



# The Rate of Non-Invasive Group A Streptococcal Infections in Northern Cyprus Before and During the Pandemic

## Kuzey Kıbrıs'ta Pandemi Öncesi ve Pandemi Sırasında Non-İnvaziv A Grubu Streptokok İnfeksiyon Oranı

Ayşe ARIKAN<sup>1</sup>([iD](#)), Emrah GÜLER<sup>2</sup>([iD](#)), Kaya SÜER<sup>3</sup>([iD](#))

<sup>1</sup> Department of Medical Microbiology and Clinical Microbiology, Near East University Faculty of Medicine, Nicosia, Turkish Republic of Northern Cyprus

<sup>2</sup> Department of Molecular Biology and Genetics, European University of Lefke Faculty of Medicine, Lefke, Turkish Republic of Northern Cyprus

<sup>3</sup> Department of Infectious Diseases and Clinical Microbiology, Near East University Faculty of Medicine, Nicosia, Turkish Republic of Northern Cyprus

**Cite this article as:** Arkan A, Güler E, Süer K. The rate of non-invasive group a streptococcal infections in Northern Cyprus before and during the pandemic. FLORA 2023;28(4):688-694.

### ABSTRACT

**Introduction:** Acute pharyngitis is a common infection mainly in school-age children. This study aims to evaluate the rate of non-invasive group A streptococcal (GAS) infections in pre-pandemic and pandemic periods in Northern Cyprus.

**Materials and Methods:** A total of 3643 cases exhibiting upper respiratory tract symptoms and admitted to the university hospital between 2017 and 2022 were included in the study. GAS detection was performed either by rapid antigen testing or conventional throat culture. SPSS Demo Ver. 22 software was used for all statistical analyses. Pearson's Chi-square test, Fisher's Exact test, and One-Way ANOVA tests were employed to determine statistical significance, with p-values less than 0.05 considered statistically significant.

**Results:** GAS positivity was detected in 13% of the admissions. A remarkable and statistically significant decrease was observed in the number of cases until 2021 ( $p \leq 0.0001$ ). The rate of GAS infections was reported at 16.5%, 16.4%, 13.3%, 6.9%, 2.9%, and 7.4% in 2017, 2018, 2019, 2020, 2021, and 2022, respectively. During the pre-pandemic period, the GAS positivity rate was 16%. However, this rate decreased to 6% during the pandemic. There was a reported resurgence in the burden of GAS infections in the later stages of the pandemic.

**Conclusion:** Due to the relaxation of measures against SARS-CoV-2, a remarkable increase in the number of noninvasive GAS infections in the later stages of the pandemic was also reported. Rapid antigen tests can be beneficial for screening and differentiating GAS infections from other upper respiratory diseases. Early diagnosis in similar scenarios might help limit the incidence of invasive GAS infections.

**Key Words:** Pharyngitis; Streptococcal infections; COVID-19; Pandemics

Received/Geliş Tarihi: 28/07/2023 - Accepted/Kabul Ediliş Tarihi: 09/11/2023



## ÖZ

## Kuzey Kıbrıs'ta Pandemi Öncesi ve Pandemi Sırasında Non-İnvaziv A Grubu Streptokok İnfeksiyon Oranı

Ayşe ARIKAN<sup>1</sup>, Emrah GÜLER<sup>2</sup>, Kaya SÜER<sup>3</sup><sup>1</sup>Yakın Doğu Üniversitesi Tıp Fakültesi, Tıbbi Mikrobiyoloji ve Klinik Mikrobiyoloji Anabilim Dalı, Lefkoşa, Kuzey Kıbrıs Türk Cumhuriyeti<sup>2</sup>Lefke Üniversitesi Tıp Fakültesi, Moleküler Biyoloji ve Genetik Anabilim Dalı, Lefke, Kuzey Kıbrıs Türk Cumhuriyeti<sup>3</sup>Yakın Doğu Üniversitesi Tıp Fakültesi, İnfeksiyon Hastalıkları ve Klinik Mikrobiyoloji Anabilim Dalı, Lefkoşa, Kuzey Kıbrıs Türk Cumhuriyeti

**Giriş:** Akut farenjit, özellikle okul çağındaki çocuklarda sık görülen bir enfeksiyondur. Bu çalışma, Kuzey Kıbrıs'ta pandemi öncesi ve sırasında non-İnvaziv grup A streptokok (GAS) enfeksiyonlarının oranını belirlemeyi amaçlamaktadır.

**Materyal ve Metod:** 2017-2022 yılları arasında üniversite hastanesine üst solunum yolu semptomları ile başvuran toplam 3643 olgu dahil edildi. GAS tespiti, hızlı antijen testi veya geleneksel boğaz kültürü ile gerçekleştirildi. Tüm istatistiksel analizler için SPSS Demo Ver. 22 programı kullanıldı. İstatistiksel anlamlılık için Pearson Ki-kare, Fisher's exact testi ve One-Way ANOVA testleri kullanıldı ve p < 0.05 değerleri anlamlı kabul edildi.

**Bulgular:** Olguların %13'ünde GAS pozitifliği saptandı. 2021 yılına kadar vaka sayısında dikkat çekici ve istatistiksel olarak anlamlı bir düşüş gözlemlendi (p ≤ 0.0001). GAS enfeksiyonu oranı 2017, 2018, 2019, 2020, 2021 ve 2022 yıllarında sırasıyla %16.5, %16.4, %13.3, %6.9, %2.9 ve %7.4 olarak bildirilmiştir. Pandemi öncesi dönemde GAS pozitifliği %16 olarak belirlenirken, pandemi döneminde bu oranın %6'ya düştüğü saptandı. Pandeminin sonraki aşamalarında GAS enfeksiyonlarında yeniden bir artış rapor edildi.

**Sonuç:** SARS-CoV-2'ye karşı alınan önlemlerin gevşetilmesi nedeniyle, Kuzey Kıbrıs'ta pandeminin ilerleyen dönemlerinde non-İnvaziv GAS enfeksiyonlarının sayısında dikkate değer bir artış olduğu görüldü. Benzer durumlarda hızlı antijen testleri kullanılarak non-İnvaziv GAS enfeksiyonlarının taranması ve hızlıca diğer üst solunum yolu enfeksiyonlarından ayırt edilmesi İnvaziv enfeksiyon oranı artışını engelleyebilir.

**Anahtar Kelimeler:** Farenjit; Streptokok enfeksiyonları; COVID-19; Pandemi

## INTRODUCTION

Acute pharyngitis is predominantly caused by various viruses and bacteria, leading to relatively mild illnesses in humans<sup>[1]</sup>. Group A Streptococcus (Strep A), also known as *Streptococcus pyogenes*, belongs to group A beta-hemolytic streptococci (GABHS) based on its antigenic properties of the cell wall. It stands as the most prevalent bacterial cause of acute pharyngitis, primarily manifesting as streptococcal pharyngitis or sore throat<sup>[2]</sup>. *S. pyogenes* is a type of gram-positive cocci bacterium that can lead to a range of conditions, varying from asymptomatic or noninvasive to infrequent severe invasive diseases. These may include pharyngitis, impetigo, cellulitis, rheumatic fever, rheumatic heart disease, post-streptococcal glomerulonephritis, scarlet fever, streptococcal toxic shock syndrome (TSS), necrotizing soft tissue infections, among others<sup>[3]</sup>. GAS infections are notably more prevalent in developing countries and among low-income

populations within developed countries. Children, immunocompromised individuals, and the elderly are at a heightened risk for GAS infections. The transmission rate tends to be higher in environments such as schools, kindergartens, hospitals, and residential care homes, with peaks typically observed during winter and early spring<sup>[4,5]</sup>.

Despite its existence for hundreds of years, *S. pyogenes* continues to be a significant cause of global mortality and morbidity, accounting for more than 500.000 deaths annually worldwide<sup>[6,7]</sup>. In the United States (USA), it is estimated that there are approximately 14.000-25.000 cases of invasive GAS (iGAS) including cellulitis, necrotizing fasciitis, pneumonia, TSS, and more than five million noninvasive cases (pharyngitis, scarlet fever, impetigo) each year among people aged 0-64 years<sup>[8]</sup>. However, the rate of GAS infections is increasing globally each year. While 470.000 new cases of rheumatic

fever were reported in 2005, this rate was recorded as 33.45 million in 2015<sup>[8,9]</sup>. A remarkable increase in the incidence of scarlet fever and iGAS infection has been noted since December 2022, especially in France, Ireland, the Netherlands, Sweden, Northern Ireland, and the United Kingdom<sup>[7]</sup>. In the United Kingdom, there were 4622 reported cases of scarlet fever between 2022 and 2023. This rate was four times higher than the reported cases in the preceding five years<sup>[7]</sup>. Conspicuously, deaths associated with iGAS infections were also reported to be higher during the pandemic compared to pre-pandemic periods in many countries<sup>[7]</sup>.

Given the swift surge in GAS infections worldwide during the latter phases of the pandemic, there is an imperative to comprehend the prevalence of the disease in individual countries and forecast the requirement for developing a Strep A vaccine. Thus, this study aims to assess the incidence of noninvasive GAS infections during both the pre-pandemic and pandemic periods in Northern Cyprus.

## MATERIALS and METHODS

### Study Group

Patients with upper respiratory tract symptoms who were admitted to the university hospital between 2017 and 2022 were included in this study. The study assessed three distinct age groups= 0-5, 6-15, and >15 years old, examining the results based on age, gender, years, and seasons. To assess the impact of the COVID-19 pandemic on the prevalence of GAS, the study analyzed two distinct periods= 2017-2019 (pre-pandemic period) and 2020-2022 (pandemic period).

A total of 3643 cases (546 male and 942 female) aged between 0-89, were evaluated in the study. The clinical data were obtained from the hospital system and the study was conducted retrospectively.

The study was approved by the Near East University Ethical Committee (Project no: NEU/2023/116-1760). As the study was conducted retrospectively and relied on laboratory findings, patient consent was not obtained.

### GABHS Identification

GABHS detection was performed either by rapid antigen testing (BioNexia Strep A plus, BIOMERIEUX, France) or conventional throat culture on blood agar. Throat swab samples obtained from the patients were inoculated on 5% sheep blood agar and a bacitracin identification disk was used to differentiate GABHS. GAS was confirmed by the presence of gram-positive cocci in chains with gram staining, catalase test, and the presence of GAS antigen in the RAT<sup>[10]</sup>.

### Statistical Analysis

SPSS (Statistical Package of the Social Sciences) Demo Ver. 22 (SPSS Inc., Chicago, IL, USA) software was used for all statistical analyses of the data. Pearson's Chi-square test, Fisher's Exact test, and One-Way ANOVA tests were employed to determine statistical significance, with p-values less than 0.05 considered statistically significant. As the study was retrospectively conducted and the laboratory findings were used, ethics committee approval and patient consent were not taken.

## RESULTS

Among 3643 admissions, GABHS was detected in n= 475/3643 (13%) of the cases. The mean age was 12.47 years (0-89 years). Of the study group, 1878 (52%) were male, and 1765 (48%) were female. Among GAS-positive cases, 52% (n= 247) and 48% (n= 228) were male and female, respectively; and there was no significant relationship between gender and GABHS infection (p= 0.834). The demographic characteristics of the study group are given in Table 1.

Considering the distribution of GAS infection by years, as of 2019, a remarkable and statistically significant decrease was observed in the number of cases until 2021 (p≤ 0.0001). The rate of GAS infections was reported at 16.5%, 16.4%, 13.3%, 6.9%, 2.9%, and 7.4% in 2017, 2018, 2019, 2020, 2021, and 2022, respectively. In the pre-pandemic period, GAS positivity was observed in 16% of the cases, whereas this rate decreased to 6% during the pandemic period. There was noted a rise in GAS infections during the latter phases of the

**Table 1. Demographic characteristics of the study population**

Demographic factors	n, %
Gender	
Male	1878 (52)
Female	1765 (48)
Age groups	
0-5	1753 (47)
6-15	942 (26)
>15	968 (27)

epidemic in Northern Cyprus. The rates of GAS per year are presented in Figure 1.

Based on the age groups, a significant correlation was identified between age categories (0-5, 6-15, and >15 years) and GAS infections. Accordingly, GAS infections were most common in children aged between 6-15 years (n= 191/942, 20%) ( $p \leq 0.0001$ ) followed by 0-5 years (n= 200/1733, 12%) (Figure 2). In cases older than 15 years old, GAS infection was reported at 9% (n= 84/968).

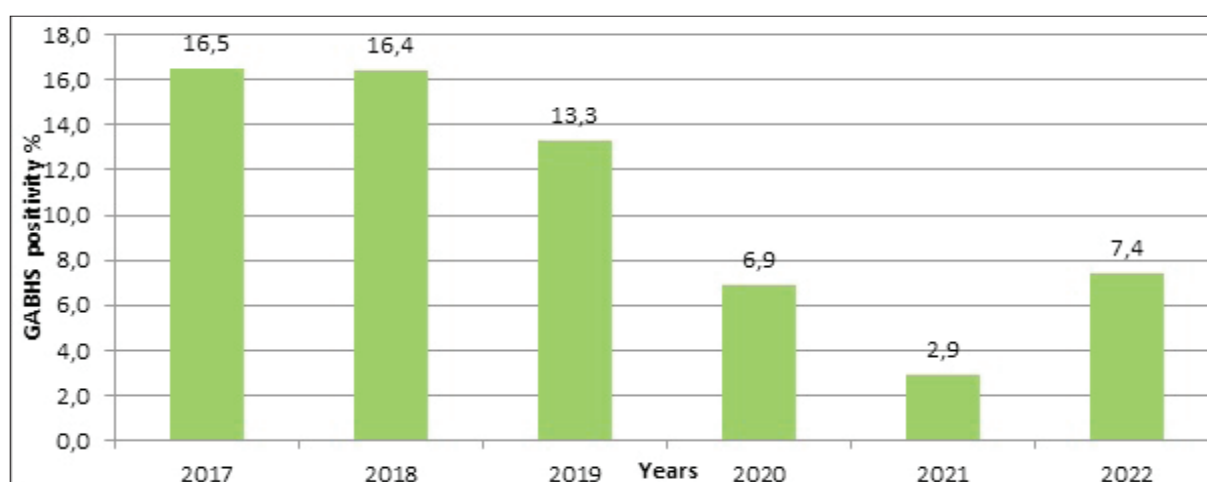


Figure 1. GABHS infections by years.

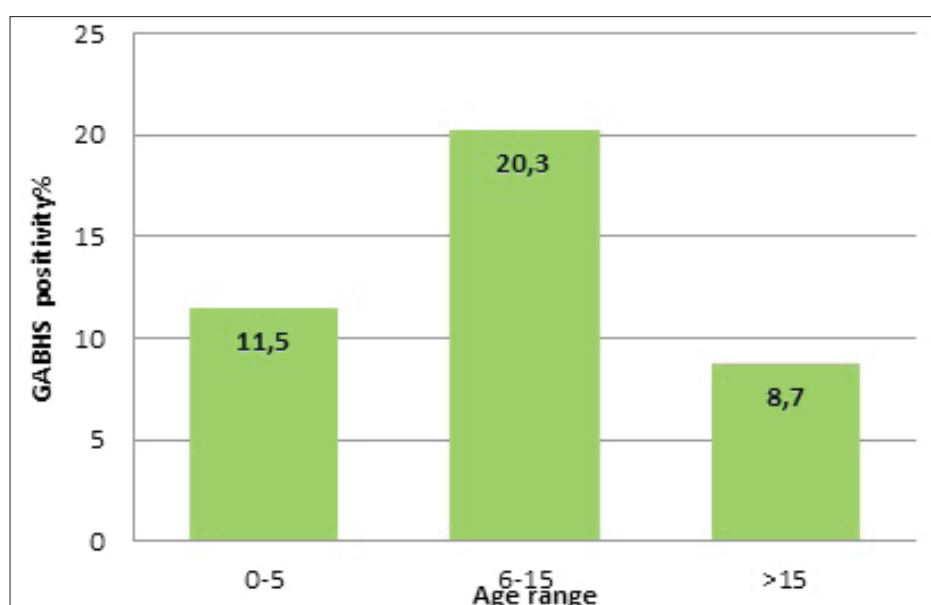


Figure 2. GABHS infections by age groups.

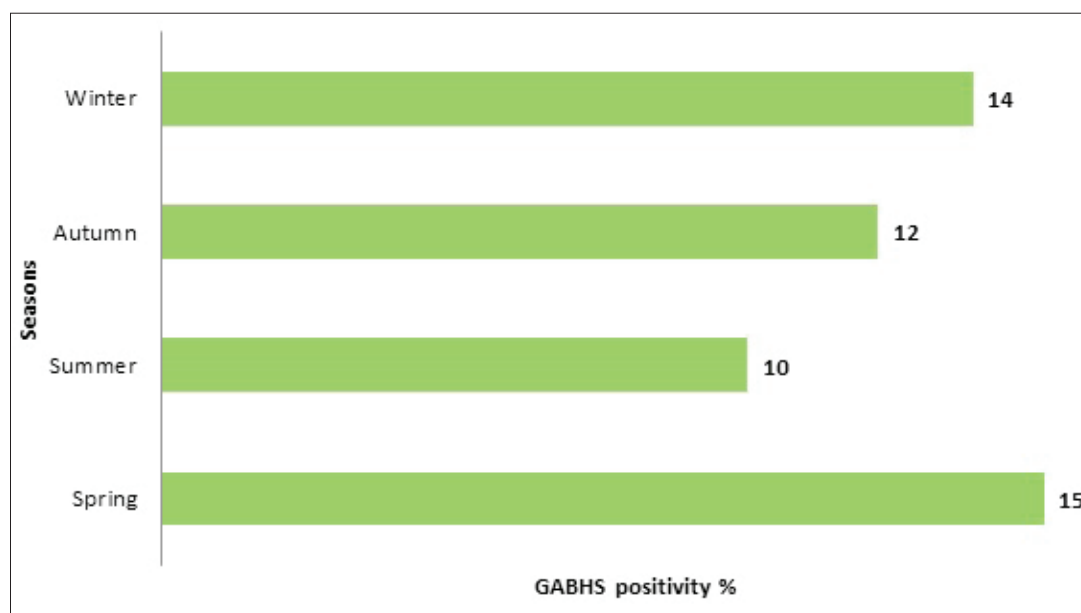


Figure 3. GABHS infection by seasons.

Furthermore, our findings unveiled the frequency of GAS infections across different seasons. The highest incidence of GAS was notably observed in the spring season ( $n=165/1106$ , 15%), followed by the winter seasons ( $n=155/1131$ , 14%), while the lowest rate was recorded during the summer seasons ( $n=68/686$ , 10%) (Figure 3). We identified a statistically significant association between the incidence of GAS and the seasons ( $p=0.016$ ).

## DISCUSSION

Streptococcal pharyngitis is a common infection mainly in school-age children<sup>[11]</sup>. In the present study, we reported the incidence of *S. pyogenes* infections in Northern Cyprus over a span of six years, encompassing both the pre-pandemic and pandemic periods. Our findings revealed that streptococcal pharyngitis was detected in 13% of the cases between 2017 and 2022. Remarkably, the frequency of GAS infections exhibited a significant decrease following the onset of the COVID-19 pandemic and began to rise again in 2022 ( $p \leq 0.0001$ ). The restrictions and measures imposed during the COVID-19 pandemic resulted in a decrease in the rate of several upper respiratory tract infections, including influenza A & B viruses, respiratory syncytial virus, and adenovirus, during

this period<sup>[11]</sup>. Nevertheless, following the gradual relaxation of numerous measures in recent months and the decline in immunity among individuals due to the COVID-19 pandemic, there have been reports of a resurgence in respiratory tract infections since December 2022 in several countries<sup>[7,12]</sup>. In Northern Cyprus, we observed a comparable scenario. From 2017, the reported rate of iGAS infections remained approximately at 16%. However, a notable decline was witnessed with the onset of the COVID-19 pandemic, followed by a substantial rebound. Due to the first case being identified in Northern Cyprus in March 2020, some restrictions were immediately implemented in the country including travel restrictions, the closure of schools, works, public areas, restaurants, etc. These restrictions likely limited the transmission of GAS infections within the country.

In the later stages of the pandemic, a surge of noninvasive GAS infections to the above pre-COVID-19 pandemic was reported in several countries including various European countries, the United Kingdom, and the United States<sup>[13,14]</sup>. A surveillance study conducted in France revealed that noninvasive GAS infections decreased during the early stages of the pandemic. However, these infections began to increase above pre-pandemic

levels since March 2022. This was followed by a rise in invasive GAS (iGAS) infections by 23.8% per month in pediatric patients<sup>[14]</sup>. The United Kingdom was one of the most affected countries with more than 6600 scarlet fever cases per 12-week period of time<sup>[15]</sup>. In the country, the case fatality rate was 9.92% in that period<sup>[15]</sup>.

Deaths were reported mainly between the ages of 10-14 years (27.3%), followed by the elderly people (16.3%)<sup>[15]</sup>. One of the reasons for this could be that acute pharyngitis is a common symptom of COVID-19, similar to GAS infection. Physicians might primarily focus on COVID-19 during the pandemic when individuals present with overlapping symptoms with SARS-CoV-2, potentially overlooking GAS infections<sup>[16]</sup>. Another reason may be due to the late diagnosis and treatment as a result of a decrease in hospital admissions.

In Northern Cyprus, GAS infections were mainly reported in the 6-15 (20%) age group. Similarly, studies up to 2017 revealed that 24.3% of GAS pharyngitis was seen in children aged 5-19 years<sup>[17]</sup>. In a similar study conducted in Northern Cyprus between 2015 and 2017, it was determined that GAS infection was most common in the 5-15 age group<sup>[18]</sup>. Although non-invasive GAS infections are known to be more common in children aged two through 17 years old, the incidence of iGAS infection increases with age<sup>[8]</sup>. Among people aged 50-64 years, 65-74 years, 75-84 years, and >85 years, the rates were given as 8.3 cases, 10.4 cases, 11.2 cases, and 15.2 cases/population, respectively in 2020<sup>[8]</sup>. Therefore, early detection and treatment of invasive GAS infections in children can limit the incidence of invasive infections in adults.

## CONCLUSION

In conclusion, reducing implementation against SARS-CoV-2 towards the end of the pandemic may lead to an increase in GAS infections in Northern Cyprus. Additionally, due to not focusing on GAS infections in patients with pharyngitis symptoms and/or late diagnosis and treatment of these cases, a burden in the rate of iGAS infections might likely be reported.

Hence, in future similar pandemics, it is crucial to consider other infections presenting with overlapping symptoms in the diagnosis. This would help prevent the progression of severe forms and reduce mortality and morbidity rates. Rapid antigen tests may be useful to screen and differentiate GAS infections from other upper respiratory diseases for early diagnosis in similar situations.

## ETHICS COMMITTEE APPROVAL

This study was approved by the Near East University Scientific Research Ethics Committee (Decision no: 2023/116, Date: 28.09.2023).

## CONFLICT of INTEREST

The authors have no conflicts of interest to declare that are relevant to the content of this article.

## AUTHORSHIP CONTRIBUTIONS

Concept and Design: All of authors

Analysis/Interpretation: AA, EG

Data Collection or Processing: EG, KS

Writing: AA

Review and Correction: All of authors

Final Approval: All of authors

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**Address for Correspondence/Yazışma Adresi**

Dr. Ayşe ARIKAN

Department of Medical Microbiology and  
Clinical Microbiology, Near East University  
Faculty of Medicine, Nicosia, Turkish  
Republic of Northern Cyprus  
E-posta: aysearikan@yahoo.com