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ACUTE ILLNESS OBSERVATION SCALE (AIOS): EFFECTIVENESS IN DIAGNOSING AND MANAGING CHILDREN 2 TO 60 MONTHS PRESENTING WITH ACUTE RESPIRATORY ILLNESS

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Abstract

Background: Paediatric respiratory diseases remain an important cause of morbidity in both the developing and the developed world. The aim of the present study was to validate the effectiveness of Acute illness observation scale (AIOS) in predicting the severity of the illness and to describe the efficacy of AIOS in determining the initial therapeutic modalities and clinical outcome of the children. **Methods:** The present study was a hospital based descriptive observational study conducted between January 2018 and August 2019 in tertiary care hospital in Central India. The study included children between 2 months and 60 months presenting to the outpatient department (OPD) with fever, cough, and difficult breathing for less than two weeks. **Results:** Majority of the children were between 13 and 36 months of age (48.0%); and more half the children included were males (62.0%). Oral antibiotics were given to 18.0% children; intravenous antibiotics to 82.0% children; nasal oxygen to 66.0% children; intravenous fluids to 64.0% children; nebulisation to 24.0% children; and mechanical ventilation to 2.0% children. Lethargy, grunt, decreased breath sounds and crepitations were significantly associated with the severity of pneumonia. Among investigations, leucocytosis and chest X ray were significantly associated with increased severity of pneumonia (AIOS scores of three or five). We also found that the presence or absence of complications were not associated with severity of pneumonia ($p>0.05$). **Conclusion:** AIOS can be used as a tool to decide on therapeutic modalities and prognosticating a child with pneumonia admitted to the hospital by a physician.

Keywords: Pneumonia, children, severity scores, AIOS, IMNCI

Introduction

Paediatric respiratory diseases remain an important cause of morbidity in both the developing and the developed world.(1) It has become the most common reason for parents taking their children to see the clinician, and to the emergency department. The global under-five mortality rates were 37.7 (90% Uncertainty Interval (UI) 36.1 to 40.8) in 2019, while in absolute numbers, the annual number of global under-five deaths were 5.2 (95% UI 5.0 to 5.6) million in 2019 (mostly from preventable and treatable causes).(2) Importantly if current trends continue, 48.1 million under-5 deaths are projected to occur between 2020 and 2030,(3) almost half of them projected to occur during the neonatal period.(4) Additionally, the geographical

and economic variation demonstrate the possibility of even lower mortality rates for children under-five years of age and point to the regions and countries with highest mortality rates and in greatest need of resources and action.(5)

Leading causes of death in children under-5 years are preterm birth complications, birth asphyxia/trauma, pneumonia, congenital anomalies, diarrhoea, and malaria, all of which can be prevented or treated with access to simple, affordable interventions including immunization, adequate nutrition, safe water and food and quality care by a trained health provider when needed.(6) Under-five children are especially vulnerable to infectious diseases like malaria, pneumonia, diarrhoea, HIV, and tuberculosis.(7-9)

The latest report of United Nations International Children's Emergency Fund (UNICEF) revealed that deaths among under-five children are mostly caused by malnourishment (45%), Pneumonia (15%) diarrhoea (8%), malaria (5%) and others (9%).(10) Using vital registration and verbal autopsy data, the Child Health Epidemiology Reference Group (CHERG) estimated the total number of pneumonia deaths in children under-five worldwide to be approximately 935,000.(11) Up to half of deaths from pneumonia occurred in sub-Sahara Africa and approximately a third in Southern Asia. There were regional variations in the percentage of deaths attributable to pneumonia – from 5% of deaths in developed regions to 16% of deaths in sub-Saharan Africa. Most notably, 96% of episodes of pneumonia, and 99% of deaths from pneumonia, take place in LMICs.(12)

In recent years, significant progress has been made reducing child deaths from diarrhoea. But diarrhoea remains a leading killer of young children, particularly in humanitarian settings. In 2019, diarrhoea killed approximately 480,000 young children across the globe, accounting for 9 per cent of all deaths among children under age five.(13) The National Family Health Survey shows that the prevalence of childhood diarrhoea has increased from 9% to 9.2% from 2016 to 2020 in India (accounting for 6.6 million hospitalizations, which contribute to 24% national disease burden with 0.37 million deaths annually).(14) These children could have been saved by simple effective interventions, such as oral rehydration salt and zinc – approximately 70 to 90 per cent of deaths caused by acute watery diarrhoea can be prevented by oral rehydration salt, while zinc is estimated to decrease diarrhoea mortality by 11.5 per cent.(15) Appropriate fluids, breastfeeding, continued feeding and selective use of antibiotics are also critical.

In India, it is essential to formulate the criteria to triage, classify and treat or refer the children presenting with symptoms of pneumonia.(16) The strategy developed by IMNCI seeks to reduce the morbidity and mortality in children by improving the management of illness in family and community practices.(17) It relies on case detection by using simple clinical assessment and research-based treatment. Though IMNCI had been showed to be effective in managing childhood pneumonia, it would be more effective if been supplemented by an illness assessment scale aiming at helping the primary care setting in quickly assessing the severity. Acute illness observation scale (AIOS) scoring system in the management of pneumonia in children less than 5 years is one such assessment tool. However, very few studies have evaluated its effectiveness.(18, 19)

Against this background, the aim of the present study was to validate the effectiveness of Acute illness observation scale (AIOS) in predicting the severity of the illness and to describe the efficacy of AIOS in determining the initial therapeutic modalities and clinical outcome of the children.

Materials and methods

The present study was a hospital based descriptive observational study conducted between January 2018 and August 2019 in tertiary care hospital in Central India. The study included children between 2 months and 60 months presenting to the outpatient department (OPD) with fever, cough, and difficult breathing for less than two weeks with any of the below mentioned signs – fast breathing (2 Months to 12 months: more than 50 breaths per minute; 12 months to 5 years: more than 40 breaths per minute); chest indrawing; stridor in a calm child; lethargy; convulsion; grunting; and inability to drink. However, we excluded children with a symptom duration of more than two weeks, known case of asthma, any underlying cardiac diseases or other conditions like IEM, chronic lung diseases, and neurological conditions like developmental delay and neurodegenerative disorders.

The content of Participant Information Sheet (PIS) in local language was provided to the parents and contents were read to them in their own language to their satisfaction. The children were enrolled in the study after obtaining written informed consent from their parents. The sample size for the present study was computed using a prevalence of 52.3%, absolute precision of 7%, with 80% power. The minimum required sample size was computed to be 196.

Method of data collection: Children between 2 months and 60 months attending the OPD with suspected pneumonia, if satisfying the prespecified inclusion criteria were enrolled as the study group and were admitted. They were then classified according to IMNCI based severity assessment. AIOS scoring was done using the 6 parameters and given scoring as 1 for normal, 3 for moderate and 5 for severe disease, in a reasonably quite state by a single observer. The final scores ranged between 6 and 30 depending on the severity. Pulse oximeter readings, vitals of each patient was recorded. Complete blood count and chest X ray was done within 24 hours. The treatment was decided according to the initial AIOS score at presentation, where children with score more than 16 were started on IV antibiotics, nasal oxygen and intravenous fluid depending on the respiratory distress. Rest of the children were treated according to the IMNCI protocol. The children were followed up until discharge from the hospital.

Data was collected from 200 participants, entered in Microsoft Excel, and analysed using Software for Statistics and Data Science (Stata) v16. Descriptive analysis was presented using numbers and percentages. Chi square test of significance (two-sided) was applied to test for association between AIOS scale scores and independent variables. Statistical significance was considered at $p<0.05$.

Acute illness observation scale (AIOS): Though IMNCI strategy is more effective in classifying and managing pneumonia, it can be supplemented by an illness assessing scoring system used along the context of primary healthcare settings that can quickly assess the severity of illness at all levels, from onset to recovery. In this view, use of AIOS illness severity scale developed by P.L. McCarthy – using simple observations (based on hydration, toxic look) instead of complex symptomatology. It is a three-point scale for six ordinal variables and the total score ranges from 6 to 30. It is a validated index for assessing risk of serious bacterial infection in children 60 months or younger presenting with febrile illnesses.(18, 20)

Table 1: Acute illness observation scale (AIOS)

	Score = 1	**Score = 3**	**Score = 5**
Quality of cry	Strong cry with normal toe or contented and not crying	Whimpering or sobbing	Weak cry/moaning or high-pitched cry
Reaction to stimulation to parent	Cries briefly and stops or is content and not crying	Cries on and off	Cries continuously or responds hardly
State variation	When awake, stays awake, or if stimulated while sleeping, awakens quickly	Closes eyes for short period when awake or awakens when stimulated for long time	Fast asleep or not arousable
Colour	Pink	Pale extremities/acrocyanosis	Pale/cyanotic/ mottled/ashen
Hydration	Normal skin and eyes and moist mucous membranes	Normal skin and eyes, mouth slightly dry	Poor recoiling of skin, mucous membrane dry and or eyes
Response to social over tunes	Smiles or alerts	Smiles for a brief period or alerts briefly	No smile, anxious face, no expressions or not alert

Results

The present study included a total of 200 children between 2 months and 60 months presenting to the outpatient department (OPD) with fever, cough, and difficult breathing for less than two weeks. Majority of the children were between 13 and 36 months of age (48.0%) followed by 2 months to 12 months of age (36.0%). More half the children included were males (62.0%). The results showed that 14.0% children has their weight for age scores less than the third percentile and 4.0% children had their weight for age scores more than the 97th percentile. The mean (SD) duration of fever among the children were 1.96 days (0.63) and the mean (SD) duration of cough was 2.49 days (0.92). The mean (SD) duration of breathlessness among the children included in the present study was 1.73 days (0.66).

The common danger signs noted in the present study were lethargy (40.0%), inability to drink (18.0%), and grunt (20.0%). None of the children included in the present study had convulsions. Using IMNCI, we found that 80.0% children had severe pneumonia and 20.0% children had pneumonia.

Oral antibiotics were given to 18.0% children; intravenous antibiotics to 82.0% children; nasal oxygen to 66.0% children; intravenous fluids to 64.0% children; nebulisation to 24.0% children; and mechanical ventilation to 2.0% children. We found that in the present study 2.0% children had complications.

In the individual item analysis of AIOS, 94.0% and 78.0% of the affected children scored normally for variables – colour and hydration status respectively. However, majority of the

children showed worst score for response to social over tunes (98.0%). At the initial presentation, of the 200 children, 76 showed normal score for quality of cry, while 62% of children (n = 124) showed abnormal scores of 3 or 5. In view of response to parent stimulation, where abnormal score was seen in 76% (n = 152) of children. 66% children scored abnormal for state variation, while majority of children had normal score in variables like colour and hydration.

The result of the present study shows that age was not statistically associated with the severity of pneumonia or in other words, the AIOS scores. Among the presenting symptoms of children, lethargy and grunt was significantly associated with the severity of pneumonia ($p<0.05$). However, inability to drink was not statistically associated with AIOS scores. We also looked at the association between signs in children and AIOS scores – decreased breath sounds and crepitations were significantly associated with severity of pneumonia. But, the capillary refill time (in seconds) and presence of wheeze were not associated with the severity of pneumonia ($p>0.05$).

Among investigations, leucocytosis and chest X ray were the variables considered – both were (presence of leucocytosis and infiltrates or consolidation in chest X ray) significantly associated with increased severity of pneumonia (AIOS scores of three or five). We also found that the presence or absence of complications were not associated with severity of pneumonia ($p>0.05$).

Table 2: Descriptive analysis of study variables

		Number (N) or Mean	**Percent (%) or SD**
Age (in months)	2 to 12	72	36.0
	13 to 36	96	48.0
	36 to 60	32	16.0
Gender	Male	124	62.0
	Female	76	38.0
Weight for age (in percentiles)	Less than 3rd	28	14.0
	3rd to 97th	164	82.0
	More than 97th	8	4.0
Duration of fever (in days)		1.96	0.63
Duration of cough (in days)		2.49	0.92
Duration of breathlessness (in days)		1.73	0.66
Danger signs	Lethargy	80	40.0
	Inability to drink	36	18.0
	Grunt	40	20.0
	Convulsion	0	0.0
	Others	44	22.0
IMNCI diagnosis	Pneumonia	40	20.0
	Severe pneumonia	160	80.0
Oral antibiotics given		36	18.0
Intravenous antibiotics given		164	82.0

Nasal O2	132	66.0
Intravenous fluids	128	64.0
Nebulisation	48	24.0
Mechanical ventilation	4	2.0
Complications (any)	4	2.0

Table 3: AIOS – individual variable analysis

	Normal score (=1)	Abnormal score (=3 or 5)
Quality of cry	76 (38.0%)	124 (62.0%)
Response to parent stimulation	48 (24.0%)	152 (76.0%)
State variation	68 (34.0%)	132 (66.0%)
Colour	188 (94.0%)	12 (6.0%)
Hydration	156 (78.0%)	44 (22.0%)
Response to social over tunes	4 (2.0%)	196 (98.0%)

Table 4: Association between study variables and AIOS scores

		AIOS score			**p value**
		≤10	**11 to 15**	**≥16**	
Age (in months)	2 to 12	24 (31.6)	16 (40.0)	32 (38.1)	>0.05
	13 to 36	36 (47.4)	16 (40.0)	44 (52.4)	
	More than 36	16 (21.0)	8 (20.0)	8 (9.5)	
Symptom correlation					
Lethargy	Yes	20 (26.3)	4 (10.0)	56 (66.7)	<0.05*
	No	56 (73.7)	36 (90.0)	28 (33.3)	
Grunt	Yes	4 (5.3)	0 (0.0)	36 (42.9)	<0.05*
	No	72 (94.7)	40 (10.0)	48 (57.1)	
Inability to drink	Yes	4 (5.2)	12 (30.0)	20 (23.0)	>0.05
	No	72 (94.8)	28 (70.0)	64 (77.0)	
Correlation with signs					
CRT (in seconds)	<3	76 (100)	40 (100)	80 (95.2)	>0.05
	>3	0 (0.0)	0 (0.0)	4 (4.8)	
Decreased breath sounds	Yes	0 (0.0)	0 (0.0)	52 (61.9)	<0.05*
	No	76 (100)	40 (100)	32 (38.1)	
Wheeze	Yes	20 (26.3)	8 (20.0)	16 (19.0)	>0.05
	No	56 (73.7)	32 (80.0)	68 (81.0)	
Crepitations	Yes	0 (0.0)	4 (10.0)	36 (42.9)	<0.05*
	No	76 (100)	36 (90.0)	48 (57.1)	
Investigations					
Leucocytosis	Yes	8 (10.5)	16 (40.0)	44 (52.4)	<0.05*
	No	68 (89.5)	24 (60.0)	40 (47.6)	
X ray	Normal	60 (78.9)	12 (30.0)	8 (9.5)	<0.05*

	Infiltrates	16 (21.1)	28 (70.0)	44 (52.4)	
	Consolidation	0 (0.0)	0 (0.0)	32 (38.1)	
Complications					
Complications (any)	Yes	0 (0.0)	0 (0.0)	4 (4.8)	>0.05
	No	76 (100)	40 (100)	80 (95.2)	
Breathlessness (n = 50), convulsions (n = 0), and tachypnoea (n =50) were not presented					

Discussion

In India, childhood pneumonia represents one of the most common infectious illness – an important cause of preventable mortality in children, particularly in under-five children. In order to overcome this global problem, WHO had introduced a strategy for effective case management that had significant impact on mortality of under-five children attributed to pneumonia in developing countries, including India. Most of the presenting symptoms in young infants and children may be associated with different illness or more than one illness. Hence, for the early detection and prompt illness management, there is a need for an effective strategy that can target children less than five years of age.(21) Against this background, the present study was conducted to validate the effectiveness of AIOS scale in predicting the severity of the illness and to describe the efficacy of AIOS in determining the initial therapeutic modalities and clinical outcome of the children.

Age is an important predictor of morbidity and mortality in paediatric pneumonias. The present study conducted among children between the age group of 2 months to 60 months, majority (48.0%) were between 13 months and 36 months. Whereas few other studies that predicted the mortality and morbidity factors in under-five children with ARI, majority with pneumonia were less than one year of age, with a prevalence of 63.2% and 52.2% respectively.(22) Regarding gender distribution, in the present study, the incidence was higher among males (62.0%) compared to females (38.0%). Similarly, Sehgal V et al. reported the incidence of pneumonia among males to be 58.3%.(23) In the present study, we included all children who presented with fever, cough, and breathlessness. However, tachypnoea (100%) and chest retractions (60.0%) were the important signs for making a clinical diagnosis of pneumonia. Palafox et al. found that tachypnoea (as defined by WHO) had a 74.0% sensitivity and 67.0% specificity for radiologically defined pneumonia.(24)

Among the 200 children included in the present study, 20.0% were diagnosed as with pneumonia and the remaining 80.0% with severe pneumonia according to IMNCI classification. On applying the AIOS scoring pattern on the patients, about 42.0% children scored more than 16, while 38.0% of them scored below ten. In the individual item analysis of AIOS, 94.0% and 78.0% of the affected children scored normally for variables, colour, and hydration. On the contrary, majority of children showed worst score for response to social overtures. In the prior study, discriminate function analysis revealed that these six items when used together had a specificity of 88.0% and sensitivity of 77.0% for serious illnesses. Another study documented that the sensitivity and specificity were 88.9% and 80.0% for colour and hydration, which was consistent with the present study.(25, 26)

In the present study, grunt, crepitations, lethargy were significantly associated with children who scored more than 16 at the time of admission. Also, the study published by Bharti et al.(18)

on the role of AIOS on managing severe pneumonia showed the percentage of children with grunt to be 55.5% and retractions to be 55.5%; a statistically significant association with children who scored more than 16 at the time of admission. In a prospective study from Zambia on clinical predictors of hypoxemia in pneumonia, severity and risk of death from pneumonia was significantly high ($p<0.05$) when hypoxaemia (SpO2 less than 92) was present.(27) In the present study abnormal radiological changes were seen in about 60.0% of children; and majority were in the form of infiltrates. While 52.4% of children with infiltrates had scored more than 16, and those with consolidation had major significance with all of them scoring more than 16 ($p<0.05$). In a recent study it was found that about 53.2% of children had abnormal X ray findings with score more than 16. This shows the significance of X ray abnormalities were more when the score was high.(28) On predicting the occurrence of complications, shock and mechanical ventilator was needed in one child, whose AIOS score was more than 16 at the time of admission and did not have much significance ($p>0.05$).

To conclude, AIOS scoring has good consistency in predicting severe pneumonia in children. The individual variables of AIOS had significant correlation and were independent predictors of severity including hypoxemia, distress in pneumonia. AIOS correlates well with abnormal X ray findings and therapeutic decision taken by the physician; with initial SpO2 reading; and with clinical outcome in community acquired pneumonia. IMNCI can be used as a tool to triage and early referral of children with community acquired pneumonia in the fields by peripheral healthcare workers. On the other hand, AIOS can be used as a tool to decide on therapeutic modalities and prognosticating a child with pneumonia admitted to the hospital by a physician.

References

1. Schuchat A, Dowell SF. Pneumonia in children in the developing world: new challenges, new solutions. Semin Pediatr Infect Dis. 2004;15(3):181-9.

2. Sharrow D, Hug L, You D, Alkema L, Black R, Cousens S, et al. Global, regional, and national trends in under-5 mortality between 1990 and 2019 with scenario-based projections until 2030: a systematic analysis by the UN Inter-agency Group for Child Mortality Estimation. Lancet Glob Health. 2022;10(2):e195-e206.

3. You D, Hug L, Ejdemyr S, Idele P, Hogan D, Mathers C, et al. Global, regional, and national levels and trends in under-5 mortality between 1990 and 2015, with scenario-based projections to 2030: a systematic analysis by the UN Inter-agency Group for Child Mortality Estimation. Lancet. 2015;386(10010):2275-86.

4. Hug L, Alexander M, You D, Alkema L. National, regional, and global levels and trends in neonatal mortality between 1990 and 2017, with scenario-based projections to 2030: a systematic analysis. Lancet Glob Health. 2019;7(6):e710-e20.

5. O'Hare B, Makuta I, Chiwaula L, Bar-Zeev N. Income and child mortality in developing countries: a systematic review and meta-analysis. J R Soc Med. 2013;106(10):408-14.

6. Ali H, Aziz S. Rising Pediatric Morbidity and Mortality in the Developing World. Cureus. 2021;13(4):e14728.

7. Bhutta ZA, Saeed MA. Childhood Infectious Diseases: Overview. International Encyclopedia of Public Health. 2008:26.

8. Keeton C. HIV drives children's pneumonia in sub-Saharan Africa. Bull World Health Organ. 2008;86(5):324-5.

9. Hansen C, Paintsil E. Infectious Diseases of Poverty in Children: A Tale of Two Worlds. Pediatr Clin North Am. 2016;63(1):37-66.

10. Ghosh K, Chakraborty AS, Mog M. Prevalence of diarrhoea among under five children in India and its contextual determinants: A geo-spatial analysis. Clinical Epidemiology and Global Health. 2021;12:100813.

11. Rudan I, Boschi-Pinto C, Biloglav Z, Mulholland K, Campbell H. Epidemiology and etiology of childhood pneumonia. Bull World Health Organ. 2008;86(5):408-16.

12. McAllister DA, Liu L, Shi T, Chu Y, Reed C, Burrows J, et al. Global, regional, and national estimates of pneumonia morbidity and mortality in children younger than 5 years between 2000 and 2015: a systematic analysis. Lancet Glob Health. 2019;7(1):e47-e57.

13. Harb A, O'Dea M, Abraham S, Habib I. Childhood Diarrhoea in the Eastern Mediterranean Region with Special Emphasis on Non-Typhoidal Salmonella at the Human–Food Interface. Pathogens. 2019;8(2).

14. Lakshminarayanan S, Jayalakshmy R. Diarrheal diseases among children in India: Current scenario and future perspectives. J Nat Sci Biol Med. 2015;6(1):24-8.

15. Lam F, Wentworth L, Cherutich P, Migiro S, Abdala K, Musyoka M, et al. An evaluation of a national oral rehydration solution and zinc scale-up program in Kenya between 2011 and 2016. J Glob Health. 2019;9(1):010505.

16. Scott JA, Wonodi C, Moïsi JC, Deloria-Knoll M, DeLuca AN, Karron RA, et al. The definition of pneumonia, the assessment of severity, and clinical standardization in the Pneumonia Etiology Research for Child Health study. Clin Infect Dis. 2012;54 Suppl 2(Suppl 2):S109-16.

17. Gera T, Shah D, Garner P, Richardson M, Sachdev HS. Integrated management of childhood illness (IMCI) strategy for children under five. Cochrane Database Syst Rev. 2016(6):Cd010123.

18. Bharti B, Bharti S, Verma V. Role of Acute Illness Observation Scale (AIOS) in managing severe childhood pneumonia. Indian J Pediatr. 2007;74(1):27-32.

19. K A, P S. Acute Illness Observation Scale in community acquired pneumonia in children aged 2 months to 59 months. International Journal of Contemporary Pediatrics. 2020;7:1394.

20. McCarthy PL, Sharpe MR, Spiesel SZ, Dolan TF, Forsyth BW, DeWitt TG, et al. Observation scales to identify serious illness in febrile children. Pediatrics. 1982;70(5):802-9.

21. McCarthy PL, Lembo RM, Fink HD, Baron MA, Cicchetti DV. Observation, history, and physical examination in diagnosis of serious illnesses in febrile children≤ 24 months. The Journal of pediatrics. 1987;110(1):26-30.

22. Clark JE, Hammal D, Spencer D, Hampton F. Children with pneumonia: how do they present and how are they managed? Archives of disease in childhood. 2007;92(5):394-8.

23. Reddaiah V, Kapoor S. ACUTE RESPIRATORY INFECTIONS IN UNDERFIVES EXPERIENCE AT COMPREHENSIVE RURAL HEALTH SERVICES PROJECT HOSPITAL, BALLABGARH. Indian Journal of Community Medicine. 1995;20(2):13-8.

24. Murali B, Mulage L. AIOS v/s IMNCI in community acquired pneumonia. Journal of Evolution of Medical and Dental Sciences. 2014;3(13):3260-7.

25. Palafox M, Guiscafré H, Reyes H, Munoz O, Martínez H. Diagnostic value of tachypnoea in pneumonia defined radiologically. Arch Dis Child. 2000;82(1):41-5.

26. Altamirano J, Govindarajan P, Blomkalns AL, Kushner LE, Stevens BA, Pinsky BA, et al. Assessment of Sensitivity and Specificity of Patient-Collected Lower Nasal Specimens for Severe Acute Respiratory Syndrome Coronavirus 2Testing. JAMA Netw Open. 2020;3(6):e2012005.

27. Weber MW, Usen S, Palmer A, Jaffar S, Mulholland EK. Predictors of hypoxaemia in hospital admissions with acute lower respiratory tract infection in a developing country. Archives of disease in childhood. 1997;76(4):310-4.

28. Addo-Yobo E, Chisaka N, Hassan M, Hibberd P, Lozano JM, Jeena P, et al. Oral amoxicillin versus injectable penicillin for severe pneumonia in children aged 3 to 59 months: a randomised multicentre equivalency study. The Lancet. 2004;364(9440):1141-8.