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Original Research Article

Revisiting Challenges in Recognizing and Treating Childhood Acquired Pneumonias in a Tertiary Referral Hospital

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Abstract

Background: Childhood acquired Pneumonias are reported to referral Hospitals in India thought the incidence has come down remarkably. Children of all age groups are affected due to rise in antimicrobial resistance to the organism. Differentiating Pneumonias of bacterial from viral etiology using rapid surrogate markers is pivotal in achieving clinical success.

Aim of the study: To study the clinical criteria and analyze the causes, laboratory investigations in the accurate diagnosis and treatment of Childhood Acquired Pneumonias.

Materials: 153 children between 3 months and 12 years diagnosed as Childhood Acquired Pneumonia (CAP) were analyzed. Children presenting with history of foreign body inhalation, fever, productive cough, purulent sputum, breathlessness, and pleurisy were included. Signs of Tachypnea, Ronchi, Rales heard over the chest, increased bronchial breath sounds, tactile fremitus, egophony and decreased tactile fremitus were included. X-Ray chest, CT scan chest were undertaken. Antigenic tests for influenza A and B and respiratory syncytial virus were undertaken. Radiological evidence of pleural effusion and Alveolar infiltrates was considered as bacterial Pneumonias. Presence of Interstitial infiltrates was taken as viral or bacterial infections. Total WBSC count, C-reactive protein and erythrocyte sedimentation rate were done

Results: There were 90 (58.82%) male children and 63 (41.17%) female children. A male to female ratio was 1:1.42 was observed. Among the 90 male children, there were 49 (32.02%) children aged between 3 months and 5 years and 41 (26.79%) were above 5 years. Among the 63 female children, there were 34 (22.22%) children aged between 3 months and 5 years and 29 (18.95%) were aged above 5 years.

Conclusions: Community Acquired Pneumonia remains a common and major disease in children causing morbidity. Hospitalization of the children with CAP was individualized resting upon their age, underlying medical risk factors, and clinical features like severity of illness. Symptoms such as tachypnea and vomiting were significant statistically in the diagnosis of CAP in this study, when correlated with the laboratory findings. Laboratory investigations like Highest WBC count, Highest CRP were statistically significant in children aged below 5 years when compared to above 5 years old children

Keywords: Community acquired Pneumonia (CAP), Lung parenchyma, Respiratory distress, and viral pneumonias.

Background

Childhood Acquired pneumonias (CAP) were defined as Infection of lung parenchyma developing in children due to various factors including foreign body inhalation, community-based infections and as a complication of upper respiratory infections. They inhibit lung function causing tachypnea, dyspnea, fever, chest pain and cough. Incidence of CAP in India is 4 million/ year; 20% requiring hospitalization [1]. The mortality rate in outpatient settings was 1%–5%, and ICUs it was 25% [1, 2]. Pneumonia was main cause of death among the infectious diseases in the USA [3]. Based on the three categories of CAP, one treated as OPD basis, admitted to the hospital and admitted to the ICUs [4, 5]; the most common pathogen was *Streptococcus pneumonia (S Pneumonia)* which was increasingly turning resistant to many antibiotics. CAP was also occurring with an atypical pathogen. These organisms may cause pneumonia or may serve as co-infecting agents along with bacteriae [6]. Atypical pathogens were *Chlamydophila pneumonia*, *Mycoplasma pneumoniae* and *Legionella* species. Other virii were adeno virus, influenza virus and respiratory syncytial virus. Among the bacteriae enteric gram-negative bacteria, Drug resistant Streptococcus Pneumoniae (DRSP), or even *Pseudomonas aeruginosa* caused CAP in outpatients. [3] Among the CAP patients admitted to ICUS, *P. aeruginosa* was the causative agent in 10%–20% of patients. [4, 7] *Staphylococcus aureus* was also reported in post Influenza infections in CAP. Methicillin-resistant *S. aureus* were also reported but their occurrence was sporadic [8]. In the management of CAP, guidelines of American Thoracic Society (ATS) and Infectious Diseases Society of America (IDSA) guidelines were quoted for the management of CAP [9]. Even though newer treatment protocols were coming into practice, risk factors, drug-resistant pathogens and short- and long-term complications occurring in them (CAP are yet to be studied [10, 11]. Biomarkers in the diagnosis of CAP, such as C-reactive protein (CRP) and procalcitonin (PCT) are the most wanted. [12, 13] Similarly other biomarkers like fibroblast growth factor (FGF) 21, pro-adrenomedullin and interleukin (IL)-6 are under study [14].

Materials

A cross sectional study was conducted prospectively between Jan 2017 to Dec 2019 in a tertiary teaching Hospital where 153 children diagnosed with Childhood Acquired Pneumonias reporting to the Department of Pediatrics in a tertiary teaching Hospital were analyzed. Institutional Ethical committee approved the study and an ethical committee approved consent performa was used. Inclusion Criteria: Children aged between 3 months and 12 years, Children presenting with fever, dyspnea, pleuritic chest pain, productive cough with purulent sputum, Children with clinical signs of raised respiratory rate, Ronchi and rales over the involved lobe or segment, bronchial breath sounds, increased tactile fremitus and egophony (increased resonance of voice sounds heard when auscultation of the lungs, often caused by lung consolidation and fibrosis) and decreased tactile fremitus and dullness on chest percussion as a result of para-pneumonic effusion or empyema were included as Inpatient Patients. Children with Hypoxemia (Oxygen saturation less than 90% in room air), Infants aged between 3 and 6 months with CAP, children with Tachypnea were included. Children with respiratory rate more than 50 breaths per minute, presenting as apnea,

grunting and difficulty in breathing were included. ICU admissions were based on acutely requiring use of noninvasive positive pressure ventilation (e.g., continuous positive airway pressure (CPAP), or bi-level positive airway pressure (BIPAP), Pulse oxymetry saturation less than 92% on Fio2 of more than 0.50, or when the child needs ventilation using a endotracheal tube were included.

Exclusion Criteria: Children with underlying co-morbidities like cardiopulmonary diseases, genetic syndromes, neurocognitive disorders and Neuro muscular disorders were excluded. Children with diabetes, hypothyroidism was not included. Children with retroviral infections and sickle cell disease empyema were excluded. All the subjects were investigated with X-Ray chest, CT scan chest. Antigenic tests for respiratory syncytial virus and influenza A and B were undertaken. X-Ray findings of pleural effusion and Alveolar infiltrates were taken as criteria for bacterial Pneumonias. Interstitial infiltrates were considered as viral or bacterial infections. C-reactive protein and white blood cell count, and erythrocyte sedimentation rate were also undertaken. In children suspected of foreign body inhalation were subjected to fibre-optic Bronchoscopy to rule out inhalation of foreign bodies into the trache-bronchial tree. Depending on the age groups, empirical treatment schedule adopted Alzomor, Omar *et al* (15) was used in this study. Children with viral CAP were administered Oseltamivir (Tamiflu) 12mg/mL mixture or 30mg, 45mg and 75 mg capsule form depending on their Age and weight. For children with weight > 15 to 23 kg, 45 mg mark on Tamiflu syringe (= ~4.0 mL on oral syringe) or 45 mg Paediatric Tamiflu capsule was used. For children weighing more than 23 to 40 kg, 60 mg demarcation on Tamiflu syringe (= 5.0 mL on oral syringe) or two, 30 mg Tamiflu capsules were used. For children ≥ 1 year > 40 kg (adult dose) 75 mg (45 mg + 30 mg mark) on Tamiflu syringe or 75 mg 'adult' capsule was used (= ~6.5 mL on oral syringe) twice daily for 5 days. The response to the treatment was recorded followed by using statistics to analyze them.

Results

153 children with lung parenchyma infections with little contact with the healthcare system (acquired outside the Hospital), clinically characterized by impaired lung function, presenting with dyspnea, fever; chest pain and cough were included. The study was conducted in the Department of Pediatrics of a tertiary teaching Hospital. There were 90 (58.82%) male children and 63 (41.17%) female children. The male to female ratio was 1:1.42. Among the 90 male children, there were 49 (32.02%) children aged between 3 months and 5 years and 41 (26.79%) were above 5 years. Among the 63 female children, there were 34 (22.22%) children aged between 3 months and 5 years and 29 (18.95%) were aged above 5 years. The youngest child was 3 months old and the eldest child was aged 144 months (12 years) old with a mean age of 47.35±6.32 months (3.94±6.32 years). Children aged between 3 months to 5 years were 83 (54.24%) and children above 5 years were 70 (45.75%). The mean age of children aged below 5 years was 2.46±0.95 years and the mean age of children aged above 5 years was 6.45±3.10 years (Table 1). The demographic data and the commonest symptoms were tabulated in the Table 1. It was observed that symptoms such as tachypnea and vomiting were significant statistically in the diagnosis of CAP in this study when correlated with the laboratory findings (Table 1.)

Table 1: Showing the clinical features and demography of children with CAP (n-153)

	3 months to 5 yrs *n* = 83 (54.24%)	**> 5 y to 12 /yrs n= 70 (45.75%)**	**Total n = 153 (100%)**	***p***
Age (y) Mean age	2.46 ± 0.9	6.45 ± 3.08	8.91 ± 3.17	< 0.012*
Sex (male) Sex (female)	49 (32.02%) 34 (22.22%)	41 (26.79%) 29 (18.95%)	90(58.82%) 63 (41.17%)	0.134 0.211
School attendance	37 (24.18%)	53 (34.64%)	90(58.82%)	< 0.024*
Underlying disease	10(06.53%)	04 (02.61%)	14 (09.15%)	0.310
Presenting Symptoms				
Fever	76 (91.56%)	67 (95.71%)	143 (93.46%)	0.480
Cough	69 (83.13%)	68 (97.14%)	137 (89.54%)	0.430
Tachypnea	48 (57.83%)	25 (35.71%)	73 (47.71%)	0.043*
Vomiting	35 (42.16%)	29 (41.42%)	65 (42.48%)	0.035
Abdominal pain	19 (22.89%)	21 (45.90%)	40 (26.14%)	0.179
Diarrhea	11 (13.25%)	08 (10.0%)	19 (112.41%)	0.581

* The *p* values in bold font indicates statistical significance.

All the investigations mentioned in the materials and methods were done in all the children and only positive results and significant results were tabulated in Table 2. 144/153 (94.11%) children showed in their sputum examination, nasopharyngeal secretions examination, positive results and the remaining 9/153 (05.88%) showed negative results. In children below 5 years virus Antigenic identification positive in 23/153 (20.26%), Bacteria positive in 36/153 (23.52%), both bacteria and viruses in 38/153 (24.83%), RV with more than 1 bacterium in 11/153 (07.18%), HMPV with more than 1 bacterium in 08/153 (05.22%), Streptococcus pneumoniae with more than 1 virus in 13/153 (08.49%) and Haemophillus influenza with more than 1 virus in 15/153 (09.80%), (Table 2). The distribution of positive sputum examination results among the children aged below and above 5 years is shown in Table 2. The mean values of Total white blood cell count, C reactive protein values, temperature recording, and X-Ray chest findings were tabulated in (* denotes p value <0.05 was taken as significant) Table 2.

Table 2: Shows Clinical findings of children with CAP with isolated virii, bacteria, combination of both, and the most common combinations of viruses and bacteria and their Laboratory results (n-153)

Characteristic	**Viruses**	**Bacteria**	**Both viruses and bacteria**	**RV with ≥1 bacterium**	**HMPV with ≥1 bacterium**	***Streptococcus pneumoniae* with ≥1 virus**	***Haemophilus influenzae* with ≥1 virus**
N (%)	23/153 (20.26 %)	36/153 (23.52 %)	38/153 (24.83 %)	11/153 (07.18 %)	08/153 (05.22 %)	13/153 (08.49 %)	15/153 (09.80 %)
Age (years) 3 months to 5 Years Above 5 Years	14 (60.86%) 09(39.13%)	25 (69.44%) 11 (30.55%)	22 (57.89%) 16(42.10%)	05 (4.45%) 06(54.54%)	04(50%0) 04(50%)	06(46.15%) 07(53.84%)	07 (46.66%) 08(53.33%)
Lab values on admission							

White blood cell count (10 ^{9}/L)	17.9 (14.6–21.4)	20.1 (14.0–26.7)	18.12 (10.30–23.4)	20.0 (10.0–28.9)*	11.3 (5.4–12.3)	22.2 (19.1–26.8)*	12.1(8.–11.4)
Serum C-reactive protein level (mg/L)	80.75(5.85–156.50)	171.2 (118.30–224.0)	122.6(38.60–182.50)	127.3 (25.70–241.40)	62.45 (22.40–238.10)	134.6(48.50–232.60)*	97.20(32.0–139.20)
Fever (°C)	40.40 (39.9–41.4)	40.8 (39.5–41.20)*	39.9 (38.65-40.4)	39.9 (38.8–40.20)	39.8 (39.7–40.30)*	39.9 (39.8–41.2)*	39.7 (39.7–40.2)
Chest radiograph findings							
Alveolar infiltrates, *n* (%)	14 (60.86%)	23 (63.88%)	21 (55.26%)	09 (81.81%)*	07 (87.5%)*	10 (76.92%)*	09 (60%)
Interstitial infiltrates, *n* (%)	06 (26.08	06 (16.66)	11 (28.94)	2 (18.18	1 (12.5%)	3 (23.07 %)	06 (40%)*

HMPV: human metapneumovirus; RV: rhinovirus.
* The *p* values in bold font indicate statistical significance.

In this study the mean duration of fever in children aged below 5 years (including before after admission) was 06.65± 4.10 days when compared to 07.15± 2.90 days and was not significant statistically (p value more than 0.05). Whereas mean values of observations like total hospitalization, Number of days in ICU admission (among 14/83 in < 5 yrs & 10/70 in >5 yrs children), Oxygen requirement and ventilator usage required were statistically significant in both below 5 and above 5 years old children (Table 3). Similarly, the mean values of laboratory data like Highest WBC count, Highest CRP and complications were also statistically significant in children aged below 5 years when compared to above 5 years old children (Table 3).

Table 3: Shows the clinical course and laboratory data of children with CAP (n-153).

Clinical course	**≤5 y/o *n* = 83 (54.24%)**	**>5 y/o *n* = 70 (45.75%)**	***p***
Observations: Mean values			
Duration of fever (days)	6.65 ± 4.10	7.15 ± 2.90	0.219
Hospitalization (days)	09.30 ± 4.10	8.40 ± 3.35	0.011*****
ICU admission (days)-(17/83 (20.48%) in < 5 yrs & 14/70 (20%) in >5 yrs children)	21.5 ±2.85	16±2.10	0.046*
O_2 requirement needed	59 (71.08%)	58 (82.85%)	0.023*
Ventilator required	16 (19.27%)	11 (15.71%)	0.048*
VATS	01(01.20%)[a]	0 (0)	0.038*
Macrolides used	44 (53.01%)	39 (55.71%)	0.020*
Laboratory data			
Highest WBC (/mm^3)	15412 ± 670	9743 ± 591	0.001*
Highest CRP (mg/dL)	15.15 ± 10.60	9.45 ± 6.45	0.018*
Complications	12 (14.45%)	05 (07.14%)	0.019*
Pleural effusion	08 (09.63%)	9 (13.6)	0.545

Pneumatocele	03 (03.61%)	0 (0%)	0.229
Respiratory failure	01 (01.58%)	1 (1.58)	0.642

*The p values in bold font indicates statistical significance.
CAP = community-acquired Pneumonia; CRP:C-reactive protein; ICU = intensive care unit; O2 = oxygen; WBC = white blood cell.

Discussion

153 children with diagnosis of childhood acquired Pneumonia matching with WHO definition were included. Clinical and laboratory signs of CAP mimic features of severe infection, such as fever, tachycardia, altered leukocyte counts, were nonspecific and were frequently present in other acute conditions. Because Biomarkers like C-reactive protein (CRP) and procalcitonin were helpful in ruling out CAP than in establishing its definitive diagnosis, frequent errors occur. Radiological interpretation by non-radiologists in the ERs caused errors in interpretation are relatively frequent [17]. Hence initial assessment of a child presenting with Signs and symptoms of LRTI and establishing final diagnosis of CAP could be often a challenge. In a study by Bahlis et al [18], in fact it was noted 1/3rd of the patients hospitalized for respiratory infections failed to meet the diagnostic features of CAP and were removed from the analysis. Once the diagnosis was established, the major guidelines suggest CAP severity should be based upon the criteria to know the treatment and antibiotic therapy [19]. Implementing the major guidelines was not possible always as the severity scores recommended were not used by all pediatricians in the emergency room or referral physicians. (19) The mean age of children aged below 5 years was 2.46±0.95 years and the mean age of children aged above 5 years was 6.45±3.10 years. Pneumonia was the most commonly encountered lung disease of children younger than 5 years of age [20]. In poor countries CAP accounts for high morbidity and mortality associated with the condition (18). CAP in children aged below 5 years resulted in high childhood mortality; an estimated 1.6–2.2 million deaths globally in children according to WHO [20]. In children below 5 years virus Antigenic identification positive in 23/153 (20.26%), Bacteria positive in 36/153 (23.52%), both bacteria and viruses in 38/153 (24.83%), RV with more than 1 bacterium in 11/153 (07.18%), HMPV with more than 1 bacterium in 08/153 (05.22%), Streptococcus pneumoniae with more than 1 virus in 13/153 (08.49%) and Haemophillus influenza with more than one virus in 15/153 (09.80%). William J and Harris P [21] concluded that Respiratory syncytial virus was reported frequently in the very young. Adenovirus, parainfluenza virus, influenza virus and meta-pneumovirus virus were known to affect the children aged below 5 years. Bacterial infections as a cause of CAP were reported commonly in older children (> 5 years). Most of the studies in the developed countries for 15 years suggested that Mycoplasma and Streptococcus pneumoniae were responsible for majority of of bacterial pneumonia cases [22, 23]. But the incidence of isolation of these organisms in children with CAP varies in different studies; the incidence of S pneumoniae from 4% [26] to 8% [23] to 21% [24]. Similar differences are seen for Mycoplasma Pneumoniae. The algorithm stressed by WHO points out the importance of tachypnea, as a crucial indicator of pneumonia. Developed world studies also support this view [25, 26]. Tachypnea was found to have sensitivity of 74% and % for radiological definition of pneumonia according to the study by Palafox [27]. Hence the job of the clinicians remains to be alert to examine the children who present early stages of the disease. Palafox also stated that tachypnea in children had a lower sensitivity and specificity of CAP, if it

appeared in less than three days [27]. But they should be cautious about the absence of tachypnea does not exclude the absence of pneumonia [28]. The mean values of laboratory data like Highest WBC count, Highest CRP and complications were also statistically significant in children aged below 5 years when compared to above 5 years old children (Table 3). The Total WBC count, CRP, and ESR were not determining the aetiology of bacterial, viral, and mixed pneumonias [29]. Hence should not be ordered as a routine in acute phase pneumonia [30]. WHO guidelines standardized and classified radiological reporting of X-Ray chest as "Normal appearance", "Infiltrates" and "end stage consolidation defined as a "significant amount of alveolar type consolidation" for epidemiological studies of pneumonia. But correlation between causative agent (Viruses or bacteria) of CAP and Radiological findings by Swischuk [31] found a 90% accuracy rate. However, Bettenay [32] reported that there was a meager chance (30%) of finding a bacterium, when the X-ray chest suggested a bacterial cause when the system designed by Swischuk was used [31]. Thus, even though consolidation was reliable to diagnose and label CAP but should not be used to presume that it was a bacterial infection. In a similar study by Virkki et al [33], while assessing 254 children to find the correlation between radiological and bacteriological aetiology, reported only in 72% of children with alveolar infiltrates had a bacterial infection. Children with primarily viral pneumonia; half of them had alveolar changes. The mean values of observations like total hospitalization, Number of days in ICU admission (among 14/83 in < 5 yrs & 10/70 in >5 yrs children), Oxygen requirement and ventilator usage required were statistically significant in both below 5 and above 5 years old children (Table 3). Depending on the age groups empirical treatment schedule (Table 1) was adopted in this study, Alzomor, Omar et al [18]. Antibiotic choice was initially empirical, based on the earlier studies, at the same time taking the child's age. The most common bacterium noted in CAP was S Pneumoniae. The BTS guidelines [3] always suggested initially oral amoxicillin for children below 5 years, with erythromycin, Clarithromycin, co-Amoxyclav, Cefaclor, , and Azithromycin as alternate choices. Mycoplasma as an aetiological agent of CAP in the younger age group ranges from 2% [35] to 39% [34]. Hence using Macrolides as the first choice remains as a dilemma to the clinicians in addition to penicillin. Studies could not provide a clear recommendation to combine macrolides with other antibiotics in treating CAP as first line treatment. [35,36] Route of administration: The choice of treating children admitted to Hospital, either with oral or parenteral antibiotics were not investigated with randomized controlled trials. The British Thoracic Society (BTS) guidelines [3] suggested parenteral antibiotics were to be used for children with severe symptoms or signs and for children who do not tolerate oral antibiotics. IV antibiotics were administered to children who were vomiting or requiring oxygen and require Hospital admission in this study. Length of treatment: Oral antibiotics were used for 5–7 days initially and the duration prolonged to 10 days in severe infections (based on the antibiotic is used). Such a practice was based on individual clinician's choice but not based on the clinical research. In India a multi-centre randomized controlled trial was conducted [36] using oral amoxicillin in hospital admitted children for the first 48 h and compared them with children at home administered with oral amoxicillin for 7 days. Literature showed treatment recommended by WHO for severe pneumonia in children at tertiary care hospitals. But the present study compared "non-severe" pneumonia children attending the OPD of Pediatric with children with established clinical diagnosis nut not confirmed on X-Ray chest. There were no complications reported in the

children during their hospital stay in this study. Follow up: A follow up clinical examination and X-ray chest was arranged for 88/153 (57.51%) children in this study at 6–8 weeks. There were no recurrences of symptoms and signs of CAP in these children, other children were los for follow up.

Conclusions

Community Acquired Pneumonia remains a common and major disease in children causing considerable morbidity. Laboratory investigations like Highest Total WBC count, Highest CRP were statistically significant in children aged below 5 years when compared to above 5 years old children. Total WBC count, CRP and ESR or their combinations had a limited role in differentiating bacterial from viral CAP in children. Higher values of these markers are point out to bacterial etiology, but low values do not rule out bacterial etiology. Accurate differentiation of viral and bacterial pneumonias based on radiological and laboratory findings was most difficult. S. pneumoniae was the common cause of paediatric CAP and co-infections with M. pneumoniae and viruses are common. Identifying the children with grave signs like inability to drink/feed, vomiting everything, convulsions, lower chest in drawing, central cyanosis, lethargy, nasal flaring, grunting, head nodding, and oxygen saturation <90%) helped in predicting and preventing death and could be used as indicators for critical care the hospital.

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