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Antibiotic susceptibility of *Streptococcus* species that cause pharyngitis in children

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Abstract

Background: Group A *Streptococcus* (GAS) significantly impacts global health, especially among children aged 5–14 years, causing approximately 288 million episodes of sore throat annually and resulting in around 100,000 disability-adjusted life years (DALYs) each year. GAS infections are particularly prevalent in developing countries.
Objective: To assess the patterns of antibiotic resistance of *Streptococcus spp.* that cause pharyngitis in children.
Patients and Methods: It was collected 100 pediatric patients. It was taken throat swabs for *Streptococcus species* culture and antibiotic sensitivity test. In addition, it was recorded the data of patient's age and gender.
Results: It was shown in this study that an average age of 4.4 ± 3.7 years for pharyngitis in children. In this study was diagnosed that Streptococcus agalactiae (24%) and *Streptococcus pyogenes* (18%) as the common causes *Streptococcus species* causes pharyngitis in children. It was noted that the differences in bacterial species according to the patient's ages. Antibiotic sensitivity testing determined that there are high sensitivity of *S. pneumoniae* and *S. parasanguinis* to multiple antibiotics. In addition, it was showed resistance of *S. pyogenes* to Metronidazole and Azithromycin.
Conclusion: In this study, it was found that the risk age for pharyngitis in children is four years old. *Streptococcus agalactiae* and *Streptococcus pyogenes* are the common bacterial causes for this infection. In addition, it was shown that S. pneumoniae appeared a high sensitivity to Ceftriaxone, Ciprofloxacin, and Meropenem, and *S. parasanguinis* was sensitive to Azithromycin, Cefixime, and Cefotaxime, and *S. pyogenes* showed a high sensitivity to Meropenem and Imipenem.
Keywords: Pharyngitis, *Streptococcus pyogenes*, Children infection, antibiotic resistance.

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Introduction

Acute pharyngitis is a widespread disease and is most common during the winter months. Over half of the cases of pharyngotonsillitis are caused by viruses [1]. It can resolve on its own and often doesn't lead to serious complications. Bacterial and fungal infections can be more severe. It was shown that Streptococcus pyogenes that are group A Streptococcus (GAS), is responsible for pharyngitis and affect up to 30% of children and 15% of adults [2]. This bacterium caused more sever and complications sore throat and tonsillitis such as peritonsillar abscesses or invasive diseases. In addition, it was reported that this bacterium infection can cause complications, including acute glomerulonephritis, rheumatic heart disease (RHD). Moreover, it was reported that RHD causes over 345,000 deaths each year and the invasive infection caused by this bacterium caused 163,000 deaths annually [3]. Acute pharyngitis/tonsillitis, commonly seen in outpatient care, involves inflammation of the posterior pharynx and tonsils, often manifesting as a sore throat and fever. While most cases are mild and resolve without the need for anti-infective treatments, it's crucial to identify when Streptococcus pyogenes (a Group A β-hemolytic Streptococcus) is the cause, as it necessitates specific treatment. This bacterium is particularly significant due to its potential to cause serious post-infection complications like acute rheumatic fever and post-streptococcal glomerulonephritis, typically appearing 1-3 weeks post-infection [4,5]. Symptoms of acute pharyngitis include fever, sore throat, possibly with tonsillar redness, swelling, exudate, or ulcerations. Streptococcal infections often begin suddenly with severe sore throat, fever, chills, general discomfort, headache, swollen and tender lymph nodes in the neck, and throat or tonsil exudate. Palatal petechial and a scarlet fever-like rash are specific but rare signs. Symptoms like cough, nasal congestion, eye inflammation, and diarrhea are less common in streptococcal infections and may indicate a viral cause [5]. The increase resistant bacteria against multiple antibiotics considers the major global health problems. It was examined that the resistant bacteria to multi antibiotics effect on 2 million people annually [6]. It is essential to prescribe antibiotics to reduce the risk of acute rheumatic fever (ARF) [7]. Recent studies on the global consumption of antimicrobials in livestock have identified hotspots of antibiotic use across continents, which are expected to have significant economic and public health impacts in the future. In food animals, antibiotics are commonly used in cattle, chicken, and pigs, with a projected increase of up to 67% by 2030 in the world's most populated countries. This anticipated rise in antibiotic use in livestock is a major concern for the continued spread and intensification of antimicrobial resistance [8,9]. Scientific literature from around the globe highlights a significant challenge in treating Streptococcal infections due to the varying levels of antibiotic resistance [10,11]. Therefore, the aim of this study determine the antibiotic resistance of *Streptococcus pharyngitis* in children to find the best antibiotic to treat this infection and prevent any complications about it.

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Patients and Methods

Study Design

This study was conducted in Al-Batoul Teaching Hospital in Baqubah city of Iraq from June 1st to the end of December. Clinical data and throat swab samples were collected from pediatric patients diagnosed with streptococcal pharyngitis. This study included a total of 100 pediatric patients. Throat swabs were taken from pediatric pharyngitis patients that suspected to isolate Streptococcus spp. from these swaps and antibiotic susceptibility tests were done for this bacterium species [12,13]. In addition, exclusion criteria was considered and was included the following patients: patients with concurrent infections other than streptococcal pharyngitis, patients with chronic diseases affecting the immune system, such as HIV/AIDS or congenital immunodeficiency, patients with incomplete medical records or missing laboratory results, and recent antibiotics within the past month.

Statistical Analysis

Data analysis was performed using IBM SPSS 27 Statistical analysis software. The chi-square test was used to calculate p values for the significance of differences in the distribution of species among different age groups and genders. The level of confidence was set at 0.05.

Results

The study recruited 100 participants to investigate streptococcal resistance. The demographic data revealed an average age of 4.4 ± 3.7 years, with a distribution of 40% female and 60% male participants. Figure 1 presents the distribution of various Streptococcus species isolated from throat swabs. The most prevalent species were Streptococcus agalactiae (24%) and Streptococcus pyogenes (18%), followed by S. salivarius (12%), S. pneumoniae (8%), and S. parasanguinis (2%). Notably, 36% of the samples showed no growth, suggesting either the absence of streptococcal infection or the presence of non-culture able organisms.

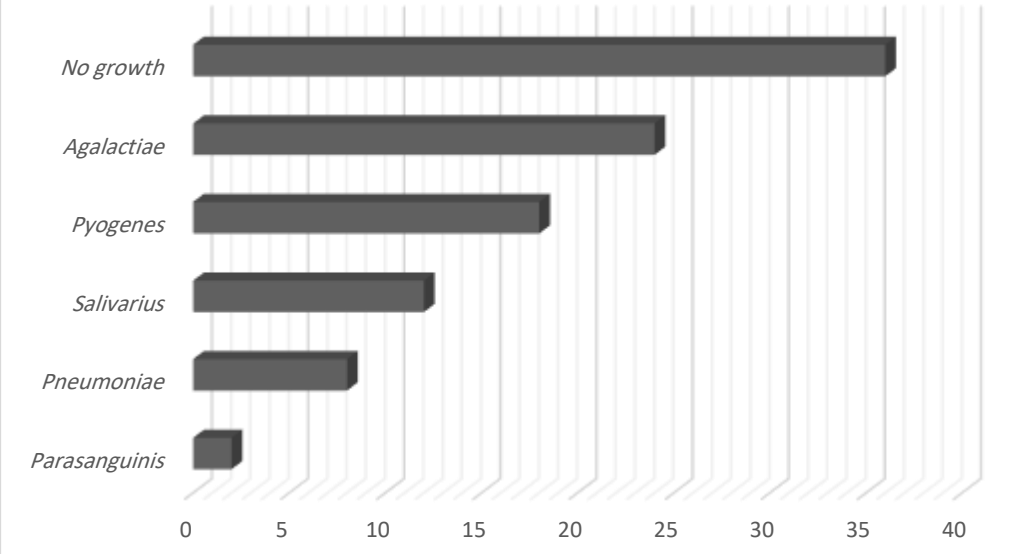

Figure (1): *Streptococcus* species isolated from throat swabs in this study (N=100)

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Figure (2) delves into species distribution among different age groups, revealing significant variances ($P < 0.01$). *S. agalactiae* was predominantly found in the 3-5 years age group (36.4%), while *S. pyogenes* showed a higher prevalence in older children (6-8 years: 40.9%, >8 years: 50%). Remarkably, there was a high rate of no growth in samples from children below 3 years (80%), suggesting a lower incidence of streptococcal infections in this age group or potential issues with sample collection in very young children.

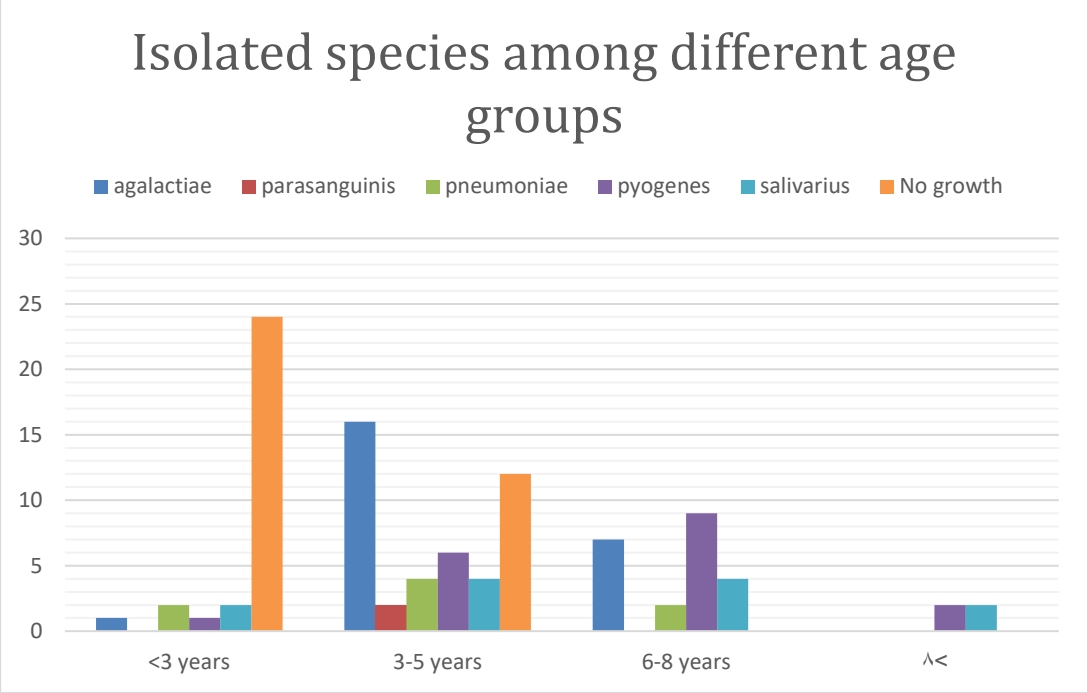

Figure (2) *Streptococcus* species that were isolated from different age groups

Table (1) outlines the antibiotic sensitivity patterns for the isolated species. *S. pneumoniae* showed a high sensitivity to Ceftriaxone, Ciprofloxacin, and Meropenem (100% sensitivity for each). Similarly, *S. parasanguinis* was highly sensitive to Azithromycin, Cefixime, and Cefotaxime (100% sensitivity). Notably, *S. pyogenes* had a high sensitivity to Meropenem (88.9%) and Imipenem (77.8%).

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Table (1): Most common antibiotics that Streptococcus showed sensitivity for them (out of 37 antibiotics)

***Streptococcus* species**	**Sensitive antibiotic**	**Percentage (%)**
Salivarius	Ceftriaxone Imipenem Meropenem	83.3 83.3 50
Agalactiae	Imipenem Cefotaxime Ceftriaxone	75.0 66.6 58.3
Pyogenes	Meropenem Imipenem Ceftriaxone	88.9 77.8 55.6
Pneumoniae	Ceftriaxone Ciprofloxacin Meropenem	100.0 100.0 100.0
Parasanguinis	Azithromycin Cefixime Cefotaxime	100.0 100.0 100.0

Table (2) highlights the resistance patterns. *S. pyogenes* exhibited significant resistance to Metronidazole (88.9%), Azithromycin (66.7%), and Ceftazidime (55.6%). In contrast, *S. parasanguinis* showed a concerning 100% resistance to Colistin, Metronidazole, and Nalidixic acid. This high resistance level to multiple antibiotics underscores the urgency in addressing antibiotic resistance in streptococcal infections.

Table (2): Resistant antibiotics for each Streptococcus species (out of 37 antibiotics)

***Streptococcus* species**	**Resistant Antibiotics**	**Percentage (%)**
Salivarius	Colistin Azithromycin Meropenem	83.3 50 33.3
Agalactiae	Colistin Trimethoprim Cefdinir	41.7 41.7 33.3
Pyogenes	Metronidazole Azithromycin Ceftazidime	88.9 66.7 55.6
Pneumoniae	Colistin Nalidixic acid Cefixime	50 50 50
Parasanguinis	Colistin Metronidazole Nalidixic acid	100 100 100

Discussion

The high prevalence of *S. agalactiae* in the 3-5 years age group and *S. pyogenes* in the 6-8 years and >8 years groups suggest age-specific transmission dynamics or varying susceptibility. This aligns with the notion that

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Streptococcus pyogenes is a common cause of pharyngitis in school children, with a higher prevalence in the 5–10-year age group [14,15,16]. This could be attributed to factors like immune system development, social behaviors including, school attendance, or differing microbiota compositions across ages [17]. This young study population is significant as it highlights the importance of pediatric considerations in streptococcal infections and resistance patterns. A study on *Streptococcus pneumoniae* found the highest prevalence of nasopharyngeal carriage in the 2-year-old group, suggesting varying susceptibility or transmission dynamics across different age groups [18].

The absence of significant gender-based differences in species distribution simplifies the diagnostic approach, suggesting that gender-specific factors do not significantly influence the prevalence of these bacterial species. Some other studies did not find significant differences in carriage rates between males and females for *Streptococcus pyogenes* and *Streptococcus pneumoniae* [19]. However, other studies suggest that in the case of group A streptococcal pharyngitis, there's a slightly higher occurrence in boys. Additionally, it was observed that rheumatic fever, an inflammatory condition following streptococcal infection, occurred more frequently in boys than in girls [20].

The high sensitivity of *S. pneumoniae* and *S. parasanguinis* to antibiotics like Ceftriaxone, Ciprofloxacin, Nitrofurantoin, Azithromycin, and Cefixime is encouraging. It suggests these antibiotics can be effective first-line treatments, subject to individual patient considerations. The sensitivity of *S. pneumoniae* to antibiotics like Ceftriaxone and Azithromycin aligns with findings that indicate high sensitivity to these antibiotics [21]. It was reported that *S. pyogenes* showed resistance to Metronidazole and Azithromycin [22]. Therefore, it is important to identify the available antibiotics to treat this bacterium that specially infect the children.

Conclusions

It was shown in this study that an average age for pharyngitis was four years old in children and the common bacterial causes this infection are *Streptococcus agalactiae* and *Streptococcus pyogenes*. In addition, it was found that *S. pneumoniae* showed a high sensitivity to Ceftriaxone, Ciprofloxacin, and Meropenem, and *S. parasanguinis* was shown highly sensitive to Azithromycin, Cefixime, and Cefotaxime. It was appeared that *S. pyogenes* had a high sensitivity to Meropenem and Imipenem.

Recommendations

It was essential to treat the pharyngitis in children after doing antibiotic sensitivity test to reduce the antibiotic resistance and prevent any complications that may be happened from this infection. In addition, it is important that to use and development more sensitive diagnostic techniques, especially for children to improve the accuracy of *Streptococcus* infection diagnosis.

Source of funding: The current study was funded by our charges with no any other funding sources elsewhere.

Ethical clearance: This study was conducted according to the approval of College of Medicine/ University of Diyala and in accordance with the ethical guidelines of the Declaration of ethical committee of the College (document no.2024RAA828).

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Conflict of interest: Nil

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حساسية المضادات الحيوية لأنواع المكورات المسبحية المسببة لالتهاب البلعوم في الأطفال

رقية عمار امين [١] , هاني حميد وادي [٢] , استبرق عبد حسن الجبوري[٣], انفال شاكر متعب[٤] , محمد حسين جابر[٥]

الملخص

خلفية الدراسة: المجموعة أ العقدية (GAS) تؤثر بشكل كبير على الصحة العالمية، وخاصة بين الأطفال الذين تتراوح أعمارهم بين ٥-١٤ سنة، مما يسبب ما يقرب من ٢٨٨ مليون أصابه من التهاب الحلق سنويا ويؤدي إلى حوالي ١٠٠٠٠٠ حالة من الإعاقة كل عام. تنتشر عدوى هذه البكتريا بشكل خاص في البلدان النامية.

اهداف الدراسة: لدراسة إلى تحديد أنماط مقاومة المضادات الحيوية لبكتيريا *Streptococcus spp.* التي تسبب التهاب البلعوم عند الأطفال.

المرضى والطرائق: تم جمع ١٠٠ طفل مريض وتم أخذ مسحات من الحلق لزراعة أنواع المكورات العقدية واختبار الحساسية للمضادات الحيوية. بالإضافة إلى ذلك، تم تسجيل بيانات عمر المريض وجنسه.

النتائج: تبين في هذه الدراسة أن متوسط العمر هو ٤,٤ ± ٣,٧ سنة للإصابة بالتهاب البلعوم عند الأطفال. في هذه الدراسة تم تشخيص أن المكورات العقدية نوع agalactiae تشكل ٢٤٪ والمكورات العقدية المقيحة هيه (١٨٪) وهما من الأسباب الشائعة لأنواع المكورات العقدية التي تسبب التهاب البلعوم عند الأطفال. ولوحظ أن الاختلافات في الأنواع البكتيرية حسب عمر المريض. حدد اختبار الحساسية للمضادات الحيوية أن هناك حساسية عالية لبكتيريا *S. pneumoniae* و *S. parasanguinis* لمضادات حيوية متعددة. وبالإضافة إلى ذلك، فقد أظهرت مقاومة S. pyogenes للميترونيدازول والأزيثروميسين.

الاستنتاجات: في هذه الدراسة وجد أن عمر خطر الإصابة بالتهاب البلعوم عند الأطفال هو عمر أربع سنوات. تعد المكورات العقدية *agalactiae* والمكورات العقدية المقيحة من الأسباب البكتيرية الشائعة لهذه العدوى. بالإضافة إلى ذلك، فقد تبين أن *S. pneumoniae* أظهرت حساسية عالية للسيفترياكسون، والسيبروفلوكساسين، والميروبينيم، وكانت *S. parasanguinis* حساسة للأزيثروميسين، والسيفيكسيم، والسيفوتاكسيم، وأظهرت *S. pyogenes* حساسية عالية للميروبينيم والإيميبينيم.

الكلمات المفتاحية: التهاب البلعوم، *Streptococcus pyogenes* ، عدوى الأطفال، مقاومة المضادات الحيوية.

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