

## Epidemiology of group A streptococcal infection: are we ready for a new scenario?



Group A streptococcal (GAS) infections have been attracting increasing attention, as many countries were overwhelmed by a rapid surge of invasive GAS (iGAS) infections in late 2022 and 2023 after an overall low incidence during the years of the COVID-19 pandemic.<sup>1</sup>

GAS infections, which are common among children, range from asymptomatic infections and mild infections (such as impetigo, pharyngitis, and scarlet fever) to iGAS infections (such as pneumonia, streptococcal toxic shock syndrome, and necrotising fasciitis) and autoimmune diseases.<sup>2</sup> iGAS infections account for 1.8 million cases worldwide, with a mortality rate of up to 20%, affecting both young and old individuals. These infections are often characterised by non-specific symptoms such as fever and pharyngodinia.<sup>3</sup> Recent research has highlighted the appearance of new and more virulent GAS strains;<sup>4</sup> the emergence of these strains could be related to the introduction of non-pharmacological interventions used to decrease virus circulation during the COVID-19 pandemic, leading to the so-called immune debt.<sup>5</sup> The spread of iGAS infections highlights the need for strict surveillance programmes aimed at monitoring their circulation.

We aimed to study the epidemiology of GAS infections over a period of 6 years (2018–23) at our tertiary centre (Policlinico Agostino Gemelli, Rome, Italy). We retrospectively collected data regarding the number of specimens analysed and the positive cultures on pharyngeal swabs obtained from patients aged 0–18 years who showed tonsillopharyngitis, scarlet fever, and other signs of GAS infection.<sup>6</sup> Samples collected for hospital surveillance programmes were excluded (appendix p 1). A total of 2230 swabs were obtained from 1839 patients during the study period. The total number of pharyngeal swabs remained substantially stable in 2018 and 2019 (428 and 425 specimens, respectively) and subsequently decreased by approximately 50% in 2020 (225 specimens), with a further reduction of almost 30% in 2021–22 (137 and 123 specimens, respectively). This trend was followed by a burst in 2023, with 501 specimens collected in that year. The GAS positivity rate decreased from 13% in the pre-pandemic period (data from 2019) to 2% in 2022; eventually, the rate increased again to 13% in 2023, when a spurt of positive samples was observed in winter

and spring (appendix p 1). In contrast, GAS cases were more widespread over time in the pre-pandemic period than in the post-pandemic period. To study the yearly GAS positivity rate by age, patients were divided into five categories: infants-toddlers (aged 0–2 years), preschoolers (aged 3–5 years), children in middle childhood (group 1, aged 6–8 years and group 2, aged 9–11 years), young teens (aged 12–15 years), and teenagers (aged 16–18 years). In particular, the incidence of GAS infection in those aged 6–8 years (middle childhood group 1) remained approximately 20% from 2018 to 2020, increased to 40% in 2021, and gradually decreased to 33% in 2022 and 26% in 2023. The preschoolers (aged 3–5 years) showed an overlapping trend from 2018 to 2022; however, the incidence of GAS infection in this group increased to 46% in 2023.

Our data are consistent with the observed decrease in the number of Emergency Department visits all over Europe, which might explain the decreased number of pharyngeal swabs collected from 2020 to 2022.<sup>7</sup> Nevertheless, the increased focus on respiratory infections led to an increase in the number of swabs collected in 2023. Consequently, an increased incidence of GAS infections was reported since 2022, with levels superior to those observed in the pre-pandemic period.<sup>6</sup> Furthermore, our research highlights two interesting characteristics of GAS infection epidemiology in 2023. Firstly, a sudden peak in infections, higher than that observed in the previous years, was reported in winter and spring; secondly, the affected population included individuals who were younger (preschoolers) than those affected in previous years (middle childhood and young teen age groups). Notably, a shift in respiratory virus seasonality and patient age was reported after the pandemic,<sup>8</sup> and viral infections in the upper respiratory tract were suggested to facilitate iGAS pathogenesis.<sup>9</sup> This effect could be attributed to the increased exposure following the use of non-pharmacological interventions during the COVID-19 pandemic period, despite no observed change in incidence.<sup>10</sup>

One of the limitations of our study was that some clinical reports were incomplete; therefore, we could not accurately evaluate the incidence of iGAS infections in

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our cohort, along with the number of viral co-infections and disease severity. Further studies are needed to elucidate why the increased incidence of GAS infections was associated with a specific age group, identify the strains circulating within the population, and understand further possible changes in GAS epidemiology that we might observe in 2024.

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### **Supplementary appendix**

This appendix formed part of the original submission. We post it as supplied by the authors.

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### Figure legend

**Fig.1.** a. Number of pharyngeal swab samples collected in our pediatric population during the years 2018-2023 and GAS yearly incidence. b. Seasonality of GAS incidence in our population. c. Spider chart shows the percentage of GAS positive samples between 2018 and 2023. Our population was divided into: infants-toddlers (aged 0–2 years), preschoolers (aged 3–5 years), middle childhood people (group 1: aged 6–8 and group 2: 9–11 years), young teens (aged 12–15) and teenagers (aged 16–18).

