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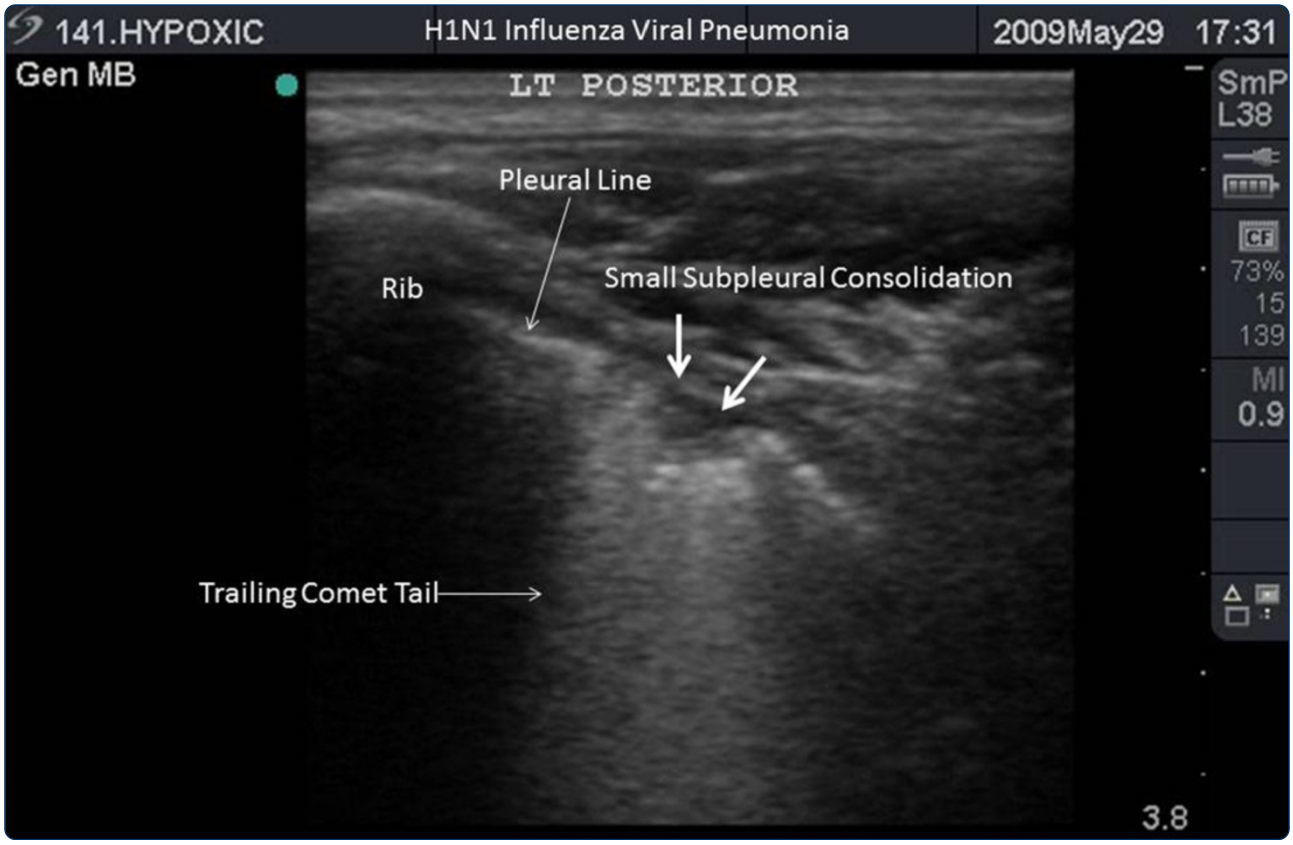

Prospective application of clinician-performed lung ultrasonography during the 2009 H1N1 influenza A pandemic: distinguishing viral from bacterial pneumonia

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ORIGINAL ARTICLE Open Access

Prospective application of clinician-performed lung ultrasonography during the 2009 H1N1 influenza A pandemic: distinguishing viral from bacterial pneumonia

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Abstract

Background: Emergency department visits quadrupled with the initial onset and surge during the 2009 H1N1 influenza pandemic in New York City from April to June 2009. This time period was unique in that >90% of the circulating virus was surveyed to be the novel 2009 H1N1 influenza A according to the New York City Department of Health. We describe our experience using lung ultrasound in a case series of patients with respiratory symptoms requiring chest X-ray during the initial onset and surge of the 2009 H1N1 influenza pandemic.

Methods: We describe a case series of patients from a prospective observational cohort study of lung ultrasound, enrolling patients requiring chest X-ray for suspected pneumonia that coincided with the onset and surge of the 2009 H1N1 influenza pandemic.

Results: Twenty pandemic 2009 H1N1 influenza patients requiring chest X-ray were enrolled during this time period. Median age was 6.7 years. Lung ultrasound via modified Bedside Lung Ultrasound in Emergency protocol assisted in the identification of viral pneumonia (n = 15; 75%), viral pneumonia with superimposed bacterial pneumonia (n = 7; 35%), isolated bacterial pneumonia only (n = 1; 5%), and no findings of viral or bacterial pneumonia (n = 4; 20%) in this cohort of patients. Based on 54 observations, interobserver agreement for distinguishing viral from bacterial pneumonia using lung ultrasound was κ = 0.82 (0.63 to 0.99).

Conclusions: Lung ultrasound may be used to distinguish viral from bacterial pneumonia. Lung ultrasound may be useful during epidemics or pandemics of acute respiratory illnesses for rapid point-of-care triage and management of patients.

Keywords: Ultrasound, H1N1 virus, Pneumonia, Emergency medicine, Point-of-care, Pandemic, Pediatric

Background

Emergency department visits quadrupled with the initial onset and surge during the 2009 H1N1 influenza pandemic in New York City (NYC) from April to June 2009 (Figures 1 and 2) [1,2]. This time period was unique in that >90% of the circulating virus was surveyed to be the novel 2009 H1N1 influenza A according to the New York City Department of Health. Five-hundred sixty-seven patients requiring hospitalization were confirmed with the 2009 H1N1 influenza A in NYC [1]. In NYC, there were 16 deaths, 46% of admitted patients were <18 years old and 20% were <5 years old [2]. Eighty percent of confirmed cases had a known underlying risk condition, most commonly asthma (40% of confirmed cases) [1].

This fourfold increase in patient volume presented logistical challenges for emergency departments [1]. In response to mass casualty incident-type conditions and overcrowding, emergency departments in New York City added staffing and created alternate sites of care to

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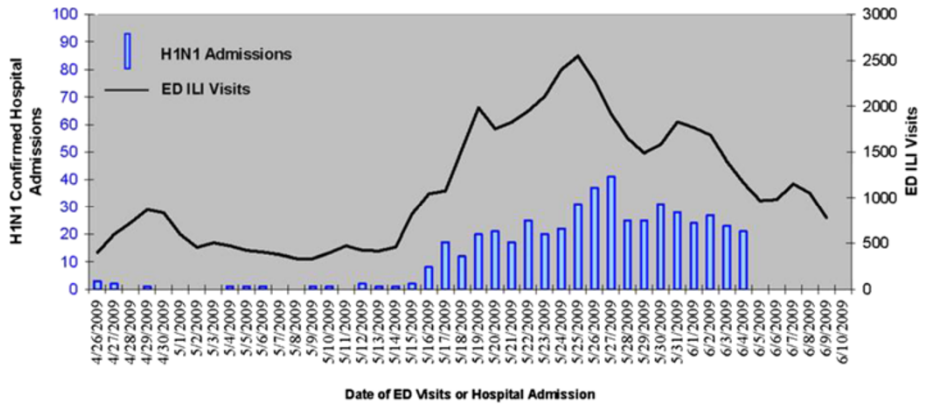

Figure 1 Laboratory-confirmed H1N1 hospital admissions and emergency department visits for influenza-like illnesses in NYC. 26 April to 10 June 2009. ED visits quadrupled at peak surge. Adapted from [1].

accommodate the increased patient volume. Increased demand for chest radiography for those patients with more severe disease led to increased delays and length of stay for those patients with suspected, but non-severe pneumonia.

Clinicians are challenged by the diagnostic dilemma that influenza cannot reliably be distinguished from other acute respiratory illnesses on the basis of clinical presentation alone [3]. Rapid viral antigen testing for diagnosis, which under ideal situations can yield results within 30 min, is not practical nor cost-effective in pandemic conditions [3]. Point-of-care ultrasound has been demonstrated to identify, in real-time, various pathologies of the lung, such as pneumonia, viral pneumonia, and acute respiratory distress syndrome (ARDS) [4-10] An algorithm for differentiating between various respiratory pathologies has been described (Figure 3) [4], and evidence-based recommendations regarding the use of point-of-care lung ultrasound have recently been published [11]. The use of lung ultrasound during the 2009 H1N1 influenza pandemic in adults has also been recently described [12]. We describe a prospective case series of children in whom clinician-performed lung ultrasonography was used to differentiate between different respiratory pathologies and assessed interobserver agreement of these ultrasound findings during the initial onset and surge of the 2009 H1N1 pandemic (April to June 2009).

Methods

Study design and setting

We describe a subcohort of patients who required chest X-ray for suspected pneumonia and were enrolled into a prospective study of lung ultrasound for diagnosing pneumonia that coincided with the onset and surge of the 2009 H1N1 influenza pandemic from April to June 2009 [1,2,13]. We also describe the application of a modified Bedside Lung Ultrasound in Emergency (BLUE) protocol [4] with posterior thorax scanning (Figure 3) during the

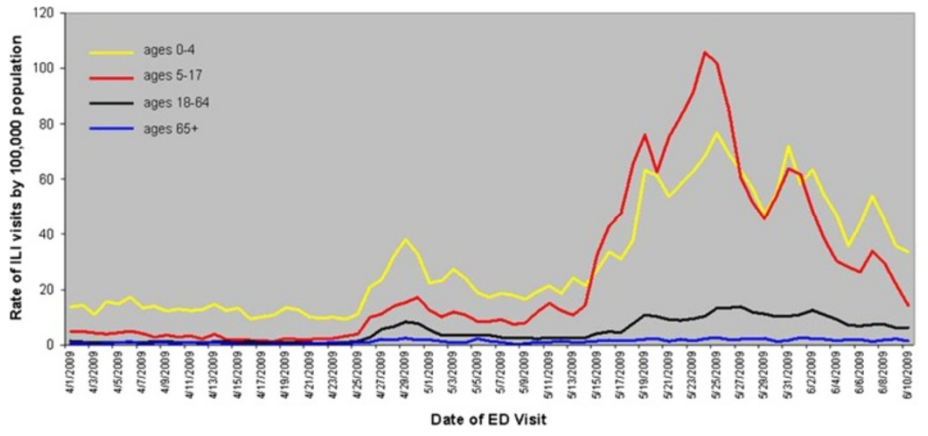

Figure 2 Rate of influenza-like illness syndrome visits to NYC emergency departments by age group. Based on chief complaint. 01 April to 01 June 2009. Adapted from [1].

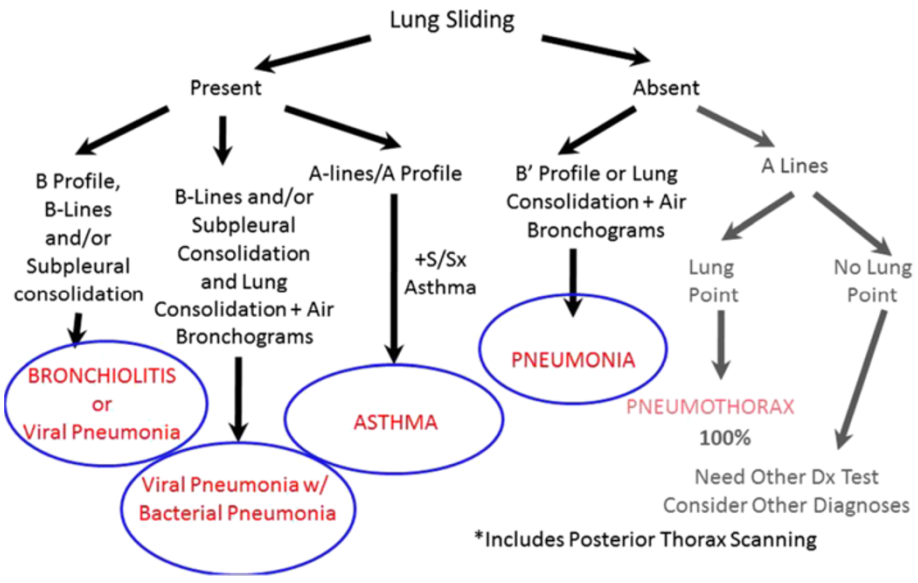

Figure 3 Bedside Lung Ultrasound in Emergency protocol - modified for ED. Includes posterior thorax scanning.

onset and surge of pandemic patients in an urban emergency department.

This study was approved by our institutional review board. The study population consisted of a convenience sample of patients who met predetermined inclusion criteria and in whom informed consent had been obtained and documented from the patient or guardian for enrollment into the study.

Selection of participants

Inclusion criteria consisted of patients < 21 years of age presenting to the emergency department with clinical suspicion of pneumonia requiring chest X-ray for evaluationWe excluded those patients who presented the following: (1) arrival in the emergency department with a chest X-ray, (2) a confirmed diagnosis of pneumonia by diagnostic imaging, or (3) hemodynamic instability.

Methods of measurement and outcome measures

Enrolled patients had a screening history and physical examination performed at the time of triage to determine eligibility into the study. After informed consent was obtained, enrolled patients had clinical exam findings documented on a standardized form and underwent point-of-care lung ultrasound examination. An ultrasound machine with a linear array transducer at 7.5 to 10 MHz (Sonosite Micromaxx, Bothell, WA, USA) was used to image the lungs in perpendicular planes (transverse, parasagittal, and coronal) in the midclavicular line anteriorly and posteriorly on the chest and the midaxillary line from the axillae to diaphragm (Figure 4).

Using a six-zone lung ultrasound scanning protocol similar to that described by Copetti et al. [7], we defined and classified patients as positive or negative for viral pneumonia based on the presence of small subpleural consolidations usually <0.5 cm (Figure 5 and Additional file 1) and/or individual B-lines or confluent B-lines (echogenic vertical lines arising from the pleural line to the bottom of the ultrasound screen; Figure 6 and Additional file 2) [7]. These ultrasound findings are similar to those described in interstitial syndrome which is defined as three or more B-lines in a given lung region [10,14,15]. A-lines (horizontal, reverberation artifacts of the pleural line; Figure 7 left) which indicate areas of the normal lung were also noted when present [10,14]. Patients were classified as positive or negative for bacterial pneumonia based on the presence or absence of lung consolidation with air bronchograms [6,7,16] seen on ultrasound (Figures 7 right, 8, and Additional file 3). A clinical course with follow-up after 2 weeks (via electronic medical record and telephone interview) was used to determine disposition and outcomes of enrolled patients. Clinicians performing and interpreting ultrasound were blinded to chest X-ray results, and when performed per hospital protocol for possible admission, viral antigen testing results. Bacterial pneumonia on chest X-ray (posterior-anterior and lateral views) was classified based on the attending pediatric radiologist reading for 'consolidation, 'infiltrate, or 'pneumonia. For analysis purposes only, viral pneumonia on chest X-ray was defined as 'peri-bronchial cuffing, 'peri-bronchial thickening, or 'increased interstitial markings identified by the pediatric radiologist. Pediatric radiologists were blinded to the lung ultrasound results.

Ultrasound images and videos were reviewed between two blinded investigator sonologists (enrolling sonologist

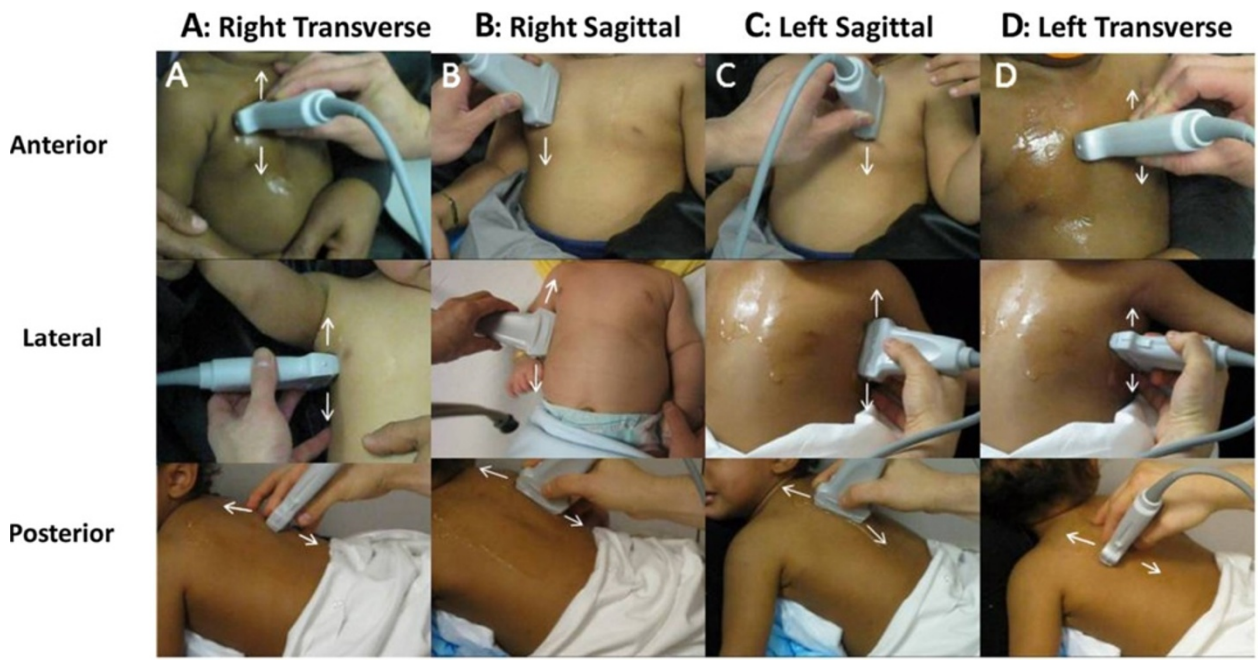

Figure 4 Six-zone lung scanning protocol. Top Row: Anterior Midclavicular Line; Middle Row: Lateral Midaxillary Line; Bottom Row: Posterior Paraspinal Line. Probes in transverse (columns in **A** and **D**) and parasagittal planes (columns **B** and **C**) in anterior and posterior lung fields, and in transverse and coronal planes (middle row) in lateral lung fields.

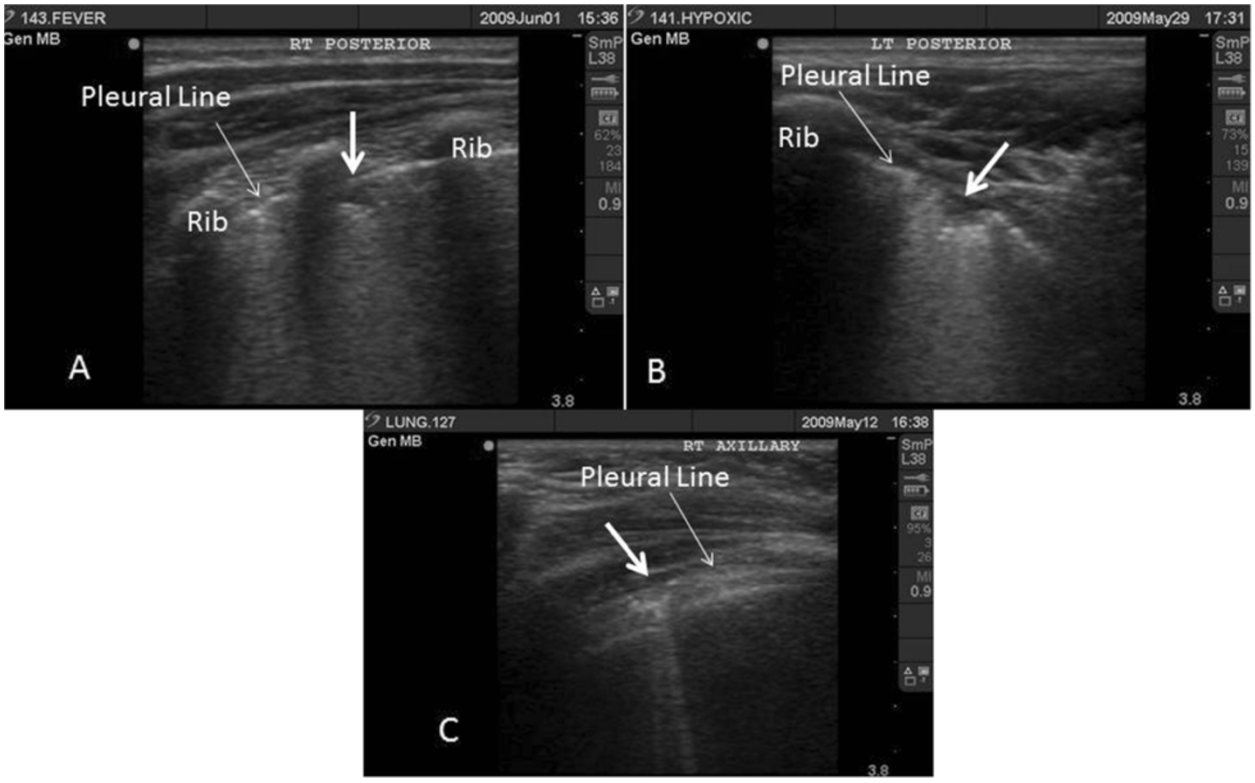

Figure 5 Small subpleural consolidations (arrows) with trailing comet tail artifacts consistent with viral pneumonia lung ultrasound pattern. (**A**, **B**, and **C**) are images of small subpleural lung consolidations in three different patients with suspected H1N1.

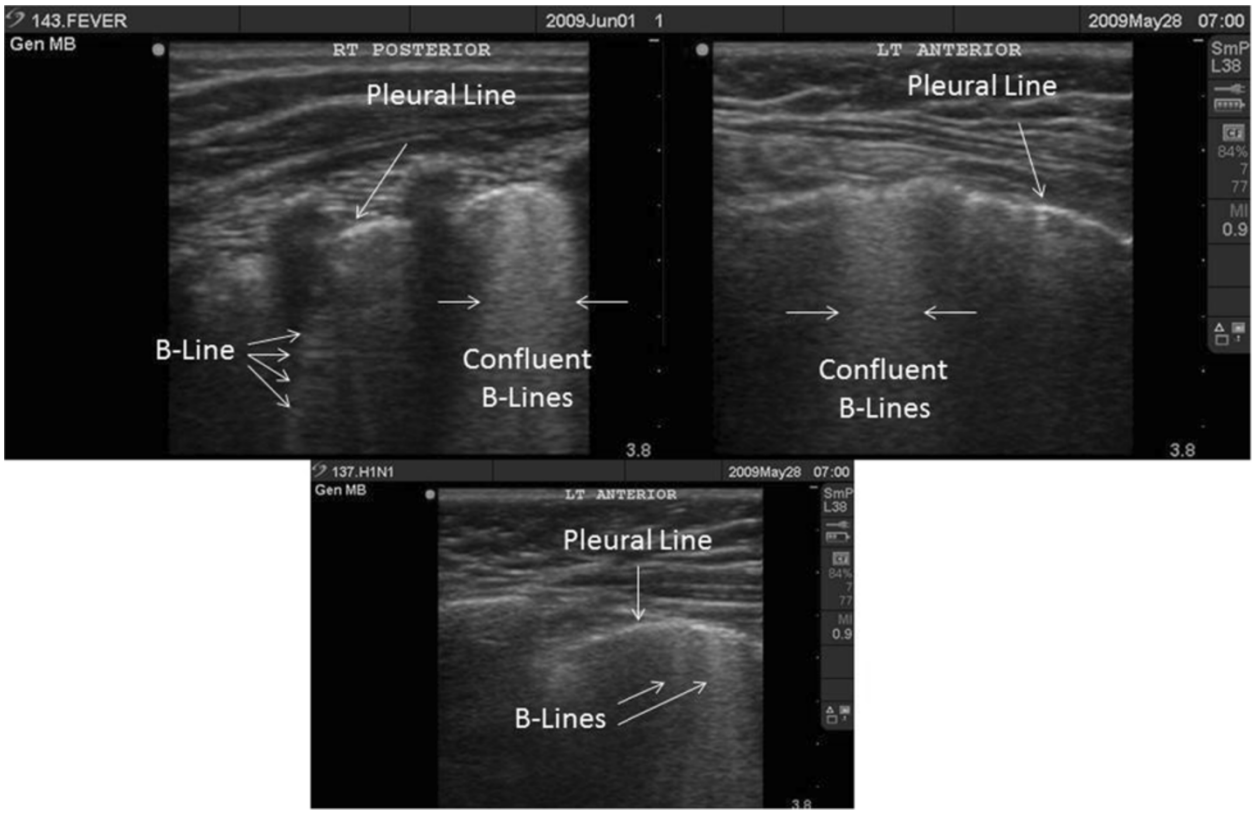

Figure 6 B-lines and confluent B-lines consistent with viral pneumonia lung ultrasound pattern.

and reviewing sonologist) to determine interobserver agreement by unweighted Cohens Kappa for viral pneumonia (small subpleural consolidation and/or B-lines), normal lung ultrasound pattern (A-lines), and bacterial pneumonia (lung consolidation with sonographic air bronchograms).

Results

Characteristics of study subjects

Patient demographic and study characteristics are presented in Table 1. Twenty pandemic 2009 H1N1 influenza patients requiring chest X-ray (CXR) were enrolled during this time period.

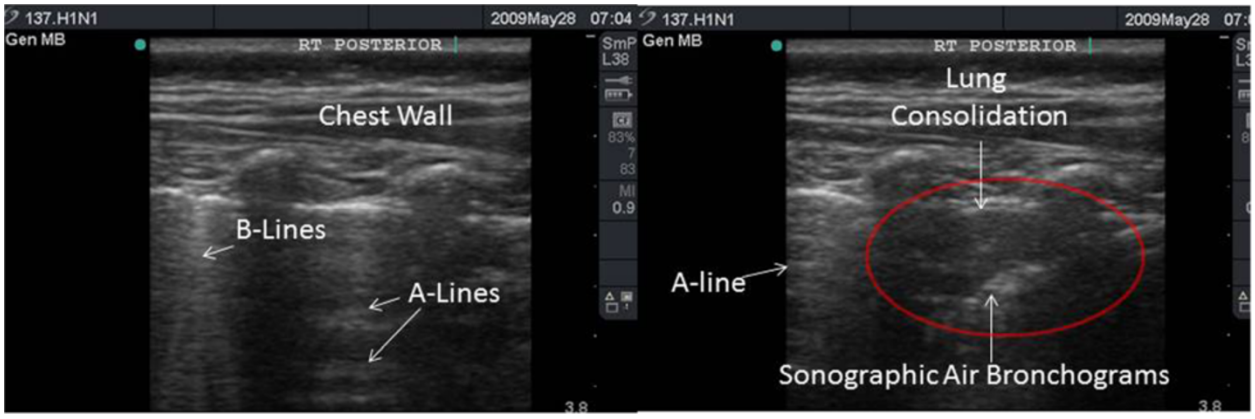

Figure 7 Viral (B-lines) and bacterial pneumonia (lung consolidation with sonographic air bronchogram) pattern. A-lines are horizontal lines that represent the normal aerated lung.

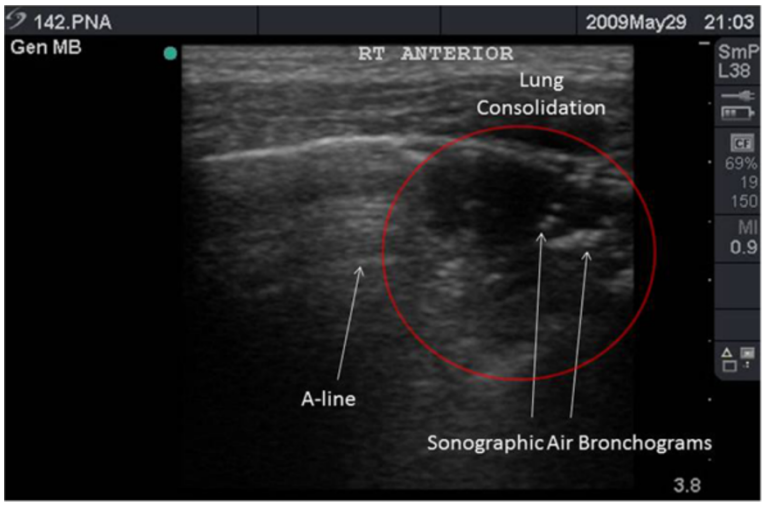

Figure 8 Lung consolidation with sonographic air bronchograms consistent with bacterial pneumonia.

Main results

Distribution of diagnoses based on lung ultrasound findings, chest X-ray findings, and clinical outcomes using a modified BLUE protocol [4] is presented in Table 2. Interobserver agreement for ultrasound findings of lung consolidation with air bronchograms, B-lines or small subpleural consolidations, and A-lines by Cohen's Kappa was 0.82 (95% confidence interval (CI), 0.63 to 0.99) (Table 3).

Ultrasound findings of lung consolidation with sonographic air bronchograms [6,7,16] correlated 100% with chest X-ray findings of bacterial pneumonia (reported as consolidation or infiltrate) in eight patients. All of these patients were confirmed to have pneumonia based on the clinical course at 2-week follow-up. This represented a doubling (40% vs. 20%) in the prevalence rate of bacterial pneumonia in our study during the H1N1influenza A onset and surge time period compared to the time period prior to the onset of H1N1 influenza A. The prevalence of viral lung ultrasound findings increased from approximately 50% for the overall study [13] to 75% during the surge of H1N1 influenza. Chest X-ray findings for viral pneumonia (most commonly described as peri-bronchial thickening or peri-bronchial cuffing) were present in 8 of 15 (53%) patients identified as having viral pneumonia on ultrasound. Seven of these 15 patients with viral pneumonia based on ultrasound had superimposed bacterial pneumonia also identified by ultrasound (Figure 7 and Additional file 4). All four patients in our series that required hospitalization had viral and bacterial pneumonia based on ultrasound.

Table 1 Clinical data

N	20
Average age	6.7 years (IQR, 3.6 to 10.7)
Gender	65% female
Median US exam time (IQR)	6 min (IQR, 4 to 8)
History of fever	95% (19/20)
History of cough	95% (19/20)
Median time to CXR from request prior to pandemic ($N = 20$)	29 min (IQR, 18 to 43)
Median time to CXR from request during pandemic surge ($N = 20$)	98 min (IQR, 79 to 125)

IQR, interquartile range.

All patients in our series were recovering or recovered from their influenza illness on follow-up after 2 weeks. All admitted patients were subsequently confirmed with the 2009 H1N1 influenza A by the New York City Department of Health. Per hospital protocol for possible hospital admission, four of nine patients tested positive for influenza A by viral antigen testing, despite the New York City Department of Health reporting >90% of the circulating virus during this pandemic time period was the novel influenza A H1N1 [1]. One infant in the cohort was co-infected with respiratory syncytial virus based on viral antigen testing. Three patients, all <5 years of age requiring hospital admission had evidence of both bacterial and viral pneumonia on ultrasound. The only patient requiring ICU admission, a 20-year-old female, was intubated after deteriorating during her ED stay with persistent hypotension and septic shock from a left lower lobe bacterial pneumonia. This patient initially presented with an influenza-like illness and acute abdominal pain.

Discussion

To our knowledge, this is the first prospective series describing the use of lung ultrasound in children as a potential real-time diagnostic triage tool during a mass

Table 2 Main results

Findings (*N* = 20)	US - *n*; % [95% CI]	CXR - *n*; % [95% CI]	Disposition[a]
Viral pneumonia	15; 75 [53 to 89]	8; 40 [22 to 61]	Oseltamivir
Bacterial pneumonia only	1; 5 [0 to 25]	5; 25 [11 to 47]	Antibiotics and oseltamivir
Viral and bacterial pneumonia	7; 35 [18 to 59]	3; 15 [3 to 38]	Antibiotics and oseltamivir
No findings	4; 20 [7 to 42]	7; 35 [18 to 59]	Discharge and observation

US, ultrasound; CXR, chest X-ray; [a]Disposition based on US findings.

casualty-type incident due to an acute respiratory illness pandemic surge [17,18]. Testa et al. have reported on similar lung ultrasound findings in adults during the 2009 H1N1 influenza A pandemic [12]. Single case reports of clinician-performed lung ultrasound to monitor the progression of H1N1 influenza-associated ARDS [19] and point-of-care echocardiography to diagnose H1N1 influenza myocarditis [20] have been described. Retrospective reports of the role of ultrasound in mass casualty incidents during disasters such as earthquakes have also been described [21,22]. Lichtenstein et al. described an algorithm using lung ultrasonography to distinguish between various respiratory pathologies of the lung [4]. We modified Lichtenstein's BLUE protocol [4] to recognize basic lung ultrasound patterns to distinguish between the normal unaffected lung, viral pneumonia pattern, and bacterial pneumonia (Figure 3). Scanning the posterior thorax was added to increase the sensitivity of the protocol [23]. Point-of-care lung ultrasound was able to identify, in real-time, four groups of pandemic patients: viral pneumonia only (subpleural consolidations and/or B-lines or confluent B-lines), bacterial pneumonia only (lung consolidation with sonographic air bronchograms), both viral and bacterial pneumonia (Figure 7), and normal lungs (A-lines only). Our calculated Kappa was 0.82, which means that the interobserver agreement in distinguishing between these ultrasound findings was excellent.

These ultrasound findings facilitated triage and immediate decision making regarding the need for respiratory isolation in a negative pressure room without waiting for chest X-ray. Our median time to chest X-ray tripled (Table 1) during the pandemic compared to a time period prior to the pandemic. Our time to chest X-ray interpretation during the pandemic was longer than the median of 98 min reported by Zanobetti et al. in the study of emergency department lung ultrasound in non-pandemic conditions [5].

Table 3 Cohen's Kappa for distinguishing viral from bacterial pneumonia on lung ultrasound between two blinded sonologists

	Viral Pneumonia	Normal	Bacterial Pneumonia	
Viral Pneumonia	13	1	0	14
Normal	1	4	0	5
Bacterial Pneumonia	0	1	7	8
	14	6	7	27
Cohen's Kappa = 0.82		95% CI (0.63 to 0.99)		

When lung consolidation with sonographic air bronchograms was visualized, point-of-care ultrasound facilitated the immediate decision to treat with antibiotics, without waiting for chest X-ray. Visualization of viral pneumonia on ultrasound may be useful to assist in the decision to initiate immediate empiric treatment with antiviral medication for future pandemic or epidemic influenza patients. In a large cohort of hospitalized H1N1 influenza A pandemic patients, only 73% of patients with radiographic evidence of pneumonia received antiviral drugs, whereas 97% received antibiotics [24]. Better recognition of viral pneumonia by ultrasound may impact outcomes, as available data have shown treatment with antiviral medication reduces mortality in hospitalized patients with influenza, even when therapy is initiated after 48 h of illness onset [24].

Limitations

Our sample size was limited by the inability to enroll during the surge of pandemic patients due to time and resource constraints. Selection bias from convenience sampling may have occurred because patients were more likely to have been enrolled at less busier or better staffed times. In general, the patients in this series had illnesses severe enough to warrant investigation with chest X-ray. Thus, information about less ill or asymptomatic pandemic patients is lacking.

Although our calculated interobserver agreement for lung ultrasound to distinguish between viral and bacterial pneumonia is high, the number of total observations was limited, and this is reflected in our wide 95% confidence intervals. However, it is notable that our point estimate Kappa for ultrasound is higher than the reported interobserver agreement for chest X-ray for pneumonia by pediatric radiologists, 0.51 (0.39 to 0.64) [25].

Due to the large numbers of patients presenting to our emergency department during the pandemic, only hospitalized patients (four patients in our series) were confirmed with 2009 H1N1 influenza A [1]. Finding small subpleural consolidations and/or B-lines on ultrasound

allows the recognition of viral pneumonia from bacterial pneumonia (lung consolidation with sonographic air bronchograms), but it is unknown if different viruses have unique lung ultrasound patterns (e.g., influenza A from RSV). We could not report test performance characteristics, such as sensitivity and specificity, as there was no practical reference gold standard for viral pneumonia at the time our study was conducted. Additionally, chest X-ray cannot be used as a gold standard for viral pneumonia. However, according to the New York City Department of Health, >90% of the circulating virus during this pandemic time period was the novel influenza A H1N1 [1].

Conclusions

Lung ultrasound may be used to distinguish viral from bacterial pneumonia with high interobserver agreement. Lung ultrasonography may be useful during epidemics or pandemics of acute respiratory illnesses for rapid point-of-care triage and management of patients.

Additional files

Additional file 1: Title: Small subpleural consolidation. Description: Small subpleural consolidation consistent with viral lung ultrasound pattern.

Additional file 2: Title: Confluent B-lines. Description: Confluent B-lines consistent with viral lung ultrasound pattern.

Additional file 3: Title: Rt anterior middle lobe lung consolidation with air bronchograms. Description:Rt anterior middle lobe lung consolidation with air bronchograms consistent with bacterial pneumonia lung ultrasound pattern.

Additional file 4: Title: Confluent B-lines and lung consolidation with air bronchograms. Description: Viral and bacterial pneumonia lung ultrasound patterns.

Competing interests

The authors declare that they have no competing interests.

Authors contributions

JWT and VPS participated in the design of the study, coordinated the study, and performed the statistical analysis. JWT, DOK, and VPS participated in the patient enrollment and data collection and drafting of the manuscript. All authors read and approved the final manuscript.

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