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Clinical Outcome of Children Hospitalized with Community Acquired Pneumonia Treated with Ampicillin in Tertiary Care Center

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Abstract
Pneumonia is the leading infectious cause of under 5 mortality. This study was done to describe the clinical outcome of children hospitalized with Community-Acquired Pneumonia receiving Ampicillin and to assess factors influencing Treatment Failure in Community Acquired Pneumonia treated with Ampicillin. Prospective observational study, in which 235 children with Severe Pneumonia between 2 months to 60 months were enrolled and started with intravenous Ampicillin according to WHO guidelines and were monitored for response to therapy. Outcomes were assessed after 48 hours of starting Ampicillin. Among 235 cases, children who responded to Ampicillin were 192 (81.7%), Forty three (18.3%) children did not respond to Ampicillin. Among 235, males were 60.85% and females were 39.15% and 51.9% of children were infants and 48.1% were above 1 year. All children (100%) had history of fever and cough. Majority were (85.1%) from low socioeconomic group and 80.85% were completely Immunized. MAM was present in 30.2% of children, 30.21% had signs of Rickets and 70.21% children had anemia There was significant improvement in general condition of the children, tachypnea, fever, chest retractions and requirement of oxygen from the time of admission to 48 hours To conclude intravenous Ampicillin is effective as the first line antibiotic for children hospitalized with severe Pneumonia.

INTRODUCTION

Pneumonia, defined as inflammation of the lung parenchyma, is the leading infectious cause of death globally among children younger than age 5 yr, killing approximately 2400 children a day accounting for an estimated 0.9 million (16%) total deaths annually[1]. The incidence of pneumonia is >10-fold higher (0.29 episodes vs 0.03 episodes) and the number of childhood-related deaths from pneumonia ˜2,000 fold higher, in developing than in developed countries[2].

These differences are due to a number of factors. First, the incidence of risk factors such as malnutrition, crowding, low birth weight, Human Immunodeficiency Virus (HIV) and the lack of measles and pneumococcal immunization is much higher among children in developing countries[3-6].

Second, they are more likely to be affected by other likely or possible risk factors such as zinc and vitamin A deficiency, poor maternal education and living in polluted areas[3-6]. Finally, there are profound differences between developing and developed countries in the organization and efficiency of their health systems[7].

India carries the largest burden of disease and deaths because of pneumonia, accounting for 43 million cases and 0.15 million deaths[1]. The median incidence of pneumonia in India is estimated to be 0.37 episodes per child per year[8]. Recent estimates in under-fives suggest that 14.2% of deaths1 and 24% of National Burden of Disease is due to pneumonia.9 Hospital based studies have reported that 20-30% of admissions in under-fives are due to pneumonia. Case fatality rates in hospitalized children are reported to be between 8.7% and 47%[10-13].

Moreover, Pneumonia is a common cause of hospitalization worldwide, which is an economic burden for the health care system[14]. In order to control the situation in developing countries, the World health organization(WHO) proposed standardized procedures to diagnose and treat children with CAP[15]. Antibiotics are the main stay of the treatment for pneumonia. In such algorithm, it is recommended that Ampicillin is given to children hospitalized with severe Pneumonia[15] (old classification was retained to avoid confusion., equivalent toPneumonia in new WHO-2014).

Older classification was chosen for its ease of application

Our study was novel and very much relevant in our setting and to our cohort selection who could not have been sent home with diagnosis of Pneumonia and followed up on oral antibiotic, lest important parameters could not have been monitored and treatment failure not assessed properly.

Hence we undertook this study with i.v Ampicillin which was more practical, operational and convenient., hence our study was novel and relevant to the circumstances and needs .

The rationale for using Ampicillin in treating bacterial CAP is the high prevalence of Streptococcus pneumonia, which is the main target[16].

To reduce infant and under five mortality, it is important to reduce mortality caused by pneumonia by selection of appropriate first line antibiotic. Even after WHO recommendation many pediatricians are using higher antibiotics to treat severe pneumonia. This study was done to support Ampicillin as the first line antibiotic for hospitalized cases of severe pneumonia, which is cost effective. This study supports mitigation of unnecessary usage of antibiotics.

Objectives: To describe the clinical outcome of children hospitalized with community-acquired pneumonia receiving Ampicillin.

MATERIALS AND METHODS

It is a prospective observational study was done on children admitted with severe pneumonia treated with injection Ampicillin aged between 2 months to 5years at Sri Balaji Medical College Hospital and Research Institute,Tirupati Andra pradesh. This study was done from Feb-2021-Dec-2023

This sample size calculator uses a normal distribution (50%) to calculate present study optimum sample size. Approximately 200-250 cases of pneumonia were recorded per year, cited in relevant records of our hospital and arbitrarily assumed to have the desired level of significance 0.05. Margin of error was 5%. The total population achieved was 235.

Inclusion Criteria: Patients fulfilled the criteria of severe pneumonia as per old WHO guidelines[12].

Age between 2-60 months

Children hospitalized with history of rapid respiration with difficulty in breathing. Rapid respiration (tachypnea) was defined as respiratory rate of more than 60, 50 or 40 per minute in children below 2 months of age, 2 months to 1 yr and 1-5 yr of age, respectively. Difficulty in breathing was defined as lower chest indrawing.

Exclusion Criteria: Pneumonia with known case of CHD or congenital malformations of the respiratory tract

Complicated pneumonia at onset like empyema/abscess/necrotizing pneumonia/pleural effusion.

Known case of active pulmonary tuberculosis

Known case of primary or secondary immunodeficiency.

Hospital acquired pneumonia.

Pneumonia with co morbid illness like diabetes/CKD/nephrotic syndrome/asthma/chronic GERD.
Those allergic to Penicillin.
Those who have received antibiotic for more than 48 hours.
Those with Severe Acute Malnutrition

Total of 235 patients who were fulfilling the inclusion and exclusion criteria after taking written informed consent from parents/guardian of the patients about the proposed study were taken for the study. Patients who left against medical advice within first 48 hours of Ampicillin were excluded from the analysis.

Details were entered in a pre defined proforma which had Following details

- Demographic details of children with severe pneumonia, detailed history of presenting complaints, relevant past and family history
- History of immunization as per National Immunization Schedule was elicited from informant/parents and verified by checking the records wherever available, socioeconomic status according to modified Kuppuswamy's classification[17] and history relevant to inclusion and exclusion criteria
- Detailed anthropometry, vitals, general and systemic examination.

All children in the study with severe pneumonia were started with intravenous Ampicillin 50mg/kg body weight

sixth hourly after giving test dose according to WHO guidelines[12] and were monitored for response to therapy.

Supportive therapy like acetaminophen was given if fever was recorded and oxygen was given whenever required.

Intravenous fluids were given in maintenance dose, till the child could take adequate oral feeds.

Outcomes were assessed after 48 hours of starting Ampicillin. If improved, child was given 5-7 days of Ampicillin. If no improvement was seen after 48 hours, it was taken as treatment failure and antibiotics were upgraded to second line and managed accordingly.

Outcomes were Measured Clinically as Follows:

- Improvement
- Persistent or worsening of fever, tachypnea, lower chest indrawing or hypoxia.
- Increase in severity that is new appearance of danger signs such as refusal of feeds, deterioration of sensorium, difficulty to wake up from sleep, stridor in a calm child, central cyanosis and convulsions.
- Occurrence of complications (empyema/ pleural effusion, pneumothorax, lung abscess, meningitis, septicemia, shock, respiratory failure).
- Fatality

Improvement was defined if all the following criteria mentioned below were met at 48 hours of starting Ampicillin

Subjective improvement (Acceptance of feed and activity)
Decrease in intensity of fever,
Decrease in respiratory rate,
Decrease in severity of chest retraction and

Decrease in requirement of oxygen/improvement in saturation\

Fever was defined as an maxillary temperature >37.5 degree celsius[18]. Hypoxia defined as spo2 <94% in right
upper limb[19].

The collected data was analysed by using SPSS statistical software and the following statistical methods were
employed to test the hypothetical results
Chi square test
Multivariate Logistic Regression

RESULTS AND DISCUSSIONS

In our study males were 143 (60.85%) and females were 92 (39.15%), majority were 122(51.91%),

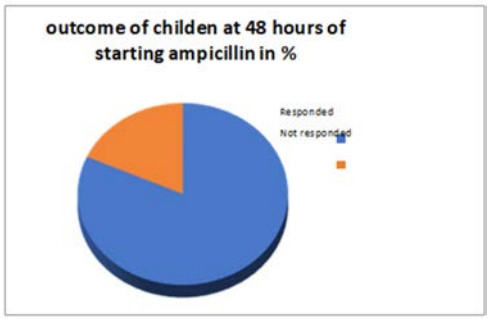

Fig. 1: Outcome of children with severe pneumonia at 48 hours of starting Ampicillin

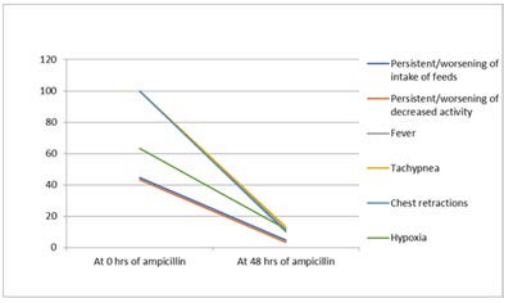

Fig. 2: Monitoring response to Ampicillin between 0 and 48 hours in children with severe pneumonia

Table 1: Monitoring response to Ampicillin between 0 and 48 hours in children with severe pneumonia

Parameters	At 0 hrs of Ampicillin (n=235)	At 48 hrs of Ampicillin (n=235)	Chi-square	p-value
Persistent/worsening of intake of feeds	105(44.68%)	11(4.68%)	25.63	0.00
Persistent/worsening of decreased activity	102(43.40%)	8(3.40%)	24.22	0.00
Fever	235(100.0%)	27(11.49%)	68.56	0.00
Tachypnea	235(100.0%)	31(13.19%)	63.22	0.00
Chest retractions	235(100.0%)	24(10.21%)	60.16	0.00
Hypoxia	149(63.40%)	26(11.06%)	18.46	0.00

between 2-12 months, 89(37.8%), 17(7.23%) and 7(2.98%) children were in age group of 13-24 months, 25-36 month and >36 months respectively. All 235(100%) children presented with history of fever and cough. Along with above complaints 197(83.82%) and 168(71.48%) cases came with complaints of hurried breathing and chest indrawing respectively. History of decreased intake of feeds was present in 105(44.68%) cases and decreased activity was present in 102(43.40%) children. In this study 195(80.85%) children were completely immunized as per NIS and 45(19.15%) children were partially immunized. None of the children were immunized with pneumococcal vaccine. Majority of 127(54.04%) children belonged to class IV socioeconomic status. 73 (31.06%) children belonged to class V and 35(14.89%) children were from class III. Among 235 cases, children who responded to Ampicillin were 192 (81.7%), Forty three (18.3%) children did not respond to Ampicillin, so they had treatment failure at 48 hours. None of the children died during the course of treatment.

In our study, there was significant improvement in oral acceptance of feeds, activity of children, tachypnea, fever and retractions from the time of admission to 48 hours of starting Ampicillin.

Age is an important predictor of morbidity and mortality in pediatric pneumonias. In our study, majority were 122(51.91%) between 2-12 months, Similar results were in study done by Jyotiranjan Champatiray[20] in odisha, India. Banstola[21] also found occurrence of pneumonia more in the age group below one year as compared to age group one year-five year. In our study, all 235(100%) children presented with history of fever and cough. Along with above complaints 197(83.82%) and 168(71.48%) cases came with complaints of hurried breathing and chest indrawing respectively.

Among the presenting complaints of children with severe pneumonia in various studies, fever and cough were the most common presentation, which is almost similar with other studies done Shekhawat[22], Jyotiranjan Champatiray[20] Ahmad Al Najjar[23] where fever found in 92.3%, 97.16%, 87.4%, cough found in 97.7%, 100%, 98%, hurried breathing was present in 89.2%, 100%, 73.5% respectively. all these shows that fever cough and tachypnea can be used as diagnostic tool for pneumonia where chest X ray is not always possible especially in rural and under equipped health settings. In our study we found that, 73 (31.06%) children belonged to class V socioeconomic status. 127(54.04%) children belonged to class IV and 35(14.89%) children were from class III, these results were comparable with other studies. In a study by Udaya[24] done in Belgaum, Karnataka, majority of children 95.2% belonged to low SES (class IV+V).

Among 235 cases, children who responded to Ampicillin were 192 (81.7%), Forty three (18.3%) children did not respond to Ampicillin., so they had treatment failure at 48 hours. None of the children died during the course of treatment.

In our study, there was significant improvement in oral acceptance of feeds, activity of children, tachypnea, fever and retractions from the time of admission to 48 hours of starting Ampicillin. To our knowledge there are no comparative studies where only Ampicillin is being used to look for outcome of severe pneumonia without comparison group. The following discussed studies which have used Ampicillin as first line drug had comparison group with other antibiotic.

Williams[25] did a study in 43 children's hospitals in the United States, they demonstrated equivalent outcomes and costs for children hospitalized with pneumonia and treated empirically with either narrow-(Ampicillin/Penicillin) or broad-spectrum (Ceftriaxone/Cefotaxime) antimicrobial therapy. Among more than 15000 children hospitalized with CAP, there were no differences in length of stay, costs, need for intensive care or readmissions between those treated with parenteral Ampicillin or Penicillin and those treated with broader spectrum third-generation Cephalosporin therapy.

In a similar study by Vuori-Holopainen[26] 154 Finnish children with pneumonia or other acute invasive bacterial infection requiring hospitalization were randomized to receive either parenteral Ampicillin or Cefuroxime. Of the included children, 47% were diagnosed with pneumonia and nearly 40% had evidence of S.pneumoniae infection. There were no differences in outcomes (time to recovery, normalization of laboratory parameters or treatment failure) between the 2 antibiotic treatment groups.

Since Penicillin falls under the same category of drugs as of Ampicillin and WHO recommends either Penicillin or Ampicillin as the first line drug for severe pneumonia, it is logical and reasonable to compare

ours with other studies which have used Penicillin as the first line drug for severe pneumonia.

A study done by Nirjala[27] in children aged between 2-60 months in Nepal and a study by Simbalista[28] conducted in Brazil showed similar results to our study i.e. significant improvement in fever, tachypnea and chest indrawing by 48 hours of treatment. In above studies Crystallin Penicillin successfully treated around 89.8% of children with CAP and Penicillin G treated the great majority (82%) of the studied hospitalized children aged more than 2 months with radio graphically confirmed CAP in comparison with broad spectrum antibiotic, respectively.

India carries the largest burden of disease and deaths because of pneumonia, accounting for 43 million cases and 0.15 million deaths annually,1 making it one of the most common indications for hospitalization in childhood. Discouraging the unnecessary use of broad-spectrum antimicrobial agents for children hospitalized with CAP therefore has the potential to markedly reduce selective pressure for antimicrobial resistance.

CONCLUSION

Children hospitalized with severe pneumonia were effectively treated with intravenous Ampicillin in the present study. The response to treatment was well appreciated within 48 hours of initiation of treatment. Children with severe pneumonia responded to Ampicillin irrespective of gender, signs and symptoms at the onset and socioeconomic status.

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