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MAJOR ARTICLE

Impact of the COVID-19 Pandemic on Group A Streptococcal Necrotizing Soft Tissue Infections: A Retrospective Cohort Study

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Background. Necrotizing soft tissue infections (NSTIs) are often caused by group A *Streptococcus* (GAS). As the number of invasive GAS infections decreased during the coronavirus disease 2019 (COVID-19) pandemic restrictions, this study aimed to compare the occurrence of GAS-NSTIs before, during, and after the COVID-19 pandemic restrictions.

Methods. This retrospective cohort study included adult patients with NSTIs admitted to the intensive care unit (ICU) of the University Hospital Zurich, Switzerland, from July 2008 to December 2023. NSTI cases were categorized as pre-, during, and postrestrictions. The primary outcome was the proportion of GAS in NSTI, and the exploratory secondary outcome was in-hospital death. A data analysis was conducted using Firth logistic regression adjusted for age, sex, diabetes, and initially affected body region.

Results. Overall, 74 NSTI cases were identified, with 49 occurring before, 8 during, and 17 after the pandemic restrictions. GAS was isolated in 27 (36%) cases, with 17 (35%) pre- and 10 (59%) postrestrictions, but none during the restrictions. NSTIs caused by other bacteria persisted during the restrictions. The odds of GAS were significantly lower during the restrictions (adjusted odds ratio, 0.02; 95% CI, 0.001–0.81) compared with after, while no significant differences were found between the pre- and postrestriction periods.

Conclusions. The significant decrease of GAS-NSTIs during the COVID-19 pandemic restrictions suggests that isolation measures may have prevented the transmission of GAS, resulting in a decline of GAS-NSTIs while NSTIs caused by bacteria transmitted by alternative routes persisted.

Keywords. COVID-19 pandemic; group A *Streptococcus*; isolation measures; necrotizing soft tissue infections.

The term necrotizing soft tissue infections (NSTIs) entails a diverse group of pathologies, including necrotizing cellulitis and necrotizing fasciitis (NF), distinguished by the depth of the tissue infection [1]. NSTIs are categorized into polymicrobial and monomicrobial infections [1, 2]. The latter are predominantly caused by group A *Streptococcus* (GAS; aka *Streptococcus pyogenes*), which may enter the tissue directly through a skin lesion or via the bloodstream [1]. Interpersonal transmission of GAS occurs through respiratory droplets as well as direct contact [1]. GAS, which commonly causes mild conditions such as pharyngitis and colonizes mucosa and skin, can become invasive. Invasive GAS shows increased expression of various virulence factors that facilitate rapid spread through host tissue and evasion of the host's immune detection and are associated with shock and high mortality [3, 4].

Since October 2022, a concerning postpandemic increase of invasive GAS (iGAS) infections, including many fatalities, mostly among children, has been reported internationally [5–7], following a markedly low incidence during the coronavirus disease 2019 (COVID-19) pandemic [8]. Simultaneously, invasive infections caused by other bacteria transmitted via the respiratory route, including *Streptococcus pneumoniae* and *Haemophilus influenzae*, were significantly reduced during the implementation of isolation measures, while those caused by microorganisms transmitted via alternative routes remained unchanged [9]. However, it is unclear whether the isolation measures implemented during the COVID-19 pandemic also led to a secondary decrease in GAS-NSTIs during the period these measures were enforced. In Switzerland, isolation

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measures to control SARS-CoV-2 spread were implemented on February 28, 2020, gradually eased, and eventually lifted by April 1, 2022 [10, 11]. This present study aimed to compare the postrestrictions occurrence of GAS-NSTIs with the during restrictions and prerestrictions periods.

METHODS

Study Design, Setting, and Participants

In this retrospective cohort study, patients aged ≥18 years hospitalized with a diagnosis of "necrotizing soft tissue infections," "necrotizing fasciitis," "Fournier's gangrene," or "necrotizing cellulitis" in the intensive care unit (ICU) of the tertiary care University Hospital Zurich (USZ), Zurich, Switzerland, between July 2008 and December 2023 were included. Time periods were defined by the start (February 28, 2020) and the end (April 1, 2022) of the COVID-19 pandemic isolation measures enforced in Switzerland [10, 11]. Between July 2019 and December 2023, the screening was performed using the USZ disposition tool (KISIM, version 5.5.0.10, Cistec AG, Zurich, Switzerland), and patients needed documentation of a valid informed consent to be included. To ensure that no NSTI cases were missed, the intermediate care units were checked in the same way, which did not yield any additional cases. Data for NSTI cases occurring from July 2008 to July 2019 were obtained from Hofmaenner et al. [12]. Representativeness between the 2 data sets is based on a consistent patient record system and stable coding practices, where diagnoses were confirmed intraoperatively according to surgical reports and coded by professional medical coders. Exclusion criteria were denial of informed consent, other documented objection to data usage for research purposes, or electronic files missing data relevant to the study such as reports of initial diagnostic workup and treatment.

This study was approved by the local ethics committee (Kantonale Ethikkommission Zurich BASEC-ID 2016-00145 and 2017-02225).

Data Collection

Basic demographical, clinical, and epidemiological data were collected, including age, sex, substance use, Charlson comorbidity index (CCI) [13], and body mass index (BMI). Obesity was defined as BMI >30 kg/m^2. Further, the following data were extracted from electronic health records: initially affected body region, site of pathogen entry, laboratory parameters, Laboratory Risk Indicator for Necrotizing Fasciitis (LRINEC) score [14] at admission, treatment, and disease course. Identification of causative microorganisms and distinction between poly- and monomicrobial infections were made based on microbiological culture results of the initial surgical samples obtained from the infected tissue. Potential commensal contaminants, such as coagulase-negative *Staphylococcus*, were considered causative if isolated in multiple specimens and targeted for treatment by the decision of the treating physicians.

Data were absent for the variables of BMI and obesity in 9 patients from the prepandemic cohort. These missing values were considered nonessential and consequently excluded when calculating the median or count for the corresponding variables.

Study Outcomes

The primary outcome was established as the proportion of GAS in mono- or polymicrobial NSTIs. In-hospital death was assessed as an exploratory secondary outcome.

Statistical Analysis

A Firth logistic regression was chosen to analyze the association of the pre-, during, and postresprictions periods with the proportion of GAS in NSTIs in order to deal with the issue of separation (0 GAS isolated in NSTIs during the pandemic restrictions). In this model, an adjustment was performed for predefined covariates including age, sex, diabetes, and initially affected body region, as those characteristics were reported to differ between GAS-NSTI and non-GAS-NSTI patients [1, 2, 15]. For the sensitivity analyses, we included exact logistic regression to investigate if the results from the Firth logistic regression were robust. Due to computational constraints, exact logistic regression was not adjusted for all covariates. The secondary outcome was exploratory without any further statistical analyses. Demographic and clinical characteristics between the 3 time periods were compared descriptively only because of the small case number during the pandemic restrictions and the risk of multiple testing.

GraphPad Prism Software for Windows (GraphPad Prism 10.2.0; GraphPad, La Jolla, CA, USA) was used for data visualization and descriptive statistics. Firth and exact logistic regression were performed using Stata 18 (Stata Corporation, College Station, TX, USA).

RESULTS

NSTI Patients Admitted to the ICU Before, During, and After the COVID-19 Pandemic Restrictions

Overall, 74 NSTI cases were included in the study (Figure 1; Supplementary Figure 1), 49 occurring pre-, 8 during, and 17 postrestrictions (Figure 2). GAS was isolated from tissue samples in 27 cases, 17 (35%, 17/49) pre- and 10 (59%, 10/17) postrestrictions (Figure 2), with no GAS-NSTIs identified during the pandemic restrictions (Figures 1 and 2). In the 11 years preceding the COVID-19 pandemic restrictions, no similar decrease in GAS-NSTIs was recorded at USZ (Figure 3). The 8 non-GAS-NSTI cases occurring during the pandemic restrictions were predominantly polymicrobial (75%, 6/8), while monomicrobial NSTIs were more prevalent pre- and postrestrictions (57%, 28/49%, and 59%, 10/17) (Figure 2).

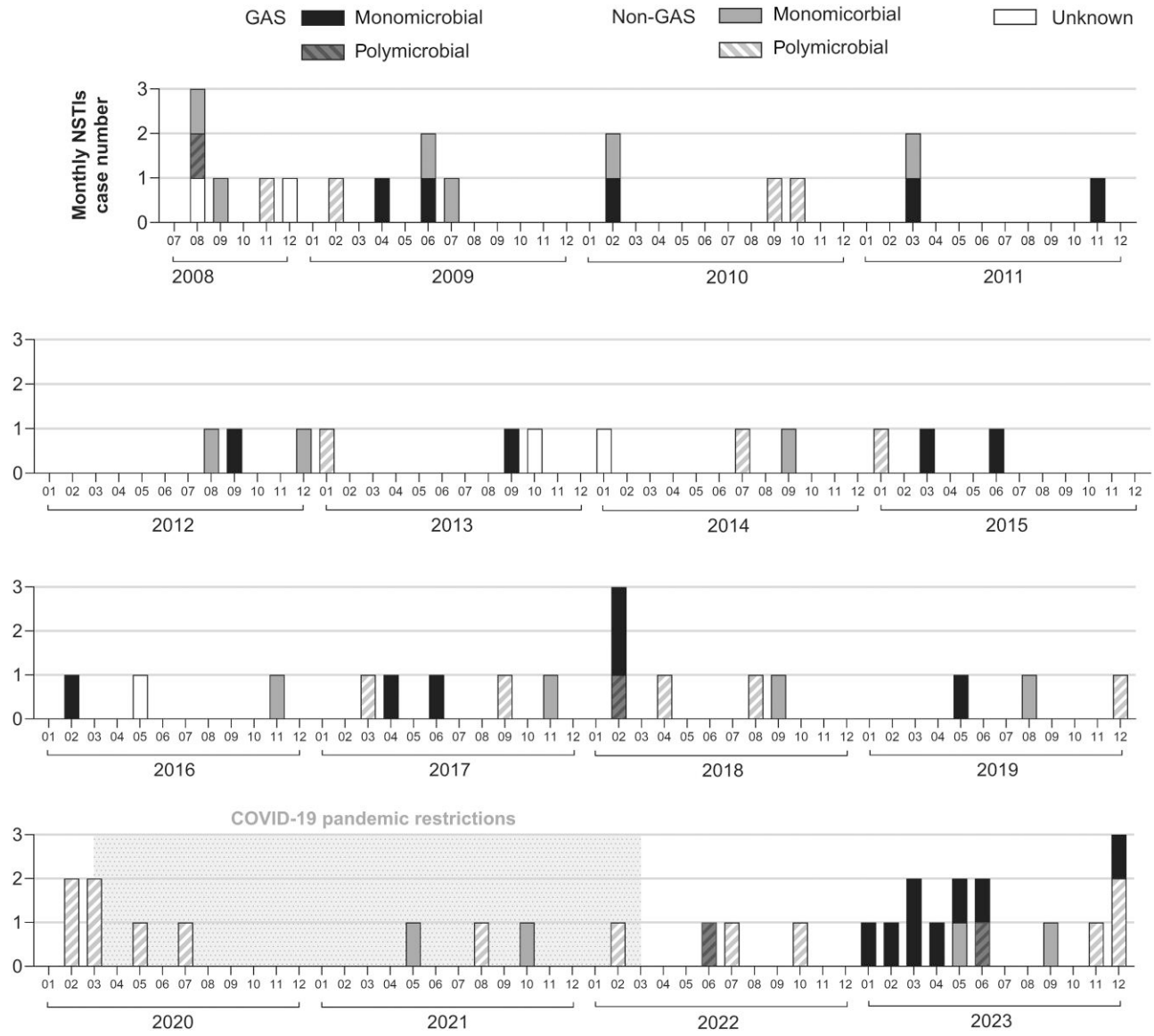

Figure 1. Monthly case numbers of NSTIs admitted to the ICU of University Hospital of Zurich from July 1, 2008, to December 31, 2023. Depicted by date of NSTI diagnosis. Abbreviations: ICU, intensive care unit; NSTIs, necrotizing soft tissue infections.

In the first year after the isolation measures were lifted (July 2022–July 2023), a notable surge of GAS-NSTIs was observed, marking a 2–8-fold increase compared with the prerestrictions era (July 2008–February 2020) (Figure 3).

Demographic and Clinical Characteristics of Patients With NSTIs

Demographic and clinical characteristics of the 74 patients with NSTIs are summarized in Table 1. Patients treated during the pandemic restrictions were older compared with the ones hospitalized pre- and postrestrictions (median [interquartile range {IQR}], 69.5 [59.25–80.75] years vs 57 [45.50–65.50] years and 61 [48.50–71.50] years, respectively). Additionally, they were more severely ill, as indicated by higher median (IQR) SAPS II score (52.5 [44.25–56.25] vs 46 [32.00–69.00] and 42 [32.00–55.50], respectively) and LRINEC score (8 [7.25–9.00] vs 6 [5.00–8.00] and 7 [5.50–8.00], respectively). The CCI was higher in the NSTI patients during the pandemic restrictions than pre- and postrestrictions (median [IQR], 3.5 [2.50–4.75] vs 3 [1.00–4.50] and 2 [2.00–4.00], respectively). The legs were the most frequently affected body region in all 3 periods, and acute traumatic wounds were the primary route for pathogen entry. Except GAS, other streptococci accounted for 10/49 pre- (20%; 5/10 *Streptococcus viridans*, 4/10 *Streptococcus* group C/G, and 1/10 *Streptococcus* group B [Supplementary Table 1]), 6/8 during (75%; 3/6 *S. viridans,* 2/6 *S.* group C/G, and 1/6 *S.* group B [Supplementary Table 1]), and 3/17 postrestrictions NSTI cases (3/3 *S. viridans* group [Supplementary Table 1]). *Escherichia coli* contributed to 9/49 pre- (18%), 2/8

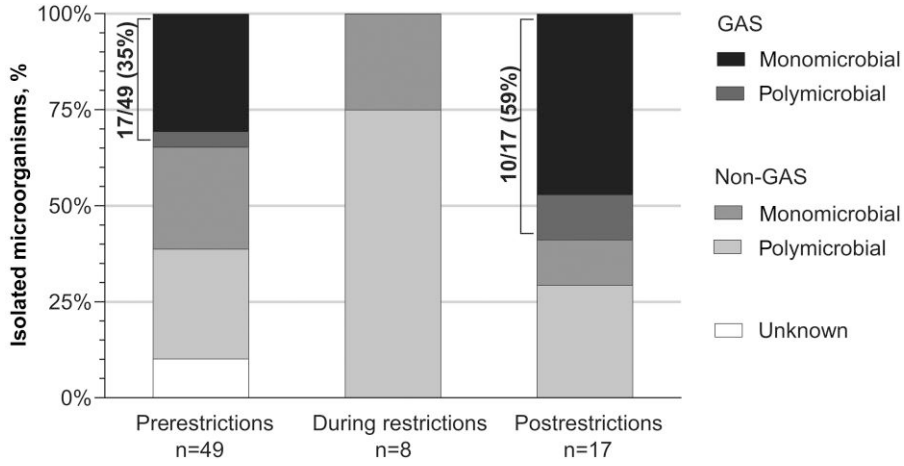

Figure 2. Percentage of isolated microorganisms before (July 1, 2008, to February 27, 2020), during (February 28, 2020, to March 31, 2022), and after (April 1, 2022, to December 31, 2023) the COVID-19 pandemic restrictions. Abbreviations: COVID-19, coronavirus disease 2019; GAS, group A *Streptococcus*.

during (25%), and 3/17 postrestrictions NSTI cases (18%). Throughout the pandemic restrictions, none of the patients died, compared with the relatively high mortality of the pre- and postrestrictions periods (29%, 14/49%, and 24%, 4/17).

Association Between GAS Proportion and COVID-19 Pandemic Restrictions

After adjustment, patients with NSTI before the pandemic restrictions had similar odds of GAS (adjusted odds ratio [aOR], 0.39; 95% CI, 0.10–1.49) as patients with NSTI after the restrictions, while during the restrictions the odds of GAS were much lower (aOR, 0.02; 95% CI, 0.001–0.81) than after the restrictions (Table 2). Using exact logistic regression in a sensitivity analysis reproduced similar results.

DISCUSSION

In summary, this retrospective, single-center study showed a significant decrease of GAS-NSTIs during the isolation measures implemented to curtail the dissemination of SARS-CoV-2. In contrast, NSTIs caused by bacteria originating likely from endogenous enteric microbiota dominated. We found an association between GAS proportion and time period when comparing during and postrestrictions, but no association when comparing pre- and postrestrictions. No in-hospital deaths occurred in the NSTI patients during the pandemic restrictions, compared with the high mortality in the pre- and postrestrictions periods.

Information on the prevalence of GAS-NSTIs is globally scarce and exhibits geographical disparities. In a study conducted in the United States (2002–2005), bacterial growth was detected in 279/323 NF cases, with GAS detected in 10% of monomicrobial and 16% of polymicrobial infections [16]. In a retrospective study from New Zealand including 247 cases of NF (2000–2006), GAS was isolated in 41% of the 228 cases with positive culture [17]. Our findings on the prevalence of GAS-NSTI before the pandemic (35%) align with data from other European studies (28%–42%) [18, 19].

Other European studies highlighted a significant increase in GAS-NSTI cases after the cessation of COVID-19 pandemic restrictions. A German study reported that 59% (7 mono- and 3 polymicrobial = 10/17 in total) of NF cases occurring after the COVID-19 pandemic restrictions in 2023 were caused by GAS, consistent with the results observed in our cohort [20]. Similarly, a Spanish study (2015–2023) including 356 patients with iGAS infections, revealed a significant iGAS decrease during the pandemic restrictions, followed by an increase after the restrictions had ended, particularly in NF cases [21].

The underlying factors contributing to the postrestrictions GAS-NSTI increase remain uncertain. Genetic analyses conducted by different research groups worldwide [7, 22, 23], including our own [24], have shown that the *emm*1 type, strongly associated with iGAS in Europe and North America [25], continued to prevail before, during, and after the pandemic. The $M1_{UK}$ strain has spread worldwide and has also emerged in Switzerland [24, 26]. The prevailing hypothesis suggests that isolation measures impeded the spread of GAS and other respiratory-transmitted pathogens. The isolation measures may have reduced GAS-NSTIs through reduction of the pharyngeal GAS carriage reservoir and reduced transmission via direct contact [27]. Missing exposure during isolation measures may have caused a decrease of immunity, leading to an increased susceptibility to GAS and other seasonal respiratory pathogens [21, 28]. A significant postrestrictions rise in circulation of influenza and respiratory syncytial

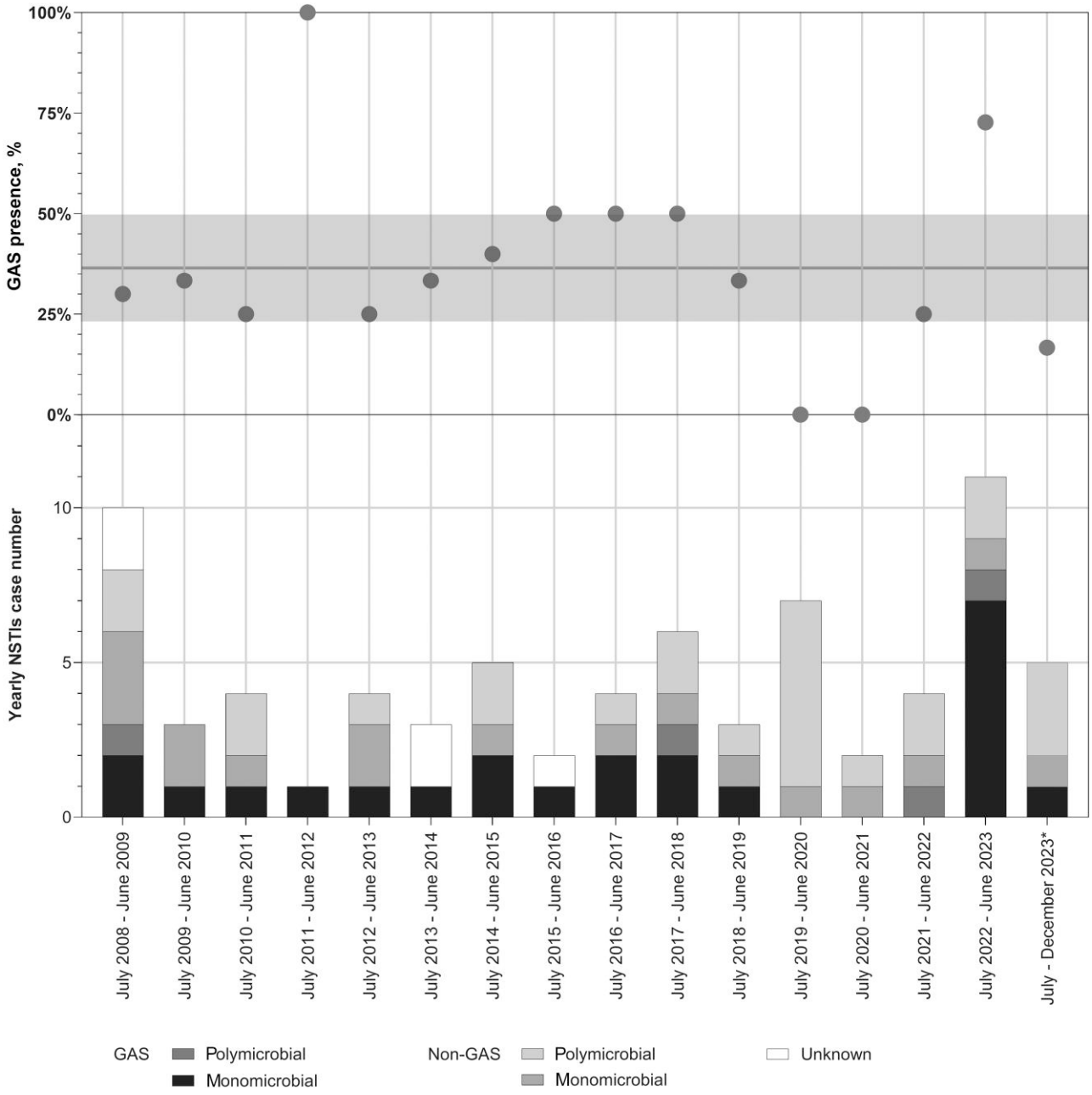

Figure 3. Lower graph: Yearly case numbers of NSTIs admitted to the ICU of University Hospital Zurich, Switzerland, from July 2008 to December 2023, grouped from July to June because of the seasonality of respiratory transmitted infections [9]. Cases were assigned to groups based on the date of NSTI diagnosis. Upper graph: Blue dots represent the percentage of GAS presence in the samples of mono- and polymicrobial NSTIs according to microbiology reports. Average and 95% CI of GAS percentages are depicted as a blue line and blue area, respectively. *The last group consists of 6 instead of 12 months. Abbreviations: GAS, group A *Streptococcus*; ICU, intensive care unit; NSTIs, necrotizing soft tissue infections.

viruses has been documented [29–31]. There are hints yet no solid scientific evidence that host susceptibility to iGAS infections might be augmented by previous infection or coinfection with respiratory viruses such as SARS-CoV-2 or influenza viruses [29, 32, 33].

Additionally, with acute traumatic wounds being the primary route for pathogen entry in our cohort, restrictions on outdoor activities during the pandemic measures may have prevented skin lesions and thus, secondarily, bacterial entry.

We found that NSTI-related in-hospital mortality pre- and postrestrictions remained similar (29%, 14/49%, and 24%, 4/17 respectively) and was in the range of previously reported data [1]. No in-hospital deaths occurred in the 8 NSTI cases during the restrictions.

Table 1. Patient Characteristics, Clinical Features, Treatment, and Clinical Outcome

	Total (n = 74)	Prerestrictions: July 1, 2008–February 27, 2020 (n = 49)	During Restrictions: February 28, 2020–March 31, 2022 (n = 8)	Postrestrictions: April 1, 2022–December 31, 2023 (n = 17)
	Median (IQR) or Count (%)	Median (IQR) or Count (%)	Median (IQR) or Count (%)	Median (IQR) or Count (%)
Patient characteristics				
Age, y	58 (46.75–69.25)	57 (45.50–65.50)	69.5 (59.25–80.75)	61 (48.50–71.50)
Male sex	41 (55)	29 (59)	4 (50)	8 (47)
Smoking	18 (24)	14 (29)	2 (25)	2 (12)
Alcohol consumption	14 (19)	9 (18)	1 (13)	4 (24)
Intravenous drug use	5 (7)	4 (8)	0 (0)	1 (6)
Systemic steroids before NSTI	11 (15)	8 (16)	0 (0)	3 (18)
Diabetes	17 (23)	13 (27)	2 (25)	2 (12)
Obesity (BMI >30 kg/m^2)	18 (n = 65, 28)	11 (n = 40, 28)	3 (38)	5 (29)
BMI, kg/m^2	26.2 (n = 65, 23.50–32.85)	26.5 (n = 40, 24.23–31.18)	25.2 (23.08–35.85)	25.7 (21.45–32.80)
Charlson comorbidity index	3 (1.00–4.00)	3 (1.00–4.50)	3.5 (2.50–4.75)	2 (2.00–4.00)
Initial presentation				
SAPS II score at ICU admission	47 (34.00–62.75)	46 (32.00–69.00)	52.5 (44.25–56.75)	42 (32.0–55.5)
LRINEC score	7 (5.00–8.00)	6 (5.00–8.00)	8 (7.25–9.00)	7 (5.50–8.00)
Initially affected body region				
Arms	11 (15)	7 (14)	0 (0)	4 (24)
Legs	38 (51)	27 (55)	4 (50)	7 (41)
Trunk	13 (18)	10 (20)	1 (13)	2 (12)
Genitals	10 (14)	4 (8)	3 (38)	3 (18)
Head/neck	2 (3)	1 (2)	0 (0)	1 (6)
Portal of entry (etiology of NSTI)				
Trauma/acute wound	17 (23)	12 (25)	1 (13)	4 (24)
Chronic wound	11 (15)	8 (16)	1 (13)	1 (6)
Dermatological disease	6 (8)	4 (8)	0 (0)	2 (12)
Postinterventional	12 (16)	8 (16)	1 (13)	3 (18)
Hematogenic	5 (7)	2 (4)	0 (0)	3 (18)
Insect/animal bite	4 (5)	4 (8)	0 (0)	0 (0)
Unknown	21 (28)	12 (25)	5 (63)	4 (24)
Causative microorganisms (both mono- and polymicrobial) from initial tissue samples[a]				
Streptococcus pyogenes (GAS)	27 (37)	17 (35)	0 (0)	10 (59)
Other streptococci	19 (26)	10 (20)	6 (75)	3 (18)
Escherichia coli	14 (19)	9 (18)	2 (25)	3 (18)
Other Enterobacterales	12 (16)	7 (14)	1 (13)	4 (24)
MSSA	8 (11)	6 (12)	0 (0)	2 (12)
MRSA	2 (3)	1 (2)	1 (13)	0 (0)
Enterococcus faecalis	4 (5)	4 (8)	0 (0)	0 (0)
Pseudomonas spp.	4 (5)	3 (6)	0 (0)	1 (6)

Table 1. Continued

	Total (n = 74)	Prerestrictions: July 1, 2008–February 27, 2020 (n = 49)	During Restrictions: February 28, 2020–March 31, 2022 (n = 8)	Postrestrictions: April 1, 2022–December 31, 2023 (n = 17)
	Median (IQR) or Count (%)	Median (IQR) or Count (%)	Median (IQR) or Count (%)	Median (IQR) or Count (%)
Clostridium spp.	3 (4)	2 (4)	0 (0)	1 (6)
Acinetobacter spp.	1 (1)	1 (2)	0 (0)	0 (0)
Others	18 (24)	11 (23)	4 (50)	3 (18)
Antibiotic treatment				
Lincosamides (clindamycin)[b]	69 (93)	44 (90)	8 (100)	17 (100)
Penicillins	55 (74)	36 (74)	7 (88)	12 (71)
Cephalosporins	43 (58)	31 (63)	3 (38)	9 (53)
Carbapenems	30 (41)	20 (41)	2 (25)	8 (47)
Glycopeptides	25 (34)	15 (31)	3 (38)	7 (41)
Quinolones	17 (23)	13 (27)	2 (25)	2 (12)
Others	21 (28)	14 (29)	3 (38)	4 (24)
IVIG treatment				
Started on IVIG	44 (60)	25 (51)	5 (63)	14 (82)
Complete IVIG treatment[c]	35 (47)	20 (41)	4 (50)	11 (65)
Surgical treatment				
No. of surgeries	6 (4.00–7.50)	6 (4.00–8.00)	6.5 (4.50–9.75)	4 (3.25–6.75)
Negative pressure wound therapy	57 (77.0%)	39 (80)	8 (100)	10 (59)
Amputation	7 (10)	5 (10)	1 (13)	1 (6)
Scrotectomy	2 (3)	2 (4)	0 (0)	0 (0)
Secondary suture	30 (41)	18 (37)	5 (63)	7 (41)
Local flap	10 (14)	4 (8)	3 (38)	3 (18)
Free flap	14 (19)	11 (23)	0 (0)	3 (18)
Mesh-graft/euroskin transplantation	47 (64)	35 (71)	4 (50)	8 (47)
Clinical outcome				
Acute renal failure	52 (70)	33 (67)	6 (75)	13 (77)
ARDS	20 (27)	12 (25)	3 (38)	5 (29)
Septic shock	46 (62)	31 (63)	6 (75)	9 (53)
ICU length of stay, d	10 (4.00–18.25)	11 (4.00–20.00)	9 (5.75–21.25)	5 (3.00–12.50)
USZ length of stay, d	26.5 (18.75–47.75)	26 (17.75–44.25)	41.5 (24.25–70.00)	24 (13.00–47.50)
In-hospital death	18 (24)	14 (29)	0 (0)	4 (24)

Abbreviations: ARDS, acute respiratory distress syndrome; BMI, body mass index; GAS, group A streptococci; ICU, intensive care unit; IQR, interquartile range (exclusive median); IVIG, intravenous immunoglobulin; LRINEC, Laboratory Risk Indicator for Necrotizing Fasciitis [14]; MRSA, methicillin-resistant *Staphylococcus aureus*; MSSA, methicillin-sensitive *Staphylococcus aureus*; NSTI, necrotizing soft tissue infection; SAPS II, Simplified Acute Physiology Score II; USZ, University Hospital of Zurich.

[a]In 2 cases, identifying the initial tissue sample was ambiguous due to preceding samples derived in the context of an earlier diagnosis of a non-necrotizing soft tissue infection. G.E., S.D.B., and D.A.H. discussed those cases and agreed on what they thought the most reasonable decision.

[b]Clindamycin was administered intravenously 600–900 mg every 8 hours in order to target potential bacterial toxins.

[c]Intravenous immunoglobulin treatment was considered complete when patients received Privigen 1 g/kg body weight at admission and 0.5 g/kg body weight for the following 2 days.

Table 2. Association of the Pre-, During, and Postrestrictions Periods With GAS in NSTIs

			Group A *Streptococcus*	
Firth logistic regression	OR	*P* Value	aOR[a] (95% CI)	*P* Value
Prerestrictions	0.38 (0.13–1.16)	.09	0.39 (0.10–1.49)	.2
During restrictions	**0.04 (0.002–0.85)**	**.04**	**0.02 (0.001–0.81)**	**.04**
Postrestrictions	1 (reference)		1 (reference)	
Exact logistic regression	OR	*P* Value	aOR[b] (95% CI)	*P* Value
Prerestrictions	0.38 (0.10–1.33)	.1	0.36 (0.09–1.37)	.2
During restrictions	**0.08 (0.00–0.61)**	**.01**	**0.07 (0.00–0.61)**	**.01**
Postrestrictions	1 (reference)		1 (reference)	

Occurrence of GAS in the initial surgical tissue samples isolated from patients suffering from mono- and polymicrobial NSTIs as recorded in the microbiology reports pre- (July 1, 2008, to February 27, 2020), during (February 28, 2020, to March 31, 2022), and postrestrictions (April 1, 2022, to December 31, 2023). Confidence intervals that do not include OR = 1 and *P* values <.05 are indicated in bold and considered significant.

Abbreviations: aOR, adjusted odds ratio; GAS, group A *Streptococcus*; NSTIs, necrotizing soft tissue infections; OR, odds ratio.

[a]Adjustment in Firth logistic regression was performed for potential covariates such as age, sex, diabetes, and initially affected body region.

[b]Adjustment in exact logistic regression was performed only for age and sex due to computational constraints.

The present study has several limitations. First, the statistical power is constrained by the small sample size, attributable to the infrequency of GAS-NSTI coupled with the study's monocentric design. Second, our screening methods could be prone to selection bias; the possibility of delayed hospital presentations [34], out-of-hospital deaths, or COVID-19 pandemic–related alterations in the patients' transfers from referring hospitals to tertiary care favor an immortal time bias and therefore underestimation of disease incidence or mortality rates. Third, as the yearly peak of respiratory transmitted infections happens during the first half of the year [8], seasonal bias may have occurred, leading to an underestimation of postrestrictions GAS-NSTIs. Lastly, the observational retrospective design of the study precludes the establishment of causal relationships between different parameters.

To our knowledge, this is the first study to report an absence of GAS-NSTIs in a center during the COVID-19 pandemic restrictions. Despite the aforementioned limitations, this study benefits from examining data over a 15.5-year period and thereby shows the distinctiveness of this significant decrease.

CONCLUSIONS

In conclusion, our findings show a lower proportion of GAS in NSTIs during the COVID-19 pandemic restrictions compared with the postrestrictions time period. An intriguing consideration is that the isolation measures may have prevented the transmission of GAS, resulting in a decline of GAS-NSTIs, while NSTIs caused by bacteria transmitted by alternative routes persisted. This would support the hypothesis that the isolation measures had broad secondary effects, potentially curbing not only respiratory infections but also soft tissue infections caused by pathogens transmitted via the upper airways and direct skin contact.

Supplementary Data

Supplementary materials are available at *Open Forum Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

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Potential conflicts of interest. All authors: no reported conflicts.

Author contributions. G.E., D.W., P.M.F., S.D.B., and A.S.Z. designed the study. S.D.B. and A.S.Z. did the ethics submission. G.E., D.W., and D.A.H. did the screening. G.E. and D.A.H. did the data acquisition. P.M.F. did the statistical model. G.E. did the descriptive statistics and visualizations. G.E., D.W., D.A.H., A.M.A., P.M.F., S.D.B., and A.S.Z. analyzed and interpreted the data. G.E. wrote the first draft of the manuscript. A.M.A. contributed to the writing progress. All authors revised the draft and read and approved the final manuscript.

Data availability. The data sets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Declaration of generative AI and AI-assisted technologies in the writing process. During the preparation of this work, the authors used ChatGPT (GPT-4, last accessed April 18, 2024) by OpenAI in order to improve language clarity and grammar of some parts of the manuscript. ChatGPT was not used to add intellectual content. After using this tool, the authors reviewed and edited the content as needed and take full responsibility for the content of the publication.

Patient consent. Documentation of the patient's informed consent was obtained as required. This study was approved by the local ethics committee (Kantonale Ethikkommission Zurich BASEC-ID 2016-00145 and 2017-02225).

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