World Journal of Medicine and Medical Science
Vol. 2, No. 3, March 2014, PP: 1 - 12, ISSN: 2330-1341 (Online)
Available online at http://www.wjmms.com

Research article

Can we predict which children with clinical pneumonia will have radiologic findings on chest radiograph?

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Abstract

Background: The majority of children with pneumonia can be managed solely based on clinical assessment. Some however require chest radiograph to detect consolidation and other lung pathologies, to guide further investigations and for follow up. The facility for chest radiography is not widely available and or affordable in resource-constrained countries even when it is indicated.

Objective: We assessed which factors can predict the presence of radiologic pneumonia on chest radiographs of children with severe pneumonia diagnosed using the WHO ARI criteria at a health centre in rural Gambia.

Methods: Four hundred and twenty consecutive under-five children with severe pneumonia were prospectively recruited and all had a chest radiograph at presentation. History and examination findings were compared between the children with and without radiologic pneumonia. Multivariate logistic regression was used to predict the presence of radiologic findings among the children with clinically diagnosed pneumonia.

Result: Two hundred and sixteen(51.4%) of the 420 children with clinically diagnosed severe pneumonia had radiologic findings on their chest radiographs. Age range 48-59 months (OR = 2.758; 95% CI = 1.110 – 2.980; p = 0.032), grunting respiration (OR = 2.053; 95% CI = 1.355 – 3.899; p < 0.016) and cyanosis (OR = 7.537; 95% CI = 1.041 – 11.925; p = 0.040) at presentation were independent predictors of radiologic pneumonia.

Conclusion: Children with severe pneumonia who in addition are older than 4 years, have grunting respiration and or cyanosis should preferentially have chest radiograph for they are likely to have radiologic pneumonia.

Key words: Childhood pneumonia, predictors, radiologic, Resource-constrained.

Introduction

Childhood pneumonia is a common cause of hospitalisation and deaths among under-five children worldwide.[1-2] This is particularly so among children living in developing countries where sadly, facilities for appropriate management of these children are not readily available and or affordable.[1-2] Caregivers who are often required to pay out-of –pocket for the treatment of their children prefer to use the available scarce resource to procure medications rather than pay for investigations.[3] Health workers are often not sure on whether to request for an investigation or treat patients empirically due largely to limited resources available to the caregivers.[4] Consequently children with pneumonia in resource-constraint regions are often managed based solely on clinical assessments which are not always accurate. [5,6]

One of the most widely used investigatory modalities in assessing children with respiratory tract infections including pneumonia is chest radiograph.[7,8] Radiologic pneumonia has been used to estimate the burden of the disease[9]and as an important outcome in many epidemiological studies. [10-12] Although it is well documented that not all clinically diagnosed pneumonia in children has radiological evidence, [13]chest radiography nonetheless remains a very important tool in the management of childhood pneumonia.[7,8] It enables easy diagnosis of associated complications like pleural effusion and pneumothorax.[8] It also assists in following up of patients as well as the identification of other childhood respiratory conditions that may mimic pneumonia.[8]It has been used to predict response of children with pneumonia to treatment[14] and it can guide clinicians to when and how to approach lung aspiration in investigating for aetiologies of childhood pneumonia.[15-16] Its use in the evaluation of childhood pneumonia is still strongly recommended if available.[8]

Interpretation of chest radiographic findings is difficult especially in centres with no appropriate man-power to do so.[17,18] Even inter-observer and intra-observer's discrepancies in the report of chest radiographs among radiologists have been reported.[19,20]Validated interpretation of what constitute significant pathology on chest radiography in childhood pneumonia still remains an uphill task.[21]

The World Health Organisation (WHO) therefore gave a guideline on the interpretation of chest radiograph. Radiologic pneumonia include end-point consolidation, infiltrates and pleural effusion on chest radiograph.[22] According to the WHO, end point consolidation is defined as a dense opacity that may be a fluffy consolidation of a portion or whole of a lobe often containing air bronchogram and sometimes associated with

pleural effusion.[22] Infiltrates on chest radiograph as the presence of linear and patchy densities (interstitial infiltrates) in a lacy pattern involving the lungs with peribronchial thickening and multiple areas of atelectasis.[22] Pleural effusion is defined as the presence of fluid in the lateral pleural space between the lung and the chest wall seen as obliteration of the costophrenic angle or as a layer of fluid adjacent to the lateral chest wall.[22]

Fortunately, majority of children with clinical pneumonia or acute respiratory tract infection can be managed without necessarily having a chest radiograph particularly when it is not easily accessible or affordable; [5,6,13] however it is of paramount importance in a few children who may have underlying pathology, complications or lung consolidation. Since cost is often an important issue in the management of children in resource-constrained countries, recognition of predictors of significant radiologic findings among children with clinically diagnosed pneumonia may assist primary health workers in these countries to take decisions on which children will benefit from taking a chest radiograph and those that can reliably be managed without a chest radiograph in order to ensure appropriate cost effective management of the children, thus the purpose of this study.

Patients and Methods

This was a prospective cross-sectional study conducted at the Basse Rural Health Centre in the Upper River Region Division of the Gambia[23] over a nine month period (November 2010 to April 2011).

Children aged 2-59 months with severe and very severe pneumonia based on the WHO criteria thus: difficult or fast breathing defined as respiratory rate >50 or 40 cycles per minute for ages 2-11, and 12-59 months respectively, in addition to any one of lower chest wall in-drawing, central cyanosis, inability to feed or drink, and altered sensorium were recruited.

The study variables included age, sex and parental socioeconomic class.The social class of parents was estimated from the average of the parental occupation and highest level of education using the method described by Oyedeji.[24]Also noted was the history of difficult or fast breathing with or without fever and cough and their duration. Associated illnesses like diarrhoea, vomiting, convulsion and their durations were also noted. Immunization status, exclusive breastfeeding, number of persons sleeping in the same room with the child and overcrowding which was defined as having three or more persons sleeping in the same room with the child[25] was documented.

Study participants were examined to obtain their weight, height or length that were used to derive the nutritional state according to the National Centre for Health Statistics and WHO (NCHS/WHO) weight-for-age, weight-for-height and height-for-age parameters. Presence of pallor, central cyanosis, nasal flaring, head nodding and grunting respiration were noted. Axillary temperature was taken at presentation using a digital thermometer.

Oxygen saturations (Osat) of the patients were measured using pulse oximeter (Nellcor^{TM}N-200, USA) with appropriately sized paediatric probe attached to the finger or toe nail bed. Hypoxaemia was defined as Osat less than 90%. Other investigations like Packed Cell volume (PCV) and blood culture were also done. Anaemia was defined as PCV less than 30.0%.[26]All the children had a chest radiograph taken at presentation which was read in digital format following the WHO guidelines.[22]The interpretation of the chest radiographs was done by at least two independent clinicians strictly following the validated and standardised guidelines for the interpretation of paediatric chest radiographs by the WHO.[22]A third senior clinician reviewed the chest radiographs if there is discordance in the readings of the two clinicians. Cardiomegaly was defined as cardiothoracic radio >0.55. [29]

The outcome variable for this study was the presence of radiologic pneumonia on the chest radiographs of children with clinical pneumonia as defined using the WHO criteria.[22]

Ethical clearance for the study was obtained from the Joint Gambian Government/MRC ethical committee. Also informed consent was obtained from the parents or care-giver of all study participants.

Data analysis

This was done using Statistical Programme for Social Sciences (SPSS) software version 17.0 (SPSS Inc standard version 2010). Continuous variables were summarised using Mean and Standard deviations (SD) for normally distributed ones while medianand interquartile range (IQR) was used for non-normally distributed continuous variables. Categorical variables were summarized using proportions and percentages.

Differences between categorical variables were analysed using Pearson's Chi square test and Fisher's exact test as appropriate (with Yate's correction where applicable), while differences between continuous variables were analysed using Student T-test (for normally distributed continuous variables) and Mann-Whitney U-test (for non-normally distributed ones). Level of significance at 95 percent confidence interval was taken at $P < 0.05$.

Association between dependent (radiologic pneumonia) and independent variables (study variables) were assessed using multivariate logistic analysis to determine their independent effect on the outcome. Diagnostic accuracy of the study variables in detecting radiological pneumonia was further assessed using sensitivity, specificity and determination of Area Under Receiver Operating Characteristic (ROC) curve. Results were interpreted with Odds ratios (OR) and 95 percent confidence interval (CI). Statistical significance was established when CI does not embrace unity.

RESULTS

Study participants

Four hundred and twenty children fulfilled the criteria for severe pneumonia during the study period. The ages of the study participants ranged from 2 to 59 months with a median age of 14.0 months, an interquartile range (IQR) of 14.0 – 24.0 months and 168 (40.0%) were infants. There was male preponderance (male to female ratio was 1.2:1). (Table I)

Socio-economic classification: Majority of the patients 381 (90.7%) were from low socioeconomic class mainly peasant farmers and petty traders with no formal education. The remaining 39 (9.3%) were from the middle socio-economic class III. There was no patient with parents were from the upper socio-economic classes I and II. (Table 1)

Immunisation status: Three hundred and forty-four (81.9%) of the patients were appropriately immunized for age according to the Gambian National Programme on Immunization while 71 (16.9%) were not appropriately immunized for age.

Weight and height of the patients: The weight of the recruited patients ranged from 2.5 to 18.5kg with a mean (SD) weight of 8.1 (2.6) kg. The mean (SD) height / length was 75.7 (12.1) cm, the height / length ranged from 49.8cm to 110.0cm. 175 (41.7%) of the study patients were undernourished, including 89 (21.2%) with moderate wasting, 86 (20.5%) with severe wasting, and 10 (2.4%) with nutritional oedema at presentation. One hundred and fifty (35.7%) were underweight while 71 children (16.9%) were stunted. (Table I).

Temperature: The axillary temperature of the patients ranged from 34.8 to 40.8^0C with a mean (SD) of 38.3 $(1.1)^0$C. Eighty-five (20.2%) of them did not have fever at presentation, 15 patients (3.6%) had subnormal temperature while one patient (0.2%) was hypothermia at presentation.

Duration of illness before presentation: The duration of illness before presentation ranged from one to 13 days with a median (IQR) duration of 3.00 (1.0 – 5.0) days. Two hundred and forty-five of the children (58.1%), presented at the health centre within three days (early presenters) of the parents or the care giver noticing the symptoms, while 176 (41.9%), were late presenters (greater than three days). (Table II)

Associated clinical features: In addition to severe pneumonia, the children also presented with grunting respiration 126 (30.0%), head nodding, 81 (19.3%), cyanosis, 17(9.0%), convulsion 23 (5.5%), lethargy 13(3.1%), inability to suck 28 (6.7%), vomiting 82 (19.5%) and diarrhoea 84 (20.0%). Also, 53 (12.6%) of the patients had features of cardiac decompensation vis-à-vis significant tachycardia, tachypnoea and enlarged tender liver.

Hypoxaemia: The mean (SD) oxygen saturation was 92.6 (7.0) %, ranged from 35.0% to 100.0% with a median (IQR) value of 94.0 (88.0 – 99.0) %. Eighty-one (19.3%) were hypoxaemic (Osat< 90.0%) while the remaining 339 (80.7%) had normal Oxygen saturation (≥ 90%) at admission.

Chest radiograph findings at presentation: About one-half of the patients i.e. 204 (48.6%) had normal chest radiographs. Two hundred and sixteen (51.4%) had radiologic pneumonia. These comprise 98 (23.3%) with classical (end point consolidation) homogenous opacities, 107 (25.5%) with infiltrates, 3 (0.7%) with pleural effusions and one (0.2%) with effusion and pneumothorax. Seven (1.7%) patients had Cardiomegaly in addition to lobar consolidation. The two clinicians who read the Chest radiograph had about 95.0% concordance in their

report. The few cases of disagreement were review by a third independent assessor and his report was taken as the final report.

Bacteraemia: Out of the 380 patients who had blood culture done at admission, 332 (87.4%) yielded no bacterial isolate while 48 (12.6%) had bacterial isolates.

Anaemia: Three hundred (71.4%) had anaemia, while the rest had normal packed cell volume.

Association between socio-demographic characteristics of the children and the presence of radiologic pneumonia

A higher proportion of children who were 48 months or older significantly had radiologic pneumonia on chest radiograph compared to children less than 48 months (73.7% vs. 50.4%; x^2 = 3.946; p = 0.047). However no significant difference in the median (IQR) ages of the children with radiologic pneumonia compared to those without radiologic pneumonia. (Mann-Whitney-U test = 20 026.500; p = 0.107).

Other socio-demographic variables like sex and parental socioeconomic class were not significantly associated with the presence of radiologic pneumonia among the children with clinical pneumonia.(Table I).

Clinical features and the presence of radiologic pneumonia

Higher proportion of children with respiratory rate in excess of 80 cycles per minute at presentation had radiologic pneumonia compared to those with respiratory rate less than 80 cycles per minute. (65.5% vs. 49.2; x^2 = 4.988; p = 0.026) Similarly, children who had head nodding at presentation were more likely to have radiologic pneumonia as 50 (61.7%) of the 81 children who head nod compared to 166 (49.0%) of the remaining 339 children who did not head nod had radiologic pneumonia. (x^2 = 4.262; p = 0.039).

Grunting respiration is significantly associated with radiologic pneumonia as 81(64.3%) of the 126 children with grunting compared to 135 (34.0%) of the 397children without grunting, had radiologic pneumonia.(x^2 = 11.912; df = 1; p = 0.001). Also the presence of cyanosis at presentation in children with clinical pneumonia was significantly associated with radiologic pneumonia (88.2% vs. 50.0%; df = 1; x^2 = 8.818; p = 0.003). Table II.

No significant difference in the mean (SD) duration of symptoms before presentation among the children with radiologic pneumonia compared to those without radiologic pneumonia. [4.1 (2.4) days vs. 3.7 (1.9) days; t = 1.89; p = 0.060]. Other clinical features at presentation like fever, vomiting, head nodding, inability to suck/feed as well as pedal oedema were not significantly associated with the presence of radiologic pneumonia among the children with clinical pneumonia (Table II).

Laboratory parameters and radiologic pneumonia

Hypoxaemia at presentation was significantly associated with radiologic pneumonia as 50 (61.7%) of the 81 children with hypoxaemia compared to 166 (50.0%) of the remaining 339 children without hypoxaemia, had radiologic pneumonia. (x^2 = 4.262; p = 0.039). Table III. The presence of anaemia or bacteraemia at presentation was not significantly associated with radiologic pneumonia on chest radiograph of the children (Table III)

Predictors of radiologic pneumonia among children with clinically diagnosed severe pneumonia using multiple regression analysis

Subjecting the variables that were significantly associated with the presence of radiologic pneumonia to further analysis using multivariate logistic regression, age range 48-59 months, grunting respiration and cyanosis were independent predictors of the presence of radiographic pneumonia on chest radiograph among the children with clinically diagnosed severe pneumonia. (Table IV)

The sensitivity and specificity of grunting in identifying radiologic pneumonia among the children with clinically diagnosed severe pneumonia was 37.5% and 77.9% respectively, while the predictive values (PV) were 64.3% and 54.1% for positive and negative values respectively; Area under Receiver Operating Characteristic (ROC) curve was 0.577 (95% CI = 0.523 – 0.632). (Table V and Figure 2)

For age range 48 -59 months with severe pneumonia, the diagnostic accuracy to identify radiologic pneumonia included sensitivity and specificity of 6.5% and 97.5% as well as positive and negative predictive values of 73.7% and 49.6% respectively; Area under Curve (AUC) = 0.520 (95%CI = 0.465 – 0.575). (Table V and Figure 1)

The diagnostic accuracy of cyanosis in recognising radiologic pneumonia in the children included sensitivity 6.9%, specificity 99.0%, positive predictive value 88.2%, negative predictive value of 50.1%, the Area under Curve was 0.530 (95% CI 0.475 – 0.585) (Table V and Figure 3)

Discussion

The present study has presented data on factors in the history, examination and investigative findings that predicted the presence of significant radiologic findings (end point consolidation, infiltrates and effusion) on chest radiograph of under-five children admitted for clinically diagnosed severe pneumonia in a rural health facility.

From our study, about one-half (51.4percent) of the children with clinical pneumonia had evidence of radiologic pneumonia. This is more than 35.5 percent reported by Lynch *et al*[13] among American children with pneumonia who had infiltrates on chest radiograph. The higher proportion recorded in our study may be due to the fact that endpoint consolidation as well as infiltrates and effusions were used as the basis for defining radiologic pneumonia in our study while only infiltrates were considered in the study by Lynch *et al*.[13]

Children older than 4 years were found to significantly have radiologic pneumonia. This may be related to the fact that older children are better able to mount appropriate immune response to infection and limit infection to a particular lobe of the lung, unlike infants and young children with limited capacity to limit infection.[7,8]Also children with severe pneumonia who additionally had grunting respiration were more likely to have consolidations and infiltrates on chest radiograph. This finding is in keeping with that of Lynch *et al*[13] in the USA where grunting was a major determinant of radiologic pneumonia among children with clinically suspected pneumonia. Grunting is a form of positive pressure ventilation employed to overcome ventilation-perfusion mismatch caused by consolidation or other causes of increased lung dead space.[27]It is usually an inspiratory sound from breathing against a closed glottis. [28]Grunting respiration and increased respiratory rates as well as head nodding in children are employed to improve oxygenation and perfusion in occasions of increased death space from consolidation and or effusion.[27,28]

Cyanosis often ensue from failure of the compensatory mechanisms of grunting respiration in addition to head nodding and fast breathing to overcome the poor oxygenation and perfusion caused by congested or consolidated lung. The resultant build up of deoxygenated haemoglobin in excess of 5g/dl which often manifest clinically as central cyanosis was found in our study to predict the presence of significant radiologic pneumonia among children with clinically diagnosed pneumonia. Cyanosis in addition to grunting often indicate the need for oxygen therapy[30] and very severe forms of childhood pneumonia.[5]Grunting and cyanosis especially in children older than 48 months were found to be highly specific though sensitivity was low in predicting the presence of radiologic pneumonia (Infiltrates, end-point consolidation with or without effusions) in children with clinically diagnosed severe pneumonia.

The setting of our study is rural with a very high burden of childhood pneumonia [10, 15-16] and our study participants have little or no assess to over- the-counter antibiotics which may have altered the natural course of the illness. These coupled with the large sample size constitute the strengths of this study. We however recognise the limitations that the chest radiographs were not reviewed by a radiologist due to the absence of one in the rural setting of the study site.[23] However, the clinicians who interpreted the chest radiographs strictly followed the standardised and validated easy – to- apply WHO guidelines with about 95% concordance. Also facilities to assess for cardiac lesions were not available in the study site; hence children with cardiomegaly and other reasons to suspect cardiac lesions were referred to better equipped centres for further management.

In conclusion, children with clinical pneumonia in resource-constrained setting who additionally had significant tachypnoea, grunting respiration, head nodding and or cyanosis particularly those older than four years should preferentially have a chest radiograph because they are more likely to have evidence of lung consolidation, infiltrates and or effusions on chest radiograph.

Acknowledgments

The authors hereby acknowledge the clinicians, nurses, X-ray technicians and fieldworkers for their contributions to this work.

Conflict of interest: None

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Table I: Association between socio-demographic characteristics of the children and the presence of radiologic pneumonia

Socio-demographic variables	Radiologic pneumonia n = 216 (%)	No radiologic pneumonia n = 204 (%)	Total 420	x^2	p-value
Sex					
Male	112 (51.9)	120 (58.8)	232	2.062	0.151
Female	104 (48.1)	84 (41.2)	188		
Age range (in months)					
2-11	82 (38.0)	86 (42.2)	168	0.769	0.381
12-23	72 (33.3)	65 (31.8)	137	0.103	0.748
24-35	24 (11.1)	32 (15.7)	56	1.300	0.254
36-47	24 (11.1)	16 (7.8)	40	1.900	0.168
48-59	14 (16.5)	5 (2.5)	19	3.946*	**0.047***
Median (IQR) age	14.5(7.0 – 24.0)	13.0 (6.0 –24.0)		20026.500**	0.107**
Parental socio-economic class					
Middle class	19 (8.8)	20 (9.8)	39	0.126	0.722
Lower class	197 (91.2)	184 (90.2)	381	0.126	0.722
Inadequate immunisation	34 (15.7)	37 (18.1)	71	0.429	0.513
Not exclusively breastfed	22 (10.2)	20 (9.8)	42	0.005	0.770
Overcrowding	20 (9.3)	16 (7.8)	36	0.592	0.442

Yate's correction applied*Mann-Whitney-U test applied. The figures in parentheses are percentages of the total in each column.**

Table II: Association between clinical features and the presence radiologic pneumonia

Clinical features	Radiologic pneumonia n = 216 (%)	No radiologic pneumonia n = 204 (%)	Total 420	x^2	p-value
Duration of illness > 3 days	96 (44.4)	80 (39.2)	176	1.178	0.278
Mean (SD)	4.1 (2.4)	3.7 (1.9)		1.890^	0.060
Fever	162 (75.0)	148 (72.5)	310	0.326	0.568
RR> 80cpm	40 (18.5)	22 (10.8)	62	4.988	**0.026**
Head nodding	50 (23.1)	31 (15.2)	81	4.262	**0.039**
Grunting	81 (37.5)	45 (22.1)	126	11.912	**0.001**
Vomiting	39 (18.1)	43 (21.1)	82	0.610	0.435
Diarrhoea	40 (18.5)	44 (21.6)	88	0.610	0.435
Cyanosis	15 (6.9)	2 (1.0)	17	8.818*	**0.003***

Convulsion	10 (4.6)	13 (6.4)	23	0.616	0.433
Heart failure	32 (14.8)	21(10.3)	53	1.944	0.163
Wasting^{+}	68 (31.5)	82 (40.2)	150	3.470	0.062
Stunting^{+}	35 (16.2)	36 (17.6)	71	0.156	0.693
Lethargy	8 (3.7)	5 (2.5)	13	0.549*	0.459*
Inability to suck or feed	19 (8.8)	9 (4.4)	28	3.241	0.072
Oedematous PEM	4 (1.9)	10 (4.9)	14	2.150*	0.142*

*Yate's correction applied; ^Student T-test applied. $^{+}$WHO/NCHS classification wasting = weight for age < -2SD; stunting = height for age <-2SD.Oedematous PEM = Kwashiorkor and Marasmickwashiorkor.The figures in parentheses are percentages of the total in each column.

Table III: Association between laboratory findings and the presence of radiologic pneumonia

Investigation	**Radiologic pneumonia n = 216 (%)**	**No radiologic pneumonia n = 204 (%)**	**Total 420**	**x^2**	**p-value**
Anaemia	158 (73.1)	142 (69.6)	300	0.644	0.422
Hypoxaemia	50 (23.1)	31 (15.2)	81	4.262	**0.039**
Bacteraemia	26 (12.0)	22 (10.8)	48	0.162	0.687

The figures in parentheses are percentages of the total in each column.

Table IV: Predictors of radiologic pneumonia on chest radiograph of children with severe pneumonia using multivariate logistic regression

Variables	**β**	**SE**	**95% CI**	**OR**	**p- value**
Age 48 – 59 months	1.154	0.536	1.110 – 2.980	2.758	**0.032**
RR > 80 cpm	0.507	0.297	0.336 – 1.079	1.849	0.088
Head nodding	0.327	0.269	0.426 – 1.221	1.681	0.224
Grunting	0.572	0.237	1.355 – 3.899	2.053	**0.016**
Cyanosis	1.641	0.798	1.041 – 11.925	7.537	**0.040**
Hypoxaemia	0.011	0.288	0.576 – 1.777	1.681	0.969

β coefficient of Regression; SE standard error; CI confident interval; OR Odds ratio

Table V: AREA UNDER THE CURVE ANALYSIS FOR PREDICTORS OF RADIOLOGIC PNEUMONIA

Test Result Variable(s)	Area	Standard Error[a]	Asymptotic Significance[b]	Asymptotic 95% Confidence Interval	
				Lower Bound	Upper Bound
Age 48 -59 months	0.520	0.028	0.475	0.465	0.575
Grunting	0.577	0.028	0.006	0.523	0.632
Cyanosis	0.530	0.028	0.291	0.475	0.585

The test result variable(s): Age range 48 - 59 months, Grunting, Cyanosis has at least one tie between the positive actual state group and the negative actual state group. Statistics may be biased.

a. Under the nonparametric assumption

b. Null hypothesis: true area = 0.5

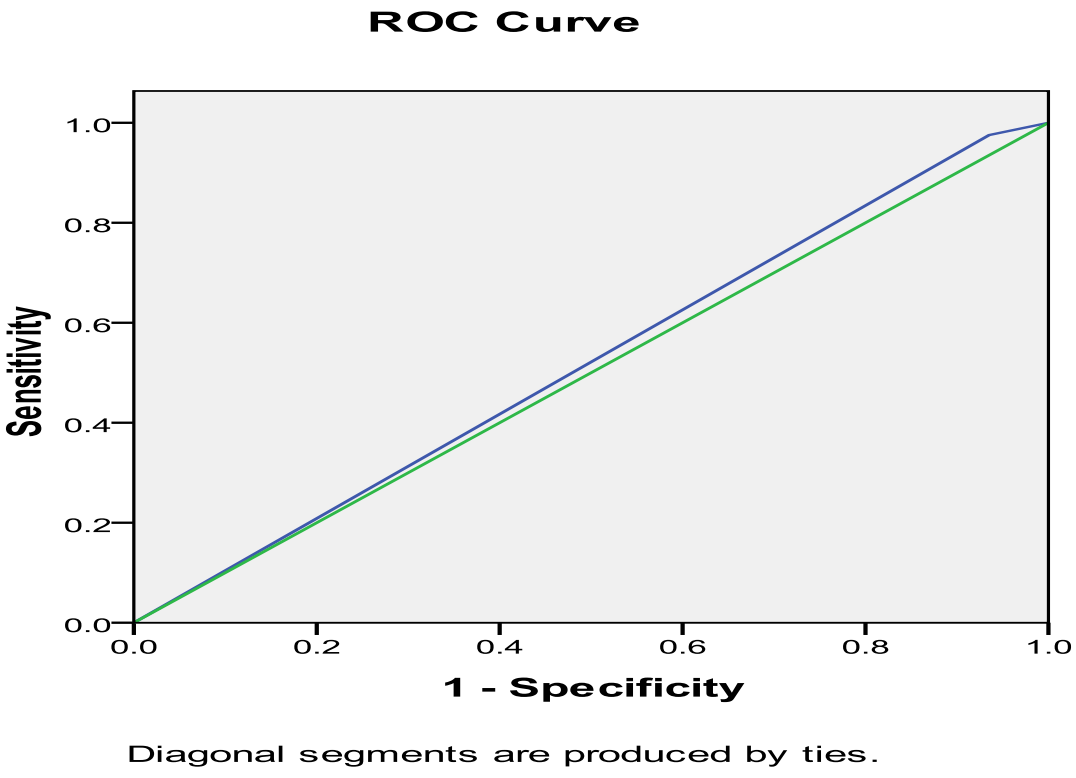

Figure 1: Receiver Operating Characteristic curve for age range 48-59months as a diagnostic tool for radiologic pneumonia

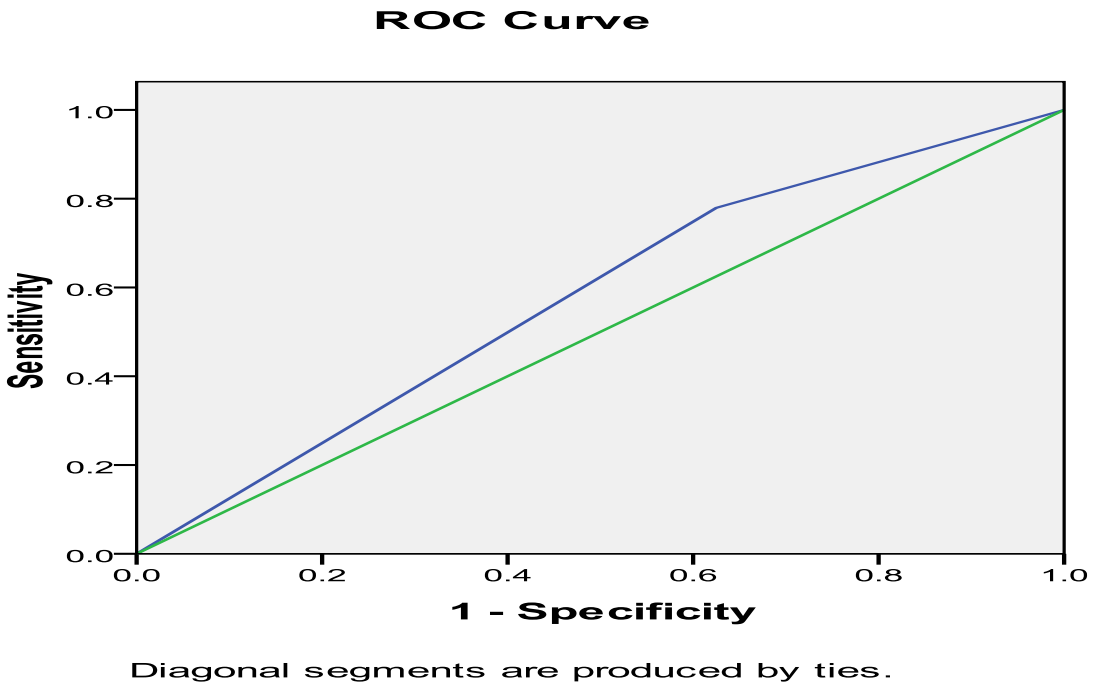

Figure 2: Receiver Operating Characteristic curve for grunting as a diagnostic tool for radiologic pneumonia

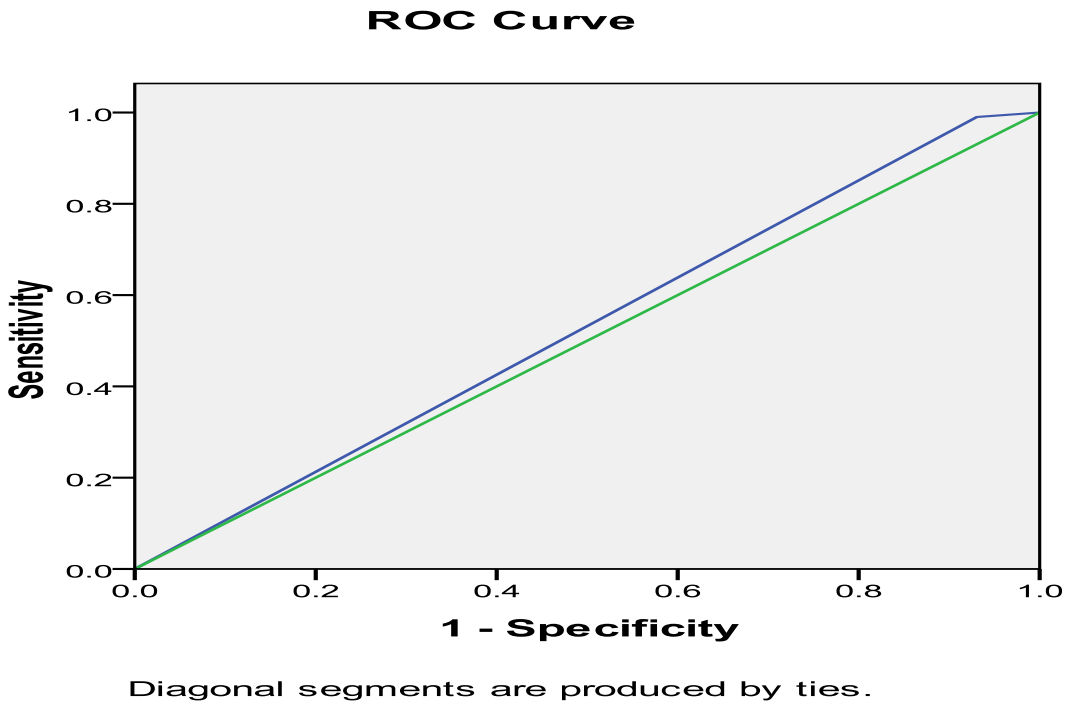

Figure 3: Receiver Operating Characteristic curve for cyanosis as a diagnostic tool for radiologic pneumonia