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ORIGINAL ARTICLE

Reappraisal of respiratory syncytial virus as an aetiology of severe acute lower respiratory tract infections in children younger than 5 years in Nigeria

Damilola M. Oladele[a,*1], Dimeji P. Oladele[a,2], Rasheedat M. Ibraheem[a], Mohammed B. Abdulkadir[a], Rasaki Adewole Raheem[b], Aishat A. Gobir[a], Olarenwaju T. Adedoyin[a] and Abdul-Wahab B. R. Johnson[a]

[a]*Department of Paediatrics and Child Health, University of Ilorin Teaching Hospital, PMB 1459, Ilorin, Kwara State, Nigeria;*
[b]*Department of Microbiology, University of Ilorin Teaching Hospital, PMB 1459, Ilorin, Kwara State, Nigeria*

*Corresponding author: Tel: +2347066983663; E-mail: d.oladele@limihospital.org
[1]Present address: Limi Hospital, Department of Paediatrics, Plot 1487, Off Constitution Avenue, Central Business District, Abuja-FCT, Nigeria.
[2]Present address: Cedarcrest Hospital, Number 2, Mbakwe Street, Gudu District, Abuja.

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Background: Acute lower respiratory tract infections (ALRIs) especially severe ALRIs, constitute a global high burden of morbidity and mortality in children <5 y of age and respiratory syncytial virus (RSV) has been documented to a play a major aetiological role. However, Nigerian reports on severe childhood RSV ALRIs are rare and most reports are old. With recent advances in RSV preventive strategy, arises the need for a recent appraisal of RSV infection in children with severe ALRI. The current study thus set out to determine the prevalence of RSV infection among hospitalized children <5 y of age and describe the related social determinants.

Methods: We performed a descriptive cross-sectional study conducted over 1 y of 120 children, ages 2–59 months, diagnosed with ALRI. Relevant data were obtained and an antigen detection assay was used for viral studies.

Results: The prevalence of RSV infection was 34.2% and its peak was in the rainy months. The proportion of infants in the RSV-positive group was significantly higher than that in the RSV-negative group (82.9% vs 54.4%; p=0.002). These findings were largely consistent with those of earlier reports.

Conclusions: RSV has remained a common cause of severe ALRI in infants, especially during the rainy months in Nigeria. It is thus suggested that more effort be focused towards implementing the current global recommendations for the prevention of RSV-associated LRI, particularly in infants.

Keywords: acute lower respiratory tract infections, bronchiolitis, Nigeria, pneumonia, prevalence, RSV

Introduction

Despite the continuing global efforts at minimizing its impact, acute lower respiratory infections (ALRIs) remain a global source of public health concern.[1–3] With about 156 million new cases per year globally,[1] ALRIs, especially pneumonia, continue to account for a significant proportion of paediatric morbidity in children <5 y of age.[4] Of this global burden, 151 million cases live in developing countries, with an average of 0.29 episodes per child.[1] Nigeria ranks fifth in the world regarding pneumonia-related morbidity, with 6 million new cases per year.[1]

Whereas several studies in developing countries have focused on identifying the causative bacterial pathogens as a useful strategy for stemming ALRI-related morbidity, there is a clear paucity of data on the causative viral agents, especially in Nigeria.[5,6] In contrast, viral studies on paediatric ALRIs emanating from the developed world have shown respiratory syncytial virus (RSV) to be the single most common pathogen of childhood ALRIs,[5,7] particularly in infants with pneumonia and bronchiolitis.

Globally, as well as in a few local reports from Nigeria and other African countries, a high contribution of RSV to severe ALRI cases has been reported.[7–10] In Nigeria, Olaleye et al.[11] reported the local prevalence of RSV infection as 23.0% among hospitalized children in southwestern Nigeria. Similar findings were also recorded by Aderele et al.[12] in the 1990s and subsequently by Johnson et al.,[8] with prevalence rates of 28.8% and 28.6%, respectively. However, most of these earlier studies were conducted 2–3 decades ago.

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With recent advances, geared towards RSV prevention on a global scale,[13] arises the need for a more recent appraisal of RSV infection in vulnerable children <5 y of age with ALRI, especially the severe forms, in Nigeria. Thus the main objectives of the current study were to determine the prevalence of RSV infection and compare the sociodemographic and risk factors of ALRI among RSV-positive and RSV-negative hospitalized children ages 2 months (age at which partial immunity from transplacentally acquired maternal anti-RSV antibodies has significantly waned[14]) to 5 y in Ilorin, North Central Nigeria.

Materials and methods

Study design and site

This was a descriptive prospective cross-sectional study conducted in the Emergency Paediatric Unit of the University of Ilorin Teaching Hospital (UITH), which is located in the Ilorin East Local Government Area (LGA) of Kwara State. Ilorin is the capital city of Kwara State, situated in the North Central geopolitical zone of Nigeria, with a yearly temperature range between 25°C and 34°C, humidity between 65% and 80% and annual rainfall of 100–150 cm.[15] The UITH is the main referral hospital in Kwara State and also receives referrals from many of the adjoining states in Nigeria. The average total yearly admission of children <5 y of age in the paediatric unit was 1773, of whom 200 were ALRI cases.

Sample size estimation

The minimum sample size required for the study was determined using Fisher's formula[16] and a total of 120 children were recruited consecutively over a 12-month period.

Ethical considerations

Ethical clearance was received from the Ethics and Research Committee of UITH and informed written consent was obtained from the parent or guardian of each subject after a clear explanation of the objectives and logistics of the study. No caregiver declined consent to the study, however, two initially recruited patients were not analysed because of difficulty in obtaining acceptable samples.

Subject recruitment

Children ages 2–59 months presenting at the Emergency Paediatric Unit of UITH with the symptom complex of one or more of the following ALRI clinical syndromes were recruited: bronchiolitis, characterized by a combination of a history or presence of fever (≥37.5°C), cough, wheeze or dyspnoea associated with bilateral expiratory rhonchi and/or fine inspiratory crepitations;[17] pneumonia, characterized by a history or presence of fever (≥37.5°C), acute cough, breathlessness, fast breathing and one or more auscultatory finding comprising reduced breath sound intensity, bronchial breath sounds and crepitations with or without the relevant radiographic findings of patchy or uniform lung opacities/consolidations and/or linear or interstitial streakiness.[17]

Inclusion criteria

Inclusion criteria were consecutive children <5 y of age (ages between 2 and 59 months) with an admission diagnosis of either bronchiolitis or pneumonia and parent/guardian informed consent.

Exclusion criteria

Exclusion criteria were: the parent/guardian declined consent, previously recruited children re-presenting within 2 weeks of onset of the initial symptoms and recruitment, children who presented with wheeze in whom a diagnosis of bronchial asthma had earlier been made and children with chronic lung disease such as bronchiectasis, lung abscess or tuberculous pneumonia.

A semistructured pro forma administered to each subject's parent or guardian was used to obtain sociodemographic information and other relevant clinical data required in making the diagnosis of ALRI. Social class categorization was based on the criteria earlier enunciated by Oyedeji.[18] Responses on exclusive breastfeeding of the child, exposure to smoking, attendance at day care settings and cooking facilities were sought and recorded.

Sample collection and testing

Nasal washings were obtained from the subjects on admission with a sterile bulb syringe by the researcher and a research assistant (both of whom were senior registrars in paediatrics). The researcher and research assistant were trained in proper sample collection prior to commencement of the study and their proficiency was assessed and ensured using role playing prior to patient recruitment.

The process of collection started with the initial filling of a bulb syringe with 2 ml of sterile saline, which was then inserted into one nostril at a time until the nostril was occluded. The saline was then instilled into the nostril, while the head was tilted back. The pressure on the bulb was then released to aspirate the specimen back into the bulb. The same process was repeated for the second nostril. The specimen obtained (ensuring up to 1 ml) was transferred into the specimen bottle provided, containing 1 ml of normal saline (to ensure a 1:1 dilution ratio of nasal wash specimen to transport medium). The specimens obtained were sent immediately to the laboratory (within 5 min) for storage at −20°C and subsequent analysis.[19]

Some a priori criteria were set to determine the acceptability of samples obtained, including immediate sample collection on presentation, retrieval of nasal aspirate in a ratio of 1:1 with viral culture medium, immediate transportation of samples to the laboratory and immediate storage in the laboratory. Two samples were not sent for analysis based on the fact that the criteria of acceptance were not met.

The RSV testing was done using the Directigen EZ RSV test (Becton Dickinson, Sparks, MD, USA), which is essentially a chromatographic immunoassay-based technique for RSV A and/or B antigen detection.[19]

During analysis of the nasal washings, the specimen was vortexed at room temperature and three drops of Extraction Reagent E was dispensed into the DispensTube. Then 250 μl of the vortexed specimen was pipetted into the DispensTube (containing Extraction Reagent E) and the sample was revortexed.

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Three drops of the revortexed specimen was introduced into the appropriately labelled RSV sample well. Test results were read at 15 min and up to 60 min after. Results that remained negative at 60 min were reported as negative. The results were interpreted as follows:

- Positive test (antigen present)—a visible reddish-purple line appeared in the 'read window' next to the test 'T' and a reddish-purple line next to the control 'C'. This was indicative of RSV antigen detection in the particular specimen.
- Negative test (no antigen detected)—no reddish-purple line is visible next to the test 'T'. This indicated RSV antigen was not detectable in the specimen. A reddish-purple line next to the control 'C' indicated proper performance of test procedure and reagents.

Chest X-rays were done for the recruited subjects within the first 24 h of presentation. Subjects were treated routinely with the most appropriate medications in accordance with the standard hospital/departmental guidelines for the two RSV-associated ALRI syndromes.

Data entry and analysis

The data recorded on the pro forma were entered into a microcomputer using numerical codes. Tables, graphs and charts were made from the data collected and subsequently translated to descriptive statistics using the relevant data with SPSS version 20 (IBM, Armonk, NY, USA). Frequency histograms were drawn for quantitative variables such as age, weight and height to determine if they were normally distributed. For normally distributed quantitative variables, descriptive statistics including the mean value and the corresponding standard deviation (SD), while median and interquartile range (IQR) values were used to describe 'skewed' quantitative variables. The Student t test or Mann–Whitney U test was used to test the significance of differences between continuous quantitative variables as applicable. Association between the various qualitative data, such as sociodemographic factors in RSV-positive and RSV-negative children with ALRI were tested using the χ^2 test. Yates corrected values were used where necessary. The level of significance was established at $p<0.05$.

Results

Age and gender distribution of the subjects

The mean ± SD age of the children with ALRI was 11.4 ± 10.3 months, with infants ages 2–<12 months accounting for 77 (64.1%) patients. Children ages 12–<24 months, 24–<36 months, 36–<48 months and 48–<60 months constituted 26 (21.7%), 11 (9.2%), 4 (3.3%) and 2 (1.7%) patients, respectively. There were 72 (60.0%) male children and 48 (40.0%) female children.

ALRI diagnoses in study subjects

Bronchopneumonia was the most common ALRI diagnosis, present in 84 (70.0%) subjects, while bronchiolitis and lobar pneumonia were found in 22 (18.3%) and 14 (11.7%) subjects, respectively.

Prevalence and monthly distribution of RSV infection

Forty-one (34.2%) of the total 120 children with ALRI were RSV positive while 79 (65.8%) were RSV negative.

Figure 1 shows monthly distribution of ALRI admissions and RSV-positive cases. The highest number of monthly ALRI cases (24 [20.0%]) was recorded in July and the lowest number (3 [2.5%]) was recorded in November. A total of 38 (92.7%) of the RSV-positive cases were reported between May and October (rainy months), compared with only 3 (7.3%) recorded during the dry season (November–April).

Prevalence of RSV infection according to the specific ALRI diagnosis

Figure 2 shows the distribution of RSV positivity among the ALRI diagnoses in the subjects. The highest RSV positivity rate (50.0%) was identified among those with bronchiolitis, while the rates among subjects with bronchopneumonia and lobar pneumonia were 31.0% and 28.6%, respectively. The distribution of RSV test positivity was not significantly different among the three diagnostic categories of ALRI ($p=0.22$).

Risk factors for ALRI in study participants

Table 1 shows the distribution of some risk factors for ALRI among the study participants. The majority of the children used kerosene or charcoal as cooking fuel and slept in crowded rooms (two or more people sharing sleeping room with child), constituting 105 (87.5%) and 90 (75.0%) of the subjects, respectively. In contrast, day care/school attendance and the presence of cigarette smoking in the home were documented in only 27 (22.5%) and 3 (2.5%) of the subjects, respectively.

Duration of symptoms prior to admission based on RSV status

The duration of symptoms among study subjects prior to admission ranged from 1 to 21 d. The median duration of symptoms of 4 d (IQR 3–5) among the RSV-positive ALRI subjects was not

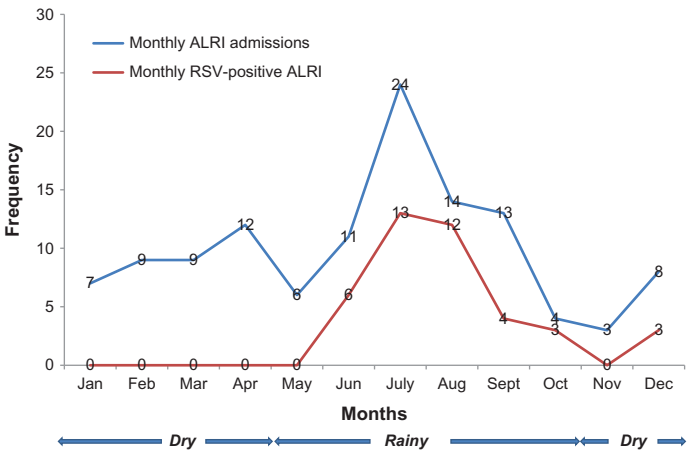


Figure 1. Monthly distribution of ALRI cases and RSV positivity.

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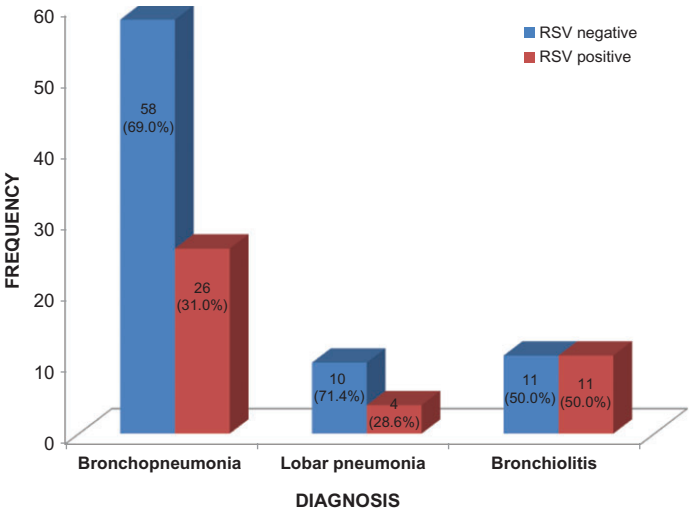


Figure 2. Distribution of ALRI diagnoses according to RSV status.

Table 1. Risk factors of ALRI among study participants

Risk factors	Frequency, n	Percentage (N=120)
Day care/school attendance		
Yes	27	22.5
No	93	77.5
Presence of other children <5 y of age in the household		
Yes	69	57.5
No	51	42.5
≥2 people sharing sleeping room with a child		
Yes	90	75.0
No	30	25.0
Cigarette smoking in the home		
Yes	3	2.5
No	117	97.5
Cooking fuel most frequently used		
Gas	15	12.5
Kerosene	50	41.7
Charcoal	18	15.0
Kerosene and charcoal	37	30.8
Exclusive breastfeeding		
Yes	57	47.5
No	63	52.5

statistically significantly different from that of 4 d (IQR 2–7) among the RSV-negative cases (p=0.22).

Comparison of sociodemographic characteristics in RSV-positive and RSV-negative children

Forty-one (34.2%) of the 120 children with ALRI were RSV positive while 79 (65.8%) subjects were RSV negative. The mean ± SD age in the RSV-positive group was 7.7 ± 8.8 months while that of the RSV-negative group was 13.4 ± 10.6 months (p=0.004). The proportion of infants in the RSV-positive group (34 [82.9%]) was significantly greater than in the RSV-negative group (43 [54.4%]) (p=0.002) [Table 2]. The gender distribution among the RSV-positive and RSV-negative groups as well as the distribution of social class among both groups showed no statistical significance.

Comparison of risk factors in RSV-positive and RSV-negative subjects

The distribution of the risk factors for ALRI based on RSV results is shown in Table 3. Greater proportions of children who slept in rooms with two or more people as well as those whose cooking fuels were kerosene and/or charcoal were recorded among the RSV-positive group compared with the RSV-negative group (82.9% vs 70.9% and 34.1% vs 29.1%, respectively). However, these were not statistically significant (p>0.05). The distribution of the other risk factors based on RSV status was also not statistically significant (Table 3).

Bacteraemia co-infection among RSV-positive isolates

With regard to RSV status and bacteraemia, 13 (31.7%) of the RSV-positive children had bacteraemia. Of the 13 subjects with concomitant bacteraemia, the predominant isolates were *Staphylococcus aureus* (5 [38.5%]) and *Klebsiella pneumoniae* (3 [23.1%]). All 13 RSV-positive children who had bacteraemia had a diagnosis of bronchopneumonia or lobar pneumonia, none had a diagnosis of bronchiolitis and the distribution was statistically significant (p=0.02).

Discussion

The identification of RSV in more than one-third of children <5 y of age with severe ALRI in the current study is comparable to the prevalence of RSV-associated severe ALRI by earlier authors from Nigeria.[8,12] Olaleye et al.[11] reported a slightly lower prevalence rate of RSV infection among hospitalized children in southwestern Nigeria. While methodological differences in the viral assay deployed in the Olaleye et al. series could account for the lower prevalence,[20] the persistently high contribution of the virus to severe ALRI in Nigeria remains a source of public health concern. Against the background of recent reports documenting a reduction in risk factors for ALRI in low–middle income countries (among which Nigeria is named),[21] the persisting high burden of RSV infection among children with severe ALRI suggests the need for focused preventive mechanisms (such as passive and active vaccination against RSV) in Nigeria, especially in children <5 y of age.

The seasonal pattern of RSV infection in the current study, where the majority of cases clustered between June and October (during rainy season), appears to be consistent with the observations in earlier reports from southwest and southern Nigeria.[22,23] However, the RSV seasonal pattern recorded in the present study is at odds with other reports from southwest Nigeria, where RSV clusters occurred in the cold and dry Harmattan months.[11,24,25] The differences in the seasonality of

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Table 2. Sociodemographic characteristics of study subjects according to RSV status

Sociodemographic characteristics	RSV positive, n (%)	RSV negative, n (%)	χ^2	p-Value
Age group (months)				
2–<12	34 (82.9)	43 (54.4)	7.215	0.002*
12–<60	7 (17.1)	36 (45.6)		
Gender				
Male	25 (61.0)	47 (59.5)	0.025	0.875
Female	16 (39.0)	32 (40.5)		
Social class				
High (class I, II)	14 (34.1)	31 (39.2)		
Middle (class III)	18 (43.9)	31 (39.2)	0.333	0.847
Low (class IV, V)	9 (22.0)	17 (21.6)		

*Statistically significant ($p<0.05$).

Table 3. Risk factors of ALRI according to RSV status

Risk factors	RSV positive, n (%)	RSV negative, n (%)	χ^2	p-Value
Day care/school attendance				
Yes	8 (19.5)	19 (24.1)	0.319	0.572
No	33 (80.5)	60 (75.9)		
Presence of other children <5 y of age in the household				
Yes	23 (56.1)	46 (58.2)	0.050	0.823
No	18 (43.9)	33 (41.8)		
≥2 people sharing sleeping room with a child				
Yes	34 (82.9)	56 (70.9)	2.087	0.149
No	7 (17.1)	23 (29.1)		
Cigarette smoking in the home				
Yes	0 (0.0)	3 (3.8)	0.419[a]	0.517[a]
No	41 (100.0)	76 (96.2)		
Most frequently used cooking fuel				
Gas	3 (7.3)	12 (15.2)	1.640	0.650[a]
Kerosene	18 (43.9)	32 (40.5)		
Charcoal	6 (14.6)	12 (15.2)		
Kerosene and charcoal	14 (34.1)	23 (29.1)		
Exclusive breastfeeding				
Yes	16 (39.0)	41 (51.9)	1.315[a]	0.252[a]
No	25 (61.0)	38 (48.1)		

[a]Yates corrected value.

the virus infection may be ascribed to temporally changing climatic conditions, as these studies were conducted several years apart.[11,25] Furthermore, the changes may also be partly attributable to the 'enigmatic nature' of the virus, a feature that has sometimes been invoked to explain the occurrence of varying epidemic burdens at different times and seasons of the year.[7,9] The relevance of this finding is the need for continuing or frequent surveillance of RSV infection in different geographical regions in planning for specific vaccine prevention for RSV infection.[26] Also, the current study finding of the peak RSV prevalence corresponding with the peak of ALRI hospitalization in the current study year underscores the role of RSV as a major aetiological agent among children <5 y of age and the need for more interventions against RSV infection.

The RSV positivity rate among children with a diagnosis of bronchiolitis in the present study was higher than the corresponding rate in those with a diagnosis of pneumonia. Even though this finding was not statistically significant, it underscores the

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predominant role of RSV as the major aetiological agent of bronchiolitis. This observation is in agreement with earlier reports.[12,26–29] Thus the current finding would partly support the need for possibly withholding the empirical use of antibiotics in children with bronchiolitis.[30] Furthermore, the current study finding of concomitant bacteraemia with RSV infection only among children diagnosed with either bronchopneumonia or lobar pneumonia, but not in subjects with bronchiolitis, further justifies this proposition.

The fact that the RSV-positive children were younger than the RSV-negative children in the current study is in agreement with the observations in most of the earlier reports.[9,12,26,29] Many of these studies recorded a preponderance of RSV-associated infections in infants, especially those <6 months of age. This finding has been attributed to the immaturity of the infant's immune system, the related lower levels of cell-mediated immunity and an equally poor antibody response in infancy, especially during the acute phase of the RSV infection.[26,31] Furthermore, the age-related variation in the airway sizes of children, with a high propensity for obstruction in the setting of an infection, is another plausible reason explaining this finding.[31] The preponderance of infants among those with RSV-associated ALRI, as well as ALRI generally in the current study, underscores the desirability and importance of RSV-targeted interventions in this most vulnerable age bracket. Such interventions are likely to impact positively on reducing the ALRI burden in children <5 y of age.

A comparison of some risk factors for ALRI showed a higher proportion of subjects sleeping in overcrowded rooms as well as those exposed to cooking fuel–related smoke (use of kerosene and charcoal) among RSV-positive subjects. However, this did not attain statistical significance, which is at odds with earlier studies in other climates where these factors were significantly associated with RSV infection.[31,32] Earlier studies in Nigeria did not examine the association of these risk factors with RSV infection.

The current study finding on risk factor comparisons between RSV-positive and RSV-negative subjects needs to be interpreted with caution, as the study was not powered to detect these differences; the risk factor analysis was a subsidiary of the RSV prevalence data set. A larger study with a larger number of RSV-positive subjects may highlight further the association of these risk factors with RSV infection. Thus it is concluded that RSV has remains a common cause of severe ALRI in hospitalized infants, especially during the rainy months in Nigeria and it is recommended that efforts at RSV prevention be focussed in this locale.

Authors' contributions: DM and ABR conceived the study. DM, DP, MB, RM, OT, RA and ABR designed the study protocol. DM and DP carried out the clinical assessment. DM, DP and RA carried out the immunoassays. DM, DP, RM and MB carried out analysis and interpretation of the data. DM drafted the manuscript. RM, MB, AA, OT and ABR critically revised the manuscript for intellectual content. All authors read and approved the final manuscript. DM is the guarantor of the paper.

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Competing interests: None declared.

Ethical approval: This research was reviewed and approved by the Ethics and Research Committee of the UITH according to the standards currently applicable to Nigeria.

References

1 Rudan I, Boschi-Pinto C, Biloglav Z, et al. Epidemiology and etiology of childhood pneumonia. Bull World Health Org. 2008;86(5):408–16.
2 Liu L, Johnson H, Cousens S, et al. Global, regional, and national causes of child mortality: an updated systematic analysis for 2010 with time trends since 2000. Lancet. 2012;379(9832):2151–61.
3 Lukšić I, Kearns PK, Scott F, et al. Viral etiology of hospitalized acute lower respiratory infections in children under 5 years of age—a systematic review and meta-analysis. Croat Med J. 2013;54(2):122–34.
4 Nair H, Simões EA, Rudan I, et al. Global and regional burden of hospital admissions for severe acute lower respiratory infections in young children in 2010 a systematic analysis. Lancet. 2013;381(9875):1380–90.
5 Weber MW, Milligan P, Sanneh M, et al. An epidemiological study of RSV infection in the Gambia. Bull World Health Org. 2002;80(7):562–8.
6 Johnson WBR, Aderele WI, Osinusi K, et al. Acute lower respiratory infections in hospitalised urban pre-school Nigerian children: a clinical overview. Afr J Med Med Sci. 1994;23:127–38.
7 Nair H, Nokes DJ, Gessner BD, et al. Global burden of acute lower respiratory infections due to respiratory syncytial virus in young children: a systematic review and meta-analysis. Lancet. 2010;375(9725):1545–55.
8 Johnson WBR, Osinusi K, Aderele WI, et al. Viral pathogens of acute lower respiratory infections in pre-school Nigerian children and clinical implications of multiple microbial identifications. West Afr J Med. 1993;12(1):11–20.
9 Nokes DJ, Ngama MJ, Bett A, et al. Incidence and severity of respiratory syncytial virus pneumonia in rural Kenyan children identified through hospital surveillance. Clin Infect Dis. 2009;49(9):1341–9.
10 Weber MW, Mulholland EK, Greenwood BM. Respiratory syncytial virus infection in tropical and developing countries. Trop Med Int Health. 2002;3(4):268–80.
11 Olaleye OD, Olawuyi AO, Baba SS. Sero-epidemiological studies of respiratory syncytial and adenoviruses in children in Ibadan, Nigeria, 1985–1988. Trans R Soc Trop Med Hyg. 1992;86(3):294–7.
12 Aderele WI, Johnson WB, Osinusi K, et al. Respiratory syncytial virus–associated lower respiratory diseases in hospitalised pre-school children in Ibadan. Afr J Med Med Sci. 1995;24(1):47–53.
13 Anderson LJ, Dormitzer PR, Nokes DJ, et al. Strategic priorities for respiratory syncytial virus (RSV) vaccine development. Vaccine. 2013;31(Suppl 2):B209–15.
14 Crowe JE Jnr. Respiratory sycytial virus. In: Kleigman R, Stanton B, St. Geme J III, et al. (editors). Nelson textbook of paediatrics. Philadelphia: Elsevier; 2015, p. 1606–9.
15 Elijah OA, Adedapo A. The effect of climate on poultry productivity in Ilorin Kwara State, Nigeria. Int J Poult Sci. 2006;5(11):1061–68.

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16 Araoye MO. Subjects selection. In: Araoye MO (editor). Research methodology with statistics for health and social sciences. Ilorin: Nathadex; 2003, p. 115–21.

17 Ibraheem RM, Johnson WBR, Abdulkarim AA, et al. Serum zinc levels as a predictor of clinical features and outcome of paediatric acute lower respiratory infections in Nigeria. Niger J Paediatr. 2013;40(4): 400–5.

18 Oyedeji GA. Socioeconomic and cultural background of hospitalized children in Ilesha. Niger J Paediatr. 1985;12:111–7.

19 Dickinson B. Directigen™ EZ RSV [package insert]. Sparks, MD: Becton Dickinson; 2010.

20 Popow-Kraupp T, Aberle JH. Diagnosis of respiratory syncytial virus infection. Open Microbiol J. 2011;5:128–34.

21 Rudan I, Brien KLO, Qazi S, et al. Epidemiology and etiology of childhood pneumonia in 2010: estimates of incidence, severe morbidity, mortality, underlying risk factors and causative pathogens for 192 countries. J Glob Health. 2013;3(1):010401.

22 Johnson A-WBR, Aderele WI, Osinusi K, et al. Acute bronchiolitis in tropical Africa: a hospital-based perspective in Ibadan, Nigeria. Pediatr Pulmonol. 1996;22(4):236–47.

23 Nwankwo MU, Dym AM, Schuit KE, et al. Seasonal variation in respiratory syncytial virus infections in children in Benin City, Nigeria. Trop Geogr Med. 1988;40(4):309–13.

24 Odaibo GN, Forbi JC, Omotade OO, et al. Incidence and burden of respiratory syncytial virus infection in a community-based cohort of under-five years children in Nigeria. Arch Basic Appl Med. 2013;1(1): 67–72.

25 Robertson SE, Roca A, Alonso P, et al. Respiratory syncytial virus infection: denominator-based studies in Indonesia, Mozambique, Nigeria and South Africa. Bull World Health Org. 2004;82(12):914–22.

26 Rodríguez DA, Rodríguez-Martínez CE, Cárdenas AC, et al. Predictors of severity and mortality in children hospitalized with respiratory syncytial virus infection in a tropical region. Pediatr Pulmonol. 2014;49 (3):269–76.

27 Fattouh AM, Mansi YA, El-anany MG, et al. Acute lower respiratory tract infection due to respiratory syncytial virus in a group of Egyptian children under 5 years of age. Ital J Pediatr. 2011;37:14.

28 Hussey GD, Apolles P, Arendse Z, et al. Respiratory syncytial virus infection in children hospitalized with acute lower respiratory tract infection. S Afr Med J. 2000;90(5):509–13.

29 Lucion MF, Juárez V, Viegas M, et al. Respiratory syncytial virus. Clinical and epidemiological pattern in pediatric patients admitted to a children's hospital between 2000 and 2013. Arch Argent Pediatr. 2014;112(5):397–403.

30 Coates B, Camarda L, Goodman D. Wheezing, bronchiolitis and bronchitis. In: Kleigman R, Stanton B, St. Geme J III, et al. (editors) Nelson textbook of paediatrics. Philadelphia: Elsevier; 2015, p. 2044–9.

31 Sommer C, Resch B, Simões EAF. Risk factors for severe respiratory syncytial virus lower respiratory tract infection. Open Microbiol J. 2011;5:144–54.

32 Jeena PM, Ayannusi E, Annamalai K, et al. Risk factors for admission and the role of respiratory syncytial virus-specific cytotoxic T-lymphocyte responses to children with acute bronchiolitis. S Afr Med J. 2003;93(4):291–4.

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