THE ACCURACY AND UTILITY OF LUNG ULTRASOUND FINDINGS WHEN COMPARED TO CHEST RADIOGRAPH FINDINGS IN DIAGNOSIS OF PNEUMONIA IN CHILDREN UNDER 12 YEARS AT KENYATTA NATIONAL HOSPITAL

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DECLARATION

I declare that the work contained herein in this proposal is my original idea and has not been presented at any other institution for an academic award to the best of my knowledge.

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ACRONYMS AND ABBREVIATIONS

AP	Aspiration Pneumonia
BTS	British Thoracic Society
CAP	Community-Acquired Pneumonia
CI	Confidence Interval
CT	Computed Tomography
CXR	Chest Radiograph
DDIRM	Department of Diagnostic Imaging and Radiation Medicine
GP	General Practitioners
HAP	Hospital-Acquired Pneumonia
Hib	Haemophilus Influenza Type b
IBM SPSS	International Business Machines Statistical Products and Service Solutions (formerly Statistical Package for Social Sciences)
IDSA	Infectious Diseases Society of America
KDHS	Kenya Demographic Health Survey
KNBS	Kenya National Bureau of Statistics
KNH	Kenyatta National Hospital
KNH/UON-ERC	Kenyatta National Hospital/University of Nairobi Ethics & Research Committee
LUS	Lung Ultrasound
PCP	Pneumocystis Jiroveci Pneumonia
PTB	Pulmonary Tuberculosis
RSV	Respiratory Syncytial Virus
UoN	University of Nairobi
US	Ultrasound

UNICEF	United Nations Children Educational Fund
W.H.O	World Health Organization

DEFINITION OF TERMS

Air bronchogram	Punctate or linear hyperechoic artefacts seen within areas of consolidation.
A-lines	Horizontal repetitive lines parallel to the pleural line. They are normal lung findings on ultrasound.
B-lines	Hyperechoic, ray-like, vertical reverberation artefacts arising from the pleural line. B-lines extend to the bottom edge of the screen, do not fade in intensity and move synchronously with lung sliding.
Dynamic air bronchogram	Denotes inspiratory movement of the air bronchogram and indicates pneumonia differentiating it from resorption atelectasis.
Fluid bronchogram	Anechoic tubular structures along the bronchial tree that develop as a result of bronchial secretions or bronchial obstruction.
Lung hepatisation	Sign demonstrated on B-mode LUS as uniform speckled tissue-like pattern resembling the liver echo pattern. It is a sign of lung consolidation resulting from reflections from alveolar interstitial interfaces due to loss of ling aeration as fluid fills the alveoli.
Lung pulse	Movement of the pleural line in synchrony with the cardiac pulse. Lung pulse is caused by the force of

	cardiac pulsations being transmitted to the lung and hence to the visceral pleura.
Lung sliding	Dynamic sign seen as a "to-and-fro" movement of the pleural line in synchrony with the respiratory cycle indicating a sliding movement of the visceral pleura against the parietal pleura.
Pleural line	A hyperechoic line seen about 0.5 cm below the rib line moving back and forth with respiration in normal lungs on LUS.
Sensitivity	(also called the true positive rate) measures the proportion of actual positives that are correctly identified as such (e.g., the percentage of sick people who are correctly identified as having the condition).
Specificity	(also called the true negative rate) measures the proportion of actual negatives that are correctly identified as such (e.g., the percentage of healthy people who are correctly identified as not having the condition).
Likelihood Ratio	Likelihood ratios are used for assessing the value of performing a diagnostic test. They use the sensitivity and specificity of the test to determine whether a test result usefully changes the probability that a condition (such as a disease state) exists.

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ABSTRACT

Background: Conventional diagnosis of pneumonia relies on clinical history, physical examination and clinically indicated chest radiographs (CXRs). Chest Computed Tomography (CT) scan is used to evaluate complications of pneumonia. CXR and CT scan of the chest are the only standardized acceptable radiological imaging tools. The utility of lung ultrasound (LUS) in the diagnosis of pneumonia has increased in the past two decades owing to its portability ease of administration and lack of ionizing radiation. LUS offers immediate results and can be used repeatedly in the diagnostic assessment of patients with pneumonia.

Aim: The purpose of this study was to assess the utility of LUS as a tool in diagnosing pneumonia in children less than 12 years at Kenyatta National Hospital (KNH) by correlating lung ultrasound and chest radiography findings in patients who have been clinically diagnosed to have pneumonia, using CXR as the reference standard.

Methodology: This was an analytic cross-sectional study carried out at Kenyatta National Hospital (KNH) Department of Radiology following approval from the University of Nairobi-Kenyatta National Hospital Ethics Research Committee (KNH-UoN ERC).

Study Population: The study population included pediatric patients (age 12 and below) with clinically suspected pneumonia and meeting the criteria for chest radiography who present to the KNH radiology department. The study participants were patients clinically suspected with pneumonia in whom a chest radiograph had been performed and informed consent obtained from the parents/guardians and assent from the patients. The time frame between the CXR and LUS was 24 hours or below. Patients with a time frame greater than 24 hours between LUS and CXR, with radiographic results known to principal investigator/sonologist, with non-diagnostic chest radiographs or in whom

parents/guardians declined consent were excluded from the study. A total of 108 patients as per inclusion and exclusion criteria were recruited. A consecutive sampling method was used and written informed consent was sought from parents/guardians of potential study participants. Basic socio-demographic and baseline clinical characteristics were obtained. Chest radiography and lung ultrasound were performed within 24 hours of each other and findings of pneumonia from the two tests were presented using 2X2 contingency tables. The diagnostic accuracy of LUS was evaluated using measures of diagnostic performance including sensitivity, specificity, negative and positive predictive values and was based on chest radiograph as the reference standard. SPSS for Windows version 21.0 statistical software was used to analyze data and results presentation was done using tables, graphs and charts.

Results: A total of 108 children with suspicion of pneumonia underwent CXR and LUS; 56.5% were male, median age was 24 months (IQR 8-84). Radiographic signs of pneumonia were demonstrated in 72/108 children while LUS detected findings consistent with pneumonia in 77 children. LUS showed consolidations in 42.6%, interstitial disease in 23.1%, pleural effusion in 7.4 % and atelectasis in 2.8%. Normal LUS were found in 27 (25%) patients. CXR showed 41.7% consolidation, 26.9% interstitial pattern, 3.7% pleural effusion and 4.6% atelectasis. 27.8 %(30) patients had normal CXR findings. LUS performed better than CXR in detection of consolidations and pleural effusions. CXR showed interstitial disease better than LUS.

The diagnostic performance of LUS with CXR as reference standard showed an accuracy of 87.9%. The sensitivity, specificity, NPV and PPV were 89.1%, 85.3%, 92.9 % and 78.4 % respectively.

Conclusion: This study showed LUS has high accuracy and is not inferior to CXR in the diagnosis of pneumonia in pediatric age group. It thus can be considered as a

replacement of or adjunct to CXR in detection of pneumonia in children without any threat of ionizing radiation.

CHAPTER ONE

1.0 INTRODUCTION

1.1Background

Early diagnosis of pneumonia is vital in the management and prevention of future complications related to the disease. Traditional diagnosis of pneumonia is done by reviewing the clinical history and performing physical examination for presenting signs and symptoms and laboratory investigations (Ayalon et al., 2013). Chest physical examination is not reliable enough to diagnose pneumonia (Wipf et al., 1999).

Differential diagnosis relies on imaging tools such as chest radiography (CXR) and computed tomography scans (CT). CXR is the first radiological investigation that is normally undertaken in the diagnosis of pneumonia followed by laboratory tests. Developing countries such as Kenya do not have widespread access to imaging diagnostic tools like CXR and CT scan that can be employed in the diagnosis of pneumonia(Shah et al., 2013).

Lung ultrasound is not considered a standard diagnostic imaging tool in the diagnosis of pneumonia. However, the recent improvement in the utility of lung ultrasound (LUS) as a diagnostic tool has increased. LUS has several advantages over CXR and CT scan of the chest such as affordability, portability, sensitivity, accuracy and safety (Reissig et al., 2012)(Reissig et al., 2012). According to a study by Balk et al. LUS can diagnose pediatric community-acquired pneumonia with significantly higher sensitivity and similar specificity compared to chest radiography The findings of the meta-analysis study indicated that LUS had a sensitivity of 95.5% and specificity of 95.3% while CXR had a sensitivity of 86.8% and specificity of 98.2% (Balk et al., 2018). These

advantages make LUS an ideal candidate as the first choice imaging diagnostic tool for suspected cases of pneumonia alongside CXR.

This study purposed to identify the spectrum of lung ultrasound findings of pneumonia, determine their prevalence, correlate them to chest radiograph and compare the accuracy of LUS in the diagnosis of pneumonia in children less than 12 years of age at Kenyatta National Hospital with CXR as the reference standard. For ethical considerations, chest CT scan was not utilized as a reference/gold standard.

1.2 Statement of the Problem

Pneumonia is the largest infectious cause of death in children in the world. Pneumonia is a high burden disease contributing to 15 per cent of deaths in children less than 5 years globally in the year 2017. (WHO, 2016, Pneumonia Factsheet). At KNH 8.9% of all admissions under 12 years in the year 2018 were pneumonia-related (KNH records).

The current main diagnostic means in identifying pneumonia infection is clinical history and physical examination. Clinical history such as cough, fever, and tachypnea cannot be relied on alone to make an accurate diagnosis of pneumonia(Shah et al., 2013). In addition, physical examination such as auscultation is unreliable (Margolis & Gadomski, 1998) (Wipf et al., 1999).

CXR is currently the only acceptable diagnostic imaging tool that is used in complementing clinical history and physical examination. CXR is indicated in hospitalized patients for management of CAP, treatment failure, checking for complications, suspected or documented hypoxemia or significant respiratory distress and screening for PTB (Bradley et al., 2011) (Andronikou et al., 2017).

CT scan is used in complementing CXR findings however it is an expensive imaging modality. Recent WHO findings have concluded that more than two-thirds of the global population lacks radiographic imaging facilities (Safdar, 2019). This has prompted general practitioners (GP) to over-rely on symptoms and signs in making their diagnosis. Lack of specific diagnostic tools has forced GPs to broaden antibiotic regimens in the management of pneumonia cases leading to increased antibiotic resistance of pathogens (Moran et al., 2012).

LUS offers simplicity, affordability, safety together with a high degree of specificity and sensitivity in the diagnosis of pneumonia (Caiulo et al., 2013) (Reissig et al., 2012)(Iuri et al., 2009). It can therefore be used as an alternative diagnostic imaging modality to complement clinical signs and physical examination. LUS also offers radiation-free follow up of patients with positive radiological findings of pneumonia (Caiulo et al., 2013).

CHAPTER TWO

2.0 LITERATURE REVIEW AND BACKGROUND

2.1 Pneumonia Disease Burden

Pneumonia is an infectious disease of global importance. The incidence of pneumonia globally is 0.29 episodes per child per year which equates to about 155 million new cases annually. The incidence in developed countries is 0.06-0.1 episodes per child per year while it's three times higher in developing countries. Seventy-four per cent of the world's pneumonia cases occur in only fifteen countries that include Kenya (WHO, 2016, Pneumonia Factsheet).

The majority of children less than 5 years of age die as a result of childhood pneumonia, with global childhood mortality standing at 29% while developing countries contributing 21%. Mortality rates for children below five years of age range from 50 to 60 per 1000 live births in most developing countries, one-fifth of these are attributed to pneumonia (UNICEF, 2015a, Level and Trends in Child Mortality). In Kenya, the childhood mortality rate is 52 per 1000 with pneumonia contributing majorly (KDHS, 2014).

2.2 Classification of Pneumonia

The traditional classification of pneumonia is based on the anatomy of the lung parenchyma. Further classification of pneumonia can be based on the causative agent, place of transmission and manner of infection (Cilloniz et al., 2016).

2.2.1 Classification Based On Anatomy of Lung Parenchyma

2.2.1.1 Lobar Pneumonia

Lobar pneumonia affects part or the whole lobe of a lung. It is mostly caused by bacterial infection. It occurs as a result of the inflammation spreading through the Khon and Lambert pore channels and affecting the whole lobe of the lung. The most common causative agents are Streptococcus pneumonia, Hemolytic streptococci and Staphylococcus aureus. Other pathogens that are less frequently associated with lobar pneumonia are *Haemophilus influenza* and *Klebsiella pneumonia* (Y. D. Singh, 2012).

2.2.1.2 Bronchopneumonia

Bronchopneumonia results from an acute bacterial infection that affects the terminal bronchioles. It presents itself as a patchy consolidation upon imaging. It is mostly caused by spreading exudates that follow the endobronchial pathway. Bronchopneumonia is mostly associated with old age and chronic debilitating conditions. The most common pathogens associated with bronchopneumonia are Streptococci, *Haemolytic streptococci*, *Haemophilus influenza*, *Staphylococcus areas, Pseudomonas pneumonia and Klebsiella pneumonia* (Y. D. Singh, 2012).

2.2.1.3 Interstitial Pneumonia

Interstitial pneumonia is mostly caused by mycoplasma or viral infection. The disease presents itself as patchy inflammations in the interstitial tissues of the lung. The infection is restricted in the interstitial tissue and does not produce exudates that spread

into the alveoli. Mononuclear filtrates and septal oedema of the alveoli is another important characteristic of interstitial pneumonia. Some of the common causative agents responsible for interstitial pneumonia are respiratory syncytial virus, adenovirus, influenza virus, and cytomegalovirus. Other less common pathogens include Coxiella and Chlamydia (Y. D. Singh, 2012).

2.2.2 Location of Infection

Pneumonia can also be classified according to the location where the infection was acquired. The two main types of pneumonia in this category are community-acquired pneumonia (CAP) and hospital-acquired pneumonia (HAP).

Pneumonia

Etiology

Pneumonia is the most common category of pneumonia. Pneumonia is one of the major categories of pneumonia contracted outside the health care setting. It responds well to treatment. CAP is more common than HAP and can be further divided into typical CAP and atypical CAP (Cilloniz et al., 2016).

Typical CAP

Typical bacteria associated with CAP include *Streptococcus pneumonia*, *Moraxella catarrhasis* and *Haemophilus influenza*. The most common viral etiologies of CAP are influenza and rhinovirus [31]. Bacteria is the main causative agent of typical CAP. These bacterial species are *S pneumoniae, M catarrhalis* and *H. influenza*. Physical examination presentation of typical CAP includes rales and tachypnea. Increased tactile fremitus, presence of egophony and bronchial breath sounds are also associated with CAP another important characteristic is decreased tactile fremitus. Emphysema may also be responsible for dullness on the chest percussion (Cilloniz et al., 2016)

Atypical CAP

Atypical CAP mostly presents subacute and indolent symptoms. CAP may present as subtle pulmonary findings. It appears as nonlabor infiltrates when viewed X-ray imaging. Other non-pulmonary manifestations may include otalgia and diarrhoea. Pathogens frequently associated with CAP include *Mycoplasma pneumoniae* and *Chlamydophila pneumonia*. Respiratory viruses such as influenza A, influenza B, rhinovirus, respiratory syncytial virus (RSV), human metapneumovirus, adenovirus 4, adenovirus 7, parainfluenza virus. Rare viruses that have also been known to cause atypical CAP include coxsackievirus, echovirus, coronavirus, hantavirus, cytomegalovirus, epstein-barr virus, human herpesvirus 6, herpes simplex, varicella-zoster virus. Fungus associated with atypical CAP include *Chlamydophila psittaci*, *Coxiella burnetti*, *Francisella tularensi*. Endemic fungi that occasionally cause chronic pneumonia and subacute pneumonia associated with atypical CAP include *Histoplasma capsulatum, Coccidioiides immitis, Cryptococcus neorformans,* and *Neoformans gattii*.

Mycobacteria that associate with atypical CAP are *Nontuberculous mycobacteria* and *Mycobacteria tuberculosis* [29].

2.3 Diagnostic Imaging Modalities for Detecting Pneumonia

2.3.1 Chest Radiography (CXR)

Studies have demonstrated that general practitioners and primary care physicians rely on CXR to diagnose pneumonia or exclude the diagnosis of pneumonia. However current guidelines advise against its routine use in the outpatient setting. International guidelines such as the British Thoracic Society (BTS)(Harris et al., 2011) recommend chest radiography in hospitalized children with severe illness or suspected complications. The guidelines for managing CAP in children may differ from place to place bearing in mind that guidelines assist clinicians in making the right decisions appropriate in their setting.

In developing countries chest radiography is used to rule out tuberculosis as the cause of lower respiratory symptoms. (Andronikou et al., 2017). According to the Kenya pediatric protocol 2016, CXR is recommended for treatment failure if none had been done prior and to look for complications such as empyema, effusion and cavitation.

According to a study by Speets et al., CXR was able to influence the diagnosis of more than 56% of the outcomes of patients with suspected pneumonia. In the study, CXR was able to rule out suspicion of pneumonia in more than 50% of the suspected pneumonia cases. In addition to ruling out or confirming the diagnosis of pneumonia, CXR was able to change patient management in 69% of the cases (Speets et al., 2006). Patient management is especially important because it changes antibiotic prescriptions and prevents the administration of a broad range of antibiotics that can eventually lead to antibiotic resistance.

A similar study by Simpson et al found out that CXR procedure influenced more than 48% of the patient's outcome during diagnosis of pneumonia (Simpson et al., 1998). The outcomes of the two studies were different because in the diagnosis of pneumonia Simpson et al used radiographic evidence while in the case of Speets et al suspicion of pneumonia was based on clinical signs and physical examination.

Pneumonia manifests in different ways when viewed in CXR. It depends on the stage of progression and level of inflammation. Mild cases or early onset of pneumonia are difficult to diagnose using CXR. This makes the positive diagnosis of pneumonia very low. According to a study conducted by Speets et al., 18% of the cases were diagnosed with CXR while in the case of Lieberman et al, only 7% of the cases were diagnosed by CXR (Speets et al., 2006)(Lieberman et al., 2003) (Lieberman et al., 2003).

The non-specific nature of radiology findings as well as the wide spectrum of causative agents is a major concern in determining imaging findings. Pneumonia infections caused by *Pneumocystis carinii* is normally characterized by diffuse alveolar consolidation can also manifest themselves as dense consolidations with pleural effusions in 5-10% of the cases (Boiselle et al., 1999).

2.3.2 Radiographic Visualizations of Pneumonia

There is a spectrum of changes seen on chest radiographs consistent with the clinical diagnosis of pneumonia. Important radiographic visualizations that may identify pneumonia range from lung tissue consolidations, interstitial patterns (simple pneumonia) to empyema and necrotizing pneumonia (complicated pneumonia). The absence of these visualizations cannot be used as a basis to rule out the presence of pneumonia. Broncho pneumonia, lobar pneumonia and interstitial pneumonia are the

most common classifications of CXR presentations (Klein, FACR, Emily N. Vinson MD, William E. Brant MD, Clyde A. Helms MD, 2018).

Lobar pneumonia is most often the result of specific bacterial infections such as Haemophilus influenza type b (Hib), S pneumonia and Klebsiella pneumonia. In this pattern of disease, the inflammatory exudate begins within the distal airspaces, spreads to produce non-segmental homogenous consolidation which may eventually involve an entire lobe. Because the airways are usually spared, air bronchograms are common and volume loss is unusual. In children, pneumococcal pneumonia may present as a spherical opacity ("round pneumonia") mimicking a parenchymal mass. Multilobar pneumonia can be a result of different bacteria and suggests a more severe disease (Klein, FACR, Emily N. Vinson MD, William E. Brant MD, Clyde A. Helms MD, 2018).

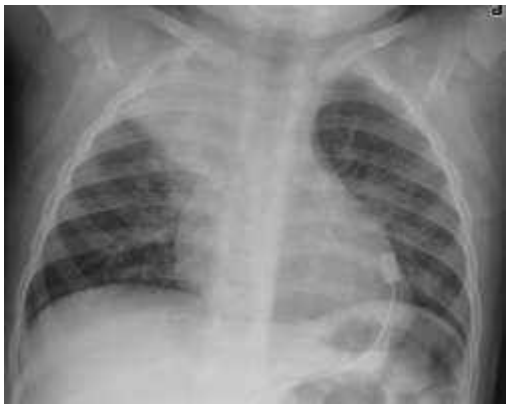


Figure 1: Right Upper Lobe Consolidation

Bronchopneumonia is the most common pattern of disease and is typically associated with infections due to staphylococcus aureus, gram-negative bacteria and some fungi. Radiological features of bronchopneumonia differ according to disease severity. In the early stages, peribronchial thickening and ill-defined airspace opacities can be present; non-uniform patchy areas of consolidation affecting several lobes reflect more severe

disease. With coalescence of affected areas, bronchopneumonia may have an appearance similar to lobar pneumonia (Klein, FACR, Emily N. Vinson MD, William E. Brant MD, Clyde A. Helms MD, 2018)

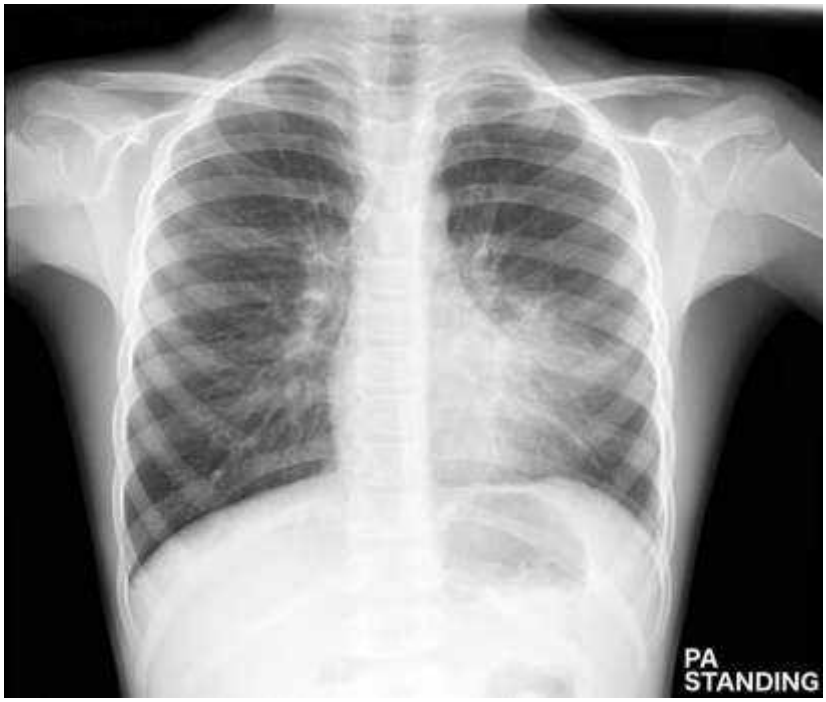


Figure 2: Bronchopneumonia 8 year Old

Case courtesy of Rad_doc, Radiopaedia.org, rID: 47997

Interstitial pneumonia is mainly associated with viral infections such as influenza virus and RSV. Some pathogens are linked to certain CXR abnormalities. The "viral" CXR is characterized by hyperinflation, peribronchial thickening and poorly defined perihilar opacities. *Pneumocystis jiroveci* pneumonia (PCP) is characterized by fine, reticular interstitial opacification usually bilateral and perihilar (Klein, FACR, Emily N. Vinson MD, William E. Brant MD, Clyde A. Helms MD, 2018)

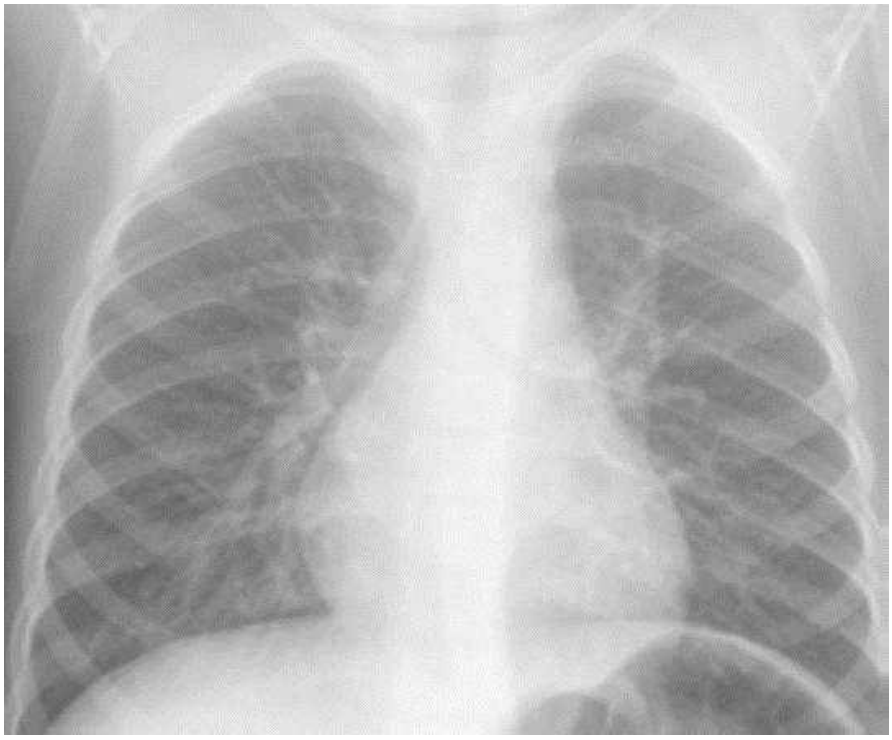


Figure 3: Chest Radiograph Showing Interstitical Pneumonia

Source (O'Grady et al., 2014).

Lung complications of pneumonia may produce characteristic radiologic findings. These may be acute or chronic and include pleural effusion, empyema, pulmonary abscess and necrotizing lung. Effusion associated with pneumonia is known as para pneumonic effusion. Peripheral parenchymal infection may produce an exudative pleural effusion due to pleural inflammation that extends into pleural space resulting in empyema. The CXR can diagnose para pneumonic fluid but not empyema. Loculated effusions may not be easily distinguished from peripheral lung abscesses. Lung abscesses appear radiologically as cavities typically with thick walls, inner smooth margin and air-fluid level.(Klein, FACR, Emily N. Vinson MD, William E. Brant MD, Clyde A. Helms MD, 2018) (King & Thomson, 2002) (Müller, 2001). Necrotizing pneumonia in the early stages have the appearance of small lucencies in a consolidation

later developing to larger cavities (Müller, 2001). CT is superior to CXR in detecting small cavities and abscesses (Donnelly & Klosterman, 1998).

2.3.3 Limitations of Chest Radiography

Chest radiography is two dimensional, thus may lead to summation shadows and obscuration of abnormalities by the heart, mediastinum diaphragm and other structures (Iuri et al., 2009). Furthermore, radiographic visualizations suggestive of pneumonia can be altered by patient-specific factors such as age, underlying diseases and immune status. In addition, obtaining a quality chest radiograph for interpretation in the context of pediatric pneumonia is problematic especially in developing countries that face challenges of quality assurance (Spijker et al., 2014). Interpretation of chest radiographs is subjective with interobserver variability noted between clinicians, between clinicians and radiologists and between radiologists(Williams et al., 2013a; Xavier-Souza et al., 2013b). To reduce interobserver variability the WHO designed standardized criteria for pediatric chest radiograph interpretation (Organization, 2001). However, the absence of abnormality on CXR does not rule out pneumonia and abnormal CXRs may be considered normal(Elemraid et al., 2014). Furthermore, CXRs cannot be reliably used in distinguishing bacterial and viral pneumonia. A systematic review of 13 studies that sought to determine the radiological differentiation between viral and bacterial pneumonia of children under18 years concluded that the accuracy of CXR was not clinically useful. (Lynch et al., 2010; Swingler, 2000). The advantage of CXR lies in the fact that it exposes patients to relatively low doses of radiation compared to CT scans. It is also relatively cheaper and available compared to CT scans (Franquet, 2001).

2.3.4 Chest CT scan Visualizations of Pneumonia

CT scan is the second line of imaging diagnostic tool that is employed to give additional information in instances where CXR findings are indeterminate. This is because a CT

scan produces higher resolution images with better contrast than CXR (Sharma et al., 2007). Visualizations that can help to identify the presence of pneumonia include the presence of consolidations, pleural effusions and interstitial patterns. When these visualizations are detected by CT scans they might be indicative of pneumonia. However, the absence of these visualizations does not rule out the absence of pneumonia.

CT imaging signs of pneumonia present themselves as alveolar consolidations in the sub pleural area. The consolidations appear with blurred margins that are often contained near fissures. In some instances, the consolidation forms into systematized segments with opacities that can affect more than one segment of the lobe. Ground glass opacities is another important indication of pneumonia. The opacities are normally located adjacent to alveolar consolidations. They form as a result of the partial filling of the alveoli by fluid. The most common cause of ground-glass opacities is a bacterial infection of the *Streptococcus pneumoniae* type(Beigelman-Aubry et al., 2012).

CT scan is the most sensitive diagnostic radiology tool for the detection of pneumonia. It provides excellent resolution of the lung that produces good quality diagnostic images which are highly detailed. It also gives good tissue contrast due to greater differences in attenuation of the different lung tissues. The different attenuation is caused by changes in parenchyma densities that result from inflammatory processes of infection. Another major advantage is that a CT scan can produce cross-sectional images(Franquet, 2001). High-resolution CT scan that makes use of thin-section CT scans has made it possible to recognize secondary pulmonary lobule images. According to Gruden et al., a CT scan of the chest is the best imaging modality that can best be able to detect consolidations, air spaces, air bronchograms, ground-glass opacities and lobular distributions (Gruden et al., 2013).

CT scan is especially helpful in determining the presence of occult pneumonia and other abnormalities such as empyema, pleural effusion and lymphadenopathy. It can also be used as diagnostic follow up of patients undergoing treatment to determine lung abscesses for a patient who does not respond well to treatment. CT is also employed in the exclusion of fungal pneumonia and pulmonary embolism. CT scan produces high contrast images with greater details and better diagnostic value than both CXR and LUS.

The main advantage of CT scan is that produces good quality diagnostic images with high contrast visualizations that provide greater detail than CXR.

2.3.5 Limitations of CT

The main draw backs are that a CT scan employs a relatively high amount of radiation doses. Despite representing just 11% of all the radiological procedures done in the united states, CT accounts for up to 67% of all the collective effective doses resulting from X-ray radiation(Mayo et al., 2003). This imaging modality is not recommended for children. The relatively high amount of radiation employed in this imaging modality can increase the susceptibility of developing cancer later in life. In this study chest, CT scan will not be used at all due to the risks involved.

CT scan is considered to be an expensive imaging modality and not easily available to the general population in developing countries. The other drawback is that CT equipment is bulky making it impossible to use it at the point of care or perform the procedure at the bed side.

2.3.6 Lung Ultrasound

Diagnosis of pneumonia using ultrasound was first described by Weinberg et al in 1986(Weinberg et al., 1986). One of the major barriers that have prevented its

widespread use was visualization difficulties caused by the presence of air in the lungs. However, recent findings of some studies have demonstrated that lung ultrasound is superior to CXR in the diagnosis of pneumonia (Iuri et al., 2009)(Reali et al., 2014).

2.3.7 Lung Ultrasound Nomenclature

Lung ultra sound acoustic artefacts are normally observed as lines with the specific designation. These lines have international designations in ultrasound nomenclature. The internationally designated lines observed in lung ultrasound are used for investigating several conditions affecting the lung parenchyma.

Pleural Line

Under normal conditions, an echogram pattern of the normal pleura appears as a hyperechoic line seen about 0.5cm below the rib line that moves in tandem with breathing movement (Francisco Neto et al., 2016). The hyperechoic line is known as the pleural line. The pleural line serves as an important landmark in the diagnosis of pneumonia and other thoracic conditions using ultrasound.

Lung sliding is dynamic demonstrating the horizontal movement of the pleural line. The absence of lung sliding also known as the lung pulse suggests the possibility of a pneumothorax.

A- Lines

Reverberation artefacts are known as A-lines. A-lines appear as horizontal, parallel lines that are evenly spaced between each other(Francisco Neto et al., 2016). A-lines are normally observed in the healthy lung parenchyma. When the lung parenchyma is infected with pneumonia the A-lines disappear. The presence of B-lines can also cause the A-lines to disappear.

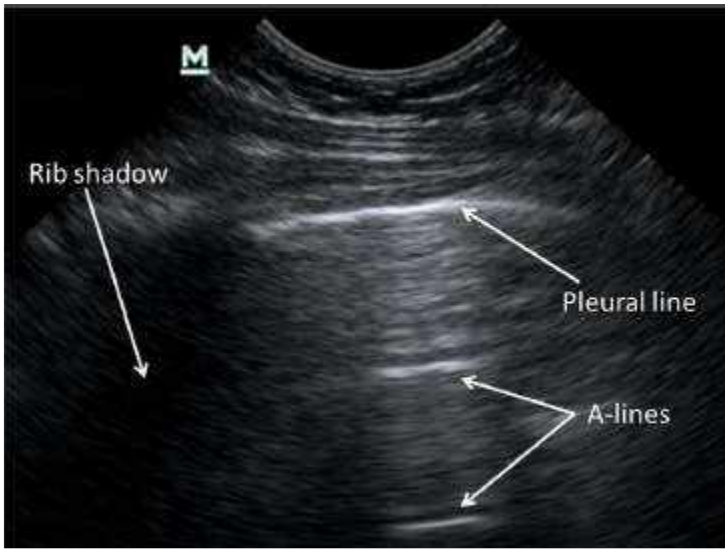


Figure 4: Hyperchoic Pleural Line, A-Lines is a 16-month old Girl

(Stadler et al., 2017)

B-Lines

These are small lines that are clearly defined. They also appear as comet tails that are perpendicular to the pleural lines. The B-lines move during the respiration process in tandem with the pleural line. The presence of B-lines erases A-lines. The presence of B-lines is suggestive of pulmonary edema or interstitial disease (Wongwaisayawan et al., 2016). Less than 3 B-lines are considered normal findings.

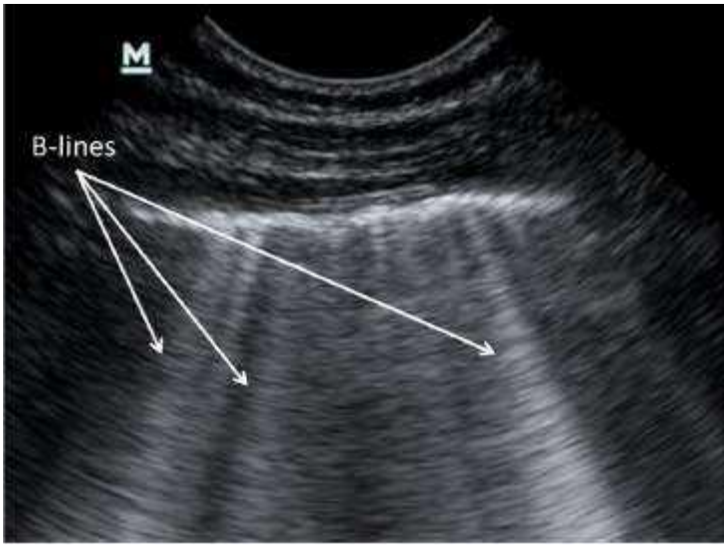


Figure 5: B-Lines representing Interstitial Pattern in a 2-Year-old Boy with Pneumonia

(Stadler et al., 2017)

C- Lines

The presence of hypoechoic focal images denotes c- lines(Francisco Neto et al., 2016). A **C line** indicates lung consolidation. The dark part of the image adjacent to the pleura represents a small focal area of consolidation. Deep into that, there is an area of "white-out" which represents a lung that is still aerated but has a very high fluid content. They do not show the presence of any gap in the visceral pleural.

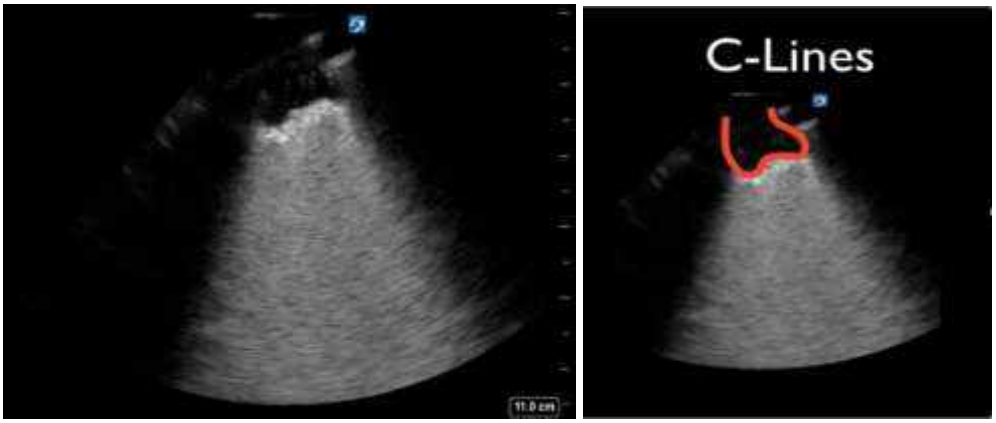


Figure 6: Showing C Line

E Lines

These are lines observed in an echogram that indicate the presence of trapped gas in the subcutaneous space. E line is used to represent emphysema. The E lines do not move in tandem with respiration movement. The presence of E lines erases A-lines. They are known as false B lines(Francisco Neto et al., 2016).

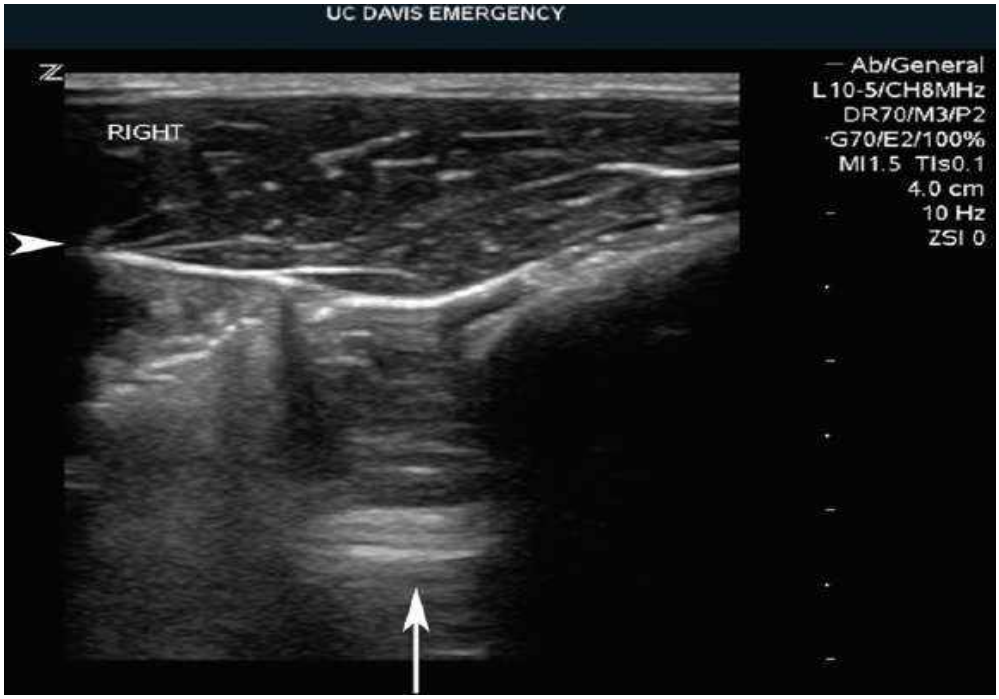


Figure 7: E-Line (arrow) arising from emphysema (arrowhead)

(Fox, 2011)

Z lines

Z lines are poorly defined vertically oriented lines originating from the pleural line and do not reach the margin of the screen. These lines do not move in tandem with respiratory movement. The presence of Z lines does not erase A-lines and do not have pathologic meaning. Z lines are sometimes confused with B lines(Francisco Neto et al., 2016).

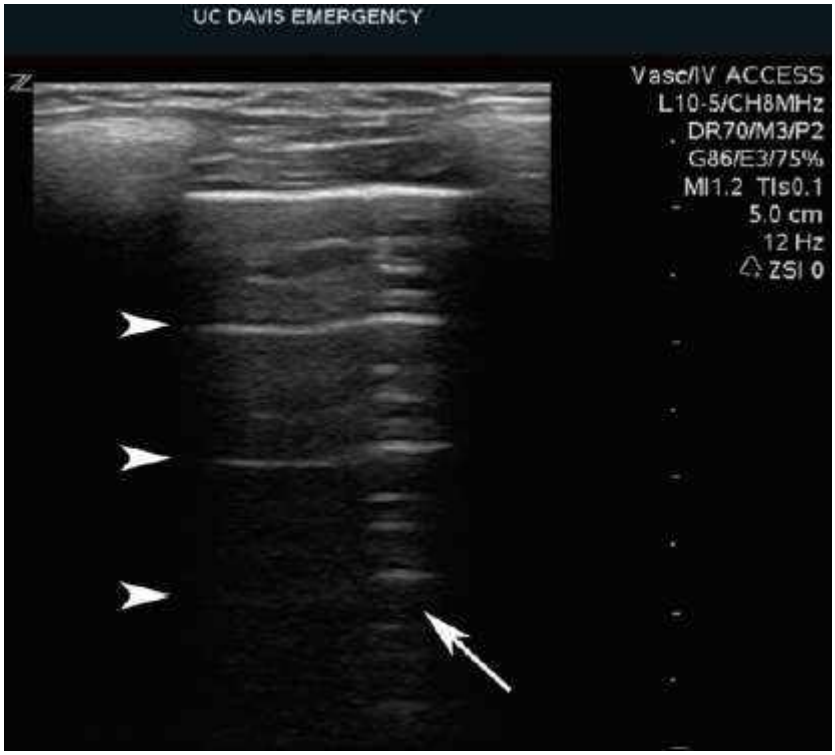


Figure 8: Normal Lung showing A-Line Artifacts (arrowheads) and Z-Line (arrow) Vertical Lines

(Fox, 2011)

2.3.8 Sonographic Visualizations Suggestive of Pneumonia

Imaging visualizations that are indicative of pneumonia are lung consolidations, interstitial patterns and pleural effusions. Other findings that indicate the presence of pneumonia are comet-tail artefacts, fluid bronchograms, air bronchograms, heterogeneous echo texture, hepatization of the lung tissue, irregular and serrated margins, tree-shaped vascular pattern hypoechoic regions with different shapes and sizes (Ho et al., 2015)(Volpicelli et al., 2012). In a recent study by Iorio et al, the incidence of sonographic signs of pneumonia was; air bronchograms at 92.8%, superficial fluid bronchograms at 75%However, the absence of these visualizations does not rule out the presence of pneumonia.

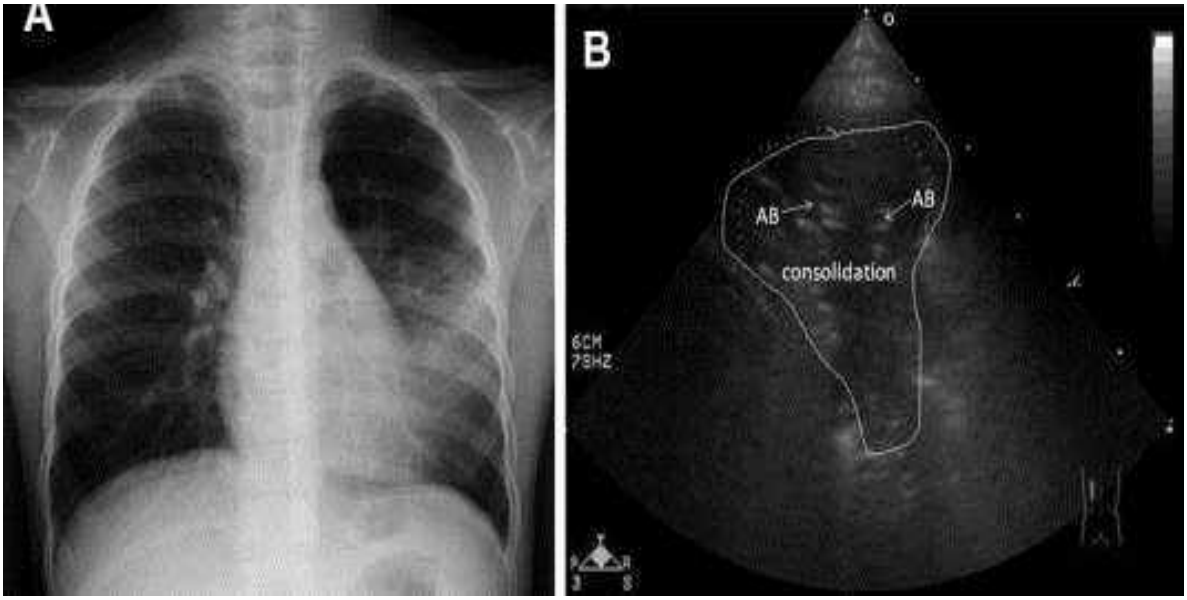


Figure 9: The Images of a 10- year old Boy

On the left (A) Radiograph showing lingular and lower lobe consolidation. On the right (B) lung ultrasound picture illustrating lower lobe consolidation**.**

(Source Ho et al. 2014).

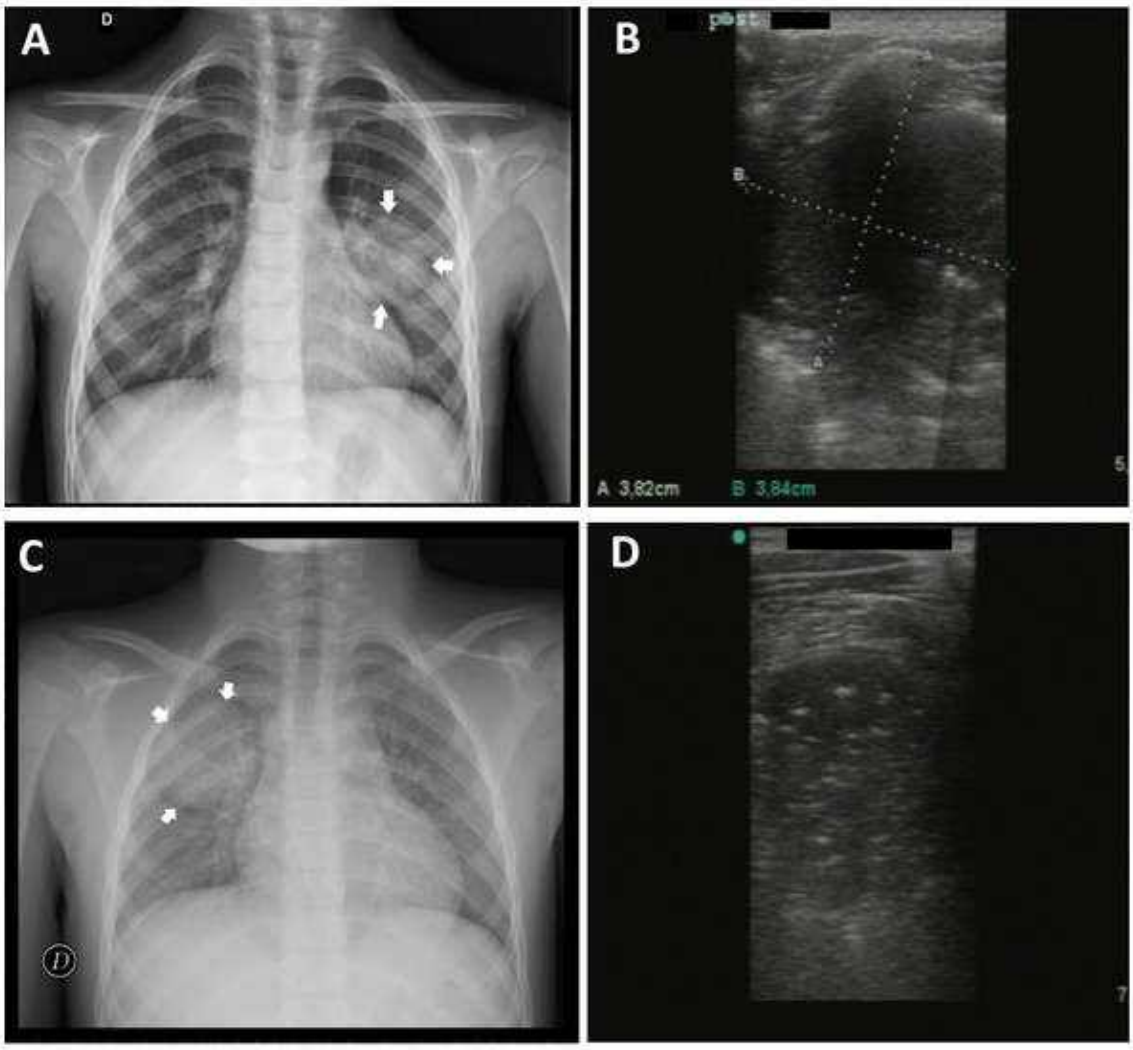


Figure 10: Case 1 above shows a 5-year old Boy with Pneumonia detected by CXR (A) and Ultrasound (B). The 2 case is of round Pneumonia detected by CXR in (C) and Ultrasound Image in (D)

Source (Iorio et al., 2015)

2.3.9 Limitations of Lung Ultrasound

The presence of air in the lungs is one of the limiting factors for the utility of LUS in the diagnosis of pneumonia. Aerated lungs cause an acoustic mismatch of the lungs with the surrounding tissues. Complete reflection of the sound waves prevents the creation and visualization of lung parenchyma imagery (Volpicelli et al., 2012).

Pulmonary abnormalities that do not reach the pleura cannot be easily detected by LUS. This is in the case of pulmonary consolidations that are surrounded by air cavities and thus cannot be detected by LUS. Some different etiologies of the pleural syndrome such as the sub pleural space cannot be detected by LUS. In addition, 8% of pneumonic lesions may appear inconspicuous when visualized by LUS. This should however not be criteria for excluding pneumonia (Gargani & Volpicelli, 2014)(Reissig et al., 2012).

Ultrasound is an operator-dependent imaging modality and previous studies have shown the correlation between accuracy of findings and operator experience.

Ultrasound examinations take considerable longer compared with chest radiography Lung ultrasonography (LUS) can be a simplified or comprehensive exam and can usually range from 5 to 15 minutes while a simple chest X-ray on an able and willing patient could take less than 1 minute (S. Singh et al., 2018).

2.4 Comparison of Accuracy of the Diagnostic Imaging Modalities in Diagnosis of Pneumonia

LUS has traditionally been used for the diagnosis of biopsy guided procedures, thoracentesis and investigation of pleural effusions. Recent studies have shown that ultrasound is effective in the diagnosis of pneumonia (Reissig et al., 2012)(Urbankowska et al., 2015) (Yilmaz et al., 2017). Portability and ease of administration have increased the utility of LUS in the diagnosis of pneumonia.

According to a study by Balk et al. LUS can diagnose pediatric community-acquired pneumonia with significantly higher sensitivity and similar specificity compared to chest radiography The findings of the meta-analysis study indicated that LUS had a sensitivity of 95.5% and specificity of 95.3% while CXR had a sensitivity of 86.8% and specificity of 98.2% (Balk et al., 2018). See Table 1.

Esposito et al conducted studies to determine the utility of point of care LUS in the diagnosis of CAP. The study included 103 children and used CXR as the reference standard. The study found out that LUS had a high sensitivity of 97.9% and specificity of 94.5% in detecting CAP at the point of care. In addition, the study revealed a positive LR of 94.0% and a negative LR of 98% according to the study LUS performed better in identifying pleural effusions compared to CXR (Esposito et al., 2014).

Boursiani et al compared the diagnostic accuracy of LUS and CXR in children with suspected pneumonia. The study included 69 patients with clinical pneumonia who underwent both CXR and LUS. The study revealed that CXR failed to reveal the diagnosis in 3 patients. In these particular cases, LUS showed consolidation in 2 and interstitial pneumonia in the other. The study was noted to have a relatively small sample. Despite this, the study concluded LUS is at least as accurate as CXR in the diagnosis of pneumonia (Boursiani et al., 2017).

Chest CT scan has been demonstrated in the literature to be the gold standard in lung evaluation. Several studies comparing the accuracy of LUS and CXR have been made with the CXR values acting as reference standards in determining the utility of LUS in the diagnosis of pneumonia. However, some studies have used CT values as the reference standard values when comparing LUS and CXR.

Table 1: Study Characteristics and Diagnostic Performance of LUS

Study	Year	Reference	Ages	Patient Number		Sensitivity (95%CI)	Specificity (95%CI)	PPV (95%CI)	NPV (95%CI)
Boursiani	**2017**	**Clinical, CXR**	**6mo-12yrs**	**69**	**LUS**	**93.9%**	**100%**	**100%**	**42.9%**
					CXR	**95.5%**	**100%**	**100%**	**50%**
Caiulo	**2013**	**Clinical, CXR**	**1yr-16yrs**	***102**	**LUS**	**98.9%**	**100%**	**100%**	**92.9%**
					CXR	**91%**	**100%**	**100%**	**61.9%**
Ianniello	**2016**	**Clinical, CXR**	**3yrs-16yrs**	**84**	**LUS**	**98.4%**	**100%**	**100%**	**95.8%**
					CXR	**77.0%**	**100%**	**100%**	**62.2%**
Iorio	**2015**	**Clinical,**	**2mo-12.5yrs**	**52**	**LUS**	**96.6%**	**95.7%**	**96.6%**	**95.7%**

Source: (Balk et al., 2018)

		CXR			**CXR**	**86.2%**	**95.7%**	**96.2%**	**84.6%**
Reali	**2014**	**Clinical,**	**0-16yrs**	**107**	**LUS**	**93.8%**	**96.2%**	**98.7%**	**86.2%**
		CXR			**CXR**	**81.5%**	**92.3%**	**97.1%**	**61.5%**
Shah	**2013**	**Clinical,**	**0-21yrs**	**209**	**LUS**	**89.6%**	**96.3%**	**87.8%**	**93.4%**
		CXR			**CXR**	**75%**	**100%**	**100%**	**93.1%**

Ambroggio et al., conducted a study comparing the accuracy of LUS and CXR in the diagnosis of childhood pneumonia. He used CT scan as the gold standard to compare the utility of CXR and LUS in the diagnosis of pneumonia. According to the study sensitivity in detecting pleural effusions, lung consolidations and interstitial disease were similar in both CXR and LUS. However, the study found out that CXR had more specificity compared to LUS. The study concluded that CXR and LUS are comparable in detecting consolidations and pleural effusions. LUS was found to be less accurate in detecting interstitial patterns compared to CXR (Ambroggio et al., 2016).

2.5 Study Justification

Currently, chest radiography is the only standard diagnostic imaging tool accepted by WHO guidelines in the diagnosis of pneumonia (Ayalon et al., 2013)(Harris et al., 2011). The reliability of Lung ultrasound as a diagnostic imaging tool with the ability to accurately diagnose pneumonia has been demonstrated extensively in the literature(Reali et al., 2014)(Boursiani et al., 2017). In a meta-analysis, lung ultrasound was found to be superior to chest radiography in the diagnosis of pneumonia with a sensitivity of 95.5% and specificity of 95.3% compared to CXR which had 86.8% and 98.2% respectively(Balk et al., 2018).

The many advantages associated with lung ultrasound compared to other imaging modalities are its portability, accuracy, safety from ionizing radiation and ease of use. Currently little or no studies have been done in Kenya to determine the utility of LUS in the diagnosis of pneumonia. This study hopes to investigate the feasibility and accuracy of using lung ultrasound as a diagnostic tool in detecting pneumonia among children. It will also be beneficial to clinicians to have alternative imaging investigations safe for their patients. It will add to the growing body of evidence of scientific knowledge on lung ultrasound diagnosis of pneumonia.

2.6 Objectives of Research

2.6.1 Broad Objective

- To determine the accuracy and utility of lung ultrasound findings when compared to chest radiograph findings in diagnosing pneumonia in children under 12 years at KNH.

2.6.2 Specific Objectives

- To determine the prevalence of lung ultrasound findings in children under 12 years at KNH.
- To correlate the lung ultrasound findings with chest radiograph findings.
- To determine the effectiveness of lung ultrasound in diagnosing pneumonia by calculating the sensitivity, specificity, positive predictive value and negative predictive value of LUS using chest radiograph as the reference standard.

CHAPTER THREE

3.0 METHODOLOGY

3.1 Study Design

The study was a cross-sectional analytic study.

3.2 Study Area

The study was conducted at the Radiology department in Kenyatta National Hospital, a National teaching and referral hospital located in Nairobi Kenya.

3.3 Study Population

The study population was pediatric patients (age 12 and below) with clinically suspected pneumonia presenting to the KNH radiology department.

3.4 Eligibility Criteria

3.4.1 Inclusion Criteria

- Patients diagnosed with suspected pneumonia who presents to the KNH radiology department for chest radiography.
- Children aged 12 years and below
- Consent for study by parents/guardians
- Assent for study by children older than 6 years

3.4.2 Exclusion Criteria

- Time frame greater than 24 hours between LUS and CXR procedures.
- Radiographic results known to the principal investigator/sonologist.
- Expiratory chest/non-diagnostic (poor technique) chest radiographs
- Parents/guardians who will decline to consent.

3.5 Sample Size Determination

The sample size was calculated using the (Daniel, 1999) formula;

$$n = \frac{Z^2 x\ P(1-P)}{d^2}$$

Sample size assumptions

n = Desired sample size

Z = value from standard normal distribution corresponding to desired confidence level (Z=1.96 for 95% CI)

P = Sensitivity of lung ultrasound in the diagnosis of pneumonia (estimated at 92.42%, a recent similar study by Boursiani et al found the sensitivity of LUS in the diagnosis of pneumonia in children between age 6months -12 years to be 92.42%(Boursiani et al., 2017).

d = desired precision (0.05)

$$n_0 = \frac{1.96^2 x\ 0.9242(1-0.9242)}{0.05^2} = 107.648$$

A sample size of **108** patients was used for the study.

3.6 Sampling Procedure

A consecutive sampling of all patients presenting to the radiology department Kenyatta National Hospital was repeated until the desired sample size was achieved.

3.7 Recruitment and Consenting Procedures

The primary point of participants' entry into the study was the waiting bay, X-ray department at KNH. Once identified, the nature and purpose of the study was clarified to potential participants and/or parents/guardians. Written informed consent was sought from those who voluntarily agree to participate.

3.8 Data Collection and Management

3.8.1 Research Instruments

An interviewer-administered questionnaire was used to obtain information such as age, sex, history of illness and comorbidities. The principal investigator or trained assistant ensured both CXR and lung ultrasound is performed for each participant.

3.8.2 Imaging Protocols

The procedure of Performing Chest Radiograph

All patients underwent either posterior-anterior or anteroposterior chest radiography. This procedure was performed by radiographers at the department. The lateral view was not be obtained under the guidelines provided by the British Thoracic Society for the management of pneumonia in children (Harris et al., 2011). Radiography was analyzed by two consultant radiologists who are blind to the LUS results. Chest radiograph findings were classified as follows:

1. Normal
2. Interstitial pattern (interstitial pneumonia)
3. Consolidation (alveolar pneumonia)
4. Atelectasis
5. Pleural effusion
6. Combination of the above findings except normal

Lung Ultrasound Procedure

Patients who had undergone CXR earlier were only enrolled if the time difference between the two procedures was within 24 hours. The LUS was done by the principal investigator/trained assistant and results were verified by a consultant radiologist who was blind to the radiographic results of the patients.

Equipment: The procedure was conducted using commercially available ultrasound machines (Philips) equipped with 6-13 MHZ linear probe.

Patient positioning: Patients were examined laterally and posteriorly in a seated position and anteriorly in a supine position as described by Coppetti and Cattarosi[41]

A systematic examination of all intercostal spaces was performed. LUS was assessed for the number, location, shape, size and breath-dependent movement of consolidations.

Technique: The probe was placed on the thorax. The reference point is the ribs in an oblique, parallel and perpendicular configuration. The thorax was divided into an anterior part that covers regions from parasternal to the anterior axillary line; the lateral part that covers regions between anterior and posterior axillary lines; posterior part covering regions from the posterior axillary line to the paravertebral line.

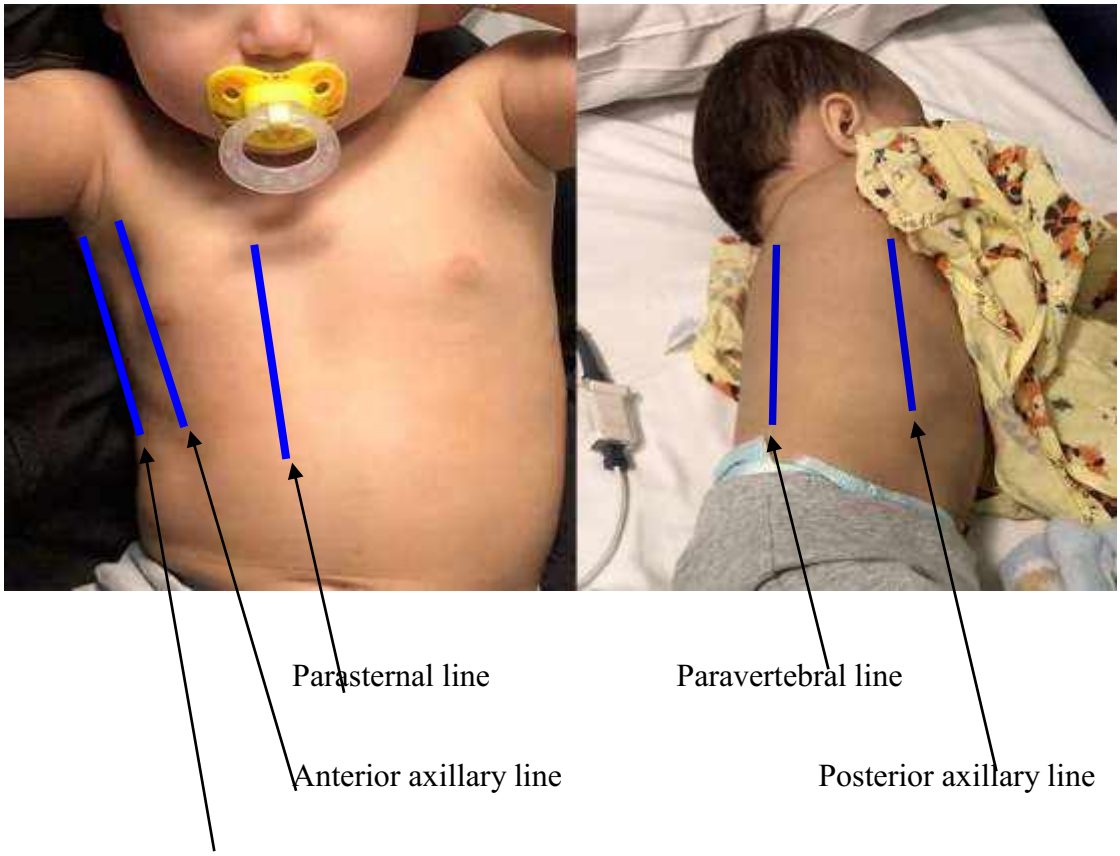


Figure 11: Showing Anterior, Lateral and Posterior Scanning Regions

Posterior axillary line

The presence of pneumonia was confirmed by confluent B lines (>3), consolidations (ill-defined hypoechoic area with air bronchograms, fluid bronchograms, increased vascularity on colour Doppler), atelectasis and pleural effusion.

LUS findings were classified as follows:

1. Normal (A-lines, lung sliding sign)
2. Interstitial pattern (more than 3 B-lines at a scan or coalescence of B-lines)
3. Consolidation (with air bronchograms or fluid bronchogram and vascularity depiction with the application of colour Doppler mode)
4. Atelectasis
5. Pleural effusion
6. Combination of some of the above findings except normal

Lung consolidations was defined as sub pleural hypoechoic regions with poorly demarcated margins while air bronchograms was defined as hyperechoic linear regions present within the hypoechoic lung that appears as consolidation.

3.9 Ethical Considerations

Ethical review and approval was sought before study commencement from the University of Nairobi-Kenyatta National Hospital Ethics Research Committee and authorization to carry out the study was sought from Kenyatta National Hospital administration.

Study procedures were thoroughly explained to the participants and/or parent/guardian, including their voluntary participation, their right to withdraw without any consequences to their management, the lack of ionizing radiation associated with LUS and disclosure of any unknown pathologies detected on LUS to their primary physicians. Subsequently written informed voluntary consent was sought from those

who have agreed to their participation. No incentives or inducements were used to lure patients to participate in the study.

There was no additional cost for the LUS study to the patient. The principal investigator uses his portable ultrasound machine and consumables (ultrasound gel, thermal paper).

Detection of additional or incidental pathologies during the study was disclosed to primary physicians for further management.

Lung ultrasonography as an additional imaging modality is safe and has no ionizing radiation. Study participants were not exposed to ionizing effects of chest CT scan, since CXR was used as the reference standard.

Confidentiality was maintained throughout the study. The data collection forms used neither contained the names of the patients nor their identification numbers. All participants' data was confidential and under restricted access. Data was stored in a password-protected computer and physical records were kept in a locked, secure cabinet during the study period.

3.10 Data Management

All data collection forms were reviewed for accurate entries. Collected data was put into a secure password-protected computer. Back-up copies were stored on flash disks and/or an external drive which remains in the sole custody of the principal investigator.

Filled data collection forms were stored by the principal investigator in a secure locked cabinet for verification during analysis.

Collected data was coded and entered in the International Business Machines Statistical Products and Service Solutions (formerly Statistical Package for Social Sciences) for

Windows software version 21.0, which was used both as a database and for data analysis.

Participants were described using age, gender and clinical information including duration of illness and comorbidities.

Lung ultrasound findings of each hemi thorax in the study participants were categorized as normal (A-lines, lung sliding sign), interstitial pattern (more than 3 B-lines at a scan or coalescence of B-lines), consolidation (with air bronchograms or fluid bronchogram and vascularity depiction with the application of colour Doppler mode), atelectasis and pleural effusion.

Chest radiograph findings of each hemi thorax in the study participants were categorized as normal, interstitial pattern (interstitial pneumonia), consolidation (alveolar pneumonia), atelectasis, pleural effusion or a combination of the above findings.

The prevalence of selected lung pathologies was determined by univariate analysis. This involved frequency distributions, percentages and graphical representation for categorical variables, and descriptive statistics (means, median and standard deviations and interquartile range) for continuous or discrete variables.

Correlation between LUS and chest radiograph was done using 2x2 contingency tables

Diagnostic accuracy was evaluated utilizing measures of diagnostic performance including sensitivity, specificity, negative (NPV) and positive predictive values (PPV) through cross-tabulation of LUS and CXR findings.

3.11 Dissemination of Results

The results of the study were disseminated to DDIRM, the University of Nairobi library and KNH. The results were also used to generate a scientific manuscript for publication in a peer-reviewed journal and presented in scientific conferences and seminars.

3.12 Study Limitations

Studies have shown operator experience, as well as training and skill directly impact ultrasound examination. In this study, the principal investigator is a senior resident and LUS was done under the supervision of an experienced senior consultant radiologist. Moreover, lung ultrasound was performed following a standardized protocol and methodology for each patient.

Research bias might have been introduced where the principal investigator was aware of findings before LUS evaluation and vice versa. In this study, the investigator performed LUS evaluation before the review of CXR findings and reviewed all findings with the consultant radiologist.

Chest CT scan is viewed as the gold standard for thoracic imaging. However, in consideration of the aforementioned associated risks of chest CT scan, CXR was applied as the reference standard for evaluation of the diagnostic accuracy of LUS. This might have presented a limitation as CXR has shown lower sensitivity and specificity in the diagnosis of lung and pleural pathology when compared to CT scans.

CHAPTER FOUR: RESULTS

From January to June 2020, 108 children met the inclusion criteria. Covid 19 patients were not included in the study. Out of the 108 participants, 61 were male (56.5%) and 47 were female (43.5%) with a median age of 24 months and Interquartile range (IQR) of 8-84 months.

Baseline characteristics are summarized in Table 2.

Table 2: Baseline Characteristics of Patients

(*N*=108)

Patient characteristics	n (%)
Demographic data	
Male	61(56.5)
Age(median(IQR) (months)	24(8-84)
Clinical History	
cough	85(78.7)
fever	91(84.3)
Difficulty in breathing	58(53.7)
Maternal Education	
Primary	22(20.4)
Secondary	55(50.9)
Tertiary	31(28.7)
Area of Residence	
Urban	74(68.5)
Rural	34(31.5)

Radiographic findings suggestive of pneumonia were demonstrated in 74 children. Lung ultrasound detected abnormalities consistent with pneumonia in 71 participants, summarized in Table 3. Other concomitant pathological findings such as effusion and atelectasis were also detected. Findings were not mutually exclusive and some patients had multiple abnormalities identified.

Table 3: Prevalance of CXR and LUS Findings

N=108

CXR findings, n (%)		
Normal		30(27.8)
Consolidation		45(41.7)
Interstitial pattern		29(26.9)
Pleural effusion		4(3.7)
Atelectasis		5(4.6)
LUS findings, n (%)		
Normal		27(25)
Consolidation		46(42.6)
Size ≥ 1cm	39(84.8%)	
Size < 1cm	7(15.2%)	
With air bronchogram	42(91.3%)	
Without air bronchogram	4(8.7%)	
Interstitial pattern		25(23.1)
Pleural effusion		8(7.4)
Atelectasis		3(2.8)

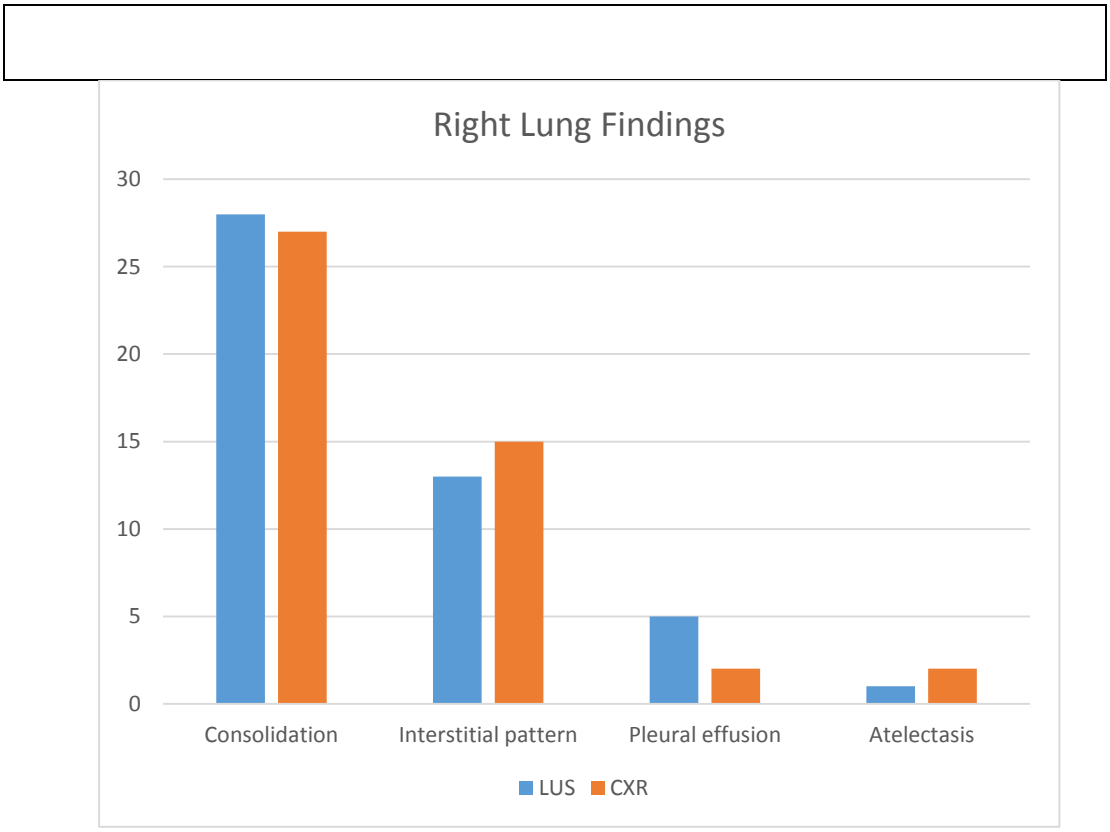
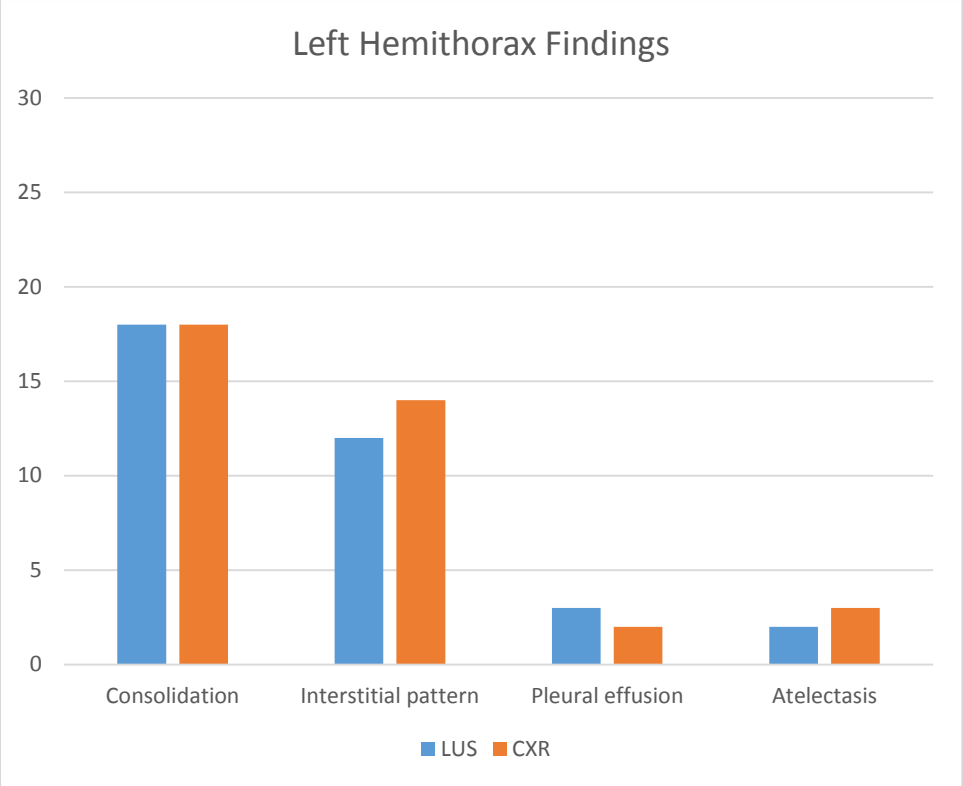


Figure 12: Distribution of Chest Radiograph and LUS Findings



Eight children with normal LUS examination had an abnormal CXR 5 showing interstitial pattern and 3 with consolidation. CXR failed to reveal the diagnosis in 5 cases. Lung ultrasound depicted consolidation in 4 of them and interstitial pneumonia in the other.

Forty-five of 74 were classified as positive for primary end-point consolidation (considered as obvious typical alveolar pneumonia) under the WHO criteria for standardized interpretation of pediatric chest radiograph for diagnosis of pneumonia. Hypoechogenic lung lesions (42 with positive air bronchograms) representing pneumonic consolidations were found in 46 patients of whom 7 had lung consolidations less than 10mm in size.

Interstitial lung ultrasound pattern was identified in 23.1%(25), while CXR detected more at 26.9%.

Associated pleural effusions were identified in 8 cases, 4 more than those seen by CXR.

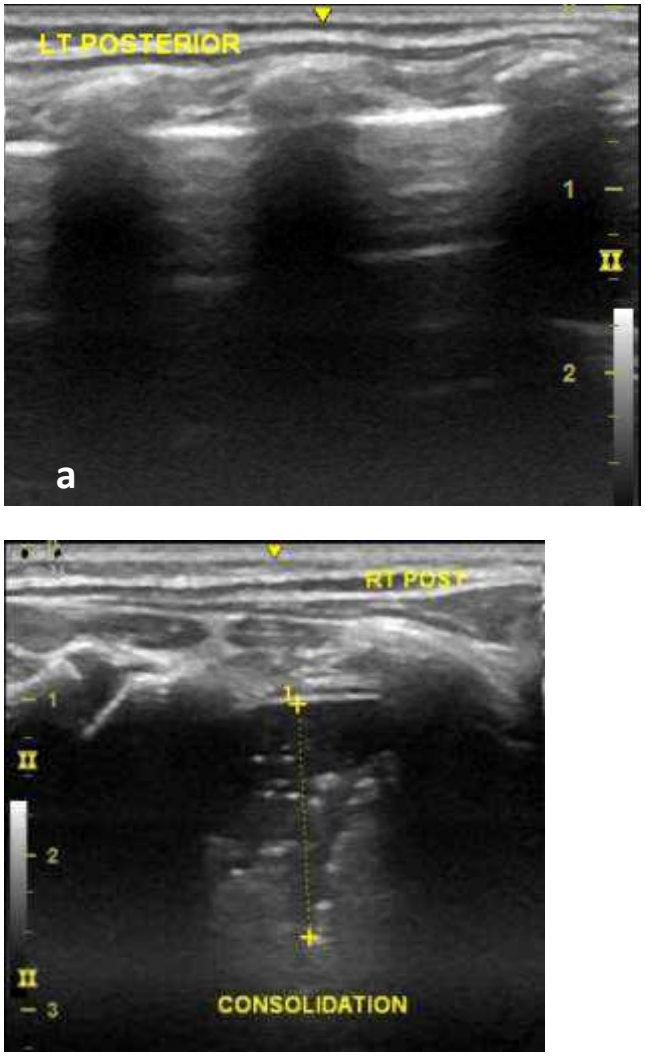


Figure 13: (a) Normal Lung, (b) Scattered and branching dot-like echogenic air bronchogram seen within subpleural consolidation

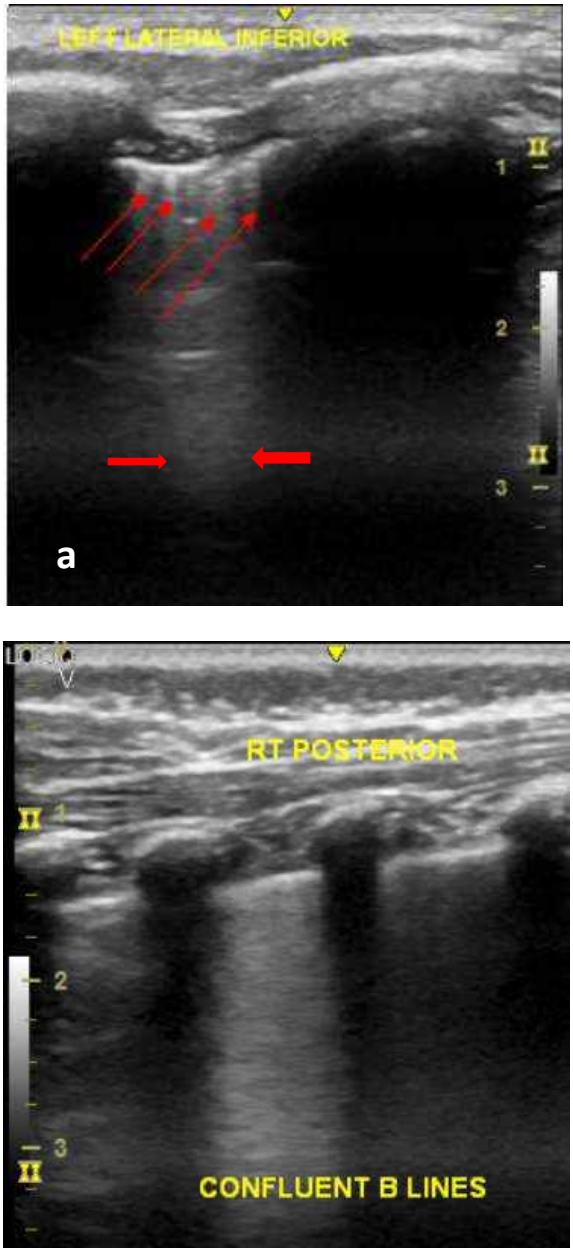


Figure 14: Interstitial disease pattern (a) Multiple B lines (red arrows), (b) confluent B lines

Table 4: Comparison of CXR and LUS in the Diagnosis of Consolidation

	LUS						
CXR	Positive	Negative	Total	Sensitivity	Specificity	PPV	NPV
Positive	42	3	45	89.2%	92.0%	91.3	95.1
Negative	4	59	63				
Total	46	62	108				

CXR, chest radiograph; LUS, lung ultrasound; PPV, positive predictive value; NPV, the negative predictive value

The Sensitivity for above is 93.3%, Specificity is 93.7%, PPV is 91.3%, NPV is 95.2% and Diagnostic accuracy is 93.5%, Cohen's Kappa, k=0.867 ($p<0.001$)

Table 5: Comparison of CXR and LUS in the Diagnosis of Interstitial Pneumonia

	LUS						
CXR	Positive	Negative	Total	Sensitivity	Specificity	PPV	NPV
Positive	24	5	29	82.7%	98.7%	96	93.9
Negative	1	78	79				
Total	25	83	108				

CXR, chest radiograph; LUS, lung ultrasound; PPV, positive predictive value; NPV, the negative predictive value

The Sensitivity for above is 82.8%, Specificity is 98.7%, PPV is 96.0%, NPV is 94.0% and Diagnostic accuracy is 94.4%, Cohen's Kappa, k=0.852 ($p<0.001$)

Applying CXR as the reference standard, the prevalence of pneumonia in our sample was 68.5%. There were five false-positive and 8 false-negative LUS results. According to the above results, lung ultrasound showed in comparison to CXR a sensitivity of 89.1%, specificity of 85.3%, a positive predictive value of 92.9% and a negative predictive value of 78.4% in the detection of pneumonia.

Table 6: Pneumonia Patient Classification by LUS (using CXR as a reference Standard)

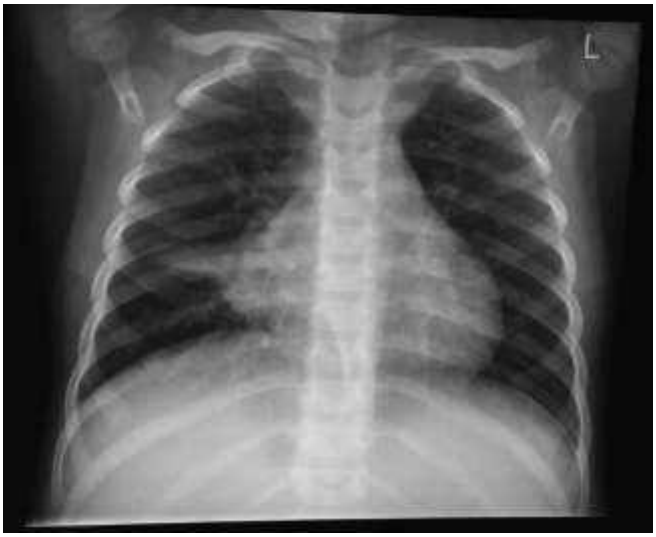
	LUS						
CXR	Positive	Negative	Total	Sensitivity	Specificity	PPV	NPV
Positive	66	8	74	89.1%	85.3%	92.9	78.4
Negative	5	29	34				
Total	71	37	108				

CXR, chest radiograph; LUS, lung ultrasound; PPV, positive predictive value; NPV, the negative predictive value

The diagnostic accuracy is 87.9% i.e. (66+29)/(66+5+8+29)

Reference cases

1-year-old boy with cough and fever 1 week



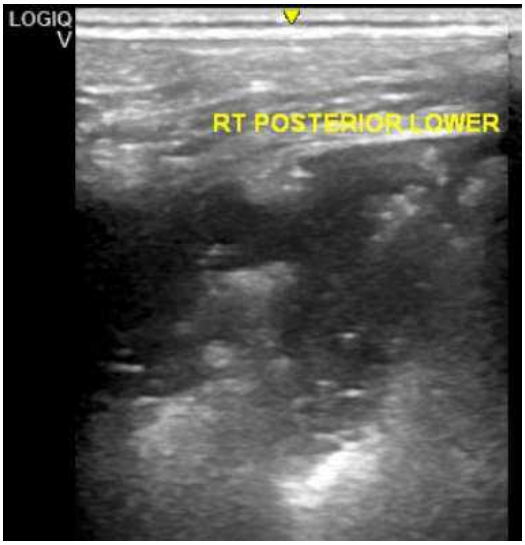


Figure 15: AP Chest Radiograph and Transverse Thoracic Scan

Irregular hypoechoic subpleural consolidation with a scattered dot-like echogenic air bronchograms in the posterior region of the right lung compatible with pneumonia. Corresponding chest radiograph shows a right pericardiac consolidation.

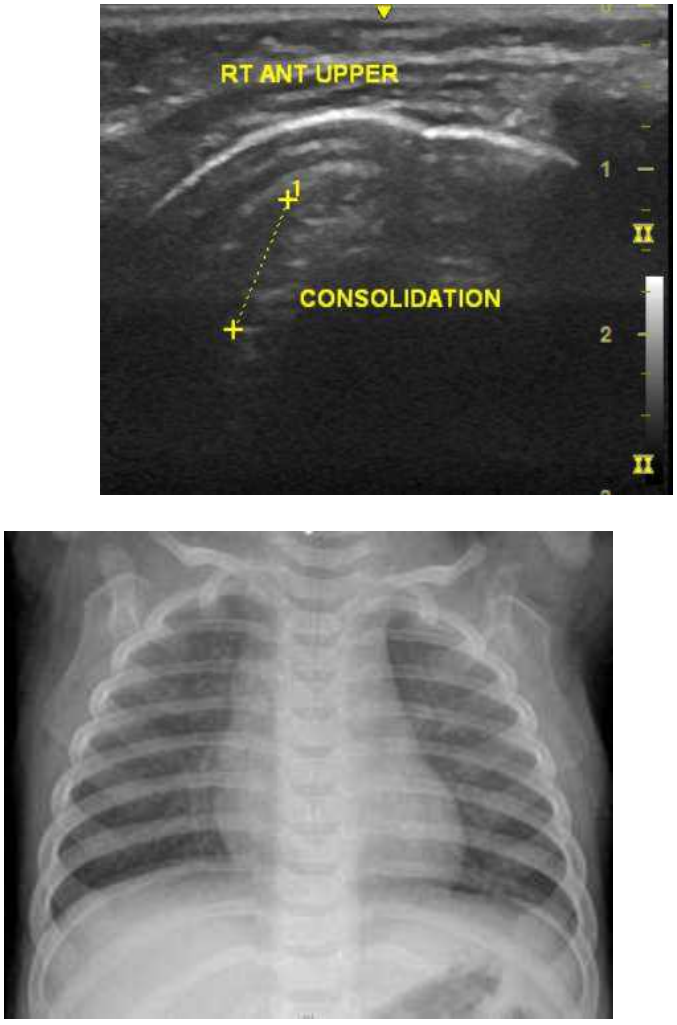
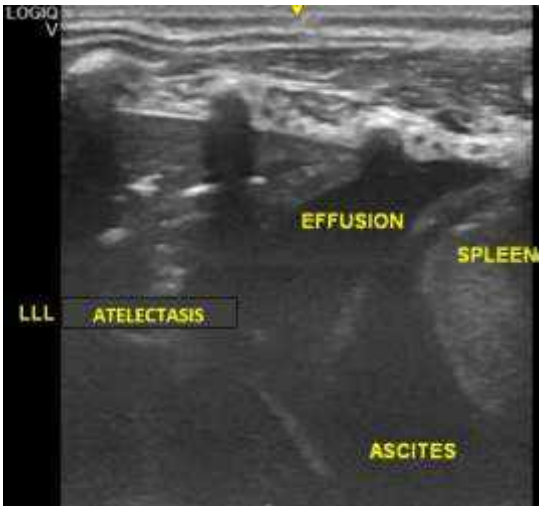


Figure 16: Transverse Thoracic Ultrasound Scan showing an irregular subpleural Consolidation measuring 0.86cm. Chest X-Ray of the same patient was normal

6-year-old complaining of cough, fever



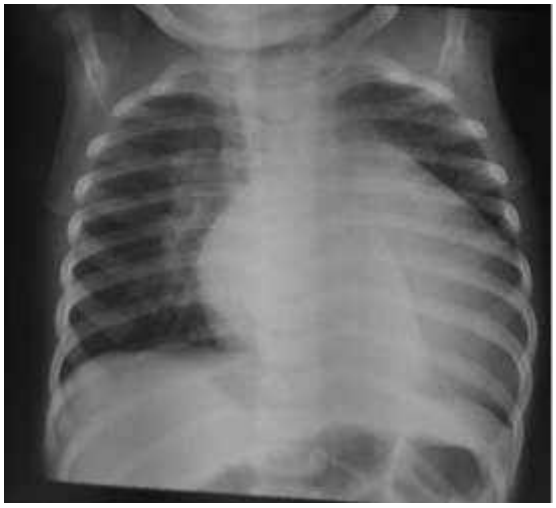


Figure 17: US Image Lower Anterior Region of the Left Lung Showing a Large Pleural Effusion adjacent to an area of Hepatization along with crowded linear echogenic air bronchograms indicating atelectatic lung

The spleen and ascites are also seen. Chest radiograph of the same patient shows

the pleural effusion with left lower lobe collapse.

CHAPTER FIVE: DISCUSSION

In our study, we demonstrated that LUS is an accurate and reliable imaging tool in identifying findings denoting pneumonia in children. LUS addresses the concerns about the potentially harmful effects of ionizing radiation from chest radiography by offering safe, low-cost imaging modalities with reproducible results in diagnosing pneumonic processes.

The sensitivity and specificity of LUS in identifying pneumonia in our study was 89.1% and 85.3% respectively. This was slightly lower than other studies that showed a sensitivity of 92%-100% and specificity 94%-100%(Esposito et al., 2014)(Urbankowska et al., 2015)(Boursiani et al., 2017). This may be explained in part by the fact that we used an imperfect reference standard, CXR. Boursiani et al. and Urbankowska et al. used ex-post diagnosis of pneumonia based on initial clinical findings, laboratory tests, radiographic results and clinical course as the diagnostic reference standard. Chest radiography interpretation has inherent intraobserver and interobserver variability. Xavier-Souza et al found agreement between 2 reporting pediatric radiologists to be 78.7% and concordance for consolidation 86.7% ($k = 0.683$) (Xavier-Souza et al., 2013a). CT would be a more precise reference standard especially for very small lung consolidations detected by LUS but not by CXR. CT would allow identification of centrally located pneumonia that may be missed by LUS. A study by Saraya et al. evaluating the diagnostic performance of LUS using chest CT as reference included 56 children who required CT for clinical reasons. In that study, LUS showed high sensitivity and specificity of 72.2% and 95% respectively when compared to the gold standard, CT(Saraya & El Bakry, 2017).CT however cannot be used as first-line due to high radiation, high cost and unavailability in some regions.

LUS detected consolidations in 4 patients which were not seen on CXR. These apparent "false positives" were among the 7 sub centimeter consolidations we found in our study. Shah et al reported that sub centimeter consolidations could go undetected on CXR((Shah et al., 2013). In addition, chest radiograph detection of consolidation is restricted in certain lung regions such retro cardiac and lung bases. In this study, LUS failed to detect 3 consolidations that CXR confirmed in perihilar locations. Literature has shown that LUS does not effectively detect deep-seated consolidations or consolidations in inaccessible lung regions such as subscapular, which results in false negatives (Iuri et al., 2009).

Interstitial pattern of radiographic findings often seen in viral pneumonia was seen in 26% of children similar prevalence to that reported in the literature in radiographs of children with clinically defined pneumonia (Mathew et al., 2015). LUS failed to pick interstitial patterns in 5 patients which were perihilar as confirmed on CXR.

In our study, LUS detected more cases of pleural effusion (8) compared to CXR (4) similar to a study by Samson et al 2016. Literature has shown ultrasound can detect very small effusions at the costophrenic angles especially in children (Volpicelli et al., 2012)

Twenty-five per cent (27) of patients had normal LUS scans compared to 30 who had normal radiographic findings. In a similar study by Samson et al prevalence of radiographic pneumonia was lower; out of 200 children with clinically suspected pneumonia, only 85(42.5%) were found to have pneumonia. In that study, however, pneumonia was defined by the presence of consolidation and effusion without the inclusion of interstitial pattern (Samson et al., 2018). Our study was cross-sectional and clinical follow up was not included to come up with the final diagnosis. The majority

of our patients were already on treatment at the time of imaging which could account for the normal findings across the two modalities.

Strengths and Limitations

This study highlights the usefulness and accuracy of LUS as a diagnostic tool in detecting lung abnormalities in children with suspected pneumonia. It aids in confirmation of pneumonia by offering immediate results taking a relatively short time to perform. In recent years there is growing evidence of the utility of LUS in diagnosing and follow up pediatric pneumonia. To our knowledge, few studies have been conducted in Kenya and Africa to assess the accuracy and utility of lung ultrasound findings in comparison to chest radiograph findings in the diagnosis of pneumonia in children.

In our region, LUS is rarely used in the diagnosis of pneumonia hence this study sets up a baseline for future studies and clinical application in hospitals where ultrasound is now commonly available.

LUS lacks ionizing which is of greater concern in the pediatric population who are more susceptible to induction of cancer(Wakeford, 2013).

However, there were certain limitations in our study. The first use of chest radiography as the reference standard pose several challenges. Previous studies have demonstrated low to the moderate diagnostic accuracy of chest radiography compared to gold standard chest CT scan as well as substantial intraobserver and interobserver variability(Williams et al., 2013b)(Johnson & Kline, 2010).

Another limitation was the inability to conclusively differentiate consolidation and atelectasis on LUS likely because early-stage, incomplete and non-resorptive atelectasis may be identical to consolidation. However, in our study, we identified very few cases of atelectasis by LUS.

Also, LUS scans have a limited role in the evaluation of lesions not in contact with the pleura, however since children have smaller chest wall thickness and smaller lungs compared to adults, these technical limitations are minimized.

The lung ultrasound examinations were done by a radiology resident and trained assistant who did not have vast experience in chest sonography but the learning curve was easier and faster than other ultrasound applications. Similar studies have been carried out successfully by other specialities such as paediatricians with minimal practical training(Zhan et al., 2018).

Conclusion and Recommendations

Ultrasound shows high sensitivity and specificity compared to chest radiography in the diagnosis of pneumonia in the pediatric age group. Lack of ionizing radiation, ability to obtain real-time dynamic imaging and portability make LUS a feasible alternative or adjunct to CXR in the detection of pneumonia in children.

CXR as a reference standard has its limitation therefore studies assessing LUS accuracy should consider incorporating clinical, laboratory and imaging evaluation to have the overall clinical picture as a reference for comparing LUS and CXR findings.

LUS diagnostic accuracy is dependent on competent operators examining as such training is key and the introduction of structured training modules in the curriculum will support its use locally.

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APPENDICES

Appendix I: Consent form to Participate in Research Study

Background

Currently chest radiography is the most acceptable diagnostic imaging tool that can be used to confirm the presence of pneumonia.

Utility of lung ultrasound in diagnosis of pneumonia has greatly increased in recent times. Lung ultra sound is inexpensive, easy to use, portable and safe from ionising radiation. Lung ultrasound can easily replace chest radiography as the first line of diagnostic imaging tool in diagnosis of pneumonia.

Study purpose

The objective of the study is to evaluate the utility of lung ultrasound in diagnosis of pneumonia at the Kenyatta National Hospital.

Study procedure

Each participant will undergo lung ultrasound and results will be documented.

Risks and benefits

This study will provide an alternative accurate imaging diagnostic tool for use for use in diagnosis of pneumonia. There are no risks involved in the study. Lung ultrasound is a safe imaging modality that uses high frequency sound waves to create image visualisations and does not involve ionising radiation.

Voluntariness of participation

Participation in this study is voluntary and you will not be denied medical care in case you refuse to participate. You may withdraw from participating in the study at any time with no consequence whatsoever.

Confidentiality

The information obtained from you will be treated with confidentiality and will only be used for the purpose of this study. The soft copy images obtained will be kept safely and no information about any participant shall be revealed to any party. You will be given a number and no names shall be used. The information may be looked at by the supervisors where relevant to the study.

All information collected will be destroyed at the end of the study.

Compensation

There will be no compensation financial or otherwise for the participants, no preferential treatment, gift or reward, for participants will be awarded during the above study.

Contact information

Should you need any further clarification regarding this study please feel free to contact the following;

Principal researcher,

Dr. Joshua Muyira (MBCHB UoN),

Postgraduate radiology resident

Cell phone number 0722588767.

DDIRM,

University of Nairobi

Or

Supervisor:

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Consent Certificate

Title of the Study: Comparing accuracy of lung ultrasound and chest radiography in diagnosis of Pneumonia in adults at Kenyatta National Hospital.

Name of the Researcher: Dr Joshua Muyira, Resident, Department of Diagnostic imaging and radiation medicine, University of Nairobi.

I hereby confirm that the above named doctor has explained the study to me and I fully understand.

I understand that my participation is voluntary and that I have not been coerced to participate.

I understand that I can withdraw at any point during the study and the quality of the medical care given to me will not be affected.

I understand that I will not receive any compensation, monetary or otherwise for participating in the above study.

I understand that my personal information will be kept confidential and will only be used for the purpose of this study.

I hereby consent to take part in the above study.

Study Number..... Signature.....Date.....

I certify that the patient has understood and consented participation in the study.

Name of person taking consent.....signature.....Date.....

Appendix II: Fomu ya Idhini ya Kushiriki Katika Utafiti

Utangulizi

Ultrasound ya mapafu ni moja kati ya zana zinazotumiwa kuchunguza magonjwa yanayohusisha kifua. Zana hii inapatikana sana,kwa gharama nafuu na ni salama ikilinganishwa na njia nyingine za kuthathmini mapafu. Lengo la utafiti huu ni kutambua mwelekeo na uenezi wa matokeo ya ultrasound ya mapafu kutathmini ugonjwa wa pumu katika watoto wa umri chini ya miaka 12 katika Hospitali Kuu ya Kitaifa ya Kenyatta.

Madhumuni ya utafiti

Kulinganisha sonographia ya mapafu na picha ya xray ya mapafu katika utathmini wa ugonjwa wa mapafu wa aina ya pumu kwa watoto chini ya umri wa miaka 12 katika Hospitali Kuu ya Kitaifa ya Kenyatta.

Utaratibu wa utafiti

Kila mshiriki atafanyiwa ultrasound ya mapafu na matokeo yake kurekodiwa.

Mtafiti: Dkt. Joshua Muyira mwanafunzi wa shahada ya juu katika radiolojia katika chuo kikuu cha Nairobi.

Ukihitaji ufafanuzi zaidi kuhusu utafiti huu tafadhali jisikie huru kuwasiliana na:

Mtafiti mkuu.

Dk Joshua Muyira (MBCHB UoN),

Nambari ya simu ya simu 0722588767.

DDIRM.

Chuo Kikuu cha Nairobi.

Msimamizi:

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Mimi natoa dhibitisho ya kwamba daktari amenieleza kiundani kuhusu utafiti huu ambao madhumuni yake yanapatikana kwenye utangulizi hapo juu. Ninakiri nimepewa fursa ya kuuliza maswali kuhusu utafiti huu na nimeridhika.

Ninaelewa kwamba kushiriki kwangu katika utafiti huu ni kwa hiari yangu mwenyewe ila sijashurutishwa.

Ninaelewa kwamba sitapokea fidia yeyote iwe ya kifedha ama vinginevyo wala sitapewa matibabu kwa upendeleo.

Naelewa kwamba taarifa zangu binafsi sitaweka siri and zitatumiwa tu kwa madhumuni ya utafiti huu pekee.

Ninatoa idhini ya kushiriki katika utafiti huu.

Nambari ya utafiti.....Sahihi.....Tarehe.....

Natoa uhakika kuwa mhudumiwa ameelewa na amekubali kushiriki kwa utafiti huu.

Jina la mchukua idhini.....Sahihi.....Tarehe.....

Appendix III: Data Collection Sheet

Date: ……

Participant No: ……...

Age (In completed years): ……

A. Demographics

1. Gender

    - Male
    - Female

2. Residence

    ……

    - Rural
    - Urban

3. Parents Education Level

    - None
    - Primary School
    - Secondary School
    - Tertiary Level
    - Other (specify) ……

B. **Clinical Findings**

1. Presenting symptoms	Duration (days)
Cough	……
Fever	…….
Difficulty in breathing	…….

- ☐ Chest pain …….
- ☐ Other (specify) …… ……..

2. Known comorbidities

- ☐ HIV
- ☐ Heart disease
- ☐ Rickets
- ☐ Others (specify)…….

C. **Lung Ultrasound Findings**

Right Hemithorax		**Left Hemithorax**	
Upper anterior		Upper anterior	
Lower anterior		Lower anterior	
Upper lateral		Upper lateral	
Lower lateral		Lower lateral	
Upper posterior		Upper posterior	
Lower posterior		Lower posterior	

1. Normal lung
2. Interstitial pattern
3. Consolidation
4. Atelectasis
5. Pleural effusion
6. Others (Specify) _____

D. **Chest Radiograph Findings**

Right hemi thorax		Left hemi thorax	
Upper zone		Upper zone	
Middle zone		Middle zone	
Lower zone		Lower zone	

1. Normal lung
2. Consolidation
3. Interstitial pattern

4. Atelectasis
5. Pleural effusion
6. Others (Specify) _____

Appendix IV: Estimated Budget

ITEM	Quantity	Unit Price (Ksh.)	Total(Ksh.)
Notebooks	5pcs	200.00	1000.00
Pens	1box	500.00	500.00
Thermal paper	5 rolls	1500	7500.00
Ultrasound gel	1 litre	1000	1000.00
Flash discs	2pcs	2 000.00	4 000.00
Files	10pcs	30 .00	300.00
Printing cartridge	1 pc	6000.00	6 000.00
Printing paper	5 reams	400.00	2 000.00
Printing of drafts and final proposal	10 copies	500.00	5 000 .00
Photocopies of data collection tool	125 copies	50.00	6250 .00
Photocopies of final proposal	6 copies	200.00	1 200.00
Binding copies of proposal	6 copies	60.00	360.00
Ethical review fee	1	5 000.00	5 000.00
Subtotal			**40 110.00**
Regional ultrasound fee	108	2 000.00	216 000.00
Biostatistician fee	1	30 000.00	30 000.00
Subtotal			**286 110.00**

Data Collection, Data Analysis and Thesis Development			
Printing of thesis drafts	10 copies	1 000.00	10 000.00
Printing final thesis	6 copies	1 000.00	6 000.00
Binding of thesis	6 copies	300.00	1 800.00
Dissemination cost			10 000.00
Subtotal			**27 800.00**
Contingency			**10 000.00**
Grand Total			**323 910.00**

Appendix V: Dummy Tables

Baseline Demographic Characteristics

Age (years) median	
Sex (male: female)	

Baseline clinical information

Presenting symptoms	**Duration (days)**
• Cough • Fever • Difficulty in breathing • Chest pain • Other (specify)	
Known comorbidities • HIV • Heart disease • Rickets • Others (specify)……	

Correlation of LUS Pattern of Consolidation and CXR Findings

	CXR findings		Total
LUS findings	**Positive**	**Negative findings**	
Positive finding			
Negative findings			

Correlation of LUS Interstitial Pattern and CXR Findings

	CXR findings		Total
LUS findings	**Positive**	**Negative findings**	
Positive finding			
Negative findings			

Correlation between LUS Atelectasis and CXR Findings

CXR Findings	LUS findings		Total
	>1 positive scan per hemi thorax	**Negative findings**	
Diffuse AIS			
Focal lung lesion and negative AIS			
Negative CXR			

Correlation of LUS pattern of Pleural Effusion and CXR findings

	CXR Findings		Total
LUS findings	**Positive**	**Negative findings**	
Positive finding			
Negative findings			

Comparison between LUS and CXR

Pathology	**LUS**	**CXR**		**Clinical**		**Sensitivity (%)**	**Specificity (%)**	**PPV (%)**	**NPV (%)**	**DA (%)**
		+	-	+	-	-				
Consolidation	**LUS +**									
	LUS -									
Interstitial pattern	**LUS +**									
	LUS -									
Atelectasis	**LUS +**									
	LUS -									
Pleural effusion	**LUS +**									
	LUS -									

Each hemi thorax is characterized as positive (?) or negative (-) for the abnormality by the presence or absence of a single positive region, respectively.

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Ref: KNH-ERC/A/13

20th January 2020

Dr. Joshua Muyira
Reg. No. H58/87916/16
Dept. of Diagnostic Imaging and Radiation Medicine
School of Medicine
College of Health Sciences
University of Nairobi

Dear Dr. Muyira

RESEARCH PROPOSAL: THE ACCURACY AND UTILITY OF LUNG ULTRASOUND FINDINGS WHEN COMPARED TO CHEST RADIOGRAPH FINDINGS IN DIAGNOSIS OF PNEUMONIA IN CHILDREN UNDER 12 YEARS AT KENYATTA NATIONAL HOSPITAL (P807/09/2019)

This is to inform you that the KNH- UoN Ethics & Research Committee (KNH- UoN ERC) has reviewed and approved your above research proposal. The approval period is 20th January 2020 – 19th January 2021.

This approval is subject to compliance with the following requirements:

a. Only approved documents (informed consents, study instruments, advertising materials etc) will be used.
b. All changes (amendments, deviations, violations etc.) are submitted for review and approval by KNH-UoN ERC before implementation.
c. Death and life threatening problems and serious adverse events (SAEs) or unexpected adverse events whether related or unrelated to the study must be reported to the KNH-UoN ERC within 72 hours of notification.
d. Any changes, anticipated or otherwise that may increase the risks or affect safety or welfare of study participants and others or affect the integrity of the research must be reported to KNH- UoN ERC within 72 hours.
e. Clearance for export of biological specimens must be obtained from KNH- UoN ERC for each batch of shipment.
f. Submission of a request for renewal of approval at least 60 days prior to expiry of the approval period. (*Attach a comprehensive progress report to support the renewal*).
g. Submission of an *executive summary* report within 90 days upon completion of the study. This information will form part of the data base that will be consulted in future when processing related research studies so as to minimize chances of study duplication and/ or plagiarism.

For more details consult the KNH- UoN ERC website http://www.erc.uonbi.ac.ke

Yours sincerely,

PROF. M. L. CHINDIA
SECRETARY, KNH-UoN ERC

c c. The Principal, College of Health Sciences, UoN
The Director, CS, KNH
The Chairperson, KNH- UoN ERC
The Assistant Director, Health Information, KNH
The Dean, School of Medicine, UoN
The Chair, Dept. of Diagnostic Imaging and Radiation Medicine, UoN
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