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Lung ultrasound as a diagnostic tool for radiographically-confirmed pneumonia in low resource settings

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ABSTRACT

Background: Pneumonia is a leading cause of morbidity and mortality in children worldwide; however, its diagnosis can be challenging, especially in settings where skilled clinicians or standard imaging are unavailable. We sought to determine the diagnostic accuracy of lung ultrasound when compared to radiographically-confirmed clinical pediatric pneumonia.

Methods: Between January 2012 and September 2013, we consecutively enrolled children aged 2–59 months with primary respiratory complaints at the outpatient clinics, emergency department, and inpatient wards of the Instituto Nacional de Salud del Niño in Lima, Peru. All participants underwent clinical evaluation by a pediatrician and lung ultrasonography by one of three general practitioners. We also consecutively enrolled children without respiratory symptoms. Children with respiratory symptoms had a chest radiograph. We obtained ancillary laboratory testing in a subset.

Results: Final clinical diagnoses included 453 children with pneumonia, 133 with asthma, 103 with bronchiolitis, and 143 with upper respiratory infections. In total, CXR confirmed the diagnosis in 191 (42%) of 453 children with clinical pneumonia. A consolidation on lung ultrasound, which is our primary endpoint for pneumonia, had a sensitivity of 88.5%, specificity of 100%, and an area under-the-curve of 0.94 (95% CI 0.92–0.97) when compared to radiographically-confirmed clinical pneumonia. When any abnormality on lung ultrasound was compared to radiographically-confirmed clinical pneumonia the sensitivity increased to 92.2% and the specificity decreased to 95.2%, with an area under-the-curve of 0.94 (95% CI 0.91–0.96).

Conclusions: Lung ultrasound had high diagnostic accuracy for the diagnosis of radiographically-confirmed pneumonia. Added benefits of lung ultrasound include rapid testing and high inter-rater agreement. Lung ultrasound may serve as an alternative tool for the diagnosis of pediatric pneumonia.

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1. Introduction

Pneumonia is a leading cause of death in children worldwide. It is responsible for 120 million episodes and 1 million deaths each year in children aged <5 years [1,2]. Despite a decrease in child mortality in the past 20 years, the proportion of pneumonia deaths has remained constant at approximately 20% [3]. In low resource settings, where skilled providers are not widely available, the World Health Organization (WHO) developed a case management algorithm for the treatment of pneumonia. This involved training community health workers to identify respiratory signs and symptoms, centered on cough, difficulty breathing, respiratory rate and danger signs, for diagnosis, treatment, and referral [5]. While this algorithm achieved important mortality reductions after implementation [6], multiple studies thereafter have shown that it lacks specificity [7–9]. A high false positive rate has resulted in overuse of antibiotics and improper therapy for children with acute bronchospasm that may instead require bronchodilators.

Pediatric pneumonia is a heterogeneous disease with bacterial and viral causes. Additionally, there is a large overlap with bronchiolitis and reactive airways disease. Therefore, the diagnosis of pneumonia can be challenging and requires integration of a variety of diagnostic tools [9,10]. In low resource settings, previous studies have tested additional, non-respiratory, diagnostic features, such as fever [10] and oxygen saturation [11,12]. But when resources are available, imaging is an important adjunct [13]. In fact, the American Academy of Pediatrics endorsed chest X-ray (CXR) as the imaging modality of choice for complicated or ambiguous cases [10]. However, CXR has its own disadvantages including radiation exposure, high inter-observer variability [14], and lack of impact on clinical outcome [15].

Lung ultrasound (LUS) is an emerging diagnostic tool for pneumonia in both adults [16] and children [17]. It also has many advantages for pediatric respiratory disease in low resource settings, including portability, rapid and repeat testing, no ionizing radiation, and ease of use [18–20]. We sought to evaluate the diagnostic accuracy of LUS as a point-of-care diagnostic tool for pediatric pneumonia in a tertiary care setting in Lima, Peru.

2. Materials and methods

2.1. Study design

Between January 2012 and September 2013, we consecutively enrolled children with respiratory symptoms in the Emergency Department, General Pediatric Wards, and Outpatient Clinics at the Instituto Nacional de Salud del Niño; a large children's hospital treating more than 170,000 children annually, in Lima, Peru. Inclusion criteria were children aged 2–59 months and the presence of respiratory symptoms. Exclusion criteria were: chronic lung disease excluding asthma, significant cardiac disease, and need for mechanical ventilation. We also enrolled children of a similar age range without respiratory complaints and acute non-respiratory illnesses (fever, vomiting or diarrhea) at the same institution. These children were usually those presenting to the hospital for well-child visits or siblings of child participants recruited into the study. We described detailed methods about study procedures elsewhere [21]. Of note, we amended the original protocol to allow for an increase in sample size. We followed STARD guidelines for the reporting of diagnostic accuracy [22]. The study was approved by the Institutional Review Board committees of the Instituto Nacional de Salud del Niño (Lima, Peru), A.B. PRISMA (Lima, Peru), and the Johns Hopkins School of Medicine (Baltimore, USA).

2.2. Clinical diagnosis

Clinical assessment included a history and physical exam performed by a pediatrician. Pediatricians on service provided a diagnosis following standard of care with input from international clinical guidelines (Table 1) [23–25]. An anteroposterior CXR was obtained for all children with respiratory symptoms. Lateral view CXRs were not obtained because they were not consistent with clinical practice in our setting. CXR used a scanner with 4800 × 4800 dots-per-inch resolution for CXR image digitation. Films were digitized and sent to a third party reading group of three study radiologists. We did not obtain a CXR on children without respiratory symptoms.

2.3. Lung ultrasound imaging

All participants underwent a complete LUS evaluation using a MicroMaxx® portable ultrasound machine (Sonosite, Bothwell, WA) with a HFL38/13-6 MHz linear transducer. This device is approximately the size of a 13" laptop computer and used at the bedside as a point-of-care tool. One of three general practitioners (LEE, MAC, and JMC) performed LUS after completing a 7-day standardized training protocol [21] based on international recommendations [26]. Both conduct and interpretation of LUS findings were performed independent of clinical evaluation or radiographic findings. LUS was conducted on almost all children who had CXR as well as on all children without respiratory symptoms (Fig. 1).

2.4. Imaging interpretation

Interpretation CXR and LUS images was performed at a later date by three board-certified pediatric radiologists (PCC, EAM, and JB) and three general practitioners (LEE, MAC, and JMC), respectively. These groups were blinded to clinical information and results from the alternative imaging modality. We used standardized protocols for interpretation of both CXR [14] and LUS [26]. We defined radiographic pneumonia as the presence of a lobar consolidation with or without a pleural effusion (Table 1). Pneumonia on LUS was defined as the identification of artifacts consistent with lobar consolidation or patchy lobar consolidation, if it occupied more than one intercostal space in vertical view, or small consolidation with a pleural effusion (Table 1). We did not consider the isolated findings of interstitial changes on LUS or CXR as positive for pneumonia. Agreement by two out of three readers was required for final diagnosis.

2.5. Laboratory assessment

We conducted laboratory testing in a subset of participants to offer additional objective data. Complete blood counts and blood cultures were obtained in a subset of 361 and 137 children, respectively. Serum or plasma levels of procalcitonin (PCT) were measured in a convenience sample of 259 children. Batched samples were maintained at −20 °C until tested in a reference laboratory. PCT levels were measured using the Kryptor chemiluminescence immunoassay (BRAHMS, Hennigsdorf, Germany) according to manufacturer specifications. The inter-assay coefficient of variation was <10%, and the functional sensitivity of the assay was 0.06 ng/mL. Pharyngeal swabs were analyzed for viruses and bacteria in a convenience sample of 251 children. Nucleic acid extraction for viral testing was accomplished utilizing the Arrow Viral NA kit (Diasorin Inc., Stillwater, MN), while bacterial extraction utilized the MagNA Pure LC with DNA Isolation Kit I (Roche Diagnostics, Indianapolis, IN). For viral testing, respiratory virus controls were utilized in each run (NATrol Respiratory