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Research Article

Diagnostic Performance of Chest Ultrasound in Diagnosing Pneumonia in Pediatric Patients at Mulago National Referral Hospital, Kampala, Uganda

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Abstract

Background: Pneumonia is a leading infectious cause of death in children under 5 years, with the greatest burden in developing countries. It is mainly diagnosed clinically using the WHO standard algorithm. Chest X-ray (CXR) which is the primary imaging modality used for the evaluation of pneumonia in children is usually reserved for severe or complicated cases of pneumonia. There is enough evidence to support chest ultrasound (CUS) as an alternative or adjunct to CXR in diagnosing community acquired pneumonia (CAP) in children. In this study we assessed the diagnostic performance of CUS in diagnosing pneumonia and the clinical correlates of radiological diagnosis of pneumonia in pediatric patients at Mulago National Referral Hospital.

Methods: We conducted a cross-sectional study, and enrolled 280 children below 13 years (age limit 2 months and 12 years), admitted with a clinical suspicion of pneumonia at acute care unit (ACU) of Mulago National Referral Hospital between January and June 2018. A clinical assessment, chest X-ray and chest ultrasound within 24hrs of admission were done on each child. Findings of CUS were compared to the composite reference standard of clinical findings plus CXR findings (final clinical diagnosis) was used to establish accuracy of CUS in diagnosing pneumonia. Logistic regression models were fitted to establish correlates of radiological diagnosis of pneumonia.

Results: Of the 280 enrolled, 252 children had complete data for analysis. Participants were predominantly < 24 months of age (68.6%) and slightly more males (52%). Overall, 81.3% had pneumonia clinically. CUS and CXR-based pneumonia prevalence was 64.7% and 37.7% respectively. Using final clinical diagnosis as reference, the accuracy was 71%. The sensitivity and specificity of CUS was 72% (95% CI [65 - 78]) and 67% (95% CI [52 - 81]), respectively. The area under receiver operating curve (ROC) of 0.7 (95% CI [0.62 - 0.77]). Significant correlates of CUS-based pneumonia diagnosis were: cough, OR = 3.9; [95%CI; 1.19 - 9.62], p = 0.022, and low oxygen saturation, OR = 1.9; [95% CI: 1.05 - 3.33), p = 0.035. While for CXR-based pneumonia, it was only low oxygen saturation, OR = 1.9 [95% CI: 1.07 - 3.26], p = 0.028.

Conclusion: Chest ultrasound has a good sensitivity and could be useful as a screening tool or/and an add-on diagnostic tool to CXR to diagnose pediatric pneumonia. Cough and hypoxia are good correlates to CUS-based pneumonia diagnosis in children with clinical suspicion of pneumonia.

Keywords: *Pneumonia; Community Acquired Pneumonia; Paediatrics; Chest Ultrasound; Chest Radiography*

Abbreviations

WHO: World Health Organization; CUS: Chest Ultrasound; CXR: Chest X-Ray; CT: Computed Tomography; MNRH: Mulago National Referral Hospital; PCV: Pneumococcal Conjugate Vaccine; CAP: Community Acquired Pneumonia; CHD: Congenital Heart Disease; SCD: Sickle Cell Disease

Introduction

Pneumonia is the single largest infectious cause of death in children worldwide. It killed 740,180 children under the age of 5 years in 2019, accounting for 14% of all deaths of children under 5 years. It is most prevalent in South Asia and sub-Saharan Africa [1]. Despite the introduction of the pneumococcal conjugate vaccine (PCV), community-acquired pneumonia is still considered as a common cause of morbidity among children aged ≤ 5 years in developing countries [2].

These numbers could further be reduced by early detection and targeted antibiotic treatment. Currently, based on World Health Organization (WHO) criteria, the clinical diagnosis of pneumonia is based on clinical history and physical examination with the presence of cough, and/or difficult breathing, fast breathing with/without chest in drawing, and with/without fever [3]. The use of CXR is normally reserved for complicated lung cases [4] and this is the current practice at the largest National Referral Hospital in Uganda. Despite these indications, chest x-ray (CXR) is also requested for mild and moderate cases because of the poor reliability of the history and physical examination [5]. In addition, CXRs could provide false negative findings in early stages of pneumonia, misses consolidations < 1 cm, causes overlap of differentials, has a low accuracy and not appropriate for patient's clinical follow-up due to risk of excessive exposure to ionizing radiation [6], but are also not easily accessible in resource-limited settings. Computed tomography (CT) which is a gold standard for the diagnosis of pneumonia is expensive, not only less accessible in resource limited settings but also exposes children to larger amounts of radiation, yet children have a greater risk of developing stochastic effects [7].

The lung ultrasonography is another alternative diagnostic method for pneumonia, that was discovered by B. Weinberg in 1986, that demonstrates sonographic air bronchograms within lung consolidations [8]. Studies done over the past three decades have reported lung ultrasonography as an accurate and reliable tool in the diagnosis of pneumonia [9-13], with possibility of use in patients' clinical follow-up without risk of exposure to radiation. However, most of these studies have been done in developed countries, leaving paucity of data for low resource settings.

Aim of the Study

The main aim of this study was to determine the diagnostic performance of chest ultrasound (CUS)in diagnosing pneumonia, and clinical correlates of radiological diagnosis of pneumonia in pediatric patients at Mulago National Referral Hospital. This was to allow bridge the knowledge gap about the use of CUS in our low resource settings and to offer evidence of CUS as a portable, reliable, fast, easily repeatable and noninvasive means in the diagnosis, follow-up and management of pneumonia.

Materials and Methods

This was a cross-sectional study conducted at ACU of MNRH in Kampala, capital city of Uganda. A total of 280 children below 13 years admitted with a clinical suspicion of pneumonia were prospectively enrolled between January and June 2018 and were evaluated with both a CXR and a CUS. Both investigations were performed in parallel within 24hrs of admission.

All children had CXRs (posterior-anterior or anterior-posterior views) done from the department of radiology at MNRH and the diagnosis of pneumonia was made in accordance with the (WHO) criteria for the standardized interpretation of pediatric chest radiographs [14] by an independent radiologist before or after the CUS.

Chest ultrasound was carried out by the principal investigator who was blinded to chest X-ray findings, using a SIUI (Shantou Institute of Ultrasound Instruments), Apogee 1000, model 2015, portable ultrasound machine with a high frequency and resolution of 7 - 12 MHz, linear array transducer. The whole chest wall was divided into 6 anatomical regions. The anterior regions were delimited by the parasternal and anterior axillary lines, the lateral regions between the anterior and posterior axillary lines, and the posterior region delimited by the paravertebral and posterior axillary lines. Each region was further divided into upper and lower regions. The anterior and lateral regions were examined in supine position with the shoulders fully straightened on the sides, the posterior regions in a sitting up or lateral decubitus positions, or on their parents' shoulders or while breastfeeding (for the younger babies), to minimize anxiety. The lung was visualized through intercostal windows with the probe placed parallel, perpendicular or oblique to the ribs in all the 12 regions, as described by Copetti R., *et al* [15].

The diagnosis of pneumonia on CUS was made basing on the presence of lung consolidations (hypoechogenic areas of varying size and shape with poorly defined borders with or without air or fluid bronchograms or B-lines (> = 3, per field view) and/or the presence of pleural effusion as defined by Reissig A., *et al* [8,16].

The final diagnosis was made by a team of clinicians who involved pediatricians, senior housing officers and medical officers, from the general pediatric wards or ACU, based on clinical presentation, physical examination findings, laboratory tests or CXR findings. The final diagnosis data was extracted from the files during or after the discharge of the patient and recorded in the data collection tool.

Informed consents were obtained from the participants or parents/guardians who were anonymized. The ethical approval was sought from both the Radiology and Paediatrics departments of MNRH and the ethical and research committees of School of Medicine of Makerere University (SOMREC) and MNRH. (Study approval number: MHREC 1312).

Data from completed questionnaires were entered into a database designed using Epi Info™ software (V7.2, 1600 Clifton Road Atlanta, GA 30329-4027 USA) and analysis was performed with Stata software (v.14, College Station, Texas, USA). Descriptive statistics were generated for participants' characteristics.

CUS diagnostic performance was calculated by estimating the sensitivity, specificity, positive and negative predictive values, positive and negative likelihood ratios, and area under Receiver Operator Characteristic (ROC) curve with their 95% confidence intervals (CIs). In bivariate analysis, based on both Chi-square test and Logistic regression, independent analysis comparing each clinical feature at presentation with pneumonia status based on CUS, and separately with pneumonia status based on CXR was performed. Unadjusted odds ratios with their corresponding 95% CI were reported. A significance level of 5% was used. All clinical variables were locked in the multivariate model to control for the confounding effect of each variable in the model. Adjusted odds ratios and 95% confidence intervals were reported for each clinical variable. A variable was considered significant in this analysis if it had a p-value < 0.05.

Results

Of the 280 children targeted, 252 had complete clinical, CXR and CUS data and so were included in the analysis. The mean age was 21.4 ± 24.2 months with slightly more males (52%).

Overall, 205 (81.3%) patients had a final diagnosis of pneumonia (based on clinical and CXR findings). No age or gender disparities were noted between those with and without final diagnosis of pneumonia, p-values > 0.05. Majority of the children were up to-date with regard to immunization, 96% and had no chronic illness 213 (84.5%) (Table 1).

Majority of the children (93%) enrolled with pneumonia suspicion had a history of cough, were febrile having a temp > 37.5°C (80.2%), had intercostal recessions (87%) and chest wall indrawing (96%).

Characteristics	Clinical Suspicion Pneumonia (N = 252) N (%)	Final Diagnosis Pneumonia (N = 205) N (%)	Final Diagnosis No Pneumonia (N = 47) N (%)	P-Value
Age (months) [Mean], sd	21.4 (24.2)	20.1 (23.8)	26.7 (25.6)	0.0944
< 6mo	57 (22.6)	49 (24.0)	8 (17.0)	0.264
6 - 11	63 (25.0)	51 (24.8)	12 (25.5)	
12 - 23	53 (21.0)	46 (22.4)	7 (15.0)	
24 - 59	54 (21.4)	42 (20.5)	12 (25.5)	
≥ 60	25 (10.0)	17 (8.3)	8 (17.0)	
Sex				0.139
Female	121 (48.0)	103 (50.2)	18 (38.3)	
Male	131 (52.0)	102 (49.8)	29 (61.7)	
Immunization				
Yes	243 (96.0)	197 (96.0)	46 (98.0)	0.554
No	9 (4.0)	8 (4.0)	1 (2.0)	
Chronic illnesses				0.262
Absent	213 (84.5)	171 (83.4)	42 (89.4)	
CHD (known)	16 (6.4)	12 (5.9)	4 (8.5)	
SCD	12 (4.8)	12 (5.9)	0	
Others	11 (4.3)	10 (4.8)	1 (2.1)	

Table 1: *Socio-demographics of the participants admitted with clinical suspicion of pneumonia at acute care unit (ACU).*

Children with final clinical diagnosis of pneumonia tended to present more with low oxygen saturation < 93% (p = 0.009), intercostal recession (p = 0.046), while those without pneumonia presented more with inability to feed (p = 0.041).

Children without the pneumonia at discharge had a greater percentage of intercostal recessions 95% as compared to those who were found to have pneumonia at 85%.

Variables	Clinical Suspicion Pneumonia N (%)	Final Diagnosis with Pneumonia N (%)	Final Diagnosis No Pneumonia N (%)	P-Value
Cough	234 (93.0)	192 (94.0)	42 (89.4)	0.302
Temp(C), mean, sd > 37.5 36.5-37.5 <36.5	38.2 (0.91) 202 (80.2) 43 (17.1) 7 (2.8)	38.2 (0.94) 163 (79.5) 35 (17.1) 7 (3.4)	38.3 (0.78) 39 (83.0) 8 (17.0) 0.0	0.436
Oxygen saturation, mean, sd < 93% ≥ 93%	92.2 (4.3) 118 (47.0) 134 (53.2)	91.9 (4.4) 104 (51.0) 101 (49.3)	93.6 (3.5) 14 (30.0) 33 (70.2)	0.009
Respiratory Rate, mean, sd	54 (7.8)	54 (8.1)	52 (6.5)	0.0960
Intercostal recessions	219 (87.0)	174 (85.0)	45 (96.0)	0.046
Chest wall indrawing	242 (96.0)	198 (97.0)	44 (94.0)	0.347
Cyanosis	7 (3.0)	7 (3.0)	0.0	0.199
Stridor	5 (2.0)	5 (2.4)	0.0	0.279
Altered mentation	6 (2.4)	6 (3.0)	0.0	0.235
Inability to feed	17(6.8)	17 (8.3)	0.0	0.041

Table 2: *Clinical features of patients admitted with suspected pneumonia at acute care unit (ACU).*

Of the 164 children admitted with clinical suspicion of pneumonia, 64.7%were found to have radiological features of pneumonia by CUS and 45.9%) were identified by CXR. This difference in yield was found to be statistically significant with a p-value < 0.001 (Table 3a).

Air space disease was the commonest radiological pattern with 149 (59%) being demonstrated by CUS and 82 (32.5%) demonstrated by CXR. CUS was able to demonstrate at least one of the patterns (alveolar or interstitial process) in 115 (46%) of the patients and 90 (35.7%) by CXR. CUS demonstrated pleural effusion in 29 (12.0%) of the patients compared to 9 (3.6%) by CXR. A total of 46 (18.3%) children were found to have cardiomegaly on CXR with 42 of these having final clinical diagnosis of pneumonia (Table 3a).

Radiological Findings	Clinical Suspicion Pneumonia N (%)	Final Diagnosis Pneumonia N (%)	Final Diagnosis No Pneumonia N (%)	P-Value
Abnormal features by CUS	164 (64.7)	147 (72.0)	16 (34.0)	< 0.001
Consolidation	149 (59.0)	134 (65.4)	15 (32.0)	< 0.001
B-Lines	62 (24.6)	58 (28.3)	4 (9.0)	0.005
At least one	115 (46.0)	102 (50.0)	13 (28.0)	< 0.001
Both	48 (19.0)	45 (22.0)	3 (6.4)	
Pleural effusion	29 (12.0)	27 (13.2)	2 (4.3)	0.084
Abnormal features by CXR	95 (37.7)	94 (45.9)	1 (2.1)	< 0.001
Pneumonia patterns				
Alveolar Process	82 (32.5)	81 (39.5)	1 (2.1)	< 0.001
Interstitial process	18 (7.1)	18 (8.8)	0	0.035
At least one (alveolar or interstitial)	90 (35.7)	89 (43.4)	1 (2.1)	
Both (alveolar and interstitial)	5 (2.0)	5 (2.4)	0	< 0.001
Pleural effusion	9 (3.6)	9 (4.4)	0	0.144
Cardiomegaly	46 (18.3)	42 (20.5)	4 (9.0)	0.055

Table 3a: *Radiological features of patients admitted with clinical suspicion of pneumonia at acute care unit.*

Investigation	Clinical suspicion pneumonia n (%)	Final diagnosis pneumonia n (%)	Final diagnosis no pneumonia n (%)	P-value
CUS (RT Lung)				
Consolidation	123 (81.5)	110 (81.0)	13 (87.0)	0.584
B-lines	42 (17.0)	38 (19.0)	4 (9.0)	0.096
CXR (RT Lung)				
Alveolar Process	77 (89.5)	76 (89.4)	1 (100)	0.731
Interstitial process	14 (74.0)	14 (74.0)	0	-
CUS (LT Lung)				
Consolidation	86 (57.0)	80 (59.0)	6 (40.0)	0.162
B-lines	40 (16.0)	39 (19.0)	1 (2.13)	0.004
CXR (LT Lung)				
Alveolar Process	24 (28.0)	24 (28.2)	0	0.531
Interstitial process	9 (47.4)	9 (47.4)	0	-

Table 3b: *Distribution of pneumonia by hemithorax.*

Most of the radiological pneumonia (both radiological patterns, but mainly airspace) was in the right hemithorax.

The demonstration of B-lines in the left hemithorax by CUS in patients was more among children with a final diagnosis of pneumonia.

Those with interstitial process on CXR in both hemithoraces were found to have pneumonia at discharge (Table 3b).

Of the 206 with final diagnosis of pneumonia, 148 (72%) were diagnosed by CUS and of the 46 without pneumonia at discharge, CUS demonstrated pneumonia in 15 (33%) children. This yielded an accuracy of 71.0% with a sensitivity of 72% [95%CI: 65 - 78], specificity of 67% [95%CI: 52 - 81], PPV 91% [95%CI: 85 - 95], NPV 35% [95%CI: 25 - 46] with likelihood ratio positive (LR+) of 2.1 [95%CI, 0.8 - 3.3] and LR negative of 0.4 [95%CI, 0.3 - 0.6] (Table 4).

Variable	Sensitivity % [95% CI]	Specificity % [95% CI]	PPV % [95% CI]	NPV % [95% CI]	LR + % [95% CI]	LR- % [95% CI]	ROC % [95% CI]
Overall	72 [65-78]	67 [52-81]	91 [85-95]	35 [25-46]	2.2 [1.4-3.4]	0.4 [0.3-0.6]	0.7 [0.6-0.8]
Age specific [months]							
<6	82 [69-91]	57 [18-90]	93 [81-99]	31 [9-61]	1.9 [0.8-4.6]	0.3 [0.1-0.8]	0.7 [0.5-0.9]
6 - 11	69 [54-81]	67 [35-90]	90 [76-97]	33 [16-55]	2.1 [0.9-4.7]	0.5 [0.3-0.8]	0.7 [0.5-0.8]
12 - 23	63 [48-77]	71 [29-96]	94 [79-99]	23 [8-45]	2.2 [0.7-7.3]	0.5 [0.3-1.0]	0.7 [0.5-0.9]
24 - 59	69 [53-82]	75 [43-95]	91 [75-98]	41 [21-64]	2.8 [1.0-7.5]	0.4 [0.2-0.7]	0.7 [0.6-0.9]
≥60	82 [57-96]	63 [25-92]	82 [57-96]	63 [25-92]	2.2 [0.9-5.5]	0.3 [0.1-1.0]	0.7 [0.5-0.9]
Sex Spec							
Female	75 [66-83]	53 [28-77]	91 [83-96]	26 [13-43]	1.6 [1.0-2.7]	0.5 [0.3-0.8]	0.6 [0.5-2.7]
Male	69 [59-78]	76 [57-90]	91 [86-96]	41 [28-55]	2.8 [1.5-5.5]	0.4 [0.3-0.6]	0.7 [0.6-0.8]

Table 4: *Accuracy of chest ultrasonography with final clinical diagnosis as a standard reference in the detection of pneumonia. Se: Sensitivity; Sp: Specificity; PPV: Positive Predictive Value; NPV: Negative Predictive Value; LR+: Positive Likelihood Ratio; LR-: Negative Likelihood Ratio; ROC: Receiver Operating Characteristics.*

Of the 95 patients with pneumonia on CXR, CUS diagnosed 91 (96.0%) and of the 157 without pneumonia on CXR, CUS identified 72 (46%) with pneumonia.

Variables	Sensitivity % [95% CI]	Specificity % [95% CI]	PPV % [95% CI]	NPV % [95% CI]	LR+ % [95% CI]	LR- % [95% CI]	ROC % [95%CI]
Overall	96 [90-99]	54 [46-62]	56 [48-64]	96 [89-99]	2.1 [1.8-2.5]	0.1 [0.0-0.2]	0.8 [0.7-0.8]
Age specific [months]							
<6	100 [86-100]	39 [23-58]	56 [39-70]	100 [75-100]	1.7 [1.3-2.2]	0.00	0.7 [0.6-0.8]
6-11	82 [57-96]	46 [31-61]	36 [21-53]	88 [68-97]	1.5 [1.1-2.1]	0.4 [0.1-1.1]	0.6 [0.5-0.8]
12-23	100 [83-100]	67 [48-82]	68 [48-82]	100 [85-100]	3.0 [1.9-4.9]	0.00	0.8 [0.8-0.9]
24-59	96 [78-100]	68 [49-83]	69 [50-84]	96 [77-100]	3.0 [1.8-5.0]	0.1 [0.0-0.4]	0.8 [0.7-0.9]
> = 60	100 [72-100]	57 [29-82]	65 [38-86]	100 [63-100]	2.3 [1.3-4.3]	0.00	-
Sex spec							
Female	98 [90-100]	50 [38-62]	61 [49-71]	97 [85-100]	2.0 [1.5-2.5]	0.0 [0.0-0.3]	0.7 [0.7-0.8]
Male	93 [81-99]	57 [46-68]	51 [39-62]	94 [85-99]	2.2 [1.7-2.8]	0.1 [0.0-0.4]	0.8 [0.7-0.8]

Table 5: *Diagnostic accuracy of chest ultrasonography using chest radiography only as a standard reference in the detection pneumonia. Se: Sensitivity; Sp: Specificity; PPV: Positive Predictive Value; NPV: Negative Predictive Value; LR+: Positive Likelihood Ratio; LR-: Negative Likelihood Ratio; ROC: Receiver Operating Characteristics.*

The above yielded an accuracy of 69.8% with a sensitivity of 96% [95% CI, 90 - 99], specificity of 54% [95%CI, 46 - 62], PPV of 56% [95%CI, 48 - 64], NPV of 96% [95%CI, 89 - 99].

The sensitivity of CUS was good across all age groups except 6 - 11 months with 82% (95%CI, 57 - 96]. The sensitivity between both sexes was almost the same. The specificity better between 12 - 59 months with values above 68% [95%CI, 49 - 83].

The specificity of CUS among children between 12 - 23 months and 24 - 59 months was slightly higher with 67 [95%CI, 48 - 82] and 68 [95%CI, 49 - 83], respectively. And it was a better diagnostic tool among the same age groups with ROC of > 0.82.

Variables	Clinical Suspicion Pneumonia N	Final Diagnosis Pneumonia N (%)	Final Diagnosis No Pneumonia N (%)	Bivariate Unadjusted OR (95%CI)	P-Value	Multivariate Adjusted OR (95%CI)	P-Value
Cough	234	155 (66.0)	79 (34.0)	2.5 (0.93, 6.46)	0.069	3.9 (1.19, 9.62)	0.022
Temp (°C)	202	129 (64.0)	73 (36.0)	0.6 (0.11, 2.96)	0.510	0.4 (0.07, 2.15)	0.271
SpO_2 (< 93)	118	87 (74.0)	31 (26.0)	2.1 (1.26, 3.65)	0.005	1.9 (1.05, 3.33)	0.035
Tachypnea	223	150 (67.3))	73 (32.7)	2.5 (1.16, 5.54)	0.020	2.2 (0.95, 4.94)	0.067
Intercostal recession	219	143 (65.3)	76 (34.7)	1.2 (0.58, 2.59)	0.600	0.9 (0.40, 2.05)	0.811
Chest wall indrawing	242	159 (66.0)	83 (34.0)	2.9 (0.79, 10.47)	0.110	2.7 (0.69, 10.50)	0.151
Cyanosis	7	6 (86.0)	1 (14.0)	3.4 (0.40, 28.39)	0.265	3.6 (0.11, 119.7)	0.472
Stridor	5	4 (80.0)	1 (20.0)	2.2 (0.24, 20.11)	0.480	0.6 (0.02, 17.71)	0.794
Altered mentation	6	5 (83.0)	1 (17.0)	2.8 (0.32, 24.22)	0.353	0.6 (0.01, 25.53)	0.757
Inability to feed	17	14 (82.0)	3 (18.0)	2.7 (0.75, 9.64)	0.128	1.6 (0.31, 8.39)	0.572

Table 6a: *The correlation between clinical findings and chest ultrasonography.*

SpO_2: Oxygen saturation.

In bivariate analysis, only oxygen saturation < 93 and tachypnea were strongly associated with CUS, with p-values < 0.005. Cough was just borderline with a p-value < 0.1.

In multivariate analysis, the odds of having a diagnosis of pneumonia on chest ultrasound were 3.9 times higher among children with cough as compared to those without cough and this was statistically significant with a p-value of 0.022, OR = 3.9; [95%CI; 1.19 - 9.62; p = 0.022]. The odds of having a diagnosis of pneumonia on chest ultrasound were 1.9 times higher in children with low oxygen saturation as compared to those with normal oxygen saturation, OR = 1.9 [95% CI: 1.05 - 3.33, p = 0.035].

Variables	Clinical Suspicion Pneumonia N (%)	Final Diagnosis Pneumonia N (%)	Final Diagnosis No Pneumonia N (%)	Bivariate Unadjusted OR (95%CI)	P-Value	Multivariate Adjusted OR (95%CI)	P-Value
Cough	234	90 (38.5)	144 (61.5)	1.6 (0.56, 4.71)	0.371	1.9 (0.63, 6.11)	0.246
Temp (C)	202	75 (37.1)	127 (62.9)	1.2 (0.23, 5.78)	0.868	0.8 (0.14, 4.96)	0.840
SpO2 (<93)	118	55 (46.6)	63 (53.4)	2.1 (1.22, 3.44)	0.006	1.9 (1.07, 3.26)	0.028
Tachypnea	223	87 (39.0)	136 (64.0)	1.7 (0.71, 3.96)	0.236	1.4 (0.58, 3.55)	0.438
Intercostal recession	219	80 (36.5)	139 (63.5)	0.7 (0.33, 1.45)	0.326	0.5 (0.22, 1.11)	0.083
Chest wall indrawing	242	93 (38.4)	149 (61.6)	2.5 (0.52, 12.01)	0.254	2.7 (0.51, 13.96)	0.247
Cyanosis	7	5 (71.4)	2 (28.6)	4.3 (0.82, 22.65)	0.085	4.1 (0.23, 74.03)	0.335
Stridor	5	3 (60.0)	2 (40.0)	2.5 (0.41, 15.40)	0.315	0.6 (0.03, 11.57)	0.723
Altered mentation	6	4 (66.7)	2 (33.3)	3.4 (0.61, 19.0)	0.162	0.6 (0.02, 16.10)	0.755
Inability to feed	11	11 (64.7)	6 (35.3)	3.3 (1.18, 9.23)	0.023	2.0 (0.53, 7.82)	0.297

Table 6b*: The correlation between clinical findings with chest radiography.*

SpO_2: Oxygen saturation.

In bivariate analysis, low oxygen saturation and inability to feed showed a strong associated with CXR with p-values < 0.05. Cyanosis was borderline with a p-value 0.085.

In multivariate analysis, the odds of diagnosing pneumonia with CXR were 1.9 times higher in patients with low oxygen saturation as compared to those with normal saturation. OR = 1.9 [95% CI; 1.07 - 3.26, p = 0.028].

Discussion

Most patients 131 (52%) were male and 121 (48%) were female, showing a slight predilection for males. The highest proportion, 90%, were below 59 months of age (limits from months to 12 years) with an overall mean age of 21.4 (Sd ± 24.2) months, this is in line with the findings of WHO that states pneumonia as a major health threat worldwide and a common cause of death in children especially those < 5yrs of age [1]. This could be because the immune systems of children < 5yrs of age are not fully develop and while the healthiest children can fight the infection with their natural defenses, younger children and those whose immune systems are compromised by chronic medical conditions are at higher risk of developing pneumonia. In this study, 243 (96%) of the patients were fully immunized or had immunization up to date. Since the immunization cards were not reviewed, we do not know if pneumococcal conjugate vaccine (PCV) was on the list of the vaccines the participants had received. The PCV was introduced in Uganda in January 2014 [17]. 213 (84.5%) of the patients did not have known chronic illness. This is important because a child's immune system may be weakened by comorbidities like HIV, CHD, SCD, asthma and malnutrition or under nourishment, especially in infants who are not exclusively breast-fed predisposing them to infections. These baseline demographic characteristics of the patients, however, did not differ much between those with a final diagnosis of pneumonia and without pneumonia, with all the p-values > 0.05.

Majority of the patients 234 (93.0%) had a history of cough, were febrile with 202 (80.2%) having a temp > 37.5C, had intercostal recessions 219 (87.0%) and chest wall indrawing 242 (96.0%). Based on the 2014, WHO criteria for diagnosing pneumonia [3], these findings show that most of the enrolled patients had pneumonia. The other predictors for severe pneumonia were not common with stridor 5 (2.0%), cyanosis 7 (3.0%), altered mentation 6 (2.4%) and inability to feed 17 (6.8%) were not common. These could have been patients who had failed on first-line treatment, according to WHO recommendation and were referred to the center of our study which is a national referral hospital.

Of the 252 patients admitted with clinical suspicion of pneumonia, CUS showed more pulmonary abnormalities consistent with pneumonia in 163 (64.7%) than CXR which was positive for pneumonia in 95 (37.7%) of the same patients. This yield was found to be statistically significant with a p-value < 0.0001 and the findings were similar to studies done by Copetti., *et al*. [15], Parlamento., *et al*. [11], Anne-Sophie., *et al*. [13], Reissig A., *et al*. [16] who found that chest ultrasound was able to demonstrate more features suggestive of pneumonia than chest X-ray (Figure 1 and 2).

Nonoccurrence of positive CUS findings with negative CXR findings could have occurred due to a number of factors; consolidations in the retro-cardiac or sub diaphragmatic which may be invisible on posterior-anterior chest radiographs but may be visible on lateral views which were not done in this study; the ability of CUS to detect very small (subcentimetre) consolidations which are not visible on CXR, as described by Shah., *et al*. [18], as seen in [Figure 3]. Jared., *et al*. [19] also found that CXR had a low sensitivity in early stages of the infection and couldn't demonstrate infiltrates until about 48 hours of the disease manifesting.

The negative CUS findings with positive CXR findings could have occurred due to; consolidations not reaching the pleural surface often located in the perihilar as highlighted by Luri D., *et al*. [20] who found 7 patients with perihilar consolidations on CXR and zero cases on CUS, in his study to evaluate the sensitivity of CUS versus CXR in detecting lung consolidations and pleural effusion; or could be due to consolidations located in hard-to- reach regions with CUS such as retro-scapular, supraclavicular or axillary regions.

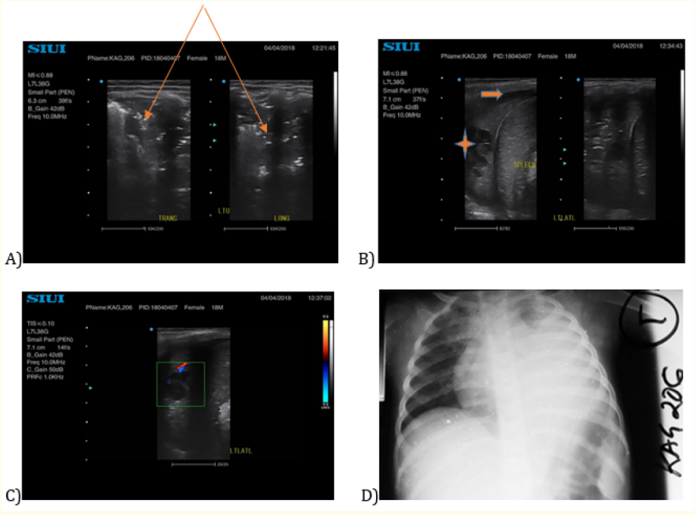

Figure 1: *A case of left lung consolidation and its different features. An 18 months old admitted with pneumonia. A; A sonogram of the left anterior upper region showing a shred sign with dot-like echogenicities representing air bronchograms (arrows). B) Sonogram of the left lateral lower region showing, the diaphragm (echogenic curve), spleen, hypoechoic collection, arrowhead (pleural effusion) and part of the consolidated lung containing sonolucent areas, (star), which have no flow on color doppler in (C), signifying necrosis. D) AP radiograph showing a homogenous opacity in the left middle and lower lung zones forming a positive silhouette sign with the left cardiac border and obscuring the left costophrenic angle.*

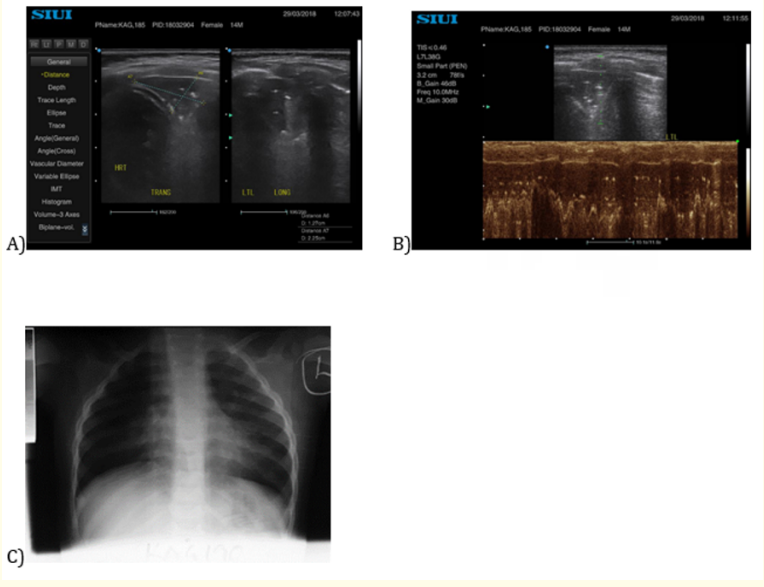

Figure 2: *A 14 months old admitted with pneumonia. A) left paracardiac wedge shaped shred sign with air bronchogram (echogenic foci). B) M-Mode showing dynamic motion of the air bronchograms. C) An AP radiograph showing a radio-opacity forming a positive silhouette sign with the left cardiac border.*

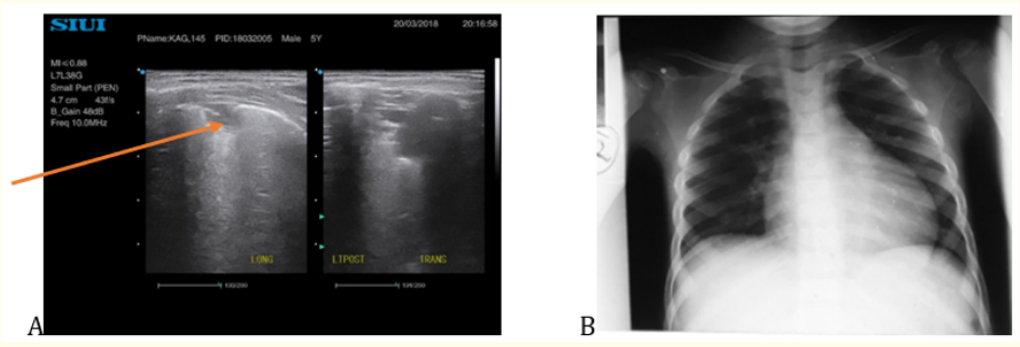

Figure 3: *A case of abnormal CUS and normal CXR. A 5yr old admitted with pneumonia. A; A shred sign seen in the left posterior lower region (arrow). B; Normal lung fields with cardiomegaly.*

Air space disease (consolidations/alveolar process) was a more common radiological pattern than interstitial disease on both CUS and CXR. CUS identified a higher percentage of patients with consolidations, 149 (59.0%) as compared to CXR which identified 82 (32.5%). This was similar to findings by Copetti., *et al.* [21], Boursiani., *et al.* [22] and Caiulo., *et al.* [23] who reported a higher percentage of consolidations detected by CUS as compared to CXR in their studies which were comparing the two investigations.

CUS demonstrated 62 (24.6%) of the interstitial disease cases and CXR 18 (7.1%) These findings differed from a study done by Boursiani., *et al.* [22] who found that CXR was better at detecting interstitial pattern than CUS which was better at detecting alveolar disease with CXR having a sensitivity of 95.5% and CUS at 92.4%. This could be because B-lines are a nonspecific feature of interstitial lung disease that cannot reliably distinguish transudative and exudative causes of interstitial edema or infective from non-infective inflammatory process [24] (Figure 4)

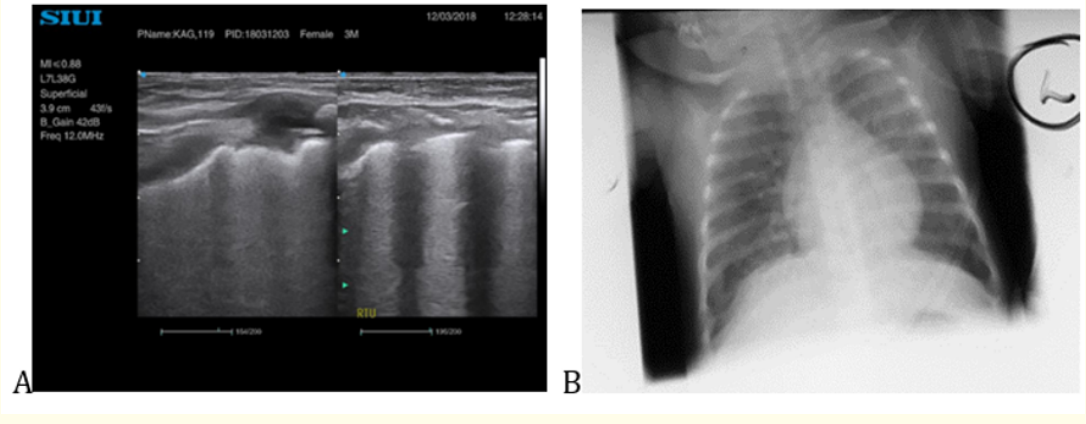

Figure 4: *A case of interstitial disease. A 3-month-old baby admitted with severe pneumonia. A; Sonogram of the right anterior upper region showing a white lung. B; An AP chest radiograph showing bilateral ground glass opacification of both lung fields.*

Most of the radiological pneumonia, in this study, was found in the right lung fields, air space disease more than interstitial process. This is attributed to the anatomical orientation of the right bronchus and consolidations in retrocardiac regions [24].

CUS demonstrated pleural effusion in 29 (12.0%) of the patients compared to 9 (3.6%) by CXR. This is because, CXR can only detect the presence of pleural effusion in patients in the orthostatic position only if the volume of the effusion is at least 200 mL and the sensitivity of this method further decreases in the supine position, whereas ultrasound can detect effusions as small as 20 ml [25]. These findings are comparable to findings by Luri., *et al*. [20] who demonstrated pleural effusion in 15 patients using CUS compared to CXR that showed only 8 patients and Urbankowski., *et al*. [26] found that pleural effusion was demonstrated by CUS in 54.3% of patients, while radiographic signs of pleural effusion were found in only 12.1% of patients.

The sensitivity of chest ultrasound in this our study was 72% [95%CI, 65 - 78], specificity of 67% [52 - 81], PPV 91% [95%CI 85 - 95], NPV 35% [95%CI 25 - 46] with likelihood ratios (LRs) 2.1 [95%CI, 0.8 - 3.3] for positives and 0.4 [95%CI, 0.3 - 0.6] for negatives (Table 4). These results were lower than those in the study done by Lorio G., *et al*. [27] who found that the sensitivity of lung ultrasound was 96.5% (95% CI [82.2% -99.9%]), specificity of 95.6% (95% CI [78.0% - 99.9%]), positive likelihood ratio of 22.2 (95% CI [3.2 -151.2]), and negative likelihood ratio of 0.04 (95%CI [0.01 - 0.25]) for diagnosing pneumonia.

When it was compared to chest X-ray alone, the sensitivity of chest ultrasound improved to 96% (95% CI, 90 - 99), specificity of 54% (95%CI, 46 - 62), PPV of 56% (95%CI, 48 - 64), NPV of 96% (95%CI, 89 - 99). (Table 5). The high sensitivity by CUS in these results, on top of the reasons stated above, could be attributed to the small body habitus and chests in children which enable easy identification of consolidations (which are usually sub-pleuric) though these may also be due to no infiltrative processes like atelectasis (obstructive and compressive) which present like consolidations (particularly in bronchiolitis or asthma). Similar findings were also presented by Esposito., *et al* [9].

In bivariate analysis with CUS, only oxygen saturation < 93% and tachypnea were strongly associated with CUS, with p-values < 0.05. Cough was just borderline with a p-value < 0.1.

In multivariate analysis, the odds of having a diagnosis of pneumonia on chest ultrasound were 3.9 times higher among children with cough as compared to those without cough and this was statistically significant with a p-value of 0.022, OR = 3.9; [95%CI: 1.19 - 9.62; P = 0.022] while the odds of having a diagnosis of pneumonia on chest ultrasound were 1.9 times higher in children with low oxygen saturation as compared to those with normal oxygen saturation. OR = 1.9[95%CI: 1.05 - 3.33; p = 0.035]. These findings were comparable to findings by Chao JH., *et al*. [28] who found a positive correlation between CUS and $SpO_2 \leq 92\%$, with p-value of 0.001, in his study to determine accuracy of CUS in diagnosing pneumonia in children with bronchiolitis.

In bivariate analysis with CXR, low oxygen saturation < 93% and inability to feed showed a strong associated with CXR with p-values < 0.05. Cyanosis was borderline with a p-value 0.085. In multivariate analysis, the odds of diagnosing pneumonia with CXR were 1.9 times higher in patients with low oxygen saturation as compared to those with normal saturation, OR = 1.9 [95% CI: 1.07 - 3.26, p = 0.028].

These findings were comparable to close the findings made by Mark I., *et al*. [29], in a study to associate clinical and history findings with radiographic findings who found that history of chest pain, focal rales, duration of fever, and oximetry levels at triage were significant predictors of pneumonia while the presence of tachypnea, retractions, and grunting were not associated with pneumonia. Hypoxia (oxygen saturation ≤ 92%) was the strongest predictor of pneumonia (odds ratio: 3.6 [95%CI, 2.0 - 6.8), though this was slightly lower in our study. Lynch., *et al*. [30] also found that history of fever, tachypnea, retractions, grunting, rales and decreased breath sounds were associated with radiographic pneumonia.

Ultrasonography of the left lower chest can be challenging, with the combination of spleen and air in the stomach being mistaken for lung consolidation and sonographic air bronchograms. In addition, the thymus has a sonographic appearance with hyper echogenic foci that can be mistaken for lung consolidation [31]. However, no errors were made in mistaking the thymus for lung consolidation. Recognition of these potential pitfalls was included in the pilot study.

There is no published work similar to this study in our setting. This study will bridge the knowledge gap about the use of chest ultrasound to diagnose pneumonia in children in resource limited areas like our setting. Some of the limitations were firstly, the final clinical diagnosis which was used as a reference standard in this study is not the gold standard for diagnosing pneumonia. Computed tomography, CT, of the chest is the best and accurate gold standard for diagnosing pneumonia, particularly for very small lung consolidations, pleural effusions and centrally located. This was however not practical for us to obtain chest CT in children enrolled in this study and is not our standard of care here in MNRH. Secondly, most of the clinical findings were recorded from the medical records/files which were made by the clinicians of different carders at ACU and admission wards. This could explain the possible false positives of those diagnosed with pneumonia clinically. There was no standardization of the gargets used to take the vitals of the patients enrolled in the study.

Conclusion

In conclusion, chest ultrasound has a higher sensitivity than chest X-ray in detection of pneumonia with the commonest radiological sign being consolidations and can therefore be used as a screening tool to diagnose pneumonia. It can also be used as an add on tool, to chest X-ray in cases of equivocal findings.

Secondly, Cough and hypoxia are good correlates to CUS-based pneumonia diagnosis in children with clinical suspicion of pneumonia.

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