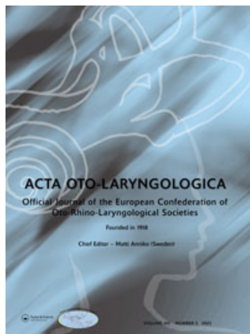

Acta Oto-Laryngologica

ISSN: (Print) (Online) Journal homepage: www.tandfonline.com/journals/ioto20

Incidence of pediatric tonsillitis, otitis and upper respiratory infectious entities in the pre and post COVID-19 quarantine eras

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To cite this article: Christophe Abi Zeid Daou, Yara Yammine, Anne-Marie Daou, Patrick A.R. Feghali, Wassim Najjar & Randa Barazi (2023) Incidence of pediatric tonsillitis, otitis and upper respiratory infectious entities in the pre and post COVID-19 quarantine eras, Acta Oto-Laryngologica, 143:5, 423-428, DOI: 10.1080/00016489.2023.2200851

To link to this article: https://doi.org/10.1080/00016489.2023.2200851

Published online: 24 Apr 2023.

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ACTA OTO-LARYNGOLOGICA
2023, VOL. 143, NO. 5, 423–428
https://doi.org/10.1080/00016489.2023.2200851

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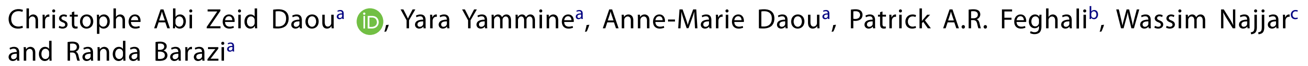

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ABSTRACT

Background: At this point of the COVID-19 pandemic, with the worldwide loosening of health restrictions, there has been an observed jump in infectious load especially of the upper airways.
Aims/Objectives: To shed light on children's immunity and potential health risks after the COVID-19 pandemic.
Methods: A retrospective chart review from May 2019 to January 2022. Pediatric patients with a discharge diagnosis suggestive of an upper respiratory or ENT infection were included. The sample was divided into three groups according to the date of presentation.
Results: A total 4356 patients were diagnosed with ENT infectious aetiology. The mean age was 4.69 years. The three periods studied were: Period-1 (May 2019–January 2020), period-2 (February 2020–April 2021) and period-3 (May 2021–January 2022). The distribution of adenoiditis and MEE is the same across all periods ($p > .05$). The incidence of URTI, AOM and tonsillitis were significantly highest during period-3 followed by period-1, which in turn was significantly higher than during period-2 ($p < .05$). The incidence of sinusitis was the highest during period-3 ($p < .001$).
Conclusion: There seems to be a heightened susceptibility to acute infection in children after the pandemic.
Significance: It is important to keep in mind the changes in microbiota and implement measures to promote healthy gut flora, timely vaccination, and prompt medical interventions.

SUMMARY BOX

- **What is already known:** We already know that quarantine has significantly decreased infectious load especially in children.
- **This study adds** an objective assessment of this decrease with an assessment of the infectious load post-quarantine.
- **This study** is a model for future pandemics on the importance of vaccinations and the importance of microbiota changes after pandemics.

ARTICLE HISTORY
Received 25 January 2023
Revised 22 March 2023
Accepted 23 March 2023

KEYWORDS
URTI; otitis; tonsillitis; sinusitis; vaccination; COVID-19

Introduction

The COVID-19 pandemic has resulted in an unprecedented global health crisis, with over 257 million confirmed cases and 5 million deaths reported worldwide as of November 2021 [1]. To curb the spread of the virus, many countries have implemented quarantine measures, including lockdowns, social distancing, and travel restrictions. These measures have been effective in reducing transmission rates and flattening the curve of new cases, as demonstrated by several studies [2].

However, the economic and social costs of quarantine measures have been significant, leading many countries to loosen their restrictions in recent months. Despite the potential risks associated with lifting quarantine measures, including an increase in infection rates, many governments have justified their actions by citing the need to balance public health concerns with economic and social needs.

Several studies have examined the effectiveness of quarantine measures in reducing the transmission of COVID-19. A systematic review and meta-analysis of 29 studies found that quarantine measures were effective in reducing the spread of COVID-19, with a pooled effect size of 0.33 (95% CI: 0.28–0.38) [3]. Another study found that quarantine measures were associated with a significant reduction in the number of COVID-19 cases, hospitalizations, and deaths [4].

The potential risks associated with lifting quarantine measures have also been documented in the literature. A study conducted in China found that the lifting of quarantine measures was associated with an increase in COVID-19 cases [5]. Another study conducted in the UK found that the lifting of quarantine measures was associated with an

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increase in COVID-19 cases in some areas, although the overall impact of lifting measures on transmission rates was unclear [6].

With the loosening of quarantine measures, we observed an increased rate of non-COVID-19-related infections, particularly in children. The number and severity of cases presenting to our tertiary care centre pushed us to ask whether children post-quarantine were more susceptible to infections, namely upper respiratory and ENT-related infections. There are no studies, to our knowledge, comparing the pre and post-pandemic burden after the re-opening of schools and the loosening of protective measures [7].

The current study aims to investigate the relationship between quarantine and pre and post-quarantine infection rates. By examining the relationship between quarantine and post-quarantine infection rates, we hope to provide valuable insights into the consequences of prolonged quarantine in children and inform public health policies aimed at reducing the risk of post-quarantine infections.

As of September 2022, a total of 614,998,314 cases of coronavirus disease 2019 (COVID-19) and 6,536,643 associated deaths have been reported worldwide [1]. Serious complications during and following infection have been seen and reported including acute respiratory distress syndrome, stroke and pulmonary embolism.

In efforts to decrease disease burden and control outbreaks, several non-pharmaceutical interventions were put in place such as prohibition and limitation of social gatherings, implementation of social distancing, wearing masks, working from home, and closing schools and public venues. Consequently, most face-to-face encounters were limited.

These implementations were associated with a significant decrease in infectious diseases disseminated through airborne and fecal-oral routes.

Respiratory viruses play an important role in airway inflammation and up-regulation of inflammatory mediators leading to impaired mucociliary clearance, changes in mucus character and upregulation of cytokines. The mentioned events eventually promote the formation of middle ear effusions, otitis medias, sinusitis, and adenoiditis. In fact, Liu et al. showed a significant decrease in the prevalence of respiratory viruses related to lower respiratory infections after school closure, namely Respiratory Syncytial Viruses, Adenoviruses, Influenza and metapneumo viruses.

It is known that children exposed to colds and viruses earlier in life will develop a stronger immune system and are less likely to become sick due to the immune response mounted against these pathogens. The hygiene hypothesis suggests that infections transmitted early in life might prevent allergies, asthma and boost the immune system. Furthermore, it was suggested that exposure to environmental microorganisms contributes to the body's microbial diversity, the latter playing an important role in host immunity.

Many studies looked at the protective role of quarantine in decreasing infectious burden, especially in the pediatric population. However, there are no studies, to our knowledge, comparing the pre and post-pandemic burden after re-opening of schools and the loosening of protective measures.

Materials and methods

The study included patients presenting to a specific tertiary care center in Beirut, Lebanon. Patients who presented to the pediatric ENT clinic, general pediatric clinic and Emergency Department between 1 May 2019 and 31 January 2022 were identified by retrospective chart review. Reporting for this study was done using the STROBE checklist.

Any pediatric patient (≤18 years of age) with a discharge diagnosis of fever, upper respiratory tract infection (URTI), viral illness, cough, sore throat, acute otitis media (AOM), suppurative otitis, ear pain, ear drainage, middle ear effusion (MEE), sinusitis, adenoiditis or tonsillitis was included. The discharge diagnosis is chosen by the treating attending physician at the end of the encounter at the time of signing the chart.

The charts were reviewed and sorted into: URTI, AOM, MEE, tonsillitis, sinusitis, adenoiditis and others. The category "other" included all entities not related to an infectious ENT cause such as diarrhea, urinary infection, pneumonia etc. Patients older than 18 and with other discharge diagnoses, than those mentioned above, were excluded.

As background information, the first COVID-19 case was recorded in Lebanon at the beginning of February 2020. Starting end of January and February 2020, health measures started to be implemented including the obligatory wearing of masks, hand hygiene, closure of schools and public places, quarantine… among others. Starting in May 2021, there was a significant loosening of restrictions and social distancing with re-opening of schools, nurseries, public offices/spaces and universities.

In order to assess the infectious load before, during and after the COVID-19 pandemic, the sample was divided into three groups according to the date of presentation. The pre-COVID era lasted from May 2019 to January 2020 (9 months). The second era (the COVID quarantine era, 15 months) was considered to span February 2020 to April 2021. The post-COVID era, therefore, includes dates starting from 01 May 2021 (9 months) till 31 January 2022.

Data analysis was done using IBM SPSS Statistics for Windows, version 27 (IBM Corp., Armonk, N.Y., USA). Frequencies and means were calculated for nominal and continuous variables. In comparing frequencies across the three periods, Levene's test showed non-equality of variance, therefore Kruskal–Wallis test was used. Significance values were adjusted by the Bonferroni correction for multiple tests.

Results

Demographic data

Six thousand, one hundred and sixty-two charts were included. Among those, 4,356 patients were diagnosed with an infectious etiology related to the ears nose and throat while 1,806 had other etiologies. Patients were aged 0 to 18 with a mean age of 4.69 ± 4.18 and the male-to-female ratio was approximately 6:5 (Table 1).

The most common discharge diagnosis was of non-ENT etiologies (29.4%) followed by URTI (28.9%), AOM (23.1%), and tonsillitis (11.8%). Most of the cases were encountered in the emergency room (56.9%) followed by the general pediatrics clinic (36.9%) and then the pediatric otolaryngology clinic (Table 1).

The COVID pandemic

The three periods studied were: Period 1 (May 2019–January 2020), period 2 (February 2020–April 2021) and period 3 (May 2021–January 2022).

The number of patients seen during these three periods was 2,749; 1,287 and 2,126 respectively.

The mean age of patients seen during each of the periods was 4.97, 5.34 and 3.87 respectively. Age distribution was significantly different between all three periods ($p < 0.05$), this was accounted for in further comparisons. Gender distribution was statistically similar across all three periods ($p > 0.05$).

The incidence of non-ENT-related discharge diagnoses (diarrhea, UTI…) was highest during periods 1 (30.8%) and 2 (52.9%). This was followed by URTI diagnoses. During period 3, the most common discharge diagnosis was URTI (32.9%) followed by AOM (27.4%) (Table 2).

The distribution of adenoiditis and MEE is the same across all three periods ($p > 0.05$).

The incidence of URTI during period 3 was the highest followed by period 1 ($p = 0.001$), which were in turn statistically higher than during quarantine (period 2, $p = 0.012$) (Figure 1).

Same for the incidence of AOM and tonsillitis, was the highest after quarantine, significantly higher than pre-quarantine era ($p < 0.001$ and 0.006 respectively). The incidence of both AOM and tonsillitis during period 1 was in turn significantly higher than during period 2 ($p = 0.012$ and $p < 0.001$ respectively) (Figures 2 and 3).

The incidence of sinusitis overall was low (0.8%). It was the highest during period 3 ($p < 0.001$), however, it did not change from pre-quarantine to during quarantine ($p = 1.00$).

Table 1. Demographic data of the study population.

	N or Mean	Standard deviation or Percentage	Range
Age (years)	4.69	4.18	0–18
Gender			
Male	3380	54.85%	
Female	2782	45.15%	
Discharge diagnosis			
URTI	1781	28.9%	
Acute otitis media	1426	23.1%	
Tonsillitis	729	11.8%	
Middle ear effusion	355	5.8%	
Sinusitis	53	0.8%	
Adenoiditis	12	0.2%	
Other	1806	29.4%	
Location of encounter			
Emergency room	3510	56.9%	
Pediatrics clinic	2277	36.9%	
ENT clinic	375	6.2%	

Discussion

The hygiene hypothesis suggests that children with frequent exposure to environmental antigens would be less susceptible to diseases that result from an imbalance in immunity [8]. During the COVID-19 pandemic, many researchers looked at the hygiene hypothesis to explain the asymmetric mortality over the globe. Case fatality was highest in Europe and lowest in South-East Asia [9]. COVID-19 mortality is surely linked to multiple hosts and environmental factors including age, viral load and nature of the infection, co-morbidities, along with other genetic and epigenetic factors. Nonetheless, many researchers have, at least partly, attributed these disparities to the hygiene hypothesis and microbiome diversity [10].

In that same thought process, exposure to multiple microbes leads to activation of the innate immunity. This response, mounted by natural killer cells, dendritic cells, macrophages, and lymphocytes, against one set of microbes can have overlapping protection against other infections [10]. In fact, researchers have found CD4 T-cells in individuals not exposed to COVID-19 that react to its expressed proteins [11].

The hygiene hypothesis has been proposed to explain susceptibility to COVID-19 infection, it also can, in a similar line of thinking be applied to host susceptibility to microbial infections post quarantine.

Reduced microbial exposure resulting from social changes, hygiene regulation, antibiotics prescription etc. is associated with a rise in acute infections and chronic autoimmune and allergic diseases [12].

This reduced exposure originates, on one hand, from the hygienic measures taken during the pandemic, including the wearing of protective equipment, frequent handwashing, continuous cleaning and bleaching of surfaces… [12] On

Table 2. Demographic data of the study population during each of the periods studied.

	Period 1 May 19–Jan 20	Period 2 Feb 20–Apr 21	Period 3 May 21–Jan 22
Age (years)	4.97 ± 4.41	5.34 ± 4.37	3.87 ± 3.03
Gender			
Male	1509 (54.9%)	698 (54.2%)	1,173 (55.2%)
Female	1240	589	953
Discharge diagnosis			
URTI	775 (28.2%)	306 (23.8%)	700 (32.9%)
Acute otitis Media	610 (22.2%)	233 (18.1%)	583 (27.4%)
Tonsillitis	328 (11.9%)	86 (6.7%)	315 (14.8%)
Middle ear Effusion	180 (6.5%)	61 (4.7%)	114 (5.4%)
Sinusitis	8 (0.3%)	6 (0.5%)	39 (1.8%)
Adenoiditis	4 (0.1%)	1 (0.1%)	7 (0.3%)
Other	844 (30.8%)	594 (52.9%)	368 (17.4%)
Location of encounter			
Emergency room	1637 (59.5%)	760 (59.1%)	1113 (52.4%)
Pediatrics clinic	997 (36.3%)	410 (31.9%)	870 (40.9%)
ENT clinic	115	117	143
Total patients seen	2749	1287	2126

Figure 1. Incidence (%) of URTI per month from May 2019 to January 2022. Legend: Blue: Period 1, Red: Period 2, Green: Period 3.

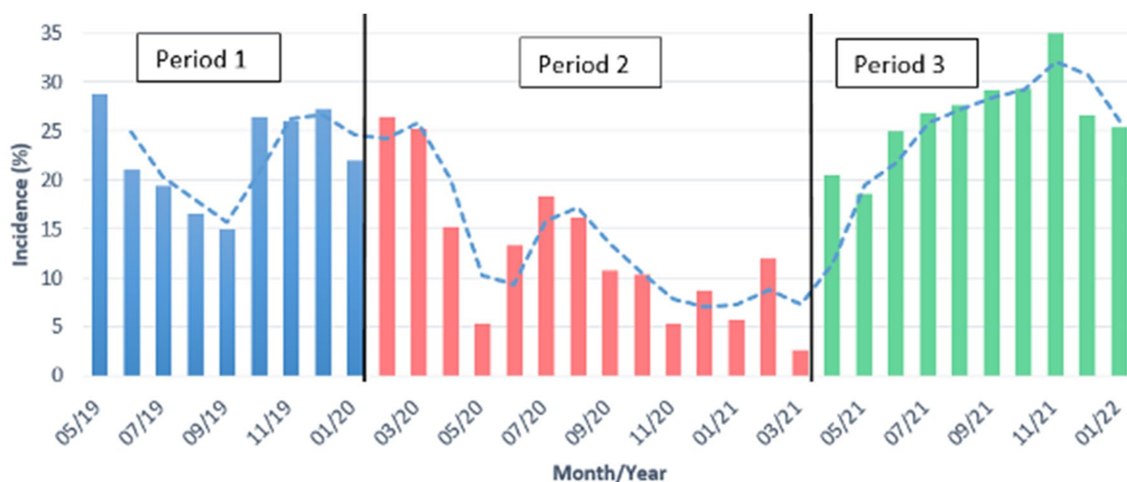

Figure 2. Incidence (%) of AOM per month from May 2019 to January 2022. Legend: Blue: Period 1; Red: Period 2; Green: Period 3.

the other hand, social confinement and segregation also leads to decreased exposure and limited diversity of the microbiome resulting from home quarantine and reinforcement of mobility and travel constraints [13]. It has also been shown in the literature that the human microbiome is negatively impacted by air pollutants, toxic metals and organic compounds, therefore people who quarantine in "unsafe" environments are more susceptible to microbiome changes and vulnerability [14].

Aside from reducing exposures, several factors during the pandemic have contributed to increased microbiota shedding and loss of diversity. Namely, the increase in the use of antibiotics during the pandemic, be it to avoid going to a hospital during the lockdown and self-medication or to treat secondary infections due to COVID-19 [15]. Also, early in the pandemic several treatment options were proposed for COVID-19 treatment and prevention, including hydroxychloroquine, ivermectin, and other antimicrobials. The increased use of these medications has been shown to substantially affect the host microbiota and hence immune system [16].

This is especially true for children and infants, as the early years of life are critical periods for establishment and development of the microbiome. Initially, the microbiome is shaped by the maternal immune system and is significantly impacted by antibiotic use, formula feeding, increased hygiene at home and increased time spent indoors [12].

The hygiene hypothesis related to reduced exposure and loss of diversity of the microbiota explains our results. The increase in infectious burden in children post-quarantine can be related, at least in part, to the COVID-19 safety measures, the increased antibiotics and antimicrobial intake and limitation in social contact.

What is interesting to note is the lower mean age of patients presenting with symptoms to the hospital post-quarantine. These children were most likely born during quarantine or spent their first few years in quarantine.

At home, the limited social interactions, the closure of schools and playgrounds affected the shaping of their immune system. Furthermore, the stress of the pandemic on the mother and caregiver also affects the child's microbiome.

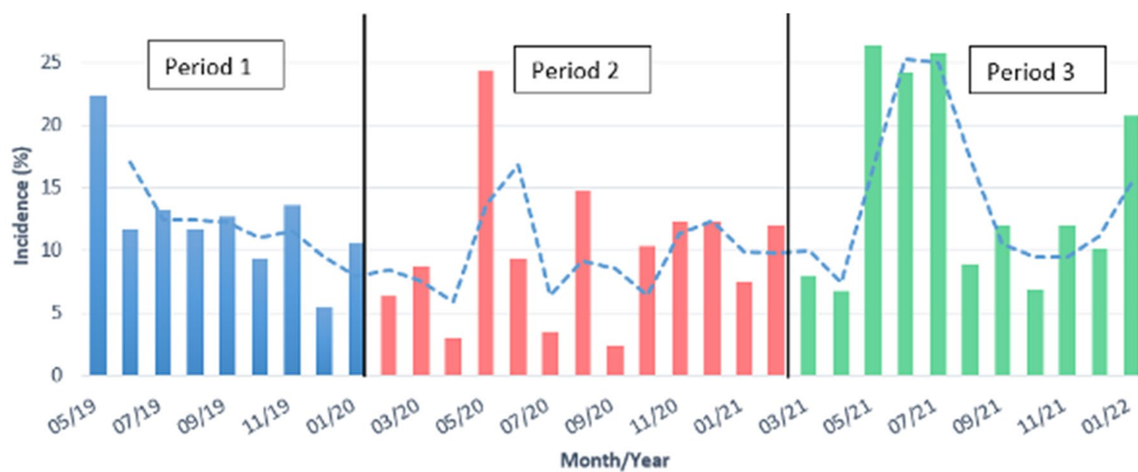

Figure 3. Incidence (%) of tonsillitis per month from May 2019 to January 2022. Legend: Blue: Period 1; Red: Period 2; Green: Period 3.

Infants during quarantine also have been noticed to fall behind in their regular vaccination schedule and routine health visits [17]. In fact, part of the innate immune training is ensured by appropriate vaccination. There have been recent claims that vaccination with MMR or BCG vaccines confer some protection against COVID-19. In the same reasoning, complete vaccination will confer protection to children against a wide array of microbes [18,19].

On the other hand, some studies have reported that there may not be significant changes in immunity after quarantine. A study of Ebola survivors who underwent quarantine found that there were no differences in immune markers between those who had been quarantined and those who had not [20].

To our knowledge, there are no studies in the literature looking at the infection rates after quarantine. It is worth noting that the impact of quarantine on immunity is likely complex and multifactorial, and may vary depending on factors such as the duration of quarantine, the age and health status of the individual, and the specific infectious agent involved.

These findings should not discourage the implementation of safety measures for the containment of a deadly disease. However, caution should be exercised especially when dealing with children born/raised in quarantine. It is important to keep in mind the changes in microbiota and implement measures to promote healthy gut flora, timely vaccination, and prompt medical interventions.

Limitations of this study include, the retrospective nature of it. The fact that it was done in one tertiary care center and the fact that only these infectious entities were looked at. What would also be interesting is to look at the severity of these infections pre and post quarantine. Further research is needed to better understand the impact of quarantine on the immune system and its implications for infection risk.

Conclusion

The COVID-19 pandemic has shifted our focus to how preventive measures and antimicrobial stewardship may have collateral damage on the collective microbiome. The consequence seems to be a heightened susceptibility to acute infection. This has been noticed in our clinics and wards with kids presenting with more frequent and more severe infections than prior to the pandemic. The increase in susceptibility to infection is surely multifactorial and should be taken into consideration with current health measures applied worldwide.

Ethical consideration

This study was approved by the Institutional Ethics Committee Institutional Review Board at the American University of Beirut) (Protocol number: BIO-2022-0165). The research was conducted ethically, with all study procedures being performed in accordance with the requirements of the World Medical Association's Declaration of Helsinki. Written informed consent was waived in accordance with ethical standards.

Author contributions

CAZD was involved in idea planning, proposal write-up, data collection, manuscript writing, and data analysis. YY, AD, PF and WN were involved in data collection. RB was responsible to oversee the project and editing the manuscript.

Disclosure statement

All authors declare that they have no conflicts of interest.

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Data availability statement

The datasets generated during and/or analysed during the current study are available from the corresponding author upon reasonable request.

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