ARTICLE

Utility of the BLUE (Bedside lung ultrasound in emergency) protocol in acute undifferentiated dyspnea among pediatric patients

Christian Anne C. Dauz, Jenina Liza Danao, Joie Aseamie Flores, Cristan Q. Cabanilla, Michael D. Cabato, Jacquelyn Olib-Velazquez

OBJECTIVE: This cross-sectional study aimed to evaluate the effectiveness of the BLUE (Bedside lung ultrasound in emergency) protocol compared to clinicoradiologic diagnosis for promptly identifying acute undifferentiated dyspnea in pediatric patients.

MATERIALS AND METHODS: Conducted at the emergency room of the Philippine Children's Medical Center from August 2022 to May 2023, the study involved performing the BLUE protocol within 2 hours of patient arrival. Chest radiography was also conducted, with images independently interpreted by a pediatric pulmonologist, emergency medicine specialist, and radiologist. The results were then compared to the clinicoradiologic findings.

RESULTS: A total of 111 participants were included, with the majority being male (55.4%) and under 1 year old (48.2%). Pneumonia was the most observed diagnosis (88.2%), followed by asthma (7.2%). Utilizing the BLUE protocol, pneumonia was identified as the most prevalent diagnosis (81%), followed by pleural effusion (12.6%) and asthma (6%). The pulmonologist, emergency medicine specialist, and radiologist exhibited high sensitivity in diagnosing pneumonia (91.01%, 89.89%, 96.77% respectively) but low specificity (26%, 21%, 57.89%). Diagnosing pleural effusion and/or congestion showed high sensitivity (89%) and low specificity (21%) based on the pulmonologist's reading, low sensitivity (37%) and high specificity (99%) based on the emergency medicine specialist's reading, and 100% specificity based on the radiologist's reading. All readers demonstrated high specificity (95%, 93%, 93%) and low sensitivity (50%, 71%, 71%) in diagnosing asthma. The ultrasound readings between the readers exhibited a high concordance rate of 98%.

CONCLUSION: The study findings show that the BLUE protocol has high sensitivity in diagnosing pneumonia and high specificity in diagnosing asthma. The high concordance rate among readers suggests consistent ultrasound findings. These results support the practical application of the BLUE protocol for promptly diagnosing acute undifferentiated dyspnea in pediatric patients within the emergency department.

KEYWORDS: *dyspnea, chest radiography, chest ultrasound*

Introduction

Breathing difficulty, or dyspnea, accounts to 5% of emergency room visits which could be explained by an array of differential diagnosis which could be determined using radiographic techniques.[1-4] A study by Shrestha et al, showed that among patients presenting with dyspnea, the most common diagnosis was involving the respiratory system in 52.3%.[5-8] In relation to this, in 2021 the emergency room consults of Philippine Children's Medical Center was 11, 727. Among these, 258 patients consulted due to difficulty of breathing and accounted for 2.2 % of emergency room visits.

A reduction in in-hospital mortality can be achieved by recognizing and responding quickly to signs of deterioration. [5-6] Resolving symptoms is best achieved by treating the underlying problem. [4] Researchers found that Point of Care Ultrasonography (POCUS) can aid in the diagnosis of respiratory and circulatory failure in critical care settings.[7] In observational studies, POCUS appears to improve the likelihood of early diagnosis and decrease the time to administration of management in both acute respiratory and circulatory failure.[7] Furthermore, POCUS use lessens diagnostic uncertainty and can detect life-threatening illnesses that would otherwise be missed.[7] The Bedside Lung Ultrasound in Emergency (BLUE) method, established by Lichtenstein et al., emphasized the use of lung ultrasonography in the evaluation of breathing difficulties in emergency room visits.[8] Respiratory failure can be accurately assessed using a short technique (less than three minutes long) which could lessen the time for a definitive diagnosis and eventually a definitive treatment.[9] On review of data, in PCMC, it takes an average of 15 minutes to 1 hour for a chest radiography to be done from the time of admission.

An easy, non-invasive approach will help identify respiratory failure early, reducing the risk of unnecessary tests and procedures. Adult studies provide examples of using lung ultrasound in determining different causes of respiratory failure.[9] Although there had been pediatric studies done at the emergency room, most studies done focused on comparing lung ultrasound and radiography with one disease entity. To date, no studies have been done to assess its applicability in the emergency room in the Philippines. The purpose of this study is to investigate the utility of the BLUE Protocol in the diagnosis of acute undifferentiated dyspnea in emergency room patients. Hence this study determined the applicability of the BLUE protocol in comparison to clinical diagnosis using clinical and radiographic findings in the immediate diagnosis of acute undifferentiated dyspnea among pediatric patients.

Materials and Methods

This is a cross-sectional study which determined the utilization of the BLUE protocol in comparison to the clinical diagnosis of the pediatric resident on duty using clinical and radiographic findings in the immediate diagnosis of acute undifferentiated dyspnea among pediatric patients.

The study was done at the emergency room of Philippine Children's Medical Center (PCMC) from August 1, 2022, to May 31, 2023, which included service patients less than 19 years old with a chief complaint of difficulty of breathing either subjective complaint of the patient or observed by the caregiver. The population computed was adjusted to a known population size. A total of 111 participants were enrolled in this study which included an attrition of 20% to account for possible drop out.

All service patients less than 19 years old with a chief complaint of difficulty of breathing either subjective complaint of the patient or observed by the caregiver and fulfilled the inclusion criteria were eligible to be part of this study, these includes: a.) patients with tachypnea based on age using the PPS guidelines (0 to 3 months: >60bpm, 3 to 12 months: >50 bpm, 1 to 5 years old: >40bpm, more than 5 years old: >30bpm); b) patients with chest indrawing or supraclavicular or intercostal or subcostal retraction. Exclusion criteria included: a) unstable patients ongoing cardiac arrest or post cardiac arrest or impending cardiac arrest with severe bradycardia; b) patients who cannot tolerate the procedure.

Purposive sampling was done. All patients who fulfilled the criteria were considered and no patient was forced to be part of this study. Once a patient who fulfilled the criteria entered the emergency department, the resident on duty informed the primary co-investigators. The primary co-investigator explained the study to the parents or caregiver and patients and secured the consent because the primary investigator was blinded in the recruitment process. The BLUE protocol was not done until the patient was assessed by the pediatric resident on duty to ensure that the patient does not need any additional medical intervention at that moment. After the initial assessment, management or resuscitative measures were done and the patient was stabilized by the pediatric resident on duty, a consent form was obtained from the parents or caregiver and patient by the primary co-investigators. An assent form was taken once the patient was stable and capable of understanding the assent. Within the first 2 hours of the patient's arrival, both BLUE protocol and chest radiography were performed whichever was available first without causing delay on the patient's management. This was assured by the primary co-investigators. No studies were found that determined the acceptable interval between the two procedures. Chest radiography with anterior posterior projection was done as the reference study for chest imaging. Only the primary co-investigators were able to know the history, physical examination and previous diagnostics done on the patient.

The BLUE protocol was performed by the primary investigator (Pediatric Pulmonology Fellow) who underwent online theoretical

theoretical training and point-of-care ultrasound workshop. The primary investigator was blinded to the clinical history and physical examination findings of the patient as well as any previous diagnostics done. The procedure was done in a properly draped area wherein the caregiver/parent, primary investigator and patient were present. Only the part to be examined was exposed. The BLUE protocol was done within 10 minutes using a GE Venue Go ultrasound with microconvex transducer with 3.1 – 12.9 MHz while the patient was on a supine position. The transducer was applied on the chest wall across the intercostal space with the marker oriented towards the head. The study followed the BLUE Protocol. [5-7] Bilateral chest wall was examined starting with the right anterior chest. Areas of investigation followed the BLUE points and protocol. With the transducer placed perpendicularly on the intercostal space, pleural line was evaluated first on the anterior upper and lower chest. Followed by the presence or absence of lung sliding on the anterior upper and lower chest wall using the M mode. Lastly, identification of A line, B Line, Consolidation and Effusion were evaluated using the zigzag technique. R1, R3 and R5 were evaluated first followed by the R2, R4 and R6, the same procedure was done on the contralateral side.

Table 1: Areas of investigation[6]

Chest	Sector	Boundaries
Anterior	R1 or L1 (anterior upper)	Upper: Clavicle Lower: 4th rib Medial: Sternal edge Lateral: Contents of axilla or clavipectoral triangle
	R2 or L2 (anterior lower)	Upper: 4th rib Lower: variable depending on habitus, abdominal contents Medial: Sternal edge Lateral: Axillary line
Lateral	R3 or L3 (lateral axilla)	Upper: axilla Lower: Axis of 4th rib Anterior: Anterior axillary line Posterior: Posterior axillary line
	R4 or L4 (lateral lower)	Upper: Axis of 4th rib Lower: variable Anterior: Anterior axillary line Posterior: Posterior axillary line
Posterior	R5 or L5 (Posterior Upper)	Upper: defined by LUS Medial: thoracic spine Lateral: medial border of scapula Lower: Inferior angle of scapula
	R6 or L6 (Posterior lower)	Upper: Inferior angle of scapula Medial: thoracic spine Lateral: Posterior axillary line

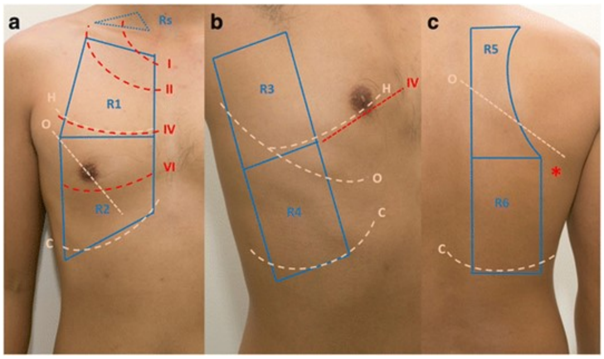

Figure 1: Areas of investigation[6]

Once BLUE Protocol was done, findings were categorized as A profile: defined as predominant bilateral anterior A lines plus lung sliding. A' profile is an A profile with abolished lung sliding. B profile defined as predominant B lines plus lung sliding. B' profile is a B profile with abolished lung sliding. A/B profile defined as massive B lines on one side and A lines on the other side. C profile designates consolidation and the PLAPS profile. There were no measurements on the findings of the BLUE Protocol. The different categories were correlated to the disease entity they likely represent and were the outcome of the BLUE protocol. The estimated time from the consent to the procedure proper lasted for approximately 30 minutes.

BLUE Protocol and Chest Radiography interpretation

The BLUE protocol images and results were recorded and saved on the ultrasound machine, copied to an external device and were given to the supervising investigators for review. All the images were interpreted by the supervising investigators: pediatric pulmonologist, emergency medicine specialist and radiologist. All the images were deleted after readings were completed. This was ensured by the primary investigator. The chest radiography was interpreted by the radiologist reader assigned to the patient. The pediatric pulmonology fellow, pulmonologist, emergency medicine specialist and radiologist were blinded with the patients' demographics, clinical history, physical examination, previous diagnostic examinations and chest radiography reading in our institution as data were kept in a secured logbook and electronic spreadsheet accessible only to the primary co-investigators at that point of the study. Interpretation was solely focused on the imaging. In the event that there was a disagreement among the readings of the pulmonologist, emergency specialist and radiologist, the BLUE protocol interpretation by the radiologist was considered the official reading. The result the BLUE protocol was compared to the immediate diagnosis of the patient using the clinical and radiologic findings.

As this was a cross-sectional study, data collection concluded upon completion of the BLUE Protocol. BLUE Protocol was not yet part of the standard of care, and the clinical decision of the pediatric resident on duty continued to be the deciding factor in the patient's care. Initial readings from the BLUE Protocol were provided to the pediatric

Throughout the duration of the trial, the researchers did not influence the clinical management of the patient.

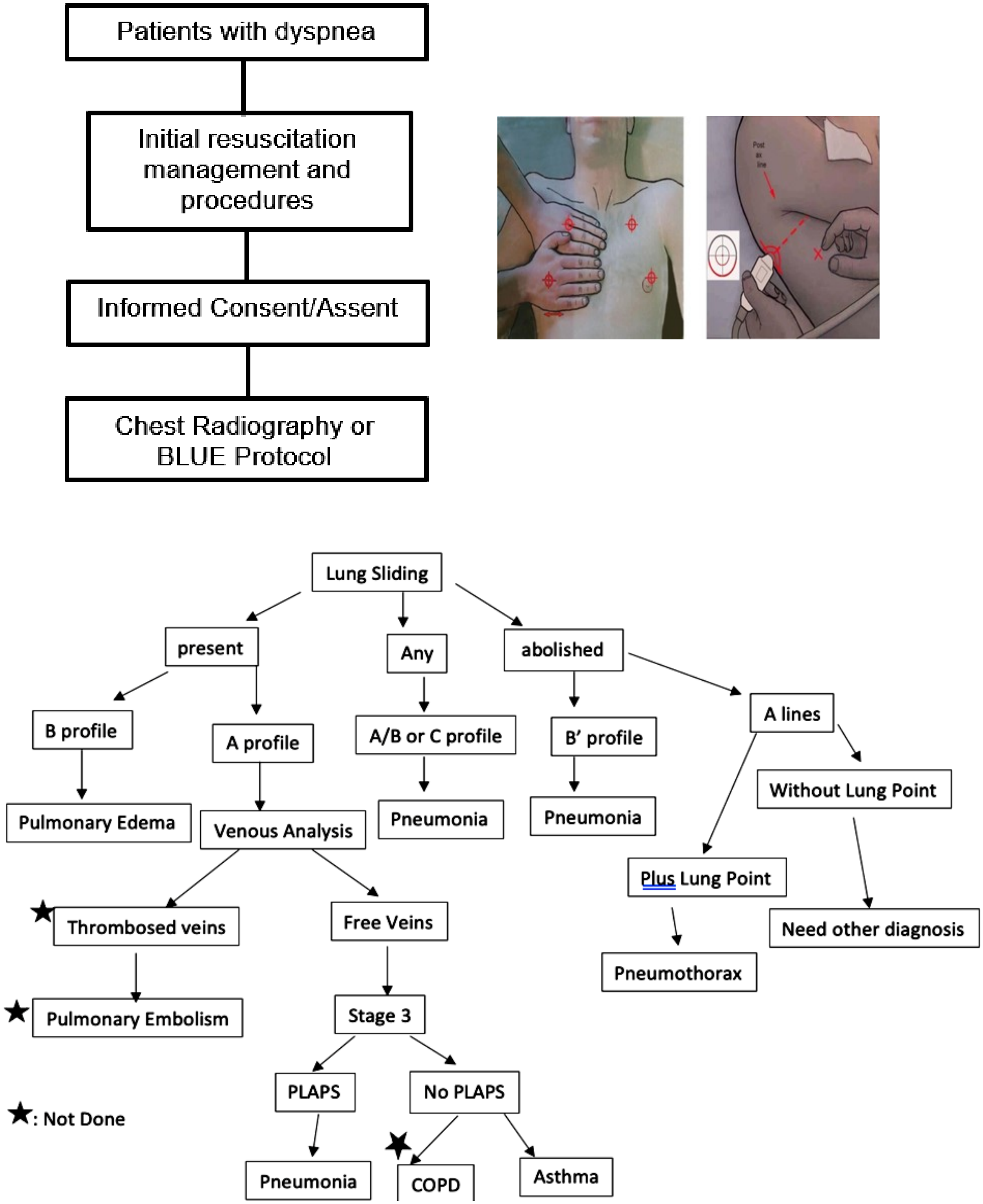

Figure 2. Study Procedure: Modified BLUE Protocol[5]

This study evaluated the applicability of the BLUE protocol in immediately diagnosing acute undifferentiated dyspnea among pediatric patients in the emergency room, compared to clinical diagnosis using clinical and radiologic findings. It also assessed the discordance between readings of emergency medicine specialists, radiologists, and pulmonologists during the BLUE protocol. Caregivers and parents were not required to withdraw during the 5 to 10-minute BLUE Protocol procedure, as patient monitoring was not conducted. Participants were given the option to withraw from the study at any point in time.

Data were logged in a laboratory logbook and encoded in Microsoft Excel worksheets coded suitable for analysis. All data were stored in a password protected laptop and will be saved for two years for reference purposes. The data yield was analyzed using the SPSS v21. Frequency, mean and percentages were the main descriptive statistical methods used. Sensitivity, Specificity, Positive Predictive Value, Negative Predictive Value, Positive Likelihood Ratio and Negative likelihood ratio were computed between the BLUE protocol results by the radiologist and chest radiography as reference study in the diagnosis of dyspnea among those included in the study. Chi square test was used to determine the presence of significant difference between the diagnosis of each reader. A p value of ≤ 0.05 was considered statistically significant.

The study had no direct monetary compensation, but patients and caregivers received nonmaterial benefits such as health education. It posed minimal risk, and adverse events were closely monitored. If successful, the BLUE protocol could be an alternative diagnostic tool for acute undifferentiated dyspnea in the emergency room, benefiting the local community by enabling early identification of respiratory failure and reducing unnecessary procedures and costs. The protocol was reviewed and approved by the Clinical Research Division and Ethics Review Board of Philippine Children's Medical Center. Consent was obtained, and participants were assigned coded identifiers for data confidentiality. Data were securely stored with limited access and kept in a locked office and locker.

Results

A total of 111 participants were included in the study with no dropout or any adverse event during the collection of data using the BLUE protocol. The majority were less than 1 year of age (48.2%) with the least number of patients coming from the adolescent age group (5.4%). Majority were male (55.4%) with Pneumonia as the predominant diagnosis (88.2%) with an average of 15.39 minutes to conduct the procedure.

Table 2: Demographic profile of patients included in the study.

Characteristic	Frequency	Percentage
Age		
<1 year old	54	48.2%
1-5 years old	40	35.7%
6 to 10 years old	12	10.7%
11 years old and above	6	5.4%
Sex		
Male	62	55.4%
Female	50	44.6%
Admitting Diagnosis		
Pneumonia	98	88.2%
Bronchial Asthma	8	7.2%
Rheumatic Heart Disease	4	3.6%
Chronic Kidney Disease	1	0.9%
Average time of POCUS in minutes (MEAN +/- SD)	15.39	(+/- 4.72)

Table 3 shows the sensitivity, specificity, positive predictive value and negative predictive value of the BLUE protocol reading in comparison to the clinicoradiologic diagnosis of each patient. Both reading from the pulmonologist (91.01%); ER specialist (89.89%) and Radiologist (96.77) have high sensitivity with low specificity at 26% (pulmonologist); 21% (ER specialist) and 57.89% (radiologist) in the diagnosis of Pneumonia. The diagnosis of pleural effusion and/or congestion showed high sensitivity (89%) and low specificity (21%) based on the pulmnologist reading; a low sensitivity (37%), high specificity (99%) on the ER specialist reading and a 100% specificity on the radiologist reading. All readers showed high specificity (95%; 93%; 93%) and lowsensitivity (50,71,71%) on the diagnosis of Asthma.

Table 3: Sensitivity and Specificity of BLUE protocol in comparison to the clinicoradiologic diagnosis of the patient. (a) Pneumonia; (b) Pleural Effusion; (c) Asthma/Normal

(a)

	Pediatric Pulmonologist Reading		ER Medicine Reading		Radiologist Reading	
PNEUMONIA	(+)	(-)	(+)	(-)	(+)	(-)
(+)	**81**	**17**	**80**	**18**	**90**	**8**
(-)	**8**	**6**	**9**	**5**	**3**	**11**
Sensitivity	**91.01% [CI 83.05%-96.04%]**		**89.89% [CI 81.67%-95.27%]**		**96.77% [CI 90.86%-99.33%]**	
Specificity	**26.09% [10.23% - 48.41%]**		**21.74% [7.46% - 43.70%]**		**57.89% [33.50% - 79.75%]**	
Positive Predicative Value	**1.23 [0.96 – 1.58]**		**1.23 [0.92 – 1.44]**		**2.30 [1.35 – 3.90]**	
Negative Predictive Value	**0.34 [0.13 -0.89]**		**0.17 [0.17 -1.25]**		**0.06 [0.02 - 0.18]**	

(b)

	Pediatric Pulmonologist Reading		ER Medicine Reading		Radiologist Reading	
PLEURAL EFFUSION	(+)	(-)	(+)	(-)	(+)	(-)
(+)	**3**	**1**	**3**	**1**	**4**	**0**
(-)	**10**	**98**	**5**	**103**	**3**	**105**
Sensitivity	**23.08% [CI 5.04%-53.81%]**		**37.50% [CI 8.52% -75.51%]**		**57.14% [CI 18.41%-90.10%]**	
Specificity	**98.99% [94.50% - 99.97%]**		**99.04% [94.76% - 99.98%]**		**100% [96.55% - 100%]**	
Positive Predicative Value	**22.85 [2.56 – 203.75]**		**39 [04.56 – 333.45]**		**-**	
Negative Predictive Value	**0.78 [0.58 -1.05]**		**0.63 [0.37 -1.08]**		**0.43 [0.18 -1.01]**	

(c)

	Pediatric Pulmonologist Reading		ER Medicine Reading		Radiologist Reading	
ASTHMA	(+)	(-)	(+)	(-)	(+)	(-)
(+)	**3**	**13**	**2**	**0**	**2**	**0**
(-)	**3**	**93**	**6**	**104**	**6**	**104**
Sensitivity	**50% [CI 11.81%-88.19%]**		**71% [CI 41.90%-91.61%]**		**71% [CI 41.90%-91.61%]**	
Specificity	**95.28% [79.94% - 93.31%]**		**93.88% [87.15% - 97.72%]**		**93.88% [87.15% - 97.72%]**	
Positive Predicative Value	**4.08 [1.58 – 10.53]**		**11.67 [5.02 – 27.11]**		**11.67 [5.02 – 27.11]**	
Negative Predictive Value	**0.57 [0.26 -1.27]**		**0.30 [0.13 -0.70]**		**0.30 [0.13 -0.70]**	

Concordance rate was also determined among the three BLUE protocol readers (Pulmonologist, Emergency medicine specialist and Radiologist) as shown in Table 4 which showed a high concordance rate at 98% and a p value >0.05 indicating no significant difference among groups.

Table 4: Concordance rate among ultrasound findings between readers.

	Pediatric Pulmonologist	P value	Emergency Medicine specialist	P value	Initial Impression	P Value
Ultrasound Reading	98.09%	0.506	98.24%	0.483	98.01%	0.621

Discussion

The study aimed to investigate the frequency of using the BLUE protocol in pediatric patients with dyspnea and evaluate its effectiveness in diagnosing different conditions. The findings indicated that the BLUE protocol had high sensitivity in detecting pneumonia and a high specificity in diagnosing asthma. Additionally, an important finding is that all readers consistently demonstrated a high concordance rate at 98% or more.

The BLUE Protocol, a point-of-care ultrasound technique, has been extensively studied in various clinical scenarios. Bekcoz et al[6] conducted a study to assess the diagnostic accuracy of the BLUE Protocol in identifying causes of acute dyspnea which revealed a high sensitivity (95%) and specificity (98%). These results highlighted the potential of the BLUE Protocol as a valuable tool in the evaluation and management of patients with acute dyspnea, aiding in the prompt identification of the underlying pathology.

Bedside lung ultrasound in emergency utilizes the immediate availability of ultrasound in the emergency room setting. If readily available, lung ultrasonography or BLUE protocol may reduce the need for unnecessary interventions or even exposure to radiation, as concluded in the study by Zieleskiewicz et al.[7] Furthermore, Potter et al emphasized that, unlike other imaging procedures, lung ultrasound does not involve ionizing radiation, provides rapid and serial bedside evaluation with real-time feedback, lessens the potential risks of transportation and importantly promotes time at the bedside of the critically unwell child.[12] While it may be accurate to highlight the positive aspects of the BLUE protocol, the reality remains that ultrasound machines are not easily accessible in every emergency room, especially in low to middle income countries like the Philippines. Therefore, this study could underscore the significance of acquiring this device due to its good diagnostic capabilities. In another study by Lichtenstein et al, the findings of the BLUE protocol showed a specificity of 90% in determining the diagnosis of acute respiratory failure.[5] This is consistent with the findings of this paper. Additionally, they reported that over 25% of patients assessed using conventional methods had an undetermined diagnosis within the first 2 hours of admission leading to incorrect management.[5] Lung ultrasound, on the other had, is nearly as effective as CT scan in identifying most disorders and is highly feasible.[5]

In a study by Potter et al, lung ultrasound demonstrated high diagnostic accuracy and increased sensitivity and specificity in comparison to chest radiography in identifying consolidation, pleural effusion and interstitial syndrome.[12] Similarly, this paper also observed similar trend, wherein the BLUE protocol diagnosed 14 cases of pleural effusion compared to the 6 cases identified by radiography. In another study by Ayuningtyas et al, lung ultrasound showed a sensitivity of 14.3% and specificity of 73% in diagnosing pleural effusion.[14] Our study showed similar results although results vary depending on the reader: pulmonologist (sensitivity 89%, specificity 21%), ER specialist (sensitivity 37%, specificity 99%), radiologist (sensitivity 57%, specificity 100%). In a study by Bourcier et al, lung ultrasound showed a sensitivity of 95% in diagnosing pneumonia.[8] Comparably, the study also showed high sensitivity in diagnosing pneumonia, although the specificity was low. It's worth noting that this could be related to the sample used, as all patients in the study had dyspnea. In another study by Attansi et al, lung ultrasound showed a specifity of 90% and sensitivity of 83% in diagnosing asthma exacerbation.[15] This is also observed in the current study wherein all readers showed high specificity (95%; 93%; 93%) although with low sensitivity (50,71,71%) on the diagnosis of Asthma. On the other hand, Asmara et al investigated the utility of the BLUE Protocol in patients with suspected acute respiratory distress syndrome (ARDS) thru meta analysis.[22] The study demonstrated that the BLUE Protocol had a high sensitivity of 97% and specificity of 94% in diagnosing ARDS. These results show that the BLUE Protocol can serve as an effective means in early identification and management of ARDS in critically ill patients, enabling timely intervention and improved patient outcomes. In a study by Scialanga et al on the accuracy of lung ultrasound in detecting pneumothorax among pediatric patients presenting with chest pain, results showed 100% sensitivity and specificity of 92%. This finding further implicates the important of POCUS as a noninvasive diagnostic tool in the Emergency department.[30]

In a meta analysis conducted by Pereda et al, studies that involved lung ultrasound performed by emergency department physicians, general practitioners, residents, or health care professionals, had a pooled sensitivity of 95% (95% CI: 91%–97%) and a specificity of 91% (87%–95%).[23-26] This is consistent with our findings which showed a low discordance among readers. Evidently, findings from studies done by highly skilled physicians had a higher specificity to diagnose pneumonia with ultrasound, nonexpert trained physicians' studies still showed a high sensitivity and specificity.[23,28] Interestingly, in the present study, despite the trainings received by the readers, results showed high concordance rate on their readings.

Taken together, these studies provide substantial evidence supporting the utility of the BLUE Protocol in different clinical scenarios. However, it is essential to consider factors such as patient population, operator expertise, and other diagnostic modalities when interpreting and applying the findings of the BLUE Protocol in clinical practice. The BLUE Protocol offers promise as a valuable tool in the assessment and management of various respiratory conditions, aiding clinicians in making timely and accurate diagnoses, ultimately improving patient care outcomes.

Conclusion

The findings of this study show that the BLUE protocol displays high sensitivity in diagnosing pneumonia and high specificity in diagnosing asthma. The high concordance rate between readers indicates consistent ultrasound findings. The results support the practical application of the BLUE protocol in diagnosing acute undifferentiated dyspnea in pediatric patients within the emergency department.

The study was limited to patients presenting with dyspnea at the emergency room of the Philippine Children's Medical Center and may not represent the whole population. BLUE protocol images reviewed by the supervising investigators were recorded and not done real time. The operator dependence of the ultrasound was another limitation. Cut off values were not determined because all participants in the study or analysis are known to be pathological. Furthermore, the absence of a healthy or non-pathological group in the dataset makes it imposible to create 2 distinct categorical datasets to separate. In statistical analysis, the determination of a cut-off value typically relies on the presence of two or more distinct groups with different characteristics or outcomes.

A prospective design which focuses not only on patients presenting with dyspnea and includes healthy patients is recommended to further asses the applicability and accuracy of the BLUE protocol furthermore a multicentered study is also recommend to determine its applicability in the low to middle income countries.

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