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The impact of social restrictions on the incidence and microbiology of severe acute tonsillitis

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ABSTRACT

INTRODUCTION. We aimed to explore the impact of social distancing on the incidence, severity and microbiology of patients with acute tonsillitis (AT).

METHODS. In this single-centre study, we retrospectively included all patients with AT referred to the Ear-Nose-Throat Department, Aarhus University Hospital, Denmark, in the two years preceding versus the two years after the COVID-19 lockdown in Denmark (11 March 2020).

RESULTS. In total, 425 patients were included. The incidence of AT was significantly lower in the post-lockdown period (n = 128) than in the pre-lockdown period (n = 297) ($p < 0.001$). Reduced incidence was observed across all age groups. No significant differences were found in patient characteristics between periods. The proportion of hospitalised patients was significantly lower in the post- than in the pre-lockdown period (36% versus 25%, $p = 0.032$). Prevalent culture findings were Streptococcus pyogenes (15%), S. anginosus group (11%) and Fusobacterium necrophorum (5%). No statistically significant differences in the relative prevalence of individual bacteria were found between periods.

CONCLUSIONS. The incidence of patients with AT referred to hospital decreased by 57% in the two-year period after the COVID-19 lockdown compared with the period leading up to the lockdown. Our findings suggest that this decrease mirrored a general decline in AT incidence rather than altered referral patterns.

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Following the lockdown due to COVID-19 on 11 March 2020, social restrictions were imposed for almost two years in Denmark. These circumstances presented a unique opportunity to study the impact of social distancing on the spread of airborne diseases. Social distancing in public health is a set of physical interventions intended to prevent transmission of contagious diseases. The cumulated effect of social distancing is particularly informative in studies of disease caused by bacterial infections arising from a heavily colonised oral mucosa as it provides an opportunity to study if these infections are contagious or develop from the patient's own flora [1-3].

Acute tonsillitis (AT) is a highly prevalent infection affecting children and adults. The most common aetiology is viral, but some bacteria are known pathogens in the development of AT. In addition to the well-described

Streptococcus pyogenes, several studies suggest that the *S. anginosus* group and *Fusobacterium necrophorum* are prevalent pathogens in AT [4]. Most cases of AT are self-limiting, but occasionally patients present with severe symptoms (fever, dysphagia, severe pain and troublesome breathing) or signs of infectious spread to the peritonsillar tissues (peritonsillar phlegmon (PP)). In these cases, management by ear-nose-throat specialists and hospitalisation are often required for correct diagnosis (differential diagnoses: peritonsillar abscess (PTA)) and to facilitate a fast and uncomplicated recovery using intravenous antibiotics.

Previous studies of the effects of COVID-19-associated social restrictions have documented a decline in referred patients with upper airway diseases, such as acute otitis media, otitis media with effusion, PTA and acute sinusitis [4-6]. No studies have explored the effects of social restrictions on the incidence or microbiological findings of patients with AT.

The aims of the present study were to explore the impact of social restriction on 1) the incidence, 2) the severity of illness and 3) the bacterial findings of patients with AT who were referred to hospital for specialised management. We hypothesised that 1) the number of patients with AT referred to hospital would be reduced because of decreased inter-person exchange of bacteria owing to social restrictions, 2) patients with AT referred to hospital would be more severely ill (higher infection markers, higher proportion of patients with PP, etc.) because of a decreased inclination for hospital management at during a pandemic by physicians and patients, and 3) that the relative prevalence of *S. pyogenes* would be decreased after the lockdown, mirroring previous findings in PTA.

Methods

Study population and setting

A retrospective analysis was performed of all patients admitted to the Department of Otorhinolaryngology, Head and Neck Surgery, Aarhus University Hospital. Data were analysed by comparing findings before and during social restrictions related to the COVID-19 pandemic. Eligible patients were all patients referred with AT in the two time periods: 1) 12 March 2018 to 11 March 2020 (pre-lockdown) and 2) 12 March 2020 to 11 March 2022 (after lockdown). Patients with PTA (defined as clinical identification of peritonsillar pus) were excluded.

Data extraction

Patients were identified through the International Classification of Diseases, 10 version (ICD-10), codes J02 and J03. Data elements extracted from the medical journals included age, sex, date of diagnosis, duration of symptoms, antibiotic treatment before admission, anamnestic fever, temperature, biochemical findings (c-reactive protein (CRP), leukocytes and neutrophilocytes), surgical intervention, presence of PP and microbiological findings. PP was defined as the clinical finding of swelling of the peritonsillar tissue without detection of pus.

Microbiological analyses

Cultures from tonsillar surface swabs were included. Culturing and identification of bacteria were performed as part of routine diagnostic procedures. Sample material was plated on blood agar, chocolate agar, anaerobic agar, selective *Fusobacterium* agar (containing 5 mg/l nalidixic acid and 2.5 mg/l vancomycin (Statens Serum Institute Diagnostica (SSID), Hillerød, Denmark), and cultured in thioglycolate broth (SSID). The plates were incubated at 35&;C in a 5% CO_2 atmosphere or anaerobically for up to three days. Cultured microorganisms were identified using standard methods [7] and often guided by identification using matrix-assisted laser desorption/ionisation time-of-flight mass spectrometry (MALDI-TOF MS) (Bruker Daltonics, Bremen, Germany). Light-to-moderate growth of *Neisseria* species, *Lactobacillus* species, coagulase-negative staphylococci, viridans streptococci,

Prevotella species and *Fusobacterium* non-necrophorum alone or in mixture was reported as "normal flora".

Statistical analyses

The binomial probability test was used for comparison of absolute numbers, the Fisher's exact test for comparison of proportions and Student's t-test for comparison of continuous variables between periods. Data normality was assessed using quantile-quantile plots. All continuous variables were normally distributed and reported as means with standard deviation. Categorical variables were reported as absolute numbers and frequencies. Statistical significance was defined as $p < 0.05$.

Trial registration: The study was approved by the Danish Data Protection Agency (-16-02-134-23) and the Danish Patient Safety Authority (-45-70-41-23).

Results

Patient characteristics and severity of disease

In total, 425 patients were included; 54% were females. No statistically significant differences were found in patient characteristics between periods concerning age, sex distribution, duration of symptoms, prevalence of fever and PP, antibiotic treatment before admission and biochemical infection markers (**Table 1**). The proportion of patients with a concurrent presence of PP was similar between the two periods (pre-lockdown: 34% (98/288) versus post-lockdown: 35% (43/124, 35%)). The presence of concurrent PP was unclear in 13 patients.

TABLE 1 Characteristics of 425 patients with acute tonsillitis stratified by period in relation to the Danish lockdown (11 March 2020).

	Period			
	pre-lockdown	post-lockdown	Patients, total	p value
Patients, n	297	128	425	< 0.001[a]
Female gender, n/N (%)	157/297 (53)	73/128 (57)	230/425 (54)	0.46[b]
Age, mean (± SD), yrs	29.0 (± 15.1)	28.6 (± 15.5)	28.9 (± 15.2)	0.81[c]
Duration of symptoms, mean (± SD), days	6.1 (± 6.4)	6.6 (± 7.9)	6.3 (± 6.8)	0.58[c]
Peritonsillar phlegmon, n/N (%)[d]	98/288 (34)	43/124 (35)	141/412 (34)	0.91[b]
Fever, n/N (%)[e]	157/226 (70)	73/108 (68)	222/334 (69)	0.80[b]
Temperature, mean (± SD), °C	38.2 (± 1.1)	38.1 (± 0.9)	38.1 (± 1.1)	0.49[c]
Antibiotic treatment prior to admission, n/N (%)				
Penicillin V	110/142 (77)	48/64 (75)	158/206 (77)	0.72[b]
Penicillin V + metronidazole	4/142 (3)	3/64 (5)	7/206 (3)	0.68[b]
Macrolides[f]	6/142 (4)	1/64 (2)	7/206 (3)	0.67[b]
Other[g]	5/142 (4)	7/64 (11)	12/206 (6)	0.12[b]
Unknown drug	17/142 (12)	5/64 (8)	22/206 (11)	0.47[b]
Subtotal	142/297 (47)	64/128 (50)	206/425 (49)	0.75[b]
Infection markers, mean concentration (± SD)				
CRP, mg/l	122 (± 92)	114 (± 88)	119 (± 91)	0.59[c]
Leukocytes, × 10^9/l	14.0 (± 5.3)	13.1 (± 5.6)	13.8 (± 5.4)	0.39[c]
Neutrophils, × 10^9/l	10.6 (± 4.9)	9.4 (± 5.4)	10.3 (± 5.1)	0.24[c]
Hospitalised, n/N (%)	106/297 (36)	32/128 (25)	138/425 (33)	0.032[b]

SD = standard deviation.
a) Binomial probability test.
b) Fisher's exact test.
c) Student's t-test.
d) Presence of peritonsillar phlegmon was unknown in 13 patients.
e) Presence of fever was unknown in 91 patients.
f) Pre-lockdown: roxithromycin (n = 2), clarithromycin (n = 2), erythromycin (n = 1), azithromycin (n = 1); post-lockdown: clarithromycin (n = 1).
g) Pre-lockdown: piperacillin-tazobactam (n = 2), amoxicillin (n = 2), dicloxacillin (n = 1); post-lockdown: amoxicillin-clavulanate (n = 3), amoxicillin (n = 1), metronidazole (n = 1), roxithromycin + metronidazole (n = 1), piperacillin-tazobactam (n = 1).

Incidence of acute tonsillitis

The incidence of patients with AT referred to hospital was significantly lower in the post-lockdown period (n = 128) than in the pre-lockdown period (n = 297) ($p < 0.001$). The proportion of patients who were hospitalised was significantly lower in the post-lockdown period (32/128, 25%) than in the pre-lockdown period (106/297, 36%) ($p = 0.032$).

Most cases (304/425, 72%) were patients aged 15-39 years (**Table 2**). A reduced incidence of patients with AT was observed in all age groups).

TABLE 2 Characteristics of 425 patients with acute tonsillitis stratified by age and period in relation to the Danish lockdown (11 March 2020).

	Period, n			
Age, yrs	pre-lockdown	post-lockdown	Patients, total, N (%)	p value[a]
0-14	29	7	36 (8)	< 0.001
15-19	58	30	88 (21)	0.004
20-29	97	51	148 (35)	< 0.001
30-39	54	13	67 (16)	< 0.001
≥ 40	59	27	86 (20)	< 0.001
Total	297	128	425	< 0.001

a) Binomial probability test.

Microbiological findings

Cultures were performed in 100 cases (**Table 3**). The proportion of patients with cultures was 26% (76/297) in the pre-lockdown period and 19% (24/128) in the post-lockdown period ($p = 0.13$). The prevalent findings were *S. pyogenes* (15%), *S. anginosus* group (11%) and *F. necrophorum* (5%). No statistically significant differences in the relative prevalence of individual bacteria were found between periods.

TABLE 3 Bacterial findings in 100 cultures from 425 patients with acute tonsillitis stratified by period in relation to the lockdown (11 March 2020).

	Period, n/N (%)			p value, comparisons	
	pre-lockdown	post-lockdown	Patients total, n/N (%)	absolute numbers[a]	relative prevalence[b]
Cultures	76/297 (26[c])	24/128 (19[c])	100/425 (24[c])	-	0.14
Normal flora	47/76 (62)	20/24 (83)	67/100 (67)	-	0.08
Positive	29/76 (38)	4/24 (17)	33/100 (33)	-	
Bacteria					
Aerobes:					
Streptococcus pyogenes	12/76 (16)	3/24 (13)	15/100 (15)	0.035	1.0
S. anginosus group	10/76 (13)	1/24 (4)	11/100 (11)	0.012	0.29
Anaerobes:					
Fusobacterium necrophorum	4/76 (5)	0/24	4/100 (4)	0.13	0.57
Other[d]	3/76 (4)	0/24	3/100 (3)	-	-

a) Binomial probability test.
b) Fisher´s exact test.
c) Proportion of patients with cultures performed.
d) *Haemophilus haemolyticus* (n = 1), *Arcanobacterium haemolyticum* (n = 1) and Enterobacterales (n = 1).

Discussion

Prevalence of acute tonsillitis and severity of disease

Compared with the pre-lockdown period, the incidence of patients with AT referred to hospital decreased by 57% in the post-lockdown period. In a similar study of 2,636 AT cases, N. Quirashi et al. found a 64% decline in the incidence of patients with tonsillitis referred to hospital in the United Kingdom [6]. The observed post-lockdown reduction in patients with AT referred to hospital may reflect an overall decreased incidence of AT or an altered threshold for referring patients to hospital. Our findings suggest that the threshold for referring patients to specialised hospital treatment remained unchanged between periods as patients exhibited a similar disease severity (duration of symptoms, prevalence of fever and PP, biochemical infection markers, etc.) before and after lockdown. Hence, our findings suggest that the marked decrease in patients with AT, who were referred to hospital because of severe symptoms and/or signs of peritonsillar involvement, mirrored an overall decrease in the incidence of patients with AT. In line with this interpretation, Kim et al. [8] reported a 58% reduced incidence of patients with AT in a study of all patients with AT treated in both primary and second care facilities in Korea in the two years leading up to versus the two years following lockdown.

In a previous study from our institution, we found a 32% reduced incidence of PTA in the two years with social restrictions compared with before the lockdown [1]. The study by Klug et al. found a modest reduction in PTA incidence in patients aged 15-29 years (6%) and a significantly higher incidence in older patients (55%). These results among PTA patients run contrary to the findings of the present study, where the reduction in the incidence of patients with AT referred to hospital was largely unrelated to age, which may be surprising considering that multiple findings suggest that PTA is a complication to AT [9]. This discrepancy indicates that the relationship between AT and PTA is complex and that additional factors are involved in the progression of infection from AT to PTA.

Microbiology

We found a statistically non-significant trend towards a decreased proportion of positive cultures in the post-lockdown period compared with before the lockdown (38% versus 17%, p = 0.08). The relative composition of bacteria was not statistically significantly different between the periods, but we noted that a markedly lower number of patients were culture-positive for *S. pyogenes*, *S. anginosus* group and *F. necrophorum* (collectively).

Admittedly, the low number of culture-positive cases prevents solid conclusions concerning potential alterations in bacterial composition after social restrictions were imposed, but our findings seem different from those in the previous study of PTA where the relative prevalence of *S. pyogenes* was significantly higher in the period before (27%) than after (16%) the lockdown, whereas the relative prevalence of *F. necrophorum* and *S. anginosus* group was significantly lower before (24% and 15%, respectively) than after (36% and 24%, respectively) the lockdown [1]. These findings suggest that the relationship between AT and PTA and the bacterial aetiology of these infections is not complex and influenced by other (yet unrecognised) factors.

Strength and limitations

The strengths of the present study are the substantial number of patients and the robust analyses associated with incidence and patient characteristics between periods. The limitations are those inherent to retrospective cohort studies: information bias and confounding. Potential confounders include differences between periods concerning antibiotic prescribing practices in primary care and the proportion of patients with cultures performed. Solid conclusions concerning microbiology are prevented by the relatively low number of cultures (which are not routinely performed), especially those positive for potential pathogens. Of note, the present study included patients referred to hospital, and our findings refer to this subgroup of patients with AT and not to the much larger group of patients with AT managed in general practice. The aetiologic cause of AT may differ when comparing patients referred to hospital with highly aggravated symptoms with those managed in general practice [10].

Conclusions

The incidence of patients with AT referred to hospital management decreased by 57% in the two-year period with social restrictions compared with the period leading up to the lockdown. No significant differences in clinical patient characteristics were found between periods. A smaller proportion of patients were hospitalised after the lockdown, which may be related to changes in the internal management of patients rather than to a change in illness severity. Hence, our findings suggest that the significant decrease in the incidence of AT mirrored a general decrease rather than altered referral patterns. No statistically significant differences in the relative prevalence of individual bacteria were found between periods.

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Conflicts of interest Potential conflicts of interest have been declared. Disclosure forms provided by the authors are available with the article at ugeskriftet.dk/dmj

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REFERENCES

1. Klug TE, Greve T, Caulley L, et al. The impact of social restrictions on the incidence and microbiology of peritonsillar abscess: a retrospective cohort study. Clin Microbiol Infect. 2024;30(1):100-6. https://doi.org/10.1016/j.cmi.2023.08.003

2. Hedin K. Sore throat-related infections - lessons learnt from non-pharmacological interventions and non-COVID-19 infections. Clin Microbiol Infect. 2024;30(1):18-9. https://doi.org/10.1016/j.cmi.2023.10.024
3. Lison A, Banholzer N, Sharma M, et al. Effectiveness assessment of non-pharmaceutical interventions: lessons learned from the COVID-19-pandemic. Lancet Pub Health. 2023;8(4):311-e317. https://doi.org/10.1016/S2468-2667(23)00046-4
4. Kjærulff AMG, Thomsen MK, Ovesen T, et al. Clinical and biochemical characteristics of patients with Fusobacterium necrophorum-positive acute tonsillitis. Eur Arch Otorhinolaryngol. 2015;272(6):1457-63. https://doi.org/10.1007/s00405-015-3535-7
5. Levy C, Cohen R. Infectious diseases in the COVID-19 era: gaps between countries. Lancet Infect Dis. 2023;23(9):987-88. https://doi.org/10.1016/S1473-3099(23)00198-6
6. Quirashi N, Ray M, Srivastava R, et al. A multicentre retrospective cohort study on COVID-19-related physical interventions and adult hospital admissions for ENT infections. Eur Arch Otorhinolaryngol. 2022;279(5):2671-8. https://doi.org/10.1007/s00405-021-07180-y
7. Carroll KC, Pfaller MA, Landry ML, et al, eds. Manual of clinical microbiology, 12 ed. ASM Press, 2019
8. Kim SY, Yoo DM, Kim JH et al. Changes in otorhinolaryngologic disease incidences before and during the COVID-19 pandemic in Korea. Int J Environ Res Public Health. 2022;19(20):13083. https://doi.org/10.3390/ijerph192013083
9. Klug TE, Rusan M, Fuursted K, et al. Peritonsillar abscess: complication of acute tonsillitis or Weber's glands infection? Otolaryngol Head Neck Surg. 2016;155(2):199-207. https://doi.org/10.1177/0194599816639551
10. Andersen C, Greve T, Reinholdt KB, et al. Bacterial findings in patients referred to hospital for the treatment of acute tonsillitis with or without peritonsillar phlegmon. BMC Infect Dis. 2023;23(1):439. https://doi.org/10.1186/s12879-023-08420-8

