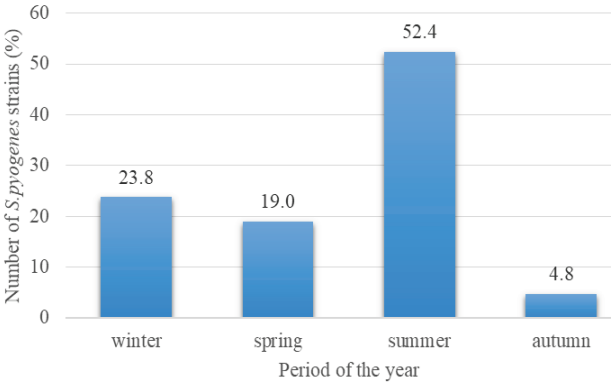

Fig. 4. Distribution of the number of *S. pyogenes* strains isolated from wounds of adult patients (n = 21) depending on the period of the year for 2021–2023 (χ^2 = 4.436, P < 0.05)

It was found that in 2021–2023, the percentage of *S. pyogenes* strains isolated from wounds of adult patients in the winter period was 23.8%, in spring – 19.0%, in summer – 52.4%, in autumn – 4.8% (correlation coefficient is –0.15; P < 0.05).

The profile of sensitivity and resistance to antibacterial drugs of *S. pyogenes* strains isolated from wounds of adults in 2021–2023 is shown in Figure 5.

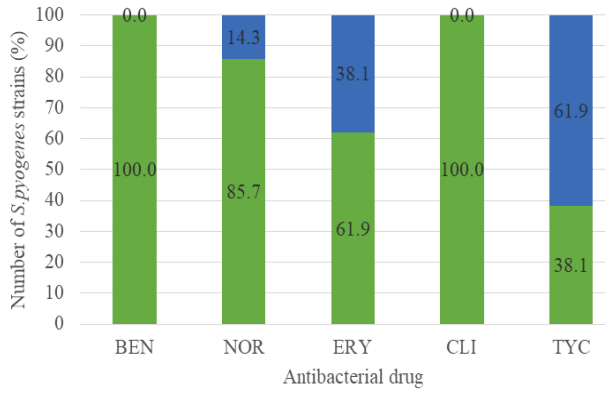

Fig. 5. Susceptibility profile to ABD of *S. pyogenes* strains isolated from wounds of adult patients in 2021–2023 (n = 21, χ^2 = 4.054, P < 0.05), green columns – number of susceptible strains, blue columns – number of resistant strains, BEN – benzylpenicillin, NOR – norfloxacin, ERY – erythromycin, CLI – clindamycin, TYC – tetracycline

It was found that in 2021–2023, the percentage of *S. pyogenes* strains (n = 21) isolated from wounds of adult patients sensitive to benzylpenicillin was 100.0%, norfloxacin – 85.7%, erythromycin – 61.9%, clindamycin – 100.0%, tetracycline – 38.1%. The ABD resistance rate of GAS strains isolated from wounds of adult patients (n = 21) for benzylpenicillin was 0.0%, norfloxacin – 14.3%, erythromycin – 38.1%, clindamycin – 0.0%, tetracycline – 61.9%.

A comparison of the susceptibility profile to ABD of *S. pyogenes* strains isolated from the oropharynx (n = 33) and wounds (n = 21) of adult patients for 2021–2023 is shown in Figure 6.

It was found that the sensitivity indicators to ABD of *S. pyogenes* strains isolated from the oropharynx (n = 33) and wounds (n = 21) of adult patients in 2021–2023 to benzylpenicillin and erythromycin do not differ, but the indicators of sensitivity to norfloxacin, clindamycin, and tetracycline do differ from each other.

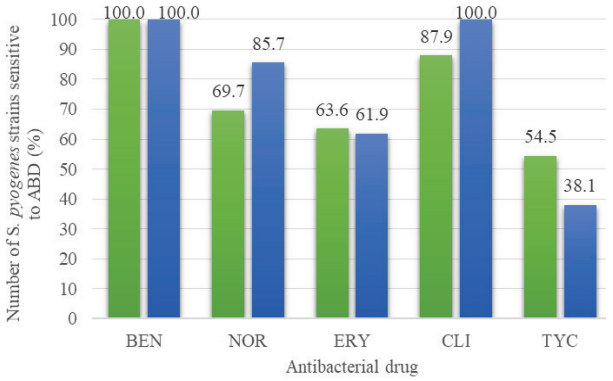

Fig. 6. Comparison of the susceptibility profile to ABD of *S. pyogenes* strains isolated from the oropharynx (n = 33) and wounds (n = 21) of adult patients in 2021–2023 (χ^2 = 7.811, P < 0.05), green columns – the number of susceptible strains from the oropharynx, blue columns – the number of susceptible strains from wounds, BEN – benzylpenicillin, NOR – norfloxacin, ERY – erythromycin, CLI – clindamycin, TYC – tetracycline

Discussion

We found that during the period 2021–2023, the number of *S. pyogenes* strains isolated from the oropharynx of children was greatest in the autumn-winter-spring period of the year, which is 88.2%, with the largest number of strains being isolated in the autumn and spring periods. These indicators correlate with the data obtained by Italian and Polish researchers (Biała et al., 2024; Di Pietro et al., 2024). Having analyzed the dependence of the number of isolated GAS strains from the oropharynx of adults, it was found that the largest number of strains was isolated in the winter-spring-summer period, especially in the spring and summer periods of the year, 33.3%, respectively. These indicators partially correlate with the data obtained by Polish and American researchers (Biała et al., 2024; Kline et al., 2024).

We found that the distribution of the number of GAS strains isolated from the oropharynx of children and adults in relation to the type of medical care provided for 2021–2023 indicates the preference of patients with *S. pyogenes* infection for outpatient hospital visits and the prescription of antibacterial therapy in outpatient settings, which correlates with the data of Australian researchers. According to the results of our study, it was found that the largest number of *S. pyogenes* strains was isolated from the oropharynx of adults aged 18 to 30 years, among children this indicator was highest in the age group up to 5 years, which correlates with the data of Australian researchers (Phakey et al., 2024).

Analysis of the distribution of the number of *S. pyogenes* strains isolated from the oropharynx of children and adults depending on gender in 2021–2023 found that GAS strains were most often isolated among adult female patients (81.8%) and among girls (64.7%), which correlates with the data obtained by Polish researchers (Biała et al., 2024). However, this indicator differs significantly from those of Australian researchers (Phakey et al., 2024), who found that *S. pyogenes* strains were most often isolated from the oropharynx of male adults and children.

We found that in 82.4% of cases, *S. pyogenes* strains isolated from the oropharynx of children were sensitive to norfloxacin, 70.6% of strains were sensitive to erythromycin, 64.7% were sensitive to tetracycline. It was found that in 69.7% of cases, GAS strains isolated from the oropharynx of adults were sensitive to norfloxacin, 63.7% of strains were sensitive to erythromycin and 54.5% were sensitive to tetracycline. In 85.7% of cases, GAS strains isolated from wounds of adults were susceptible to norfloxacin, 61.9% of strains were susceptible to erythromycin, 38.1% were susceptible to tetracycline. A comparison of the susceptibility profile to ABD of isolated *S. pyogenes* strains from the oropharynx of children and adults with the indicators of researchers from other countries is presented in Table 6.

Table 6
Comparative characteristics of the susceptibility profile to ABD *S. pyogenes* from biomaterial of children and adults with indicators of researchers from other countries

Country	Number of strains susceptible to ABD *GAS*, %				
	BEN	NOR	ERY	CLI	TYC
Dnipro, Ukraine (children, oropharynx)	100.0	82.4	70.6	94.1	64.7
Dnipro, Ukraine (adults, oropharynx)	100.0	69.7	63.6	87.9	54.5
Dnipro, Ukraine (adults, wounds)	100.0	85.7	61.9	100.0	38.1
Southern Ethiopia (Gebre et al., 2024)	100.0	–	59.1	95.5	59.1
Northern Ethiopia (Meles et al., 2024)	45.2	95.2	85.6	92.8	71.2
Bulgaria (Gergova et al., 2024)	–	100.0	60.0	100.0	100.0
Greece (Gergova et al., 2024)	–	98.0	79.6	81.3	59.2
Spain (Gergova et al., 2024)	–	100.0	91.3	96.1	88.0
Hungary (Gergova et al., 2024)	–	86.5	89.5	90.8	100.0
USA (Gergova et al., 2024)	–	98.6	77.0	100.0	77.4
South Africa (Rampersadh et al., 2024)	100.0	100.0	99.0	100.0	91.6
Turkey (Ünübol et al., 2025)	100.0	95.8	89.5	91.6	34.7

Note: GAS – group A *Streptococcus*; BEN – benzylpenicillin, NOR – norfloxacin, ERY – erythromycin, CLI – clindamycin, TYC – tetracycline.

It was established that the sensitivity indices to benzylpenicillin of isolated *S. pyogenes* strains from the oropharynx of children and adults in Dnipro, Ukraine, obtained by us, correlate with each other, therefore β-lactam antibiotics can be used in 100% of cases for the treatment of infections caused by this microorganism among children and adults. The sensitivity index we obtained for GAS strains isolated from the oropharynx of children to norfloxacin, erythromycin, clindamycin, and tetracycline is 12.7%, 7.0%, 6.2%, and 10.2% higher than that in adult patients, respectively.

The benzylpenicillin susceptibility profile of isolated *S. pyogenes* strains from the oropharynx and wounds of adult patients in Dnipro, Ukraine correlates with each other, therefore β-lactam antibiotics can be used in 100% of cases for the treatment of infections caused by this microorganism. The sensitivity index to norfloxacin and clindamycin of *S. pyogenes* strains isolated from the oropharynx of adults obtained by us is 16.0% and 12.1% lower than that of strains isolated from wounds of adult patients, respectively. The erythromycin susceptibility profile of GAS strains isolated from the oropharynx and wounds of adults is the same. The tetracycline susceptibility profile of *S. pyogenes* strains isolated from the oropharynx of adults is 16.4% higher than the susceptibility profile of strains isolated from wounds. It was found that the sensitivity index to benzylpenicillin of GAS strains isolated from the oropharynx of children and adults obtained by us correlates with the data of researchers from Turkey, South Africa, and Southern Ethiopia and differs significantly from the indicators of researchers from Northern Ethiopia. The norfloxacin susceptibility profile of *S. pyogenes* strains isolated from the oropharynx of children and adults obtained by us correlates with the data of researchers from Hungary and is lower than the indicators of other researchers. The erythromycin susceptibility profile of GAS strains isolated from the oropharynx of children and adults partially correlates with the data of researchers from the European Region, being 6.4% lower than the rates in the USA, higher than the rates in Southern Ethiopia, and lower than the rates in South Africa and Turkey. It was found that the sensitivity index to clindamycin of isolated *S. pyogenes* strains from the oropharynx of children and adults, obtained by us, correlates with the data of researchers from Ethiopia, countries of the European region and Turkey, and is 5.9% lower than the index for the USA and South Africa. The sensitivity to tetracycline of GAS strains isolated from the oropharynx of children and adults correlates with the data of researchers from Ethiopia and Greece, is lower than the indicators of other countries of the European Region and the USA, and is significantly higher than the indicators in Turkey. Thus, we achieved our goal and confirmed the hypothesis of our research.

Conclusions

β-lactam antibiotics can reasonably be used as the main group of drugs for the treatment of infections caused by *S. pyogenes* in children and adults. The ABD susceptibility profile of *S. pyogenes* strains among children and adults correlates with data from researchers in other countries. The ABD susceptibility profiles of GAS strains isolated from the oropharynx and wounds of adult patients are partially different.

The increase in the number of *S. pyogenes* strains isolated from the oropharynx of children occurs in the autumn-winter-spring period of the year, and in adults – in the winter-spring-summer period.

The results of our study established the antibacterial drug susceptibility profile of *S. pyogenes* strains, which will allow clinicians to prescribe empirical antibacterial therapy for infections caused by this microorganism among children and adults, with subsequent adjustment after receiving the antibiotic sensitivity test of the bacteriological study. Antimicrobial resistance is a global problem in the public health and healthcare system, which requires the results of analyzing the distribution of resistant strains and antimicrobial susceptibility profile indicators.

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References

Bazhar, S., El-Benaissi, Y., Benaissa, E., Ben Lahlou, Y., & Chadli, M. (2024). Invasive *Streptococcus pyogenes* infection: A case report. Access Microbiology, 6(7), 000767.v3.

Bergsten, H., & Nizet, V. (2024). The intricate pathogenicity of Group A *Streptococcus*: A comprehensive update. Virulence, 15(1), 2412745.

Biała, M., Babicki, M., Malchrzak, W., Janiak, S., Gajowiak, D., Żak, A., Kłoda, K., Gibas, P., Ledwoch, J., Myśliwiec, A., Kopyt, D., Węgrzyn, A., Knysz, B., & Leśnik, P. (2024). Frequency of group A *Streptococcus* infection and analysis of antibiotic use in patients with pharyngitis – A retrospective, multicenter study. Pathogens, 13(10), 846.

Boutin, S., Arnold, B., Alabi, A.S., Bélard, S., Toepfner, N., & Nurjadi, D. (2024). Genomic epidemiology of *Streptococcus pyogenes* from pharyngeal and skin swabs in Gabon. Microbiolology Spectrum, 12(7), e0426523.

Burckhardt, I., & Burckhardt, F. (2024). Epidemiology of *Streptococcus pyogenes* disease before, during, and after COVID-19 pandemic, Germany, 2005–2023. Emerging Infectious Diseases, 30(11), 2435–2438.

Cinicola, B. L., Sani, I., Pulvirenti, F., Capponi, M., Leone, F., Spalice, A., Montalbano, A., Macari, A., Fonte, M. T., Giampietro, P. G., Buonsenso, D., Zicari, A. M., Rongai, T., & Italian Pediatrician Federation (FIMP), Lazio Region (2024). Group A *Streptococcus* infections in children and

adolescents in the post-COVID-19 era: A regional Italian survey. Italian Journal of Pediatrics, 50(1), 177.
Di Pietro, G. M., Marchisio, P., Bosi, P., Castellazzi, M. L., & Lemieux, P. (2024). Group A streptococcal infections in pediatric age: Updates about a re-emerging pathogen. Pathogens, 13(5), 350.
Gashaw, Y., Getaneh, A., Kasewm D., Tigabie, M., & Gelaw, B. (2025). *Streptococcus pyogenes* carriage rate, associated factors and antimicrobial susceptibility profiles among urban and rural schoolchildren at Gondar city, Northwest Ethiopia. Scientific Reports, 15(1), 2057.
Gebre, A. B., Fenta, D. A., Negash, A. A., & Hayile, B. J. (2024). Prevalence, antibiotic susceptibility pattern and associated factors of *Streptococcus pyogenes* among pediatric patients with acute pharyngitis in Sidama, Southern Ethiopia. International Journal of Microbiology, 2024, 9282571.
Gergova, R., Boyanov, V., Muhtarova, A., & Alexandrova, A. (2024). A review of the impact of streptococcal infections and antimicrobial resistance on human health. Antibiotics, 13(4), 360.
Geteneh, A., Biset, S., & Reta, M. A. (2025). Emerging β-lactam non-susceptibility in group A *Streptococcus*: Implications for Ethiopia's healthcare system. JAC Antimicrobial Resistance, 7(1), dlaf020.
Karapati, E., Tsantes, A. G., Iliodromiti, Z., Boutsikou, T., Paliatsiou, S., Domouchtsidou, A., Ioannou, P., Petrakis, V., Iacovidou, N., & Sokou, R. (2024). Group A *Streptococcus* infections in children: Epidemiological insights before and after the COVID-19 pandemic. Pathogens, 13(11), 1007.
Keller, N., Boumasmoud, M., Andreoni, F., Tarnutzer, A., von Matt, M., Scheier, T. C., Epprecht, J., Weller, D., Gómez-Mejia, A., Huemer, M., von Reibnitz, D., Fontein, D. B. Y., Marques-Maggio, E., Schuepbach, R. A., Mairpady-Shambat, S., Brugger, S. D., & Zinkernagel, A. S. (2024). Investigating group A *Streptococcus* antibiotic tolerance in necrotizing fasciitis. mSphere, 9(9), e0063424.
Kline, M. C., Kissler, S. M., Whittles, L. K., Barnett, M. L., & Grad, Y. H. (2024). Spatiotemporal trends in group A streptococcal pharyngitis in the United States. Clinical Infectious Diseases, 78(5), 1345–1351.
Lapthorne, S., McWade, R., Scanlon, N., Ní Bhaoill, S., Page, A., O'Donnell, C., Dornikova, G., Hannan, M., Lynch, B., Lynch, M., & Brady, D. (2024). Rising clindamycin resistance in group A *Streptococcus* in an Irish healthcare institution. Access Microbiology, 6(6), 000772.v4.
Leśnik, P., Janc, J., Biała, M., Bartoszewicz, M., Łysenko, L., & Słabisz, N. (2025). Old bug-new challenges after COVID-19 pandemic: Severe invasive *Streptococcus pyogenes* infections in adults – A single-center experience in Poland. Pathogens, 14(2), 199.
Marco, D. N., Canela, J., Brey, M., Soriano, A., Pitart, C., & Herrera, S. (2024). Assessing the influence of the COVID-19 pandemic on the incidence, clinical presentation, and clindamycin resistance rates of *Streptococcus pyogenes* infections. IJID Regions, 11, 100349.
Martín-Delgado, M. C., De Lucas Ramos, P., García-Botella, A., Cantón, R., García-Lledó, A., Hernández-Sampelayo, T., Gómez-Pavón, J., González Del Castillo, J., Martín Sánchez, F. J., Martínez-Sellés, M., Molero García, J. M., Moreno Guillén, S., Rodríguez-Artalejo, F. J., Ruiz-Galiana, J., Burillo, A., Muñoz, P., Calvo Rey, C., Catalán-González, M., Cendejas-Bueno, E., Halperin-Benito, V., Recio, R., Viñuela-Benítez, C., & Bouza, E. (2024). Invasive group A *Streptococcus* infection (*Streptococcus pyogenes*): Current situation in Spain. Revista Española de Quimioterapia, 37(6), 454–471.
Matsui, Y., Mizuno, S., Anraku, M., Yamaguchi, T., Sugino, M., Kawahara, R., & Kasai, M. (2025). Clinical and microbiological characterization of invasive group a *Streptococcus* infection in children in Japan: A single-center experience. Journal of Infection and Chemotherapy, 31(2), 102560.
Meles, H. N., Aregawi, B. B., Gebregergis, M. W., Hailekiros, H., Weldu, Y., Thangaraju, P., Thiruvengadam, M., Alharbi, N. S., & Saravanan, M. (2024). Prevalence, antimicrobial susceptibility patterns and associated factors of *Streptococcus pyogenes* among apparently healthy school children in Mekelle city primary schools, Northern Ethiopia. Heliyon, 10(14), e34769.
Mills, J. L., Lepletier, A., Ozberk, V., Dooley, J., Kaden, J., Calcutt, A., Huo, Y., Hicks, A., Zaid, A., Good, M. F., & Pandey, M. (2024). Disruption of IL-17-mediated immunosurveillance in the respiratory mucosa results in invasive *Streptococcus pyogenes* infection. Frontiers in Immunology, 15, 1351777.
Phakey, S., Campbell, P. T., & Gibney, K. B. (2024). Epidemiology of scarlet fever in Victoria, Australia, 2007–2017. Epidemiology and Infection, 152, e116.
Ramírez de Arellano, E., Saavedra-Lozano, J., Villalón, P., Jové-Blanco, A., Grandioso, D., Sotelo, J., Gamell, A., González-López, J. J., Cervantes, E., Gónzalez, M. J., Rello-Saltor, V., Esteva, C., Sanz-Santaeufemia, F., Yagüe, G., Manzanares, Á., Brañas, P., Ruiz de Gopegui, E., Carrasco-Colom, J., García, F., Cercenado, E., Mellado, I., Del Castillo, E., Pérez-Vazquez, M., Oteo-Iglesias, J., Calvo, C., & Spanish PedGAS-Net/CIBERINFEC GAS Study Group (2024). Clinical, microbiological, and molecular characterization of pediatric invasive infections by *Streptococcus pyogenes* in Spain in a context of global outbreak. mSphere, 9(3), e0072923.
Rampersadh, K., Engel, K. C., Engel, M. E., & Moodley, C. (2024). A survey of antibiotic resistance patterns among Group A *Streptococcus* isolated from invasive and non-invasive infections in Cape Town, South Africa. Heliyon, 10(13), e33694.
Sitkiewicz, I., Borek, A., Gryko, M., Karpińska, A., Kozińska, A., Obszańska, K., Wilemska-Dziaduszycka, J., Walory, J., Bańska, A., Belkiewicz, K., Foryś, M., Gołębiewska, A., Hryniewicz, W., Kadłubowski, M., Kiedrowska, M., Klarowicz, A., Matynia, B., Ronkiewicz, P., Szczypa, K., Waśko, I., Wawszczak, M., Wróbel-Pawelczyk, I., & Zieniuk, B. (2024). Epidemiology of *Streptococcus pyogenes* upper respiratory tract infections in Poland (2003–2017). Journal of Applied Genetics, 65(3), 635–644.
Su, M. S.-W., Cheng, Y.-L., Lin, Y.-S., & Wu, J.-J. (2024). Interplay between group A *Streptococcus* and host innate immune responses. Microbiolology and Molecular Biololgy Reviews, 88(1), e0005222.
Thacharodi, A., Hassan, S., Vithlani, A., Ahmed, T., Kavish, S., Geli Blacknell, N. M., Alqahtani, A., & Pugazhendhi, A. (2024). The burden of group A *Streptococcus* (GAS) infections: The challenge continues in the twenty-first century. iScience, 28(1), 111677.
Tyrrell, G. J., Croxen, M., McCullough, E., Li, V., Golden, A. R., & Martin, I. (2024). Group A streptococcal infections in Alberta, Canada 2018–2023. Epidemiology and Infection, 153, e35.
Ünübol, N., Caglayan, N., Cebeci, S., Beşli, Y., Sancak, B., Uyar, N. Y., Ahrabi, S. S., Alebouyeh, M., & Kocagöz, T. (2025). Antimicrobial resistance and epidemiological patterns of *Streptococcus pyogenes* in Türkiye. Journal of Infection and Public Health, 18(2), 102633.
Woldan-Gradalska, P., Gradalski, W., Gunnarsson, R. K., Sundvall, P. D., & Rystedt, K. (2024). Is *Streptococcus pyogenes* a pathogen or passenger in uncomplicated acute sore throat? A systematic review and meta-analysis. International Journal of Infectious Diseases, 145, 107100.