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LETTER

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Is there an increased number of community-acquired pneumonia requiring drainage placement in children after COVID-19 pandemic in Italy?

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To the Editor,

Community-acquired pneumonia (CAP) represents one of the most common causes of hospital admission and morbidity among children worldwide, accounting (according to the World Health Organisation) for 14% of all deaths of children under 5 years old (1). Community-acquired pneumonia can be caused by bacterial pathogens such as Streptococcus pneumoniae and Haemophilus influenzae type B, the most frequent, or viral pathogens such as the most common respiratory syncytial virus.[1] After the coronavirus disease 2019 (COVID-19) pandemic, some studies revealed a significantly decreased proportion of children hospitalized with CAP,[2] but the literature is still inconclusive on this topic.

This cross-sectional observational study was conducted from October 1, 2023 to October 31, 2023 at IRCCS Arcispedale Santa Maria Nuova of Reggio Emilia in Italy.

The hospital serves a large area, accounting for more than 500,000 inhabitants and more than 75,000 children.

The primary outcome of this study was to quantify the incidence of CAP during the prepandemic period, the pandemic period, and the post pandemic period. The incidence was defined as the number of episodes of CAP in individuals residing in the surveillance area, divided by the total population at risk during the study period. The ratio of the three rates (the incidence rate ratio) R1/R2/R3 with its 95% was considered significant. The secondary output was to estimate the incidence of CAP complicated by pleural effusion/empyema requiring chest drain insertion during these three periods.

We reviewed the electronic registry and medical records of all patients aged between 1 and 15 years discharged with a final diagnosis of pneumonia. We categorized the disease with ICD-9 or ICD-10 codes indicating "acute pneumonia" or "acute pneumonia from other specified organisms." We excluded patients with hospital-acquired pneumonia. CAP was defined clinically, according to the British Thoracic Society guidelines.[3]

Abbreviations: CAP, community-acquired pneumonia; COVID-19, coronavirus disease 2019; CRP, C-reactive protein.; HFNC, high flow nasal cannula; ICU, intensive care unit; PCT, procalcitonin; WBC, white blood count.

As this study used pre-existing, deidentified data, the Institutional Review Board considered this study exempt. According to Italian law, the Authorization to Process Personal Data for Scientific Research Purposes (Authorization No. 9/2014) declared that retrospective archive studies that use ID codes, preventing the data from being traced back directly to the data subject, do not need ethics approval.[4]

Categorical variables were reported as counts and percentages, and continuous variables were referred as mean and standard deviation or median and interquartile range, based on the results of the Shapiro-Wilk normality test previously performed. We evaluated the differences between groups using the Chi-square test (Fisher's exact test, when appropriate) for categorical variables and the oneway ANOVA or the non-parametric analogue (i.e., Kruskal–Wallis test) for continuous variables.

In case of significant between-group differences, the effect of the observation period on the outcomes of interest was estimated with univariate logistic regression and median regression for categorical and continuous non-normal variables, respectively.

We set the significance level at 0.05. and performed all the statistical analyses using Stata software (version 18).

Based on the period of the diagnosis of pneumonia, we assigned patients to three categories, namely the prepandemic group (ranging from September 1, 2018 to March 9, 2020), the pandemic group (ranging from March 9, 2020 to September 30, 2022), the postpandemic group (ranging from October 1, 2022 to September 30, 2023).

For each subject, we anonymized and then recorded demographical data, including age, gender, previous pneumococcal vaccination with PCV-13, ibuprofen usage before the admission, symptoms at the admission, laboratory data (white blood cells-WBC-count,

TABLE 1 Demographical, laboratory, microbiological, and clinical data.

Variables	Period			*p* Value
	Pre-Covid *N* = 128	Covid *N* = 34	Post-Covid *N* = 69	
Age (years), median (IQR)	4.9 (3.1-7.3)	3.5 (2.4-6.5)	4.9 (3.3-6.7)	0.317
Gender, *n* (%)				0.904
Male	66 (51.6)	19 (55.9)	36 (52.2)	
Female	62 (48.4)	15 (44.2)	33 (47.8)	
Viral (interstitial) pneumonia, *n* (%)	68 (53.1)	24 (70.6)	25 (36.2)	*<0.001*
Bacterial (lobar) pneumonia, *n* (%)	60 (46.9)	10 (29.4)	44 (63.8)	*0.004*
WBC, median (IQR)	11.4 (7.8-19.6)	12.7 (10.6-17.2)	15.2 (10.3-20.9)	*0.028*
Neutrophils, median (IQR)	7.7 (4.9-14.6)	11.3 (6.3-15.9)	12.6 (7.6-16.4)	0.052
Neutrophils (%), median (IQR)	72.5 (61.1-79.8)	72.7 (59.9-82.9)	78.0 (68.3-85.1)	0.084
CRP, median (IQR), mg/dL	5.1 (2.2-12.6)	3.8 (1.7-11.0)	8.0 (4.3-17.9)	*0.009*
PCT, median (IQR), ng/mL	0.3 (0.1-3.5)	1.7 (0.4-5.5)	2.2 (0.3-10.6)	*0.005*
Pleural effusion, *n* (%)	11 (8.6)	5 (14.7)	21 (30.4)	*<0.001*
Drainage placement, *n* (%)	5 (3.9)	1 (2.9)	7 (10.1)	0.172
Duration of drainage placement, days, *n* (%)				0.331
0 days	123 (96.1)	33 (97.1)	62 (89.9)	
1−7 days	3 (2.3)	0	3 (4.3)	
>7 days	2 (1.6)	1 (2.9)	4 (5.8)	
Positive blood colture, *n* (%)	1 (0.8)	0	3 (4.3)	0.185
Antibiotic therapy, duration in days, median (IQR)	11 (8-14)	7 (7-10)	8.5 (12.5)	*<0.001*
Ultrasound performed, median (IQR)	0 (0-1)	0 (0-1)	2 (1-3)	*<0.001*
Need for oxigen supplementation, *n* (%)	78 (60.9)	26 (76.5)	44 (63.8)	0.244
HFNC, *n* (%)	26 (20.3)	9 (26.5)	22 (31.9)	0.192
Admission to pICU, *n* (%)	3 (2.3)	2 (5.9)	7 (10.1)	*0.056**

Abbreviations: CRP, C-reactive protein; HNFC, High Flow Nasal Cannula; PCT, procalcitonin; pICU, pediatric intensive care unit; WBC, white blood cells count.

C-reactive protein-CRP-, procalcitonin-PCT-, microbiological data (blood culture and eventually pleural fluid culture) and data regarding the clinical management (hospital length of stay, antibiotic administered, need for oxygen/High Flow Nasal Cannula-HFNC-, supplementation and drainage placement along with pediatric intensive care unit-pICU-admission).

Children were categorised according to the onset of symptoms at home, to limit the possible effect of the pandemic on possibly delayed CAP evaluations, admissions, and diagnosis.

Two hundred seventy-nine children were initially included in the study. Forty-eight patients were excluded for incomplete data. Two hundred thirty-one patients were enrolled in the final analysis: one hundred twenty-eight in the prepandemic period, thirty-four in the pandemic period and sixty-nine in the post pandemic period. Results are displayed in Table 1, 2, and 3. Whereas the cumulative incidence of pneumonia significantly reduced during the pandemic with a subsequent increase after the pandemic (with a final incidence lower than in the prepandemic period), the cumulative incidence of pneumonia with pleural effusion doubled in the postpandemic group when compared to the prepandemic period. Postpandemic groups significantly displayed higher incidence of bacterial pneumonia, pleural effusion, higher values of CRP and PCT, longer antibiotic course and slightly significant admissions to pICU. File S1 shows the multivariate logistic regression for interstitial pneumonia, pneumonia with effusion and days with hospitalization. File S2 indicates the trend in the vaccinated group prevalence among children before,

TABLE 2 Univariate logistic and median duration.

	Univariate logistic regression			
Outcome	**Variables**	**OR**	**95% CI**	***p* Value**
Interstitial pneumonia	Period (reference: Pre-Covid)			
	Covid	2.96	[1.33; 6.58]	*0.008*
	Post-Covid	1.37	[0.76; 2.48]	0.289
Pleural effusion	Period (reference: Pre-Covid)			
	Covid	1.83	[0.59; 5.69]	0.294
	Post-Covid	4.65	[2.08; 10.39]	*<0.001*
	Univariate median regression			
	Variables	**Coeff.**	**95% CI**	***p* Value**
Antibiotic duration (days)	Period (reference: Pre-Covid)			
	Covid	1.04	[−6.04; −1.96]	*<0.001*
	Post-Covid	0.81	[−3.59; −0.41]	*0.014*
In-hospital length of stay, days	Period (reference: Pre-Covid)			
	Covid	0	[1.20; 1.93]	1.000
	Post-Covid	1.00	[0.07; 1.93]	*0.035*
Number of ultrasounds performed	Period (reference: Pre-Covid)			
	Covid	0	[−0.36; 0.36]	1.000
	Post-Covid	2.00	[1.72; 2.28]	*<0.001*
WBC	Period (reference: Pre-Covid)			
	Covid	1.12	[0.86; 3.08]	0.325
	Post-Covid	3.59	[0.52; 6.66]	*0.022*
CRP	Period (reference: Pre-Covid)			
	Covid	−1.08	[−4.52; 2.37]	0.538
	Post-Covid	2.97	[0.30; 5.64]	*0.029*
PCT	Period (reference: Pre-Covid)			
	Covid	1.13	[0.08; 1.58]	0.138
	Post-Covid	1.85	[0.86; 2.84]	*<0.001*

Abbreviations: CRP, C-reactive protein; PCT, procalcitonin; WBC, white blood cells count. *$p < 0.05$

TABLE 3 Incidence of pneumonia and pneumonia with pleural effusion over time in the three periods considered in the study.

	Pre-covid (2017–2018–2019–2020)	Covid period (2020–2021–2022)	Post-Covid (2022–2023)	*p* Value
Total number of pneumonia				
Population at risk (0–15 years) at the beginning of the period, *N*	76,654	76,515	75,109	
Cumulative incidence (per 10,000)	17.7	4.4	9.2	<0.001
Pneumonia with pleural effusion				
Population at risk (0–15 years) at the beginning of the period, *N*	76,654	76,515	75,120	
Cumulative incidence (per 10,000)	1.4	0.7	2.8	<0.001

during and after the pandemic era. File S3 reports the association between ibuprofen usage, pneumococcal vaccination before hospital admission, and CAP with pleural effusion and drainage placement.

This study revealed an increasing incidence of bacterial CAP and o CAP requiring chest drainage after the pandemic compared to both pandemic and prepandemic periods in a paediatric population. Univariate logistic regression and univariate median regression proved an increased trend of interstitial pneumonia during the pandemic compared to another period. In contrast, we observed a rise in the number of pleural effusions, antibiotic days of treatment, WBC count, CRP and PCT in the postpandemic period compared to other periods (Table 2).

Conversely, we did not notice significant differences between groups regarding demographical data. The overall incidence of CAP was similar in the postpandemic group but with a higher rate of bacterial CAP and an increased disease severity in the postpandemic group. This last evidence was supported by significantly higher WBC count, CRP and PCT values, a higher antibiotic duration, and augmented use of HNFC. As displayed in multivariate linear regression (File S1), this last finding is strictly linked to a subsequently more extended hospital stay and additional intensive care unit admissions, in contrast with the existing literature outside Europe.[2] These findings can only partially explain the decline in invasive pneumococcal disease during the pandemic because of the reduced microbes spreading,[5] with a subsequent breakthrough after the pandemic era.

The increase in the last period could be due to a reduced prevalence of pneumococcal vaccinated children, which shifted from 96% in the prepandemic period to 91% in the postpandemic period, with a more severe course of CAP. The vaccination rate was directly linked with a diminished incidence of invasive pneumococcal disease, even if a rebound in complicated forms was reported after some years, as a possible consequence of a change in serotype prevalence.[6] Another potential role could be represented by the growth of the viral and bacterial spreading and subsequent rise in ibuprofen usage, related to the increased number of days of fever associated with the ample rate of complicated pneumonia.[7]

Finally, we could hypothesize a change in paediatricians' attitudes after the COVID-19 pandemic.

In particular, the switch to the extensive use of remote patient-doctor interactions, common in the postpandemic period, could reflect a more severe course of CAP determined by a delayed assessment of patients.

This study's primary limits were the retrospective nature and the limited number of patients enrolled. Due to its retrospective nature, we could not rule out possible misclassifications of patients in clinical records, the absence of standardized clinical scores in the clinical records, and the patient's decision-making. Furthermore, some data regarding prehospital management (use of ibuprofen, duration of symptoms before diagnosis) were missing for some patients. Another limitation was the absence of pneumococcal serotype determination, which was not routinely performed in our hospital.

Finally, the different time intervals (respectively 2 and 1 year) chosen before and after the pandemic reduced the strength of this report.

However, given the substantial growth in complicated CAP, this choice was justified by the need to share a relevant epidemiological aspect to increase awareness in the paediatric community of the rising risk of facing complicated pneumonia.

Indeed, this was the first study investigating the rate of CAP requiring chest drain insertion before and after the COVID-19 pandemic.

In conclusion, our study showed a strikingly increased incidence of bacterial CAP complicated by pleural effusion/empyema after the pandemic in Italy in a setting with a relatively stable overall incidence of CAP.

AUTHOR CONTRIBUTIONS

Luca Barchi and Andrea Trombetta wrote the first draft of the manuscript. Egidio Barbi, Alessandro De Fanti and Lorenzo Iughetti revised the manuscript. Giulia Zamagni performed the statistical analysis.

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CONFLICT OF INTEREST STATEMENT

The author declare no conflict of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

ETHICS STATEMENT

We obtained written consent from the patient's parents for publication in all forms and media. This study used pre-existing, deidentified data; therefore, the Institutional Review Board considered this study exempt. According to Italian law, the Authorization to Process Personal Data for Scientific Research Purposes (Authorization No. 9/2014) declared that retrospective archive studies that use ID codes, preventing the data from being traced back directly to the data subject, do not need ethics approval.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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