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Point-of-care lung ultrasound to differentiate bacterial and viral lower respiratory tract infections in pediatric age: a multicenter prospective observational study

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Distinguishing between bacterial and viral etiologies in children with Lower respiratory tract infections (LRTIs) is challenging. This study investigates the association between lung Point-of-Care ultrasound (POCUS) characteristics and the etiologic diagnosis of LRTI. This multicenter, prospective, observational study included children admitted with suspected LRTI to three pediatric centers in Italy. Lung POCUS was performed within six hours of clinical diagnosis, alongside collection of clinical, laboratory, microbiological, and radiological data. Patients were stratified into groups based on presumed microbial etiology: bacterial pneumonia (confirmed or probable) and viral pneumonia (confirmed or probable). 162 children were admitted, 90 with viral pneumonia (74 confirmed, 16 probable), and 72 with bacterial pneumonia (15 confirmed, 57 probable). The lung POCUS score was higher in bacterial infections compared to viral ones (mean score of 32 vs. 27.5, $p < 0.001$). Receiver operating characteristic (ROC) curves showed that models incorporating POCUS (AUC = 0.88) or chest X-ray (CXR) findings (AUC = 0.89), along with a minimal amount of clinical and laboratory findings, were both accurate in establishing the pneumonia etiology. The study indicates that lung POCUS is a valuable tool that can support clinical and laboratory items in the diagnostic process of LRTI. These results also suggest that POCUS can be as effective as CXR in aiding diagnosis, providing solid evidence for a radiation-free alternative.

Lower respiratory tract infections (LRTIs) are a major public health concern with a specific burden and a great impact on pediatric morbidity and mortality[1,2]. They are among the most common causes of admission to pediatric emergency departments (PEDs) and pediatric wards worldwide[3]. According to the World Health Organization (WHO), pneumonia is the single largest infectious cause of death in children worldwide, killing 1.2 million children under the age of 5 each year. This accounts for 18% of all deaths in children under the age of 5[4].

In the majority of patients, complaints associated with pneumonia are nonspecific, including cough, fever, tachypnea, and difficulty breathing[5]. According to the British Thoracic Society guidelines, bacterial pneumonia should be considered in patients with persistent fever along with chest recessions and increased respiratory rate, in a previously healthy child[5]. However, these symptoms and signs may widely overlap among different etiologies, making it challenging to make an appropriate distinction, which is critical for antibiotic stewardship.

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Even if viruses are the most common cause of LRTI, the majority of diagnosed children still undergo empiric and even unnecessary antibiotics, giving a major contribution to a widespread antibiotic resistance[6].

LRTI is recommended to be a clinical diagnosis, but it should have solid support from the history of present illness, laboratory tests, and imaging modalities as well[7]. So far, laboratory findings and clinical items are not able to make a strict distinction between different etiologies[8,9]. Even in a study where biomarkers were significantly associated with bacterial infection, a reliable threshold was far from being established[10].

Traditionally, chest radiography (CXR) and computed tomography (CT) have been used to aid in diagnosis, but they have several drawbacks, including exposure to ionizing radiation and the need for specialized equipment and pediatric expertise[1].

Point-of-Care ultrasound (POCUS) offers pediatricians a suitable tool to address specific issues in clinical practice, narrow differential diagnoses, and improve the security of routine procedures[11,12], being increasingly used and particularly for lung pathologies, where it has been demonstrated to have good accuracy to recognize LRTI[13–17].

A few studies have suggested POCUS may be a useful tool in discerning between pediatric bacterial and viral LRTI[6,18] since they show different ultrasound patterns. Consolidations in viral pneumonia are mostly smaller, compared to atypical bacterial and to bacterial LRTI[19], whereas air bronchograms are more associated with bacteria and atypical pneumonia compared to viral ones[6].

Since similar ultrasound findings may overlap in different etiologies and due to the limited available body of evidence, especially in large-scale multicenter studies, a standardized and shared classifying system is far to be recognized. Therefore, the primary aim of the present study was to investigate if there is an association between lung POCUS characteristics and the etiological diagnosis of LRTI in the pediatric population.

Material and methods

Study design

This is a multicenter, prospective, observational study involving three Italian centers (Fondazione Policlinico Universitario A. Gemelli of Rome, Bambino Gesù Children's Hospital of Rome and Giovanni XXIII Children's Hospital, Bari).

We analyzed patients aged from 6 months to 17 years admitted between March 2023 and June 2024 who were hospitalized for a clinical diagnosis of LRTI according to the British Thoracic Society Guidelines[5].

For each patient included in the study, history, clinical parameters, microbiological data, and ultrasound data were collected. The study was approved by the Ethics Committee of Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome, Italy (ID 5474, Prot N 0003293/23), Bambino Gesù Children Hospital in Rome (ID 5474), and Policlinico di Bari (ID 7717)). Informed consent was obtained by all participants and their legal guardians. There is no identifying information or image in the article.

Inclusion criteria

We performed Lung Ultrasound (LUS) in all children evaluated with a clinical diagnosis of LRTI having at least two of the following signs and symptoms: fever (> 38 °C), cough, dyspnea, abnormal auscultatory findings, with or without chest or abdominal pain. Only children who underwent LUS within six hours of the first clinical assessment and for whom clinical information on the outcome was available were included.

Exclusion criteria

Patients with underlying diseases, including respiratory tract anomalies, immunodeficiency, cerebral palsy, neuromuscular diseases, congenital heart disease, and malignancy were excluded. Patients with other infection than LRTI or without parental consent were excluded as well. For this study, LRTI due to *M. pneumoniae* were excluded as they will undergo a separated analysis.

Lung POCUS

POCUS was performed by pediatricians using the ESAOTE MyLab ™ 40 ultrasound device, which complies with the Medical Device Directive (MDD) 93\42\EEC and subsequent amendments. In accordance with this Directive, Esaote has classified it as a Class IIa device. It was performed within 6 h of clinical diagnosis of LRTI, without knowledge of microbiological, laboratory and CXR (if performed) results. Linear probe (12–6 MHz) was used in preschool children, usually the procedure being done with parents holding children to make them quitter and never using sedatives. In older children, we used a curved probe (8–5 MHz).

Images and clips were stored and archived. All LUS was made by the same physician in each center to reduce inter-operator differences.

The scans were made by investigating the anterior, lateral and posterior regions of the thorax and placing the probe according to a methodical scheme first described by Soldati et al.[20]. According to them, seven areas (3 posterior, 2 lateral, and 2 anterior) in each hemithorax ought to be explored per patient for 10 sec. Scans need to be intercostal to cover the widest surface possible in a single scan[20]. This score was used because it has been extensively studied and used worldwide since the beginning of the pandemic and already readapted for used in children[21]. In addition, this score was adapted after a careful multidisciplinary meeting of our team members from four different institutions and part of the Italian Academy of Thoracic Ultrasound (ADET) which has played a pivotal role in the international diffusion of lung ultrasound. In addition, this score was not only based on a decades-lasting clinical experience of ADET in Lung Ultrasound, but also on basic-science studies from the same academy demonstrating how ultrasound findings correlate with both preclinical and anatomopathological findings[22–25].

They adopted a standard evaluation sequence using landmarks on the anatomical lines of the chest. Ultrasound scans can be identified with progressive numbering starting from the right posterior basal regions. For a patient able to maintain a sitting position, the following areas were identified:

1. Right basal on the paravertebral line above the curtain sign;
2. Right middle on the paravertebral line at the inferior angle of the shoulder blade;
3. Right upper on the paravertebral line at the spine of the shoulder blade;
4. Left basal on the paravertebral line above the curtain sign;
5. Left middle on the paravertebral line at the inferior angle of the shoulder blade;
6. Left upper on the paravertebral line at the spine of the shoulder blade
7. Right basal on the midaxillary line below the internipple line
8. Right upper on the midaxillary line above the internipple line
9. Left basal on the midaxillary line below the internipple line
10. Left upper on the midaxillary line above the internipple line
11. Right basal on the midclavicular line below the internipple line
12. Right upper on the midclavicular line above the internipple line
13. Left basal on the midclavicular line below the internipple line; and
14. Left upper on the midclavicular line above the internipple line.

The following ultrasound features were recorded:

- A comprehensive qualitative overview (A-Lines, short vertical artifacts, multiple B lines, white lung, subpleural consolidation, mixed consolidation and multiple B lines) as a summary interpretation of the LUS assessment
- Size of the main lesion in each analyzed zone, that we generally define as subpleural lung parenchymal lesion (consolidation and atelectasis)
- Presence of bronchograms, its characteristics (air, fluid), morphology (arboriform or linear), position (deep if > 2 cm far from the pleura or superficial if close to the pleura), dynamicity during breath (static or dynamic)
- Presence of vertical artifacts or B lines, characteristics (short or long, spared (when the pleaural line was clearly visible between each vertical artifact) or confluents (when several distinguishable vertical artifacts were close enough that the pleural line was not clearly recognized between the vertical lines)), position (unilateral or bilateral, perilesional or not);
- Presence and type of pleural effusion: small (less than 2 cm depth)[26] or moderate/large, simple (anechogenic and dependent to gravity) or complex (presence of septa, hyperechogenic spot, following the lung through the apex and not dependent to gravity, requiring drainage).

A number of key parameters are evaluated in the estimation of a lung ultrasound score, each of which contributes to the overall score on the basis of specific criteria, as illustrated below.

- Short vertical artifacts do not contribute to the score regardless of their presence or absence.
- If B lines are present, they are scored as follows:
  - Isolated B lines: 1 point
  - Confluent B lines: 2 points
- If a white lung pattern is observed, it is scored as follows:
  - White lung: 3 points
  - Its localization and distribution do not contribute to the score.
- If a consolidation is present, it is scored based on several sub-criteria:
  - Presence of consolidation: 4 points
  - Size of the consolidation:
    - Less than 1 cm depth: 0 points
    - 1–3 cm depth: 1 point
    - Greater than 3 cm depth: 2 points
  - The absolute number of consolidations does not contribute to the score
  - Locations of consolidations:
    - Bilateral: 1 point
    - Unilateral: 2 points
- Air bronchograms are scored based on their presence and characteristics:
  - Absent: 0 points
  - Present:
    - Static: 1 point

    - Dynamic: 1 point
    - Superficial (within 2 cm from the pleural line): 1 point
    - Deep (greater than 2 cm from the pleural line): 2 points

- Fluid bronchograms are scored as follows:
    - Absent: 0 points
    - Present: 1 point

- Effusions are scored as follows:
    - Effusion absent: 0 points
    - Effusion present:
        - Small: 0.5 points
        - Moderate/large: 1 point
    - Type of effusion:
        - Simple: 1 point
        - Complex: 2 points

By summing the points from each of these categories, a comprehensive lung ultrasound score can be calculated, providing a detailed assessment of lung condition.

Etiological stratifications of patients

Patients have been stratified into different groups according to the presumed microbial etiology: patients with bacterial pneumonia (divided in either confirmed or probable), patients with viral pneumonia (divided in either confirmed or probable). A panel of three expert in pediatric infectious diseases have assessed the final database, blinded to the clinical discharge charts, and classified the etiological diagnosis according to the following data.

Bacterial pneumonia was considered in patients with documented bacterial infection (either culture- or PCR-based methods) in clinically significant samples (bronchoalveolar lavage, pleural drainage, blood cultures) (in this case, bacterial pneumonia was defined as confirmed), or when a mix of the the following three criteria were obtained along with the clincal decision of the evaluating doctors to codify the case as of probable bacterial origin needing antibiotics: lobar pneumonia or significant effusion on chest X-ray or CT scan (when performed), and/or leucocytosis ($>15\times109$/L), and/or raised inflammatory markers (either C-reactive protein > 40 mg/l or procalcitonin > 0.5 µg/L, according to clinical decision and local availability), even when viruses were detected in the nasopharyngeal swab, (in this case, bacterial pneumonia was defined as probable).

Patients with detected viral infection on nasopharyngeal swab have been included into the viral pneumonia group only after the exclusion of bacterial superinfection, according to a comprehensive assessment of clinical, laboratory, radiology, and microbiological findings, according to a recently proposed classification[27], and the absence of the previously mentioned criteria for bacterial pneumonia (confirmed viral pneumonia). When no viruses were detected, but patients had absence of criteria for bacterial pneumonia, they were classified as probable viral pneumonia.

Statistical analysis

Descriptive data are shown as absolute numbers and percentages for categorical variables, and median and interquartile range (IQR) for continuous ones. Categorical variables' associations were studied with Chi-Squared tests while continuous variables' associations with Student's T test.

Logistic regression models have been applied to study the outcomes "confirmed viral pneumonia", "confirmed plus probable viral pneumonia" and "confirmed plus probable bacterial pneumonia".

A multivariable logistic regression model was constructed starting from clinical baseline and progressively adding laboratory data (both hematologic and microbiologic) and radiologic findings (either conventional or LUS). POCUS findings eligible for inclusion in the models were obtained from a preliminary analysis performed on the enrolled patients. In all models, CRP levels were converted into a dummy variable coded 1 if CRP was less than 40 mg/l and 0 if CRP was greater than 40 mg/l. We evaluated how the addition of these new types of data affected the performance of the model. The models showed an increasing trend in AUC as new items are added to the clinical baseline. The equivalence of the ROC curve was tested for the two final specified models, the one with POCUS and the one with CXR use, with the De Long's method. Data were analyzed with Stata 18.0 B.E. (StataCorp LLC, USA). Two-tailed tests were used. P values < 0.05 were considered significant.

Results

Study population

A total of 162 children with suspected LRTI (79 male and 83 female) were enrolled in the study. The complete study enrollment flow chart is shown in Fig. 1. Results were stratified between the probable/confirmed viral cohort and the probable/confirmed bacterial cohort whereas results depicting only confirmed viral and bacterial pneumonia are shown in supplementary materials.

The most common etiology of LRTI was viral (55.55%), with a slight prevalence in females (57.7% of cases), while males were more numerous in bacterial forms (56.9%). The mean age in months was significantly lower in viral infections compared to bacterial ones (20.5 vs. 64; $p < 0.001$). The main epidemiologic and clinical features

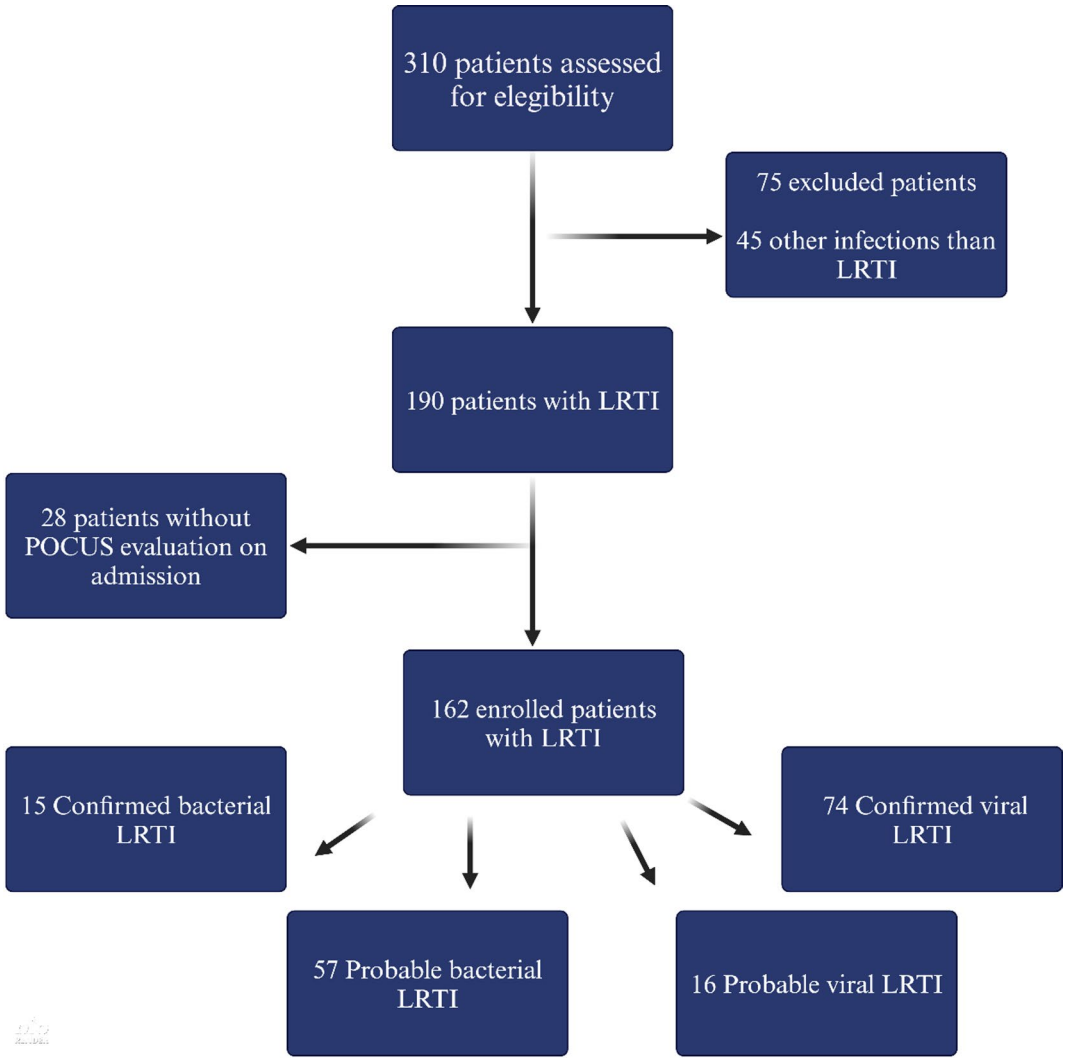

Fig. 1. Study enrolment flow chart.

of the children involved are described in detail in Table 1. Among the various clinical items analyzed, fever was slightly more associated to bacterial forms whereas rhinitis resulted to be more represented in the viral cohort in a statistically significant way ($p < 0.001$). The mean duration of fever was one day longer in the bacterial forms.

In terms of clinical auscultatory findings, crackles were most often associated with viral infections when diffuse and with bacterial infections when localized, while wheezing was more often associated with viral forms. Focal reduced ventilation was also mostly seen in bacterial forms. The main laboratory and radiological findings are presented in Table 2 and Table 3, respectively. In the univariate analysis, white blood cell count, neutrophils count and C-reactive protein level were more elevated in bacterial LRTI ($p < 0.05$), although with overlap of values between the two groups. More than half in percentage (87.5%) of patients with a bacterial form were prescribed an oral antibiotic therapy compared to children with a viral form (44.4%). Intravenous antimicrobials were used in 50% of bacterial cases and 15.5% of viral cases.

When performed, chest x-ray showed more frequently an interstitial pattern in viral forms and consolidations in bacterial ones ($p < 0.001$). LUS score resulted significantly higher in bacterial infections compared to viral ones (27.5 vs 32, $p < 0.001$).

Discrimination of bacterial and viral pneumonia

In the confirmed viral model, baseline clinical items were significant predictors, reaching AUC = 0.75. The addition of laboratory parameters, i.e. C-reactive protein levels and nasopharyngeal swab result, significantly improved the performance of the model with AUC = 0.91. With the augmentation of CXR findings the model reached an AUC = 0.89. For POCUS artifacts, isolated B-lines and posterior confluent B-lines were identified as the best predictors with AUC = 0.92. The AUC for both radiologic techniques overlapped to a large extent and no significant difference was found between the two ROC curves. The models for each combination of clinical, laboratory and imaging findings to discriminate confirmed viral LRTI, confirmed and probable viral LRTI, confirmed and probable bacterial LRTI are fully illustrated in supplementary materials.

	Viral confirmed /probable	Bacterial confirmed/probable	
	N = 90	N = 72	*p* value
Mean age (months)	20.5 (6.0–58.0)	64.0 (32.5–108.5)	< 0.001
Female	52 (57.7%)	31 (43.1%)	0.053
Male	38 (43.3)	41 (56.9)	
Asthma	7 (7.8%)	5 (6.9%)	0.84
Allergy	2 (2.2%)	3 (4.2%)	0.47
Other chronic respiratory	4 (4.4%)	0 (0.0%)	0.07
Celiac disease	0 (0.0%)	1 (1.4%)	0.26
Fever	60 (66.7%)	61 (85.0%)	0.005
T max (IQR)	39.0 (38.0–39.5)	39.0 (38.6–39.4)	0.22
Days of fever	3.0 (2.0–4.0)	4.0 (3.0–6.0)	< 0.001
Cough	88 (97.8%)	66 (91.7%)	0.25
Rhinitis	65 (72.2%)	17 (23.6%)	< 0.001
Conjunctivitis	13 (14.4%)	3 (4.1%)	0.034
Dyspnea	45 (50.0%)	19 (26.3%)	0.003
Vomiting	8 (8.9%)	3 (4.2%)	0.25
Diarrhea	2 (2.2%)	0 (0.0%)	0.22
Abdominal pain	6 (6.7%)	5 (7.0%)	0.9
Wheezing	26 (29.0%)	8 (11.4%)	0.007
Crackles and rales on auscultation			
No	8 (8.9%)	17 (23.6%)	< 0.001
Localized	35 (38.9%)	45 (62.5%)	
Diffuse	47 (52.2%)	10 (14.0%)	
Reduced ventilation			
No	73 (81.1%)	28 (38.8%)	< 0.001
Yes, localized	12 (13.3%)	42 (58.3%)	
Yes, bilateral	5 (5.6%)	2 (2.7%)	
Wbc count	11.4 (9.4–16.8)	16.0 (9.9–21.7)	0.007
Neutrophils count	6.9 (4.0–11.0)	11.9 (7.2–16.7)	< 0.001
Lymphocytes count	3.5 (2.1–5.0)	2.0 (1.5–3.2)	< 0.001
C reactive protein value	18.0 (3.6–46.5)	90.0 (45.2–179.0)	< 0.001
Procalcitonin value	0.1 (0.0–0.3)	0.7 (0.2–3.8)	< 0.001
Received intravenous antibiotic therapy	14 (15.6%)	36 (50.0%)	< 0.001
Received second intravenous antibiotic therapy	1 (1.1%)	9 (12.5%)	0.003
Received oral antibiotic	40 (44.4%)	63 (87.5%)	< 0.001
Duration of oral antibiotic (days)	3.5 (1.0–7.0)	7.0 (2.0–10.0)	0.005
Received second oral antibiotic	3 (3.3%)	13 (18.1%)	0.002

Table 1. Epidemiological and clinical features stratified according to the causative agent**.**

We used the same model applied to the diagnosis of "confirmed and probable viral pneumonia". Baseline clinical items were significant predictors, reaching AUC = 0.83 in combination with C-reactive protein level. Empowerment with an interstitial pattern on CXR and another laboratory parameter, i.e. nasopharyngeal swab result, considerably boosted the performance of the model with AUC = 0.89. The model generated through POCUS artifacts showed a great performance as well (AUC = 0.88).

Figure 2 shows the comparison of ROC curves for the models including respectively lung ultrasound and chest x-ray, in addition to clinical, laboratory and microbiological data, for the detection of probable and confirmed viral LRTI. Their AUCs widely overlapped and no significant difference was found between the two ROC curves ($p = 0.31$).

In the model applied to confirmed and probable bacterial pneumonia, clinical parameters (namely presence of localized crackles and rales and localized reduced ventilation) showed a good performance with AUC = 0.78. When C-reactive protein level was added, the AUC was 0.84. The addition of a consolidation pattern on CXR lead to a significant increase in AUC up to 0.93. When considering POCUS artifacts, we used the presence of large consolidations, the presence of effusion, and fluid bronchograms as predictors, achieving an AUC of 0.91, 0.92, and 0.92, respectively. Even in this case, comparisons of the ROC curves for the models including POCUS and CXR respectively, were performed and showed no significant difference.

Due to the small amount of confirmed bacterial forms, an independent reliable model was not feasible.

		Viral confirmed/probable	Bacterial confirmed/probable	*p* value
		N = 90	N = 72	
Nasopharyngeal swab culture	Negative	31 (34.4%)	26 (36.1%)	0.13
	Adenovirus	40 (44.4%)	23 (31.9%)	
	Rhinovirus	6 (6.7%)	1 (1.4%)	
	RSV	6 (6.7%)	0 (0.0%)	
	Influenza A	1 (1.1%)	0 (0.0%)	
	Metapneumovirus	2 (2.2%)	1 (1.4%)	
	Influenza B	2 (2.2%)	0 (0.0%)	
	Haemophilus Influenzae	1 (1.1%)	3 (4.2%)	
	Veillonella	0 (0.0%)	1 (1.4%)	
	Not performed	1 (1.1%)	17 (23.6%)	
PCR nasopharyngeal swab	Adenovirus	77 (85.6%)	44 (61.1%)	< 0.001
	RSV	24 (26.7%)	3 (4.1%)	< 0.001
	Rhinovirus	24 (26.7%)	11 (15.3%)	0.08
	Metapneumovirus	13(14.4%)	1 (1.4%)	0.003
	Influenza A	4 (4.4%)	1 (1.4%)	0.264
	Influenza B	4 (4.4%)	0 (0%)	0.07
	Parainfluenza	7 (7.8%)	2 (2.8%)	0.167
	Haemophilus influenzae	2 (2.2%)	0 (0%)	0.2
	Not performed	5 (5.5%)	6 (8.3%)	
	Negative	7 (7.7%)	4 (5.6%)	
Blood culture	Negative	10 (11.1%)	13 (18.1%)	0.19
	Haemophilus Influenzae	0 (0.0%)	0 (0.0%)	
	Steptococcus Hominis	0 (0.0%)	1 (1.4%)	
	Not performed	80 (88.9%)	58 (80.6%)	
Broncho-Alveolar Lavage (BAL) culture	Negative	0 (0.00%)	1 (1.4%)	0.72
	Streptococcus Pneumoniae	0 (0.00%)	2 (2.8%)	
	Streptococcus Pyogenes	0 (0.00%)	1 (1.4%)	
	Moraxella Catarralis	0 (0.00%)	1 (1.4%)	
	Haemophilus Influenzae	0 (0.00%)	1 (1.4%)	
	Not performed	90 (100.00%)	66 (98.25%)	
Pneumococcal antigen in urine	Negative	3 (3.3%)	9 (12.5%)	< 0.001
	Positive	0 (0.0%)	5 (6.9%)	
	Not performed	87 (96.7%)	58 (80.6%)	
Pleural fluid culture	Negative	0 (0.0%)	2 (2.8%)	0.076
	Not performed	90 (100.0%)	70 (97.2%)	
Pleural fluid PCR	Negative	0 (0.0%)	1 (1.4%)	0.33
	Not performed	90 (100.0%)	71 (98.6%)	

Table 2. Laboratory features stratified according to the causative agent.

Discussion

This is one of the largest prospective studies that explored the potential of lung POCUS in discriminating viral and bacterial LRTIs. Given the alarmingly high proportion of antibiotic prescriptions in pediatric respiratory infections raises concerns about antibiotic overuse[28], antimicrobial stewardship interventions and targeted therapies are needed to tackle the rising threat of antibiotic resistance[28]. With good coverage of pneumococcal conjugate vaccine and *Haemophilus influenzae* B vaccine, an increasing proportion of childhood pneumonia cases are caused by viral infections[29]. Thereby an etiological discrimination is essential in this setting to ensure a prompt treatment only when needed. Still, most children with LRTI receive antibiotics, both in the outpatient and inpatient settings[28].

In the last decade lung ultrasound has been widely applied as a Point-of-Care tool able to assess lung superficial pathologies[11]. A bunch of metanalysis confirmed its diagnostic role in detecting pneumonia in children[17,30,31]. POCUS is a promptly available, quite inexpensive and radiation-free technology, making it an attractive support for the detection and follow-up of pediatric pneumonia. On the other hand, fewer studies have focused on the discriminative power of LRTI etiology based on POCUS scoring compared to clinical items or chest x-ray. According to our findings, POCUS lung patterns vary consistently depending on the underlying etiology, and was at least as similarly accurate as chest X-ray. Specifically, the higher median lung ultrasound score observed in bacterial infections, along with specific ultrasound findings such as major consolidations and fluid bronchogram pointed out how bacterial forms show a more severe lung involvement and specific

		Viral confirmed/probable	Bacterial confirmed/probable	
		N = 90	N = 72	*p* value
Chest x ray		76 (84.4%)	67 (93.1%)	< 0.001
Interstitial pattern (CXR)		56 (62.2%)	17 (23.6%)	< 0.001
Consolidation (CXR)		48 (53.3%)	66 (91.6%)	< 0.001
Consolidation side (CXR)	Unilateral	30 (33.3%)	55 (76.4%)	< 0.001
	Bilateral	18 (20.0%)	10 (13.9%)	
Air bronchogram (CXR)		9 (10.0%)	25 (34.72%)	0.045
Pleural effusion (CXR)	Absent	68 (75.6%)	27 (37.5%)	< 0.001
	Present	8 (8.9%)	40 (55.6%)	
	Not performed	14 (15.6%)	5 (6.9%)	
CT scan	Not done	88 (97.8%)	62 (86.1%)	0.044
	Done	2 (2.2%)	10 (13.9%)	
Interstitial pattern (CT scan)	Absent	2 (2.2%)	6 (8.3%)	0.027
	Present	0 (0.0%)	4 (5.6%)	
	Not performed	88 (97.8%)	62 (86.1%)	
Consolidation (CT scan)	Unilateral	1 (1.1%)	9 (12.5%)	0.017
	Bilateral	1 (1.1%)	1 (1.4%)	
	Not performed	88 (97.8%)	62 (86.1%)	
Air broncogram (CT scan)	Absent	1 (1.1%)	4 (5.6%)	0.07
	Present	1 (1.1%)	6 (8.3%)	
	Not performed	88 (97.8%)	62 (86.1%)	
Pleural effusion (CT scan)	Absent	0 (0.0%)	1 (1.4%)	0.072
	Present	2 (2.2%)	9 (12.5%)	
	Not performed	88 (97.8%)	62 (86.1%)	
Pleural effusion (CT scan)	Fluid density	2 (2.2%)	4 (5.6%)	0.023
	Sovrafluid density	0 (0.0%)	2 (2.8%)	
	Characteristics not available	0 (0.0%)	3 (4.2%)	
	Not performed	88 (97.8%)	63 (87.5%)	
Total lus score		27.5 (18.0–41.0)	32 (20.0–50.0)	< 0.001

Table 3. Radiological features stratified according to the causative agent.

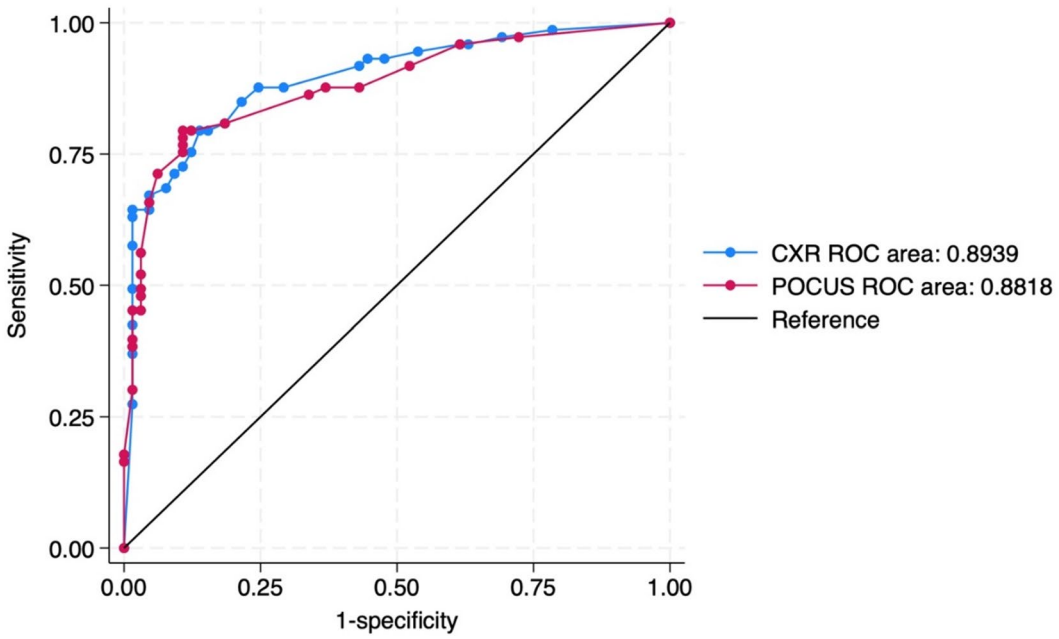

Fig. 2. ROC curves of models including chest X-ray or POCUS in addition to other clinical findings.

sonographic structures compared to viral infections. These findings greatly corroborate the even limited actual body of evidence of previous studies in the literature[1,6,13]. Musolino et al. reported that early sonography features on diagnosis and after 48 h of treatments were able to predict the development of complicated LRTI, more than clinical data and laboratory results[13]. In addition, Buonsenso et al. provided an analysis of ultrasound patterns that were highly consistent with LRTI etiology in pediatric patients, even though clinical and laboratory data did not allow for a clear etiologic distinction[6]. Similarly, in their analysis of 147 children with LRTI Berce et al. detected significantly smaller consolidations in viral CAP, with a median diameter of 15 mm, compared to 20 mm in atypical bacterial CAP ($p=0.05$) and 30 mm in bacterial CAP ($p<0.001$)[19]. The peculiarities of viral infections in terms of sonographic features have also been fully described by other studies[32–34].

Our results confirm that epidemiologic, clinical and laboratory features are useful in establishing the etiology of LRTI, but poorly specific when taken alone. As a matter of fact, clinical signs that are more specific for bacterial LRTI (decreased ventilation, local crackles) are not consistently present (58 and 62%, respectively). Therefore, they are missing in a noteworthy amount of our cases, making them insufficiently reliable items.

Our data showed that laboratory findings (white blood cell count, neutrophils count, lymphocytes count, and C-reactive protein level) are reliable in discriminating the etiologic diagnosis of LRTI, since a high value in WBC, neutrophils count, and C-reactive protein is highly consistent with a bacterial form, whereas a high lymphocyte count stands for a viral one. These data are supported by a structured body of evidence in the literature. In 2017 the PERCH study stated that CRP ≥ 40 mg/l was positively related to confirmed bacterial pneumonia (particularly S. pneumoniae and H. influenzae)[35], and negatively associated with RSV.

As mentioned above, community acquired pneumonia is a clinical diagnosis without the need for imaging or laboratory tests[5]. Therefore, unlike clinical features, which are an essential step, laboratory items are useful only when a diagnostic suspicion of LRTI is already established and could allow progress towards a defined etiology.

According to our data, lung POCUS in the hands of an experienced physician is a noteworthy tool, able to add useful information regarding the etiological diagnosis. Moreover, we have shown through a stepwise approach of models that the utility of POCUS and chest x-ray is increasingly enhanced when used in combination with clinical and laboratory data.

Furthermore, in addition to what has been previously reported in the literature, our study demonstrated that the performances of CXR and POCUS models for the detection of probable and confirmed viral pneumonia are highly overlapping (Fig. 2). The same findings are shown in the detection of confirmed and probable bacterial LRTI and for solely confirmed viral LRTI in supplementary materials.

In light of these findings and considering the numerous pros of ultrasound (radioprotective, easily transportable, feasible at the bedside, easily archived and reproducible, cost-saving, performable by non-radiologist providers), POCUS should replace CXR as a supportive diagnostic tool for LRTI. This is consistent with the conclusions of two recent meta-analyses, which showed that the diagnostic performance of POCUS and CXR in detecting pneumonia in children was similar[2,3]. Besides, Harel-Sterling et al. in a retrospective cohort study showed that lung POCUS performed by emergency physicians was associated with reduced length-of-stay and financial cost in comparison to CXR[36]. Although the routine use of CXR is discouraged by all guidelines[37,38], it is still widely used in the real world, as it was in our real-world study, where radiographic evidence of pneumonia was not mandatory for study inclusion.

Even though widely explored in the literature, barriers to capillary diffusion of POCUS among pediatricians still exist: lack of training, supervision, quality assurance processes (archiving and image review), handheld devices, and time to perform POCUS during shifts[39]. In terms of training, in contrast to other specialties, a small number of residency programs have a specific POCUS rotation (340. A POCUS core curriculum is well established in other specialties, such as emergency medicine, where it is a core component of the Accreditation Council for Graduate Medical Education program requirements for residency training[41]. Consequently, much disparity persists in pediatrics in the acquisition of quantitative and qualitative skills.

In terms of prescribed antibiotic therapy, we reported a high level of antibiotic use for bacterial forms, but the data for viral LRTIs are also notable. In a future prospective interventional study, researchers should test if a model based on our findings is able to safely reduce antibiotic prescriptions (or its duration) in children with clinical, laboratory and POCUS findings suggestive of viral infections, as previously hypothesized.

Our study has limitations to address. Firstly, the diagnosis of LRTI was made on a clinical basis, but the gold standard for detection (CT scan) was rarely used. CT scan is not widely applicable due to ethical issues related to radiation exposure, especially in pediatric patients with a long-life expectancy. CT scans are generally reserved for cases with worse clinical evolution, complicated pneumonia with pleural effusions, necrotizing pneumonia or lung abscesses. In addition, microbiologic stratification of patients may not be 100% accurate, as this stratification is at times based on nasopharyngeal swabs analyzed by PCR or culture, because bronchoalveolar lavage is an invasive procedure that is difficult to obtain in nonventilated patients. This could be a bias because the microbiological nature of the upper airways does not necessarily reflect the status of the lower airways. However, this is an intrinsic limitation of any microbiological study of LRTIs, and we have used the most comprehensive recently proposed classification for the purpose of such a stratification[27]. In this regard, a typical example of how may be difficult to distinguish viral and bacterial infections, also using upper respiratory tract swabs, is the case of adenovirus, which was isolated in a significant proportion of patients with confirmed/probable bacterial pneumonia (36.1% on culture, 61% on PCR). This can reflect a posssible confounding factor (viral pneumonia with subsequent bacterial superinfection, or coinfections), also in light of recent studies showing that adenoviral infections are associated with strong inflammatory responses in children[40–42]. We also acknowledge the existence of other scores, and we have motivated the reasons for our choice. Although would be interesting to see if similar findings are obtained with similar scores, we think that this would probably be the case as different scores provide similar information by using slighlty different codes or languages. Last, our study included a low number of confirmed bacterial LRTI, which made it difficult to build a reliable model

exclusive for confirmed bacterial infections based solely on these data. This is due to the low number of children undergoing invasive procedures for the identification of bacteria in sterile specimen.

In conclusions, our study shows that POCUS, in addition to a minimum set of clinical and laboratory findings, is accurate in discriminating viral and bacterial LRTI. Since the discriminatory power of this imaging modality is comparable to CXR and due to its non-invasive nature, POCUS should replace CXR as the main supportive diagnostic tool for LRTI. Future studies should be designed aiming to validate how our model can safely spare or reduce antibiotic prescriptions in children with LRTI having POCUS findings suggestive of a viral infection.

Data availability

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

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Author contributions

DB conceptualized the study. AC was responsible for statistical analyses. CDR, RM, LDS, LT, AO, MF, MS, AV, ACM contributed with data collection and patient management. DB, AC, LDS, MF contributed to drafting the initial version of the manuscript. All authors have participated in the preparation of the manuscript, all authors have read and approved the final manuscript.

AI disclosure statement

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Declarations

Competing interests

The authors declare no competing interests.

Ethics approval and consent to participate

The study was approved by the Ethics Committee of Fondazione Policlinic Universitario A. Gemelli IRCCS, Rome, Italy (ID 5474, Prot N 0003293/23) and conducted according to the Helsinki Declaration of Human Rights.

Consent for publication

Consent for publication was obtained by all participants and/or their legal guardians.

Informed consent

Was obtained by all participants and/or their legal guardians. There is no identifying information or image in the article.

Additional information

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