

**AMPICILLIN & GENTAMICIN V/S 3<sup>RD</sup> GENERATION CEPHALOSPORIN FOR  
THE MANAGEMENT OF COMMUNITY-ACQUIRED PNEUMONIA IN  
CHILDREN; A COMPARATIVE ANALYSIS**

**ABSTRACT**

**BACKGROUND**

Community acquired pneumonia (CAP) is a common cause of childhood morbidity, attributed to every 1 in 500 hospitalization of children under the age of 5 years. While science made therapeutic advancements to battle CAP, the pathogens too have acquired resistance to many drugs. In this fight for dominance, Ampicillin plus Gentamicin and 3<sup>rd</sup> Gen Cephalosporins are nowadays the cornerstone of treatment. However, their efficacy varies in different parts of the world owing to differing levels of drug resistance.

**OBJECTIVE**

To compare the effect of Ampicillin and Gentamicin vs. third generation cephalosporin in treatment of severe community acquired pneumonia.

**METHODOLOGY**

This Randomized Controlled Trial was conducted at the Dept. of Pediatrics (Ziauddin University Hospital) upon a sample of 74 patients (in two equal groups) of either gender, aged 2 months to 5 years, presenting with CAP. After taking written informed consent, data was recorded onto a pre-structured questionnaire containing inquiries pertaining to basic biodata, sociodemographic details, presenting complaints, immunization status of the pneumococcal and HIB vaccine, laboratory values, and treatment outcome.

**RESULTS**

The mean age of the sample stood at 15 months (SD ± 3) with a majority of the sample comprising of male children (52.7%). The mean weight stood at 8.7 kg (SD ± 0.9) and the mean height was recorded to be 74.2 cm (SD ± 11). The commonest symptoms included fever, fast breathing, chest in-drawing and added sounds. It was revealed that

both treatments achieved successful treatment outcomes in all patients with no mortality. The resolution of symptoms however varied with faster resolution observed in the Cephalosporin group.

### **Conclusion**

After careful consideration, it can be concluded that 3<sup>rd</sup> generation cephalosporins is more efficacious at treatment of CAP with significantly faster resolution of disease symptoms and a shorter hospital stay.

### **KEYWORDS**

Community Acquired Pneumonia,

Gentamicin,

Ampicillin,

3<sup>rd</sup> Gen Cephalosporin,

&Therapeutic Efficacy.

### **INTRODUCTION**

Community acquired pneumonia (CAP) is a common cause of childhood morbidity, attributed to every 1 in 500 hospitalization of children under the age of 5 years. *S. Pneumoniae* and *Haemophilus Influenza* are the commonest organisms isolated in children under five years with CAP; accounting for up to 50% and 30%, respectively. Around 50% of the total mortality incurred by the disease can be attributed to the two aforementioned bacterial pathogens. <sup>[1 - 4]</sup>

In this modern era of medicine when many pharmaceutical interventions to CAP are present, such a high burden of disease is not acceptable and one may assume that despite availability of the many interventions, effective selection and use is probably not being practiced. <sup>[5]</sup>

Bacterial Pneumonia should be treated with antibiotics. Most cases of pneumonia require oral antibiotics. <sup>[6]</sup>In last decade, several guidelines identified the best antimicrobial regimen for CAP in children considering spectrum of activity, antimicrobial susceptibility, tolerability, bioavailability, safety, and cost. World health organization recommends domiciliary treatment with oral Amoxicillin (40 mg/kg/dose) two times in a day for 3 days for pneumonia without chest in-drawing and 5 days for pneumonia with chest in-drawing. <sup>[7, 8]</sup>

If there is no improvement in 48 h, Amoxicillin should be replaced with 2nd line drug therapy. Injectable Ampicillin plus Gentamicin is now first choice for hospital-based treatment of severe CAP. In absence of satisfactory improvement in next 48 h, antibiotics should be changed to ceftriaxone. A randomized trial study on children under 5 years of age reported higher treatment failure in oral cotrimoxazole group (39.1%) than oral amoxicillin group (8.1%).<sup>[9,10]</sup>

Immunization status in children with respect to *S. pneumoniae* and *H. influenzae* type B is one of key factor in antibiotic selection. First-line choice for appropriately immunized children with CAP is amoxicillin/ampicillin. According to Infectious Disease Society of America and other supporting guidelines; if the child is not immunized appropriately for pneumococcus and Hib first-line choice IV ceftriaxone with move to oral therapy as able.

Another determinant of the antibiotic choice is the resistance pattern of the local populace. It is a fact that “various biologic or biochemical mechanisms may lead to bacterial resistance; ample evidence points to the fact that antimicrobial resistance is directly linked to antibiotic usage. While overuse and misuse of antibiotics have been observed globally, both in industrialized and developing countries, this problem has assumed immense proportions in the latter.”<sup>[11, 12]</sup>

Studies on antibiotic usage for inpatients have demonstrated that antibiotics may have been prescribed unnecessarily. Cephalosporin were often reported to be the class with higher rates of prescription for CAP treatment, as reported by many centers in different countries, like Ethiopia, Saudi Arabia, Nepal, Serbia, Sudan, US, Italy, and other European countries.<sup>[13 - 20]</sup>

Pakistan has no published data regarding prescription of IV antibiotics in children but it is reported that ceftriaxone in adults is most commonly prescribed IV antibiotic with severe CAP. In India ceftriaxone is the second common IV antibiotic after ampicillin/calvulanic acid prescribed in severe community acquired pneumonia. Current WHO recommendation is Ampicillin and Gentamicin for severe community acquired pneumonia, but it is observed that ceftriaxone is usually prescribed in severe pneumonia.<sup>[21, 22]</sup>

## **MATERIALS AND METHODS**

This Randomized Controlled Trial was conducted at the Dept. of Pediatrics (Ziauddin University Hospital) upon a sample of 74 patients (in two equal groups) of either gender, aged 2 months to 5 years, presenting with CAP. After taking written informed consent, data was recorded onto a pre-structured questionnaire containing inquiries

pertaining to basic biodata, sociodemographic details, presenting complaints, immunization status of the pneumococcal and HIB vaccine, laboratory values, and treatment outcome.

Inclusion Criteria:

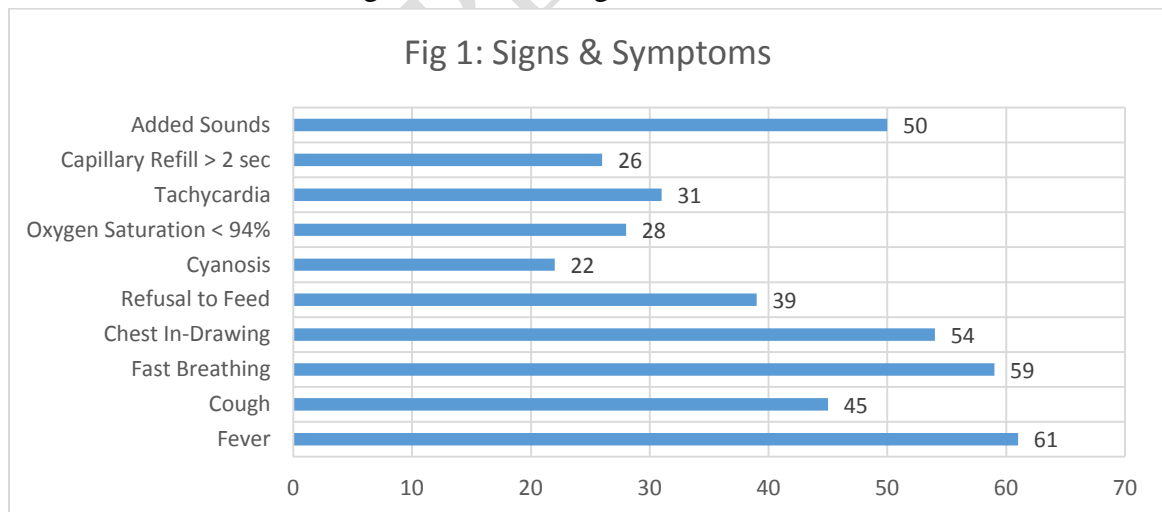
- Children of consenting parents
- Children aged between 2months to 5years of age
- Either gender
- Children with sign and symptoms of severe community acquired pneumonia (cough, chest in drawing, refused to feed, lethargic/unconscious, convulsion) as per operational definition.

Exclusion Criteria:

- Children who need ventilator support at the time of admission
- Severe malnutrition/immunocompromised patient
- Chronic lung diseases like cystic fibrosis, bronchiectasis
- Patient with Congenital heart defect

**RESULTS**

The mean age of the sample stood at 15 months ( $SD \pm 3$ ) with a majority of the sample comprising of male children (52.7%). The mean weight stood at 8.7 kg ( $SD \pm 0.9$ ) and the mean height was recorded to be 74.2 cm ( $SD \pm 11$ ). The commonest symptoms included fever, fast breathing, chest in-drawing and added sounds.



It was revealed that both treatments achieved successful treatment outcomes in all patients with no mortality. The resolution of symptoms however varied with faster resolution observed in the Cephalosporin group.

**Table 1: Comparative Trajectory of Treatment**

Variable	Day 01		Day 2		Day 3		Day 4	
	G1	G2	G1	G2	G1	G2	G1	G2
Fever	30	31	25	21	18	14	07	01
Cough	21	24	26	13	16	06	-	-
Chest In - Drawing	26	28	20	21	15	15	-	-
Tachycardia	14	17	08	12	02	01	-	-
Refusal to Feed	22	17	08	04	-	-	-	-
Fast Breathing	26	33	14	16	05	01	-	-
Oxygen Sat < 94%	14	14	04	-	-	-	-	-

**Table 2: Outcome Comparison**

Variable		Group A	Group B
Antibiotic Change		-	-
Adv Airway Support		8.1%	-
Length of Stay (days)		5	5
Final Outcome	Discharge	100%	100%
	Expired	-	-

## DISCUSSION

The mean age of the sample stood at 15 months ( $SD \pm 3$ ) with a majority of **the sample comprising of male children (52.7%)**. This is comparable with the statistics yielded by the latest Pakistan Demographic Health Survey wherein it is reported that the gender ratio is 51.3%, and thus it matches the gender ratio of our study participants. Additionally, disease (CAP) specific research conducted in different parts of the country have yielded information suggesting that the incidence of community acquired pneumonia is slightly higher 1.1:1 to 1.3:1.<sup>[23,24]</sup>

The mean weight stood at 8.7 kg ( $SD \pm 0.9$ ) and the mean height was recorded to be 74.2 cm ( $SD \pm 11$ ). Though this is not ideal and falls short of meeting the reference values laid out by World Health Organization (WHO), however, this is expected from a developing and low-income country wherein the nutritional needs of the population are not met and

hence the weight, height, and BMI are sub-par in comparison to the international standards. <sup>[25, 26]</sup>

Additionally, CAP is a serious ailment, which manifests strong effects on a child's body. It is only natural to assume that the disease state leads to a decrease in the weight and BMI. Additionally, prolonged diseases states may stunt the growth of a child and decrease the height of the child. This is substantiated by a large pool of literature. <sup>[27, 28]</sup>

The commonest symptoms included fever, fast breathing, chest in-drawing and added sounds. Published evidence reports fever, coupled with respiratory symptoms to be the commonest manifestations of CAP. In this research we operationally defined CAP as a disease state characterized by cough or difficult breathing and tachypnoea. The symptoms may vary with disease severity, but the common symptoms remain the same. <sup>[29]</sup>

It was revealed that both treatments achieved successful treatment outcomes in all patients. Again, this was outcome since both the treatment regimens are not experimental and have been used and recommended as the treatments of choice by several drug regularity authorities and health administrative services (national and international).

One interesting finding though is that the mortality rate, despite falling everywhere else in the world, is high in Pakistan as reported in literature. But in this research, no mortality was reported which is an encouraging observation giving hope that if either of these treatment regimens are administered to children with CAP, a good chance at survival and eventual recovery awaits the child. <sup>[30, 31]</sup>

In this modern world of specialized medicine, the healthcare needs of the patients have become more and more demanding with many patients not only seeking a recovery but one that is achieved the fastest with minimal risk of adverse events. In this research, it was noted that the resolution of symptoms however was faster in the Cephalosporin group, than the other group. <sup>[32]</sup>

Contradictory evidence is available on the matter with certain research suggesting the Cephalosporin to act as a superior therapeutic agent while just as many report ampicillin and gentamicin to yield better results. The trends are different in different parts of the world and may vary according to disease strains and patterns of antibiotic resistance noted in the regions. However, this research confirms that the use of third generation Cephalosporins is ideal in our region. <sup>[32, 33]</sup>

## **CONCLUSION**

After careful consideration, it can be concluded that 3<sup>rd</sup> generation cephalosporins is more efficacious at treatment of CAP with significantly faster resolution of disease symptoms and a shorter hospital stay.

#### **COMPETING INTERESTS DISCLAIMER:**

**Authors have declared that no competing interests exist. The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.**

**Ethical Approvals: we conducted our research after obtaining proper IEC approval.  
Consent**

**As per international standard or university standard, patients' written consent has been collected and preserved by the author(s).**

#### **REFERENCES**

1. *Thoracic Society guidelines for the management of community acquired pneumonia in children: update 2011. Thorax. 2011;66Suppl 2:ii1-23.*
2. *McCulloh RJ, Patel K. Recent Developments in Pediatric Community-Acquired Pneumonia. Curr Infect Dis Rep. 2016;18(5):14.*
3. *Falade AG, Ayede AI. Epidemiology, aetiology and management of childhood acute community-acquired pneumonia in developing countries--a review. African journal of medicine and medical sciences. 2011 Dec;40(4):293-308.*

4. Donà D, Luise D, Da Dalt L, Giaquinto C. Treatment of community-acquired pneumonia: are all countries treating children in the same way? a literature review. *International journal of pediatrics*. 2017;2017.
5. Sujatha K, Ushasri GV, Rao JV, Kathi A. Disease spectrum of PICU admissions in a Tertiary Care Center in Hyderabad, Telangana. *Int J Scientific Res*. 2018 Sep 15;6(9).
6. Berti E, Galli L, de Martino M, Chiappini E. International guidelines on tackling community-acquired pneumonia show major discrepancies between developed and developing countries. *ActaPædiatrica*. 2013 Dec;102:4-16.
7. Dekate P, Mathew J, Jayashree M. Acute community acquired pneumonia in emergency room. *Indian J Pediatr*. 2011;78:1127–35.
8. Bradley J.S., Byington C.L., Shah S.S., Alverson B., Carter E.R., Harrison C. The Management of Community-Acquired Pneumonia in Infants and Children Older Than 3 Months of Age: Clinical Practice Guidelines by the Pediatric Infectious Diseases Society and the Infectious Diseases Society of America. *Clinical Infectious Diseases*. 2011;53:e25–e76.
9. Abera B, kibert M, Mulu W. Knowledge and beliefs on antimicrobial resistance among physicians and nurses in hospitals in Amhara Region, Ethiopia. *BMC PharmacolToxicol*. 2014;15:26.
10. Rajesh S, Singhal V. Clinical effectiveness of co-trimoxazole vs. amoxicillin in the treatment of non-severe pneumonia in children in India: a randomized controlled trial. *Int J Prev Med*. 2013;4:1162–68.
11. Feleke M, Yenet W, Lenjisa JL. Prescribing pattern of antibiotics in pediatric wards of Bishoftu Hospital, East Ethiopia. *International Journal of Basic & Clinical Pharmacology*. 2017 Feb 2;2(6):718-22.
12. Alakhali KM, Asif Ansari Shaik Mohammad A. Prescribing pattern of antibiotics in pediatric patients in the Jazan Region, Kingdom of Saudi Arabia. *RGUHS Journal of Pharmaceutical sciences*. 2014;4(3):120-4.
13. Thapaliya K, Shrestha S, Bhattarai S, Basnet D, Chaudhary RK. Prescribing pattern of antibiotics in pediatric hospital in Chitwan district in Nepal. *World J Phar Pharm Sci*. 2015 Sep 14;4(11):1631-41.
14. Zec SL, Selmanovic K, Andrijic NL, Kadic A, Zecevic L, Zunic L. Evaluation of Drug Treatment of Bronchopneumonia at the Pediatric Clinic in Sarajevo. *Medical Archives*. 2016 Jun;70(3):177.
15. Salih KE, Bilal JA, Alfadeel MA, Hamid Y, Eldouch W, Elsammani E, et al. Poor adherence to the World Health Organization guidelines of treatment of severe pneumonia

*in children at Khartoum, Sudan. BMC research notes. 2014 Dec;7(1):531.*

16. Brogan TV, Hall M, Williams DJ, Neuman MI, Grijalva CG, Farris RW, et al. Variability in processes of care and outcomes among children hospitalized with community-acquired pneumonia. *The Pediatric infectious disease journal. 2012 Oct;31(10):1036.*
17. De Luca M, Donà D, Montagnani C, Vecchio AL, Romanengo M, Tagliabue C, et al. Antibiotic prescriptions and prophylaxis in Italian children. Is it time to change? Data from the ARPEC project. *PLoS One. 2016 May 16;11(5):e0154662.*
18. Amadeo B, Zarb P, Muller A, Drapier N, Vankerckhoven V, Rogues AM, et al. European Surveillance of Antibiotic Consumption (ESAC) point prevalence survey 2008: paediatric antimicrobial prescribing in 32 hospitals of 21 European countries. *Journal of antimicrobial chemotherapy. 2010 Aug 16;65(10):2247-52.*
19. Khan MA, Ali SI, Kashif SS, Zafar F, Ali H, Fatima R, et al. Profile and management of community acquired pneumonia in a tertiary care hospital in Karachi. *International Journal of Medicine and Medical Sciences. 2018 Feb 28;10(2):31-5.*
20. Choudhury DK, Bezbaruah BK. Antibiotic prescriptions pattern in paediatric in-patient department Gauhati medical college and hospital, Guwahati. *Journal of Applied pharmaceutical science. 2013 Aug 1;3(8):144.*
21. Lakhanpaul M, Atkinson M, Stephenson T. Community acquired pneumonia in children: a clinical update. *Arch Dis Child Educ Pract Ed 2004;89:ep29–ep34.*
22. Khan AJ, Hussain H, Omer SB, Chaudry S, Ali S, Khan A, Yasin Z, Imran JK, Mistry R, Baig IY, White F. High incidence of childhood pneumonia at high altitudes in Pakistan: a longitudinal cohort study.
23. Kerai S, Nisar I, Muhammad I, Qaisar S, Feroz K, Raza A, Khalid F, Baloch B, Jehan F. A community-based survey on health-care utilization for pneumonia in children in peri-urban slums of Karachi, Pakistan. *The American journal of tropical medicine and hygiene. 2019 Nov 6;101(5):1034-41.*
24. Mushtaq MU, Gull S, Mushtaq K, Abdullah HM, Khurshid U, Shahid U, Shad MA, Akram J. Height, weight and BMI percentiles and nutritional status relative to the international growth references among Pakistani school-aged children. *BMC pediatrics. 2012 Dec;12(1):1-2.*
25. Shah SM, Selwyn BJ, Luby S, Merchant A, Bano R. Prevalence and correlates of stunting among children in rural Pakistan. *Pediatrics international. 2003 Feb;45(1):49-53.*
26. Victora CG, Barros FC, Kirkwood BR, Vaughan JP. Pneumonia, diarrhea, and growth in the first 4 y of life: a longitudinal study of 5914 urban Brazilian children. *The American journal of clinical nutrition. 1990 Aug 1;52(2):391-6.*
27. Shaheen SO, Sterne JA, Tucker JS, du V Florey C. Birth weight, childhood lower respiratory tract infection, and adult lung function. *Thorax. 1998 Jul 1;53(7):549-53.*

28. Hussain R, Lobo MA, Inam B, Khan A, Qureshi AF, Marsh D. *Pneumonia perceptions and management: an ethnographic study in urban squatter settlements of Karachi, Pakistan. Social science & medicine. 1997 Oct 1;45(7):991-1004.*
29. Owais A, Tikmani SS, Sultana S, Zaman U, Ahmed I, Allana S, Zaidi AK. *Incidence of pneumonia, bacteremia, and invasive pneumococcal disease in Pakistani children. Tropical Medicine & International Health. 2010 Sep;15(9):1029-36.*
30. Soofi S, Ahmed S, Fox MP, MacLeod WB, Thea DM, Qazi SA, Bhutta ZA. *Effectiveness of community case management of severe pneumonia with oral amoxicillin in children aged 2–59 months in Matiari district, rural Pakistan: a cluster-randomised controlled trial. The Lancet. 2012 Feb 25;379(9817):729-37.*
31. Atkinson M, Lakhanpaul M, Smyth A, Vyas H, Weston V, Sithole J, Owen V, Halliday K, Sammons H, Crane J, Guntupalli N. *Comparison of oral amoxicillin and intravenous benzyl penicillin for community acquired pneumonia in children (PIVOT trial): a multicentre pragmatic randomised controlled equivalence trial. Thorax. 2007 Dec 1;62(12):1102-6.*
32. Pallares R, Linares J, Vadillo M, Cabellos C, Manresa F, Viladrich PF, Martin R, Gudiol F. *Resistance to penicillin and cephalosporin and mortality from severe pneumococcal pneumonia in Barcelona, Spain. New England Journal of Medicine. 1995 Aug 24;333(8):474-80.*
33. Pallares R, Linares J, Vadillo M, Cabellos C, Manresa F, Viladrich PF, Martin R, Gudiol F. *Resistance to penicillin and cephalosporin and mortality from severe pneumococcal pneumonia in Barcelona, Spain. New England Journal of Medicine. 1995 Aug 24;333(8):474-80.*