

Distribution Of Streptococcus Pyogenes In The Pediatric Population

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ABSTRACT: Introduction: *Streptococcus pyogenes* (*S. pyogenes*) is a beta-hemolytic streptococcus of serological group A. This Gram-positive bacterium produces a wide range of extracellular products that are crucial for its virulence. Infections caused by them vary depending on the site of infection, the patient's age, and their immune status. It can cause a range of diseases such as tonsillopharyngitis, scarlet fever, acute rheumatic fever, acute post-streptococcal glomerulonephritis, skin infections (impetigo and erysipelas), and rare neuropsychiatric disorders. Objective: to analyze the representation of *S. pyogenes* according to gender, age, and different types of tested samples, and to compare the obtained results according to months/years, and to analyze the antimicrobial sensitivity/resistance of isolated bacterial strains. Methods: This retrospective, clinical, and epidemiological study was conducted in a microbiology laboratory from January 2021 to December 2023. Results and Conclusions: The study included 320 patients, 184 males and 136 females. The highest positive cases were recorded in 2023 (78%). Most patients were in the age group from 6 to 10 years, while the lowest percentage was recorded in the age group above 15 years. Sensitivity tests showed that the highest percentage was sensitive to penicillin (99%). The highest resistance was seen with trimethoprim (80%).

KEYWORDS: *S. pyogenes*, tonsillopharyngitis, infection, pediatric population

I. INTRODUCTION

S. pyogenes is a serogroup A beta-hemolytic streptococci (GAS), a gram-positive bacterium that exclusively infects humans. It is the cause of a wide range of diseases, from uncomplicated ones to more serious and invasive diseases with high morbidity. It is thought to cause millions of infections and at least 517,000 deaths each year worldwide.[1]. It is one of the most common causes of infections in the pediatric age group (children of preschool age who stay in kindergartens and children of early school age). Diseases can occur in the form of mild forms or in the form of acute tonsillopharyngitis and its purulent complications, up to forms associated with high mortality, including complications after infection in the form of rheumatic fever and poststreptococcal glomerulonephritis. The main risk factors for invasive disease are age <5 years, immunosuppressive conditions, varicella, diabetes, and skin lesions [2,3]. The source of infection caused by *S. pyogenes* is most often a sick person or a carrier, and it is transmitted by droplets. The entrance gate for streptococcus is the mucous membrane of the pharynx. The adhesive ability of *S. pyogenes* to bind to the respiratory epithelium also contributes to the development of the infection. Three properties of these bacteria are manifested in pathogenesis: invasive, toxic, and allergic. Invasive action can be local or general. Local streptococci manifest themselves in inflammatory-purulent processes, while the spread of streptococci into the subcutaneous tissue and blood vessels results in a general infection. Allergic action is manifested by allergic manifestations in the heart, kidneys, and joints due to the hypersensitivity of the organism to the re-entry of the pathogen. [4]. *S. pyogenes* strains produce a wide range of extracellular products, many of which are virulence factors due to their role in promoting the disease and/or survival of this pathogen in the host. Virulence factors that are secreted and released from the surface of bacteria include: hemolysins, streptolysin O (SLO) and streptolysin S (SLS), erythrogenic toxin (streptococcal pyrogen erythrogenic toxin-SPE), streptokinase, DNase, and hyaluronidase. Many of these virulence factors also function as digestive enzymes that provide the bacteria with nutrients from the host [5].

II. MATERIALS AND METHODS

According to the type, the research is a retrospective, descriptive, analytical, clinical, and epidemiological study, conducted at the department of the microbiology laboratory of the Hospital in Travnik in the period from January 2021 to December 2023.

A total of 320 patients were treated. The study involved nasopharyngeal and other types of swabs and sputum, which were collected from patients. After the collection of samples from patients, were transported to the microbiological analysis. –After processing the tested samples and isolating and identifying the cause of the infection, the samples were inoculated onto appropriate nutrient media, then incubated at 37°C for 24 hours with 5% to 10% CO₂, which stimulates growth and hemolysis in the medium. A positive result is indicated by typical gray-white, smooth, shiny β-hemolytic colonies surrounded by a zone of growth inhibition that is several times larger than the diameter of the colony itself. The negative plates are incubated for an additional 24 hours, and then the final results are documented. After it was proved that these were beta-hemolytic colonies, for identification and differentiation of *S. pyogenes* from other beta-hemolytic streptococci, a bacitracin test and antimicrobial susceptibility testing were performed.

III. RESULTS

In the period from 2021 to 2023, there were 320 patients with confirmed *S. pyogenes* infection; male patients were more represented - 57.5% (184). (Table 1)

Table 1. Gender structure of patients positive for *S. pyogenes*

Gender	Number of patients	%
Men	184	57.5%
Women	136	42.5%
Total	320	100%

The highest percentage of both male (54.9%) and female (54.4%) patients belongs to the age group of 6-10 years, while the lowest percentage of representation (6%) is in the age group older than 15 years. (Table 2)

Table 2. Age structure of patients positive for *S. pyogenes*

Age groups	Men		Women	
	Number of patients	%	Number of patients	%
1-5	37	20.1%	33	24.3%
6-10	101	54.9%	74	54.4%
11-15	35	19.0%	26	19.1%
16-20	11	6.0%	3	2.2%
Total	184	100%	136	100%

According to the sampling period, we observe that the largest number of positive samples was isolated during the year 2023, as many as 248 (78%), and the least during the year 2021, 17 (5%). The number of positive isolated samples during 2022 was slightly higher than the previous year, 55 (17%). (Figure 1)

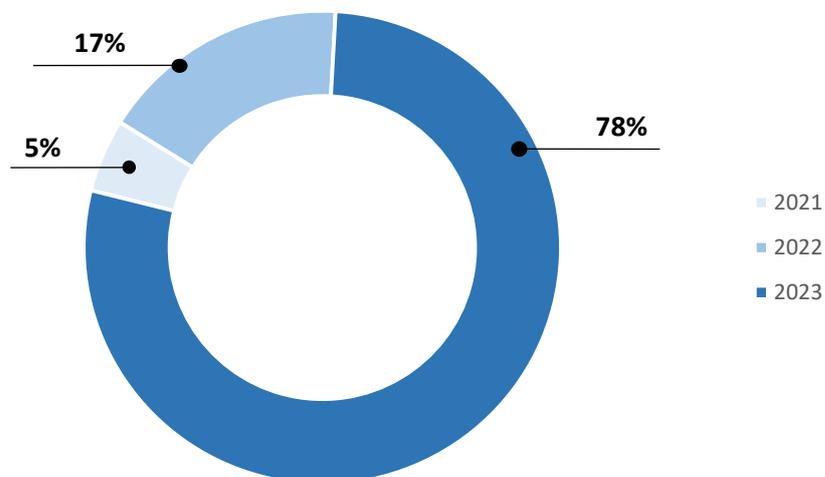


Figure 1. Percentage of isolated patients with *S. pyogenes* during the years of sampling

Furthermore, the highest percentage of positive samples during 2021 and 2022 was isolated during the month of December (17.6% and 23.6%), while during 2023 the highest percentage of positive samples was recorded during the month of April, 19%. (Figure 2)

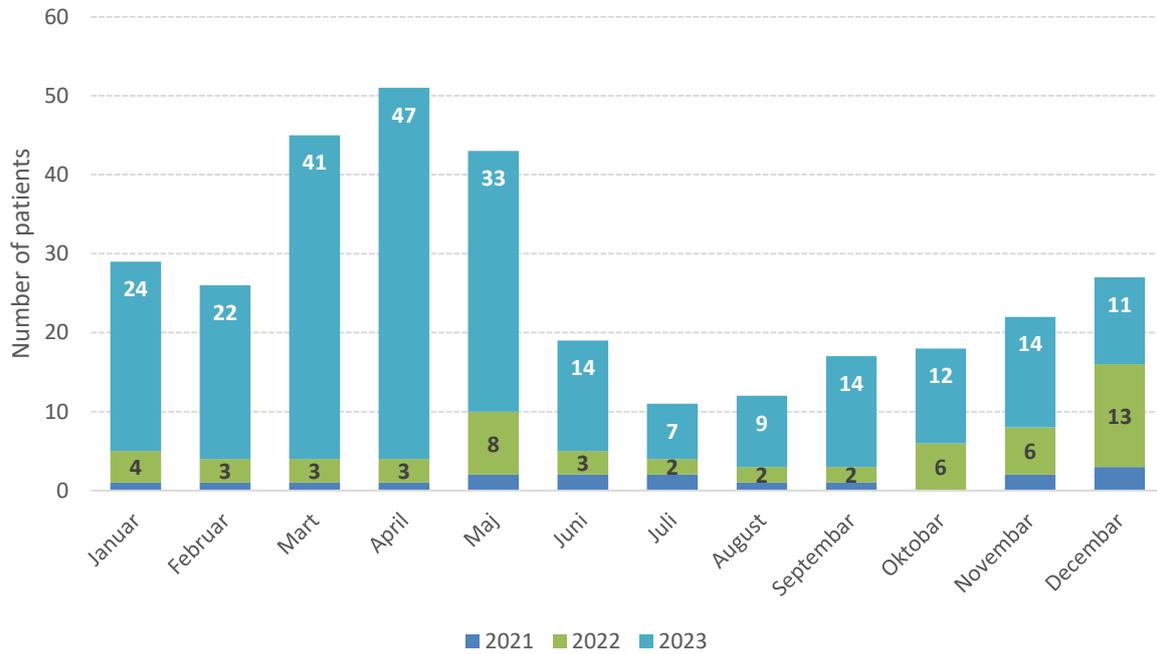


Figure 2. Number of patients with confirmed *S. pyogenes* infection on a monthly basis according to the years of sampling

The highest percentage of *S. pyogenes* is isolated from throat swabs (54.7%), less from throat and nose swabs (25.6%), and nasal swabs (16.3%), while the proportion of other samples is relatively negligible (<1%). (Figure 3)

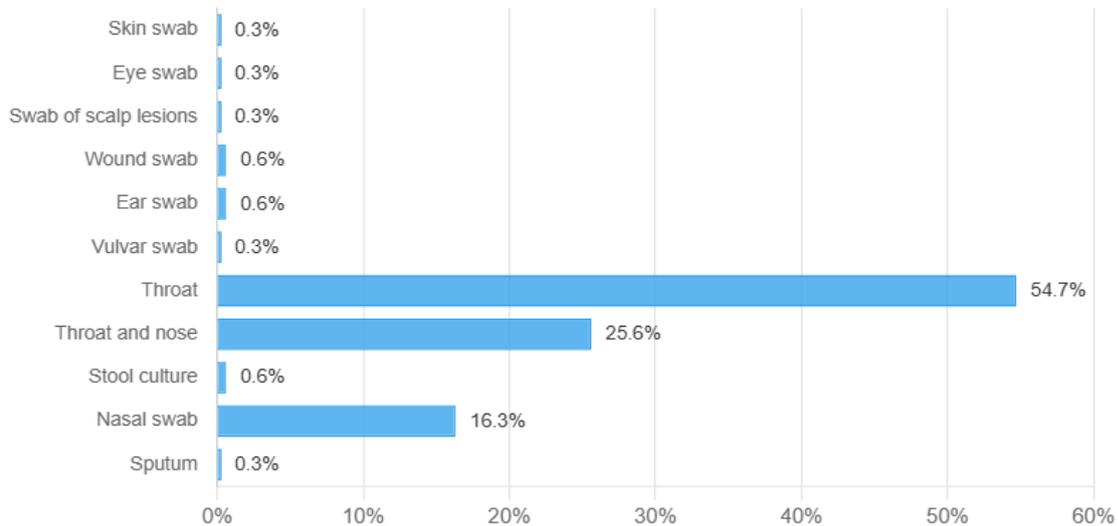


Figure 3. Percentage of isolated positive samples for *S. pyogenes*

The results of the conducted sample (only 76) show that the highest percentage of bacterial isolates, at 99%, showed sensitivity to penicillin. Furthermore, high sensitivity is also present with rifampicin (89.5%), ampicillin (82.9%), erythromycin (82.9%), amoxiclav (81.6%), and doxycycline (77.6%). When it comes to resistance, we observe that the highest percentage of bacterial isolates showed resistance to trimethoprim (as much as 80.3%).

After that, resistance was also present with doxycillin (17.1%), erythromycin (15.8%), clindamycin (13.2%), and in a small percentage with linezolid, azithromycin, moxifloxacin, levofloxacin, and norfloxacin (1.3%/2.6%/7.9%/1.3%/1.3%).

IV. DISCUSSIONS

The study included 320 patients with proven *S. pyogenes* infection. The largest number of registered cases was recorded in 2023, as many as 248 (78%), while only 17 positive samples were isolated during 2021 (5%). In our research, a sharp increase in the number of infections was observed in 2023 (248; 78%) compared to 2021 (17; 5%) and 2022 (55; 17%). Nygaard and colleagues obtained similar results in a study conducted in Denmark (2024), in which 76 children and adolescents with invasive group A beta-hemolytic streptococcus (iGAS) infection were identified during 2022-2023, while 98 patients were identified between 2016-2017 and 2021-2022. There was an increase in the incidence of iGAS from an average of 22.6 (95% CI 14.7–33.1) per 1,000,000 children and adolescents during 2016–17 by 2018–19 to 66.0 (52.0–82.6) per 1 000 000 during 2023–23 (RR 2.9, 95% CI 1.9–4.6; $p < 0.0001$) [6]. Gier et al. in the Netherlands (2022) also observed an increase in the number of invasive *S. pyogenes* infections (iGAS) in children aged 0-5 compared to the years before the COVID-19 pandemic. Between 2016 and 2019, the percentage of non-puerperal iGAS infections that occurred among children aged 0 to 5 years ranged 2% to 7%. In 2022, this percentage was 13%. In absolute numbers, the annual number of iGAS cases has increased sevenfold: from an average of six cases in 2016-19, respectively three and two in 2020 and 2021, to 42 cases of in 2022 [7].

As already mentioned, the therapy of streptococcal infections is based on oral or parenteral administration of penicillin. The results of the conducted sample (76 patients) show that the highest percentage of isolates, as much as 99%, showed sensitivity to penicillin. The result of our research is similar to the results of the study by Kebeda et al., which was conducted in Ethiopia and published in 2021. The aforementioned study showed that all isolates were susceptible to penicillin and ampicillin [8]. Research conducted over a period of 6 years (2018-23) in a tertiary center (Policlinico Agostino Gemelli, Rome, Italy) showed that the incidence of infection caused by group A beta-hemolytic streptococcus is highest in preschool children (3-5 years). The study also showed that the incidence of infection in the age group 6-8 years was 20% from 2018 to 2020; while in 2021 it increased to 40%, and gradually decreased to 33% in 2022 and 26% in 2023. The group of preschool children (3-5 years old) showed an overlapping trend from 2018 to 2022. However, the incidence of infection in this group increased to 46% in 2023 [9]. By analyzing the presence of *S. pyogenes* in different types of samples, it was observed that in the largest number of patients, it was isolated from the throat sample, 54.7%. The result is in accordance with the results obtained by Espadas-Maciá et al. in a study conducted in Spain over a period of ten years, in which out of a total of 2192 positive samples, 92.7% were pharyngeal samples [10]. According to the CDC report, cases of invasive *S. pyogenes* infections decreased by 25% during the COVID-19 pandemic compared to the years immediately before the pandemic. The reduced frequency of both invasive and less severe forms of infection was particularly observed in the pediatric population. At the end of 2022, the CDC reported and issued a warning about an increase in the number of pediatric cases, while the WHO issued a warning about the increased incidence of these infections [11].

V. CONCLUSION

In our research, it was observed that there is a statistically significant difference in the percentage of isolated positive cases of *S. pyogenes* when comparing the throat sample with other types of sample. The increase in invasive infections caused by *S. pyogenes* is associated with the return to normal social activities after the COVID-19 pandemic, which has affected the epidemiological patterns of many infectious diseases.

Conflict of interest

The authors have declared no conflict of interest.

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