



# Group A Beta Hemolytic Streptococcus Infections in Children; Change According to Age and Years

Çocuklarda A Grubu Beta Hemolitik Streptokok Enfeksiyonları;  
Yıllara ve Yaş Gruplarına Göre Değişimi

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## Abstract

**Objective:** Group A streptococcus (GAS) is the most common bacterial reason of tonsillopharyngitis cultured rarely in children under three years old and above 15 years old of age. We aimed to determine the changing pattern in *Streptococcus pyogenes* isolates according to cultured site, years, age of the patient, and invasive disease between 2010 and 2019.

**Material and Methods:** Children with cultured *Streptococcus pyogenes* isolates in Keçiören Research and Training Hospital between January 2009 and July 2019 were included. Primary symptoms, sociodemographic characteristics, site of culturing, year and month of culturing were recorded.

**Results:** Totally, 3899 patients with a mean age of  $83 \pm 34.5$  months, including 1880 (48.2%) females and 2019 (51.8%) males, were included in the study. *Streptococcus pyogenes* were cultured from throat culture in 3703 (90%) patients, wound culture in 66 (1.7%) patients, otorrhea/middle ear aspiration fluid in 30 (0.8%) patients, blood culture in 12 (0.3%) patients, sputum culture in three (0.1%) patients. Sixty-six (1.7%) patients were hospitalised, 3748 (98.3%) patients were outpatients. In patients with invasive *S. pyogenes* infections, 66 (61.1%) samples were isolated from wound culture, 30 (27.8%) from middle ear aspiration culture, 12 (11.1%) from blood culture. Invasive *S. pyogenes* infection was present in 53 (49.1%) of children under three years old of age, nine (8.3%) of children between the ages of 3-5 years of age, 46 (42.6%) of children over five years old of age. Incidence of invasive *S. pyogenes* infections was found to increase during years ( $p < 0.001$ ).

## Öz

**Giriş:** Grup A streptokoklar (GAS) veya diğer adıyla *Streptococcus pyogenes* (*S. pyogenes*) tonsillofarenjitin en yaygın bakteriyel etkenidir. Üç yaşından küçük ve 15 yaşından büyüklere daha az rastlanır. Bu çalışmada 2010-2019 yılları arasında üreyen *S. pyogenes* izolatlarının retrospektif olarak incelenmesi, üreme yerleri, üreme yıllarının yaş grupları ve mevsimlere göre değişiminin araştırılması planlanmıştır.

**Gereç ve Yöntemler:** Çalışmaya Keçiören Eğitim ve Araştırma Hastanesi'ne başvuran Ocak 2009-Temmuz 2019 tarihleri arasında alınan kültürlerde grup A beta hemolitik streptokok üremesi olan hastalar dahil edilmiştir. Hastaların primer başvuru şikayetleri, üreme yerleri, üreme zamanı yaş grubu, cinsiyet gibi sosyodemografik özellikleri kaydedilmiştir.

**Bulgular:** Çalışmaya ortalama yaşı  $83 \pm 34.5$  ay olan, 1880 (%48.2)'i kız, 2019 (%51.8)'u erkek toplam 3899 hasta dahil edilmiştir. Altmış altı (%1.7) üreme yatan hastalardan, 3748 (%98.3) üreme ayaktan başvuran hastalardan izole edilmiştir. Çalışmaya en sık boğaz kültüründen (%90) olmak üzere, yara yeri kültürü (%1.7), kulak akıntısından/aspirasyon sıvısından (%0.8), kan kültüründen (%0.3), balgam kültüründen (%0.1) olmak üzere *Streptococcus pyogenes* üremesi ve semptomu olan toplam 3899 hasta dahil edilmiştir. İnvaziv *S. pyogenes* enfeksiyonu saptanan hastaların 66 (%61.1)'sında etken yara yeri kültüründen, 30 (%27.8) 'unda kulak aspirasyon sıvısından, 12 (%11.1)'sinde kan kültüründen izole edilmiştir. İnvaziv *S. pyogenes* enfeksiyonu saptanan 108 hastanın 53 (%49.1)'ü üç yaş altında, 9 (%8.3)'ü 3-5 yaş aralığında, 46 (%42.6)'sı beş yaş üstü çocuk hastalarda saptanmıştır. Yıllara göre invaziv hastalık görülme sıklığının istatistiksel anlamlı olarak arttığı saptanmıştır ( $p < 0.001$ ).

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**Conclusion:** Invasive disease caused by GAS was found more common in children under three years old, and increase in cases was noted. *Streptococcus pyogenes* is an important pathogen, especially under three years old of age, with a potential to cause invasive infection.

**Keywords:** *Streptococcus pyogenes*, invasive disease, children, Group A Beta hemolytic streptococcus

**Sonuç:** GAS'a bağlı invaziv hastalık üç yaş altı çocuklarda daha sık olarak saptanmış ve yıllara göre hasta sayılarında artış dikkat çekmiştir. *Streptococcus pyogenes* özellikle üç yaş altı çocuklarda invaziv hastalık potansiyeli olan önemli bir mikroorganizmadır.

**Anahtar Kelimeler:** *Streptococcus pyogenes*, invaziv hastalık, üreme bölgeleri, çocuklar

## Introduction

Group A streptococcus (GAS), in other terms, *Streptococcus pyogenes* (*S. pyogenes*), is the most common bacterial agent of tonsillopharyngitis. While streptococcal pharyngitis is seen at every age, it is mostly encountered in school-aged children and adolescents. Geographically, while GAS pharyngitis and pyoderma are seen everywhere, pyoderma is more frequent in tropical climates and hot seasons. *Streptococcal pharyngitis* is seen at the end of autumn, in winter and spring in mild climates possibly due to close living conditions in schools (1).

Sinusitis, otitis, mastoiditis, peritonsillar abscess, septic arthritis, osteomyelitis, cavernous sinus thrombosis and bacteremia are suppurative complications. Non-suppurative complications include acute rheumatological fever (ARF) and acute glomerulonephritis.

In young children (aged 1-3 years) with GAS respiratory tract infection, the disease may start with moderate fever and serous rhinitis and may cause a long-lasting clinical picture with fever, unease and loss of appetite (streptococcal fever). Classical clinical picture of streptococcal upper respiratory tract infection as acute pharyngitis is seen rarely in children aged under three years, and acute rheumatic fever is also scarce in this age group. Scarlet fever commonly manifests with pharyngitis, is rarely seen with pyoderma or infected surgical or trauma-related wound, and characteristic erythema caused by erythrogenic exotoxin is observed (2-7). Necrotizing fasciitis and other invasive GAS infections in children are generally seen as varicella complications (4).

It is estimated that there are 616 million pharyngitis cases, 111 million pyoderma cases and 517 thousand deaths related to invasive diseases worldwide due to *S. pyogenes* infections (3,8).

In this study, a retrospective review of *S. pyogenes* isolates' growth sites and growth times according to age groups was planned to cover the years 2010 up to 2019.

## Materials and Methods

The study included pediatric patients in whom group A hemolytic streptococcus grew in cultures taken between January 2009 and July 2019. Sociodemographic characteristics such as primary presenting complaints of the patients, growth sites, age group at growth times, and sex were recorded. Pri-

mary aim of the study was to investigate *S. pyogenes* growth in children and to investigate the growth of invasive *S. pyogenes*.

Invasive group A streptococcal infection is defined as isolating the agent from normally sterile site or isolating *S. pyogenes* from the wound site in streptococcal toxic shock syndrome and necrotizing fasciitis patients (9-12).

Ethics board approval was obtained for the study. Information of all patients included into the study were retrospectively reviewed from computer logs following the approval of the ethics board. The study included patients aged under 18 years in whom *S. pyogenes* had grown.

SPSS (Statistical Package for Social Sciences) for Windows 21 was used for statistical analyses. Compatibility of the variables to normal distribution was investigated with visual (histogram and probability graphics) and analytic methods (Kolmogorov-Smirnov/Shapiro-Wilk tests). Descriptive statistics were performed as number and percentage for categorical variables, as mean  $\pm$  standard deviation for normally-distributed continuous variables and as median (minimum-maximum) for non-normally-distributed continuous variables. In the comparison of categorical variables, Pearson Chi-square test was used. The variables were compared between groups using Student's T test and Mann-Whitney U test. Statistical significance was set at p value under 0.05.

## Results

The study included a total of 3899 patients, 1880 (48.2%) girls and 2019 (51.8%) boys, with a mean age of 83 months  $\pm$  34.5 months between January 2009 and July 2019. *Streptococcus pyogenes* growths were isolated from throat culture in 3703 (90%), wound-site culture in 66 (1.7%), ear discharge in 30 (0.8%), blood culture in 12 (0.3%), and sputum culture in 3 (0.1%) patients. Sixty-six growths (1.7%) were isolated from inpatients, and 3748 (98.3%) were isolated from outpatients (Table 1).

Mean age of 3703 patients presenting due to tonsillitis with *S. pyogenes* growth in throat culture was  $84 \pm 33.5$  months (minimum: 9 months, maximum: 196 months). Of the patients with *S. pyogenes* growth in throat culture, 139 (3.8%) was aged under three years, 575 (15.5%) was aged between three and five years, 2969 (80.2%) was aged between five years and 15 years, and 20 (0.5%) were aged 15 years and

**Table 1.** Sociodemographic characteristics of patients with *Streptococcus pyogenes* growth

Throat culture (n)	3703
Age*	83 ± 34.5 months
Sex**	
Male	2019 (51.8)
Female	1880 (48.2)
Age group**	
<3 years	139 (3.8)
3-5 years	575 (15.5)
5-15 years	2969 (80.2)
>15 years	20 (0.5)
Wound site culture (n)	66
Age*	4.8 ± 3.8 years
Sex**	
Male	24 (36.4)
Female	42 (63.6)
Age group**	
<3 years	24 (36.4)
3-5 years	4 (6.1)
5-15 years	38 (57.6)
>15 years	0 (0)
Ear discharge/aspiration culture (n)	
Age*	34.7 ± 35.3 months
Sex**	
Male	18 (60)
Female	12 (40)
Age group**	
<3 years	20 (66.7)
3-5 years	4 (13.3)
5-15 years	6 (20)
>15 years	0 (0)
Blood culture (n)	12
Age*	34 ± 34.2 months
Sex**	
Male	9 (75)
Female	3 (25)
Age group**	
<3 years	9 (75)
3-5 years	1 (8.3)
5-15 years	2 (16.7)
>15 years	0 (0)
*Mean ± standard deviation	
**n (%).	

over. *S. pyogenes* growth in throat culture was most commonly found in spring (n=1388, 37.5%), followed by winter (n= 1147, 31%), autumn (n=661, 17.9%), and summer (n= 507,13.7%). Mean age of a total of 44 patients, including 12 girls (27.3%), with *S. pyogenes* growth in throat culture under the age of two years was detected as 18 ± 3.5 months (9-23 months). Presenting symptoms of the patients aged under three years in whom *S. pyogenes* growth was confirmed through throat culture in-

cluded upper respiratory tract infection in 31 (70.5%), rash in 9 (20.5%), lymphadenitis in 1 (2.3%), and fever of unknown origin in 2 (4.5%), and throat culture for screening purposes in 1 (2.3%) (Figures 1,2).

Mean age of 66 patients with *S. pyogenes* growth in wound site was 4.8 ± 3.8 years (8 days-14 years). Of the patients with *S. pyogenes* growth in wound site culture, 24 (36.4%) were aged under three years, 4 (6.1%) were aged between 3 and 5 years, and 38 (57.6%) were aged between 5-15 years (Figures 1,2). Different from throat culture growths, patients with *S. pyogenes* growth in wound site culture presented most commonly in winter (n= 19, 28.8%), followed by spring (n= 18, 27.3%), summer (n= 15, 22.7%) and autumn (n= 14, 21.2%).

Mean age of 30 patients, 12 of whom were girls (40%), presenting with perforated otitis media and with *S. pyogenes* growth from ear discharge/aspiration fluid was recorded as 34.7 ± 35.3 months (36 days-9 years). Of the patients with *S. pyogenes* growth from ear discharge/aspiration fluid, 20 (66.7%) were aged under three years, 4 (13.3%) were aged between three and five years, and 6 (20%) were aged between 5 and 15 years (Figures 1,2). Just as in throat culture growths, patients presenting with perforated otitis media and with *S. pyogenes* growth from ear discharge were most frequently seen in spring (n= 12, 40%), followed by winter (n= 10, 33.3%), autumn (n= 6, 20%) and summer (n= 2,6.7%).

Mean age of 12 patients, three of whom were girls (25%), with *S. pyogenes* growth in blood culture was 34 ± 34.2 months (1 day-8 years). Of the patients with *S. pyogenes* growth in blood culture, 9 (75%) were aged under three, 1 (8.3%) was aged between three and five years, and 2 (16.7%) were aged between 5 and 15 years (Figures 1,2). Presenting diagnoses of 12 patients with *S. pyogenes* growth in blood culture were lymphadenitis (n= 4, 33.3%), acute otitis media (n= 4, 33.3%), fever of unknown origin (n= 2,16.7%), septic arthritis (n= 1, 8.3%), and sepsis (n= 1, 8.3%). Presenting symptoms of nine patients aged under three years with *S. pyogenes* growth in blood culture were lymphadenitis (n= 4), unknown fever (n= 2), acute otitis media (n= 2), and sepsis (n= 1).

*S. pyogenes* growth was confirmed in the sputum culture of 3 patients aged four years, six years and 13 years admitted due to acute lower respiratory tract infection.

The agent in invasive *S. pyogenes* infection was detected from wound site culture in 66 patients (61.1%), ear aspiration fluid in 30 patients (27.8%), and blood culture in 12 patients (11.1%). Of the 108 patients in whom invasive *S. pyogenes* infection was detected, 53 (49.1%) were aged under three years, nine (8.3%) were aged between three and five years, and 46 (42.6%) were aged over five years. The incidence of invasive disease was determined to have statistically significantly in-

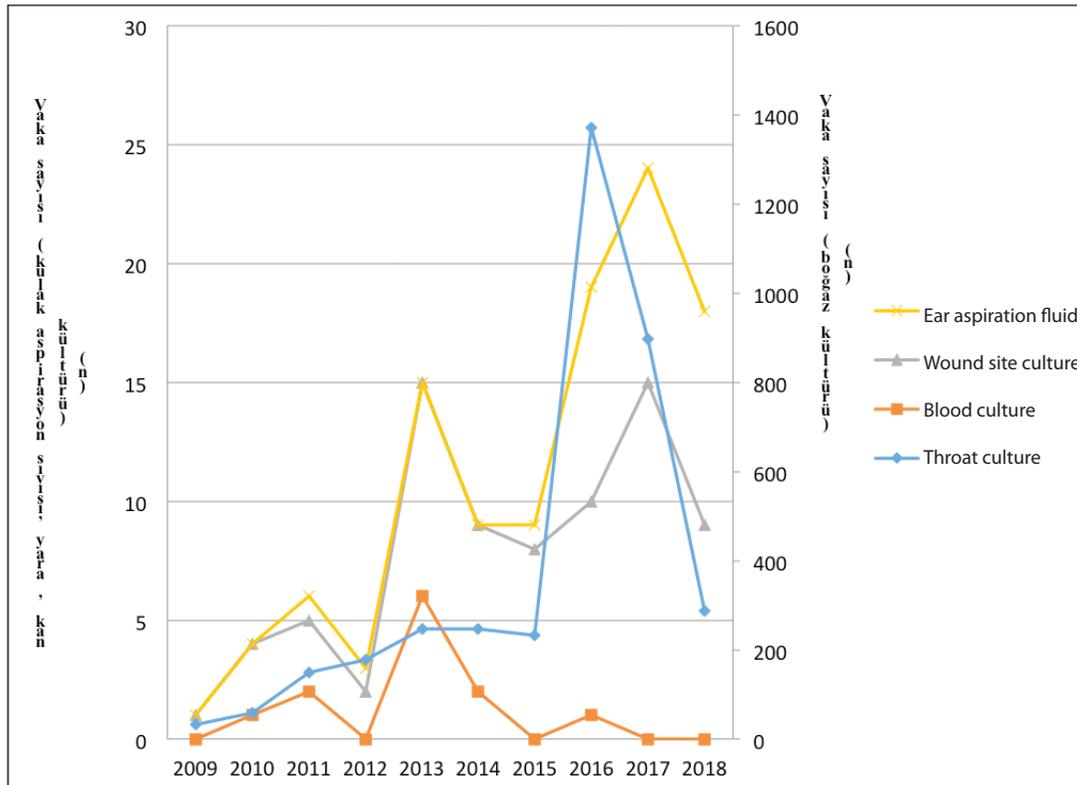


Figure 1. Change in growth sites of *Streptococcus pyogenes* growth over the years

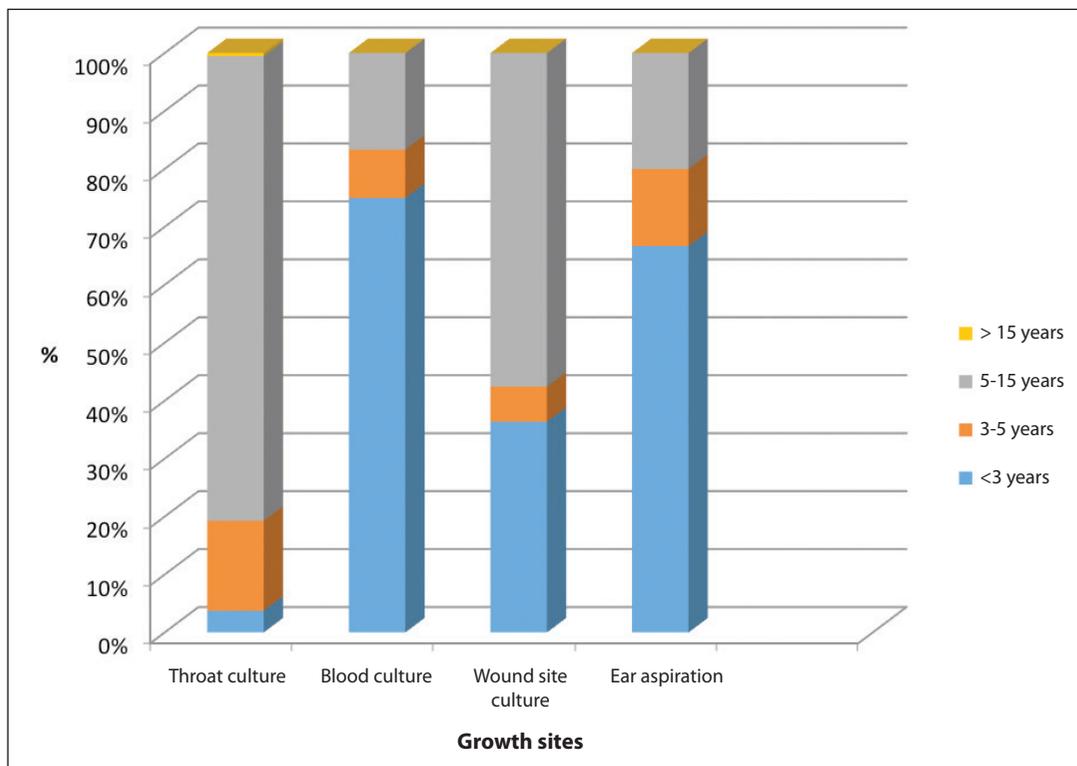


Figure 2. Change in *Streptococcus pyogenes* growth sites according to age groups.

creased over the years ( $p < 0.001$ ) (Figure 3).

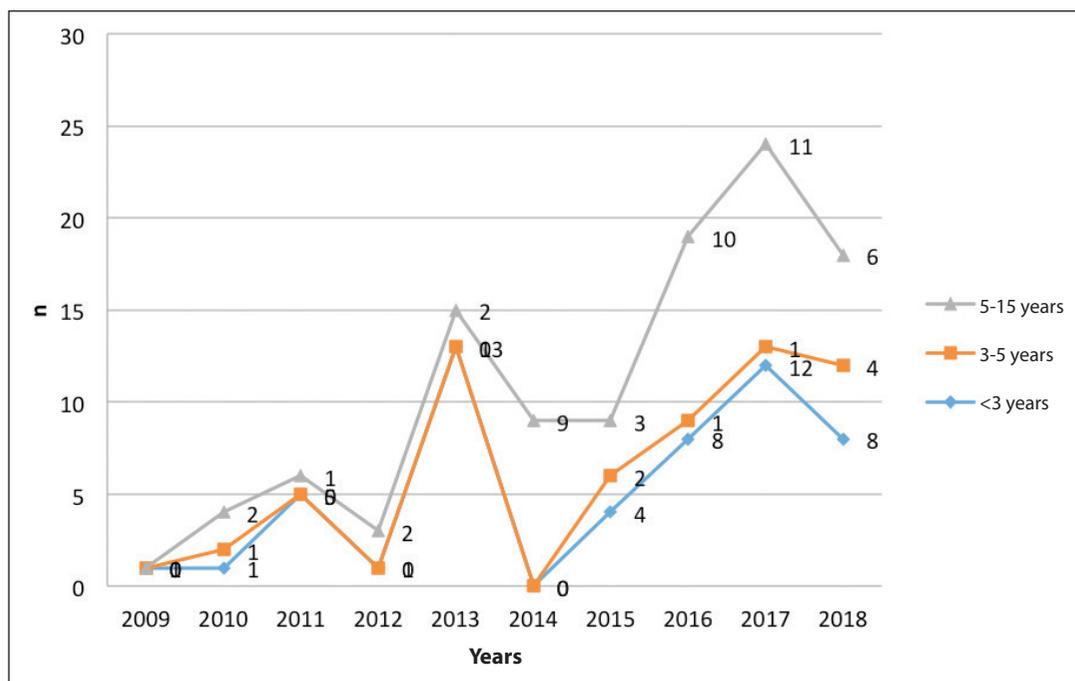


Figure 3. Change in patient numbers of invasive group A streptococcus according to years and age.

## Discussion

The study included a total of 3899 patients in whom *Streptococcus pyogenes* was most commonly isolated from throat culture, followed respectively by wound site culture, ear discharge/aspiration fluid, blood culture, and sputum culture. Compatible with the literature, majority of the cases with *S. pyogenes* growth in throat culture were in the 5-15 years age group. Again, compatible with the literature, *S. pyogenes* growth in throat culture was detected most commonly in spring, followed respectively by winter, autumn and summer. *Streptococcus pyogenes* bacteremia and perforated otitis media incidence was detected higher in cases aged under three years. The incidence of invasive disease due to *Streptococcus pyogenes* was detected to have increased over the years.

*S. pyogenes* was isolated in the throat culture of 139 (3.8%) patients aged under three years with upper respiratory tract infection symptoms. In the literature, there are studies having detected *S. pyogenes* as the agent of tonsillopharyngitis in cases under three years of age (12,13). In 30% of 78 symptomatic pediatric patients aged under three years, *S. pyogenes* was detected as the agent (13).

In the study, *S. pyogenes* growth at wound site was most commonly seen in the group aged 5-15 years and as the most frequent presentation of invasive disease. In a study investigating invasive *S. pyogenes* infection in 370 pediatric cases, 70% of the agent, similar to the results of our study, have been isolated from wound site cultures (14). In a study, the most common agent in 13 pediatric patients presenting with necrotizing fasciitis has been found as *S. pyogenes* (15).

The most common bacterial agents of acute otitis media are *Streptococcus pneumoniae* (40-50%), non-type *Haemophilus influenzae* (30-40%), and *Moraxella catarrhalis* (10-15%). *Staphylococcus aureus* and anaerobes are scarcely seen. Group A streptococci are common in older children and related more with perforation and mastoiditis (16). Segal et al. have reported in 11.300 acute otitis media pediatric cases that *S. pyogenes* is detected in the aspiration culture at a rate of 3%, and compared to other agents, the patients have been demonstrated to present with perforated otitis as in our study (17). In our study, *S. pyogenes* growth was confirmed in all patients presenting with perforated otitis and in whom ear discharge culture was taken.

Seventy-five percent of the patients with *S. pyogenes* growth in blood culture were seen in the group aged under three years. In the literature, in a study including 52 patients with invasive *S. pyogenes*, *S. pyogenes* have been found most commonly in patients under the age of three years and at a rate of 11%, just as in our study (18).

The incidence of invasive GAS infections started to decrease in the middle of 1900s, but an increase in incidence has recently been reported in many countries (19,20). In a study by Meehan et al. conducted in 561 patients with invasive GAS infection, the highest incidence has been reported in groups aged  $\leq 4$  years and  $\geq 75$  years, with septic arthritis most commonly reported in children (21). In our study, 53 (49.1%) of 108 patients detected to have invasive *S. pyogenes* infection were aged under three years. In our study, *S. pyogenes* was isolated in the blood culture of an 8-year-old patient presenting with septic arthritis.

The incidence of GAS-related invasive diseases has been rising since the 1980s all over the world. Though the reason for this increase is not fully understood, focus has been turned on to the epidemiological and microbiological changes in GAS. It is seen in recent studies that while the rate of invasive infections in developed countries is 2.3-3.5%, mortality rate has been reported as 7-15%. When invasive infections and mortality rates are compared, the rates of developing countries are significantly higher than those of developed countries (19,20). According to limited epidemiological and microbiological data of developing countries, invasive diseases with a mortality rate reaching 95% have been detected. In our study, GAS-related invasive disease was more commonly detected in patients aged under three years, and the increase of patient numbers over the years caught our attention.

To conclude, *S. pyogenes* should be kept in mind in patients presenting with wound site infection and perforated otitis. More epidemiological studies are required since an increase in invasive diseases has been determined in recent years.

**Ethics Committee Approval:** The approval for this study was obtained from Ankara Keçiören Research and Training Hospital, Ethics Committee (Decision no: 43278876-929, Date: 2019).

**Informed Consent:** Patient consent was obtained.

**Peer-review:** Externally peer-reviewed.

**Author Contributions:** Concept - KA; Design - All of authors; Supervision - KA; Resource - KA; Data Collection and/or Processing - KA; Analysis and/or Interpretation - All of authors; Literature Search - KA; Writing - KA; Critical Review - All of authors.

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