INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES
[ISSN: 0975-4725; CODEN(USA): IJPS00]
Journal Homepage: https://www.ijpsjournal.com

OPEN ACCESS

Research Article

To Study The Safety And Efficacy Of Injection Ceftriaxone Monotherapy Versus Injection Ceftriaxone Plus Oral Azithromycin Dual Therapy In Enteric Fever

Swathi Boddupally*[1], Goreti Shivani[2], DR.Gangadhara Rao[3], Jetram Omprakash Reddy[4], Jakkula Vagdevi[5]

[1]Assistant Professor, Bharat School of Pharmacy, Mangalpally, Ibrahimpatnam, Ranga Reddy District,Telangana, India
[2,4,5]Department of Pharmacy Practice, Bharat School of Pharmacy, Mangalpally, Ibrahimpatnam, Ranga Reddy District, Telangana, India.
[3]Department of Paediatrics, Durgabai Deshmukh Hospital and Research Centre, Vidyanagar, Hyderabad, Telangana, India.

ARTICLE INFO

Published: 16 July. 2026
Keywords:
Enteric Fever, Ceftriaxone, Azithromycin, Dual Therapy, Monotherapy, Paediatric Patients
DOI:
10.5281/zenodo.21390541

ABSTRACT

Introduction:Enteric fever remains a major public health concern in developing countries, particularly among children, due to inadequate sanitation and the emergence of antimicrobial resistance. Ceftriaxone is widely used for the treatment of enteric fever; however, combination therapy with azithromycin may provide improved clinical outcomes. This study aimed to evaluate the safety and efficacy of injection ceftriaxone monotherapy versus injection ceftriaxone combined with oral azithromycin dual therapy in paediatric patients with enteric fever. Materials and Methods: A comparative prospective study was conducted in the Department of Paediatrics at Durgabai Deshmukh Hospital and Research Centre over a period of six months. A total of 100 paediatric patients aged 1–15 years diagnosed with enteric fever were included. Patients received either ceftriaxone monotherapy (n=51) or ceftriaxone plus oral azithromycin dual therapy (n=49). Demographic data, clinical symptoms, laboratory investigations, Widal test results, white blood cell counts, and fever trends were collected and analyzed using appropriate statistical methods. A p-value of <0.05 was considered statistically significant. Results and Discussion: Both treatment groups showed improvement in clinical outcomes.

***Corresponding Author:** Swathi Boddupally
Address: *Assistant Professor, Bharat School of Pharmacy, Mangalpally, Ibrahimpatnam, Ranga Reddy District,Telangana, India*
Email ✉: Swathisniz92@123

Relevant conflicts of interest/financial disclosures: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

No significant differences were observed in gender distribution, chief complaints, baseline temperature, or Widal test positivity. However, the dual therapy group demonstrated significantly faster fever reduction on Day 2 (p=0.001) and Day 3 (p<0.001) compared with the monotherapy group. White blood cell counts were significantly higher in the dual therapy group on Day 3 (p=0.010),indicating better recovery and immune response. Safety profiles were comparable between both treatment regimens, with no significant increase in adverse effects observed in the dual therapy group. Conclusion: Ceftriaxone plus oral azithromycin dual therapy was found to be more effective than ceftriaxone monotherapy in achieving faster fever clearance and improved clinical recovery in paediatric enteric fever patients. The combination regimen may be considered a superior therapeutic option, particularly in areas with increasing antimicrobial resistance.

INTRODUCTION

Enteric fever, comprising typhoid and paratyphoid fever, is a systemic infectious disease caused primarily by Salmonella enterica serovar Typhi and Salmonella enterica serovar Paratyphi. The disease remains a significant public health problem in developing countries, particularly in regions with inadequate sanitation, poor hygiene practices, and limited access to safe drinking water. Children are among the most affected populations, contributing substantially to the global burden of morbidity associated with enteric fever.

Despite advances in healthcare, enteric fever continues to pose therapeutic challenges due to the emergence of multidrug-resistant and extensively drug-resistant strains of *Salmonella*. Antimicrobial therapy remains the cornerstone of treatment, with ceftriaxone and azithromycin being among the most commonly prescribed antibiotics. Ceftriaxone, a third-generation cephalosporin, has demonstrated good efficacy against susceptible strains and is widely used in hospitalized patients. Azithromycin, a macrolide antibiotic, has also shown effectiveness against enteric fever and offers the advantage of excellent intracellular penetration and activity against resistant organisms.

The increasing prevalence of antimicrobial resistance has raised concerns regarding treatment failures, delayed clinical recovery, and disease relapse. Consequently, combination therapy using ceftriaxone and azithromycin has been proposed as a potential strategy to enhance therapeutic outcomes, achieve faster symptom resolution, and reduce the risk of resistance development. However, evidence comparing the effectiveness and safety of ceftriaxone monotherapy with ceftriaxone plus azithromycin dual therapy in paediatric enteric fever remains limited.

Therefore, the present study was undertaken to evaluate and compare the safety and efficacy of injection ceftriaxone monotherapy versus injection ceftriaxone combined with oral azithromycin dual therapy in paediatric patients with enteric fever. The study hypothesized that dual therapy would provide superior clinical outcomes, including faster fever clearance and improved recovery, while maintaining a comparable safety profile to monotherapy.

MATERIALS AND METHODS STUDY DESIGN

A comparative prospective study was conducted to evaluate the safety and efficacy of Injection Ceftriaxone monotherapy versus Injection Ceftriaxone combined with Oral Azithromycin dual therapy in paediatric patients diagnosed with enteric fever.

STUDY SETTING

The study was carried out in the inpatient and outpatient departments of Paediatrics at Durgabai Deshmukh Hospital and Research Centre,

Hyderabad, Telangana, India, a 300-bedded multispecialty teaching hospital.

STUDY DURATION

The study was conducted over a period of six months.

STUDY POPULATION

A total of 100 paediatric patients diagnosed with enteric fever were enrolled in the study. Patients were allocated into two treatment groups based on the prescribed therapeutic regimen:

- Monotherapy Group (n = 51): Patients receiving Injection Ceftriaxone.
- Dual Therapy Group (n = 49): Patients receiving Injection Ceftriaxone along with Oral Azithromycin.

DRUGS USED IN THE STUDY

Injection ceftriaxone

Generic Name: Ceftriaxone Sodium

Dosage Form: Intravenous/Intramuscular Injection Class: Third-Generation Cephalosporin Antibiotic

Oral Azithromycin

Generic Name: Azithromycin

Dosage Form: Oral Suspension/Tablet Class: Macrolide Antibiotic

INCLUSION CRITERIA

- Paediatric patients aged 1–15 years diagnosed with enteric fever.
- Patients treated with Injection Ceftriaxone alone or Injection Ceftriaxone plus Oral Azithromycin.
- Patients whose clinical and laboratory records were available for evaluation.

EXCLUSION CRITERIA

- Patients admitted for less than 7 days.
- Patients younger than 1 year of age.
- Patients older than 15 years of age.
- Patients with incomplete clinical records.

DATA COLLECTION

Relevant data were collected from patient case records, laboratory investigation reports, prescriptions, and interviews with patient attendants. Demographic characteristics, clinical symptoms, treatment details, laboratory findings, and treatment outcomes were documented using a structured data collection form.

EFFICACY ASSESSMENT

Treatment efficacy was evaluated based on:

- Reduction in fever over the study period.
- Time required for symptom relief.
- Changes in White Blood Cell (WBC) count.
- Clinical recovery and treatment response.

STATISTICAL ANALYSIS

Data were entered into Microsoft Excel and analyzed using appropriate statistical methods. Continuous variables were expressed as mean ± standard deviation, whereas categorical variables were expressed as frequencies and percentages.

The following statistical tests were applied:

- Unpaired Student's t-test for comparison of normally distributed continuous variables.
- Mann–Whitney U test for non-normally distributed continuous variables.

- Chi-square test or Fisher's Exact test for categorical variables.
- A p-value less than 0.05 was considered statistically significant.

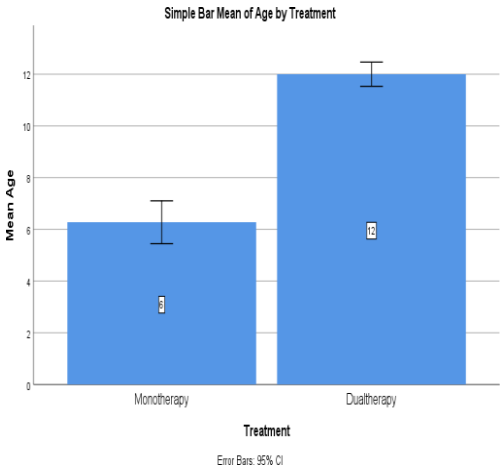
ETHICAL CONSIDERATIONS

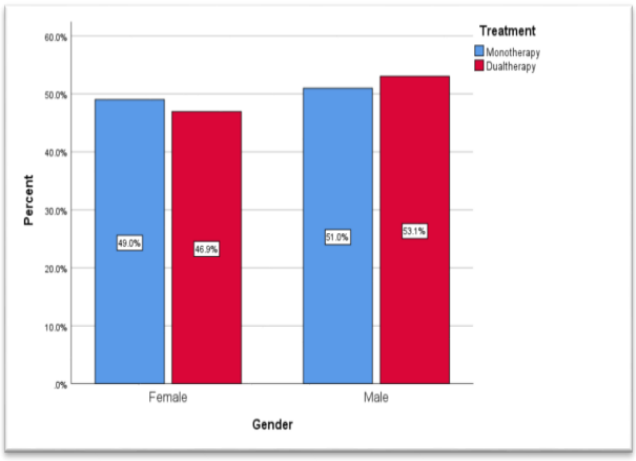
The study was conducted only after obtaining approval from the Institutional Ethics Committee of Durgabai Deshmukh Hospital and Research Centre. Written informed consent was obtained from the parents or legal guardians of all participating children before inclusion in the study.

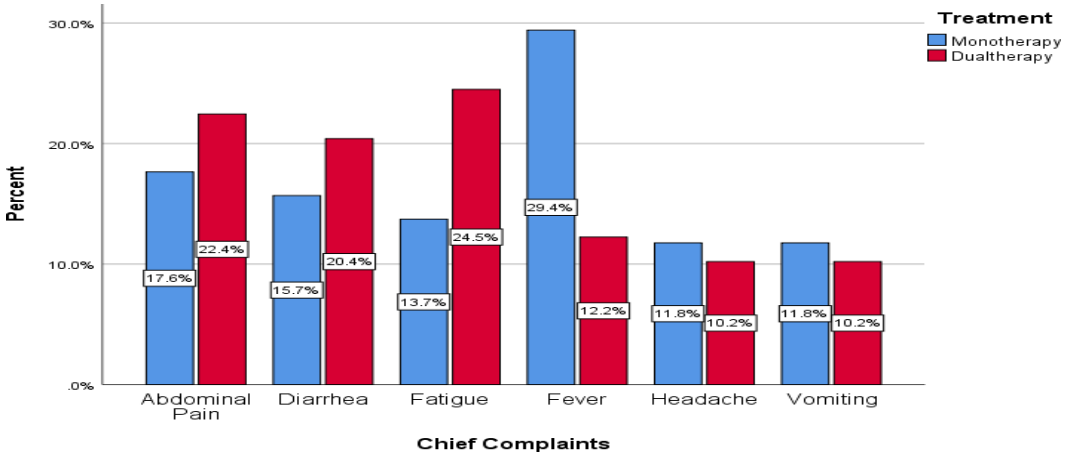
Ethics Approval Number: Year of Approval:RESULTS AND DISCUSSION

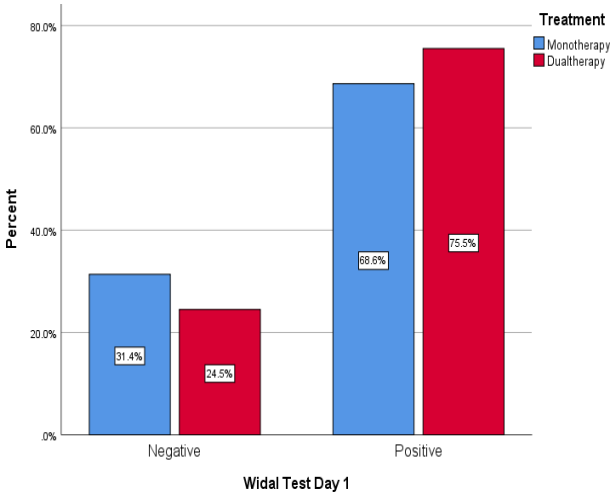
A total of 100 paediatric patients diagnosed with enteric fever were included in the study. Among them, 51

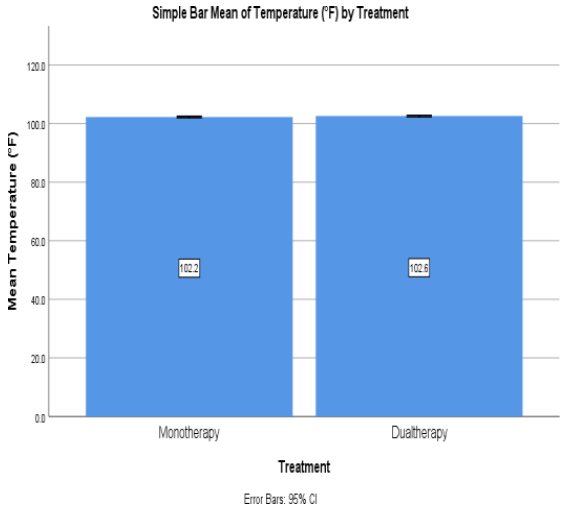
patients received Injection Ceftriaxone monotherapy and 49 patients received Injection Ceftriaxone combined with Oral Azithromycin dual therapy.

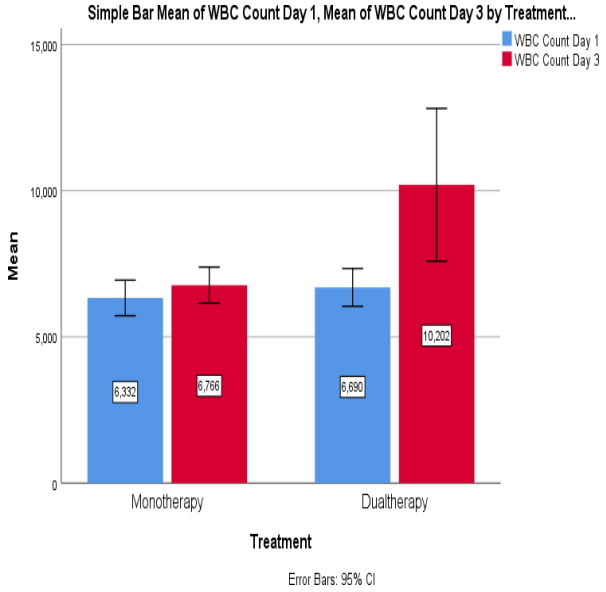


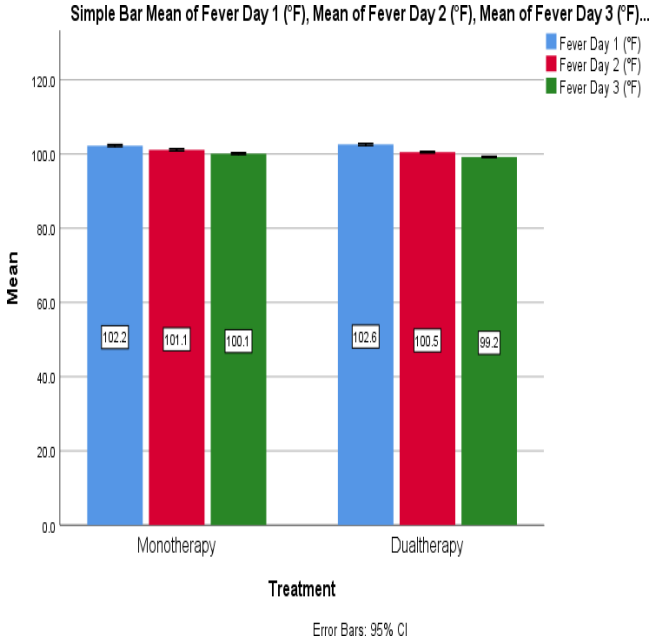












DISCUSSION:

Enteric fever continues to be a major cause of morbidity among paediatric patients in developing countries. Effective antimicrobial therapy is essential to achieve rapid symptom resolution and prevent disease-related complications.

The present study compared the efficacy and safety of Injection Ceftriaxone monotherapy with Injection Ceftriaxone plus Oral Azithromycin dual therapy in paediatric patients with enteric fever.

The findings demonstrated that both treatment regimens were effective; however, dual therapy produced superior clinical outcomes in terms of fever reduction and recovery rate.

The absence of significant differences in gender distribution, chief complaints, baseline temperature, and Widal test positivity suggests that both treatment groups were clinically comparable at the beginning of the study. This strengthens the validity of the treatment outcome comparison.

One of the most important observations was the significantly faster reduction in fever among patients receiving dual therapy. By the second and third days of treatment, fever reduction was significantly greater in the dual therapy group. Rapid fever clearance is an important indicator of therapeutic success and patient recovery in enteric fever.

CONCLUSION:

The present comparative prospective study evaluated the safety and efficacy of Injection Ceftriaxone monotherapy versus Injection Ceftriaxone combined with Oral Azithromycin dual therapy in pediatric patients with enteric fever. Both treatment regimens were found to be effective and well tolerated; however, the dual therapy regimen demonstrated superior clinical outcomes.

Patients receiving ceftriaxone plus azithromycin showed faster fever clearance and better clinical recovery compared with those receiving ceftriaxone monotherapy. The dual therapy group also exhibited significant improvement in white blood cell counts during treatment, indicating enhanced therapeutic response. Furthermore, the addition of azithromycin did not result in any significant increase in adverse effects, confirming the safety of the combination regimen.

The findings of this study suggest that ceftriaxone plus azithromycin dual therapy may be a more effective treatment strategy for pediatric enteric fever, particularly in regions where antimicrobial resistance is increasing. Although ceftriaxone monotherapy remains a useful therapeutic option, combination therapy appears to offer improved clinical benefits, reduced risk of treatment failure, and faster recovery.

Therefore, ceftriaxone combined with azithromycin can be considered a preferred therapeutic approach for the management of enteric fever in children, especially in patients at higher risk of resistant infections. Further multicenter studies with larger sample sizes are recommended to validate these findings and strengthen clinical treatment guidelines.

ACKNOWLEDGEMENT:

The authors express their sincere gratitude to the Department of Paediatrics, Durgabai Deshmukh Hospital and Research Centre, Hyderabad, for providing the necessary facilities and support to conduct this study. The authors are thankful to the physicians, nursing staff, hospital administration, and all study participants and their parents/guardians for their cooperation throughout the study period.

The authors also acknowledge the guidance and support provided by the faculty members of the Department of Pharmacy Practice in the successful completion of this research work.

CONFLICT OF INTEREST

The authors have no conflicts of interest regarding this investigation.

TABLES

TABLE-1: Effectiveness of mono therapy verses dual therapy across different age groups

Age	Treatment	Mean	Std. Deviation	P value
1-10	Monotherapy	6.27	2.947	<0.001
11-15	Dual therapy	12.00	1.633	

The table and bar graph shows that comparision of treatment effects between two Age groups [1-10] years and [11-15] years

- Conclusion for age: The mean treatment duration for the 1–10 age group receiving monotherapy is 6.27,
- The mean duration for the 11–15 age group receiving dual therapy is 12.00.
- The standard deviation for monotherapy is 2.947, whereas for dual therapy, it is 1.633, indicating that treatment duration in the dual therapy group is more consistent.
- The p-value is less than 0.001
- The age distribution was similar in both groups, as indicated by the statistical comparison of age, which revealed a significant difference [P value <0.001].

TABLE-2: Gender Distribution in Monotherapy and Dual Therapy Groups

Gender	Treatment		Total	P value
	Monotherapy No. (%)	Dual therapy No. (%)		
Female	25 (49)	23 (46.9)	48	0.835
Male	26 (51)	26 (53.1)	52	
Total	51	49	100	

The table and bar chart presents a monotherapy and dual therapy treatment distribution based on gender

- Among females, 49% received monotherapy, while 46.9% received dual therapy.
- Among males, 51% received monotherapy, and 53.1% received dual therapy.
- The p-value is 0.835
- The p-value (0.835) is significantly greater than the customary threshold of 0.05, indicating that there is no significant connection between gender and the type of treatment received. It appears that the decision to provide solo or dual treatment is not influenced by a patient's gender.

TABLE-3: Comparison of Chief Complaints Between Monotherapy and Dual Therapy Groups

Chief complaints	Treatment		Total	P value
	Monotherapy No. (%)	Dual therapy No. (%)		
Abdominal pain	9 (17.6)	11 (22.4)	20	0.332
Diarrhea	8 (15.7)	10 (20.4)	18	
Fatigue	7 (13.7)	12 (24.5)	19	
Fever	15 (29.4)	6 (12.2)	21	
Headache	6 (11.8)	5 (10.2)	11	
Vomiting	6 (11.8)	5 (10.2)	11	
Total	51	49	100	

- The table and bar chart present a comparison of chief complaints between patients receiving monotherapy and dual therapy
- The most common complaints include fever (29.4% in monotherapy vs. 12.2% in dual therapy), fatigue (13.7% in monotherapy vs. 24.5% in dual therapy), and abdominal pain (17.6% in monotherapy vs. 22.4% in dual therapy).
- The p-value is 0.332. there is no significant association between the type of treatment (monotherapy or dual therapy)

TABLE-4 :Comparison of Widal Test Results Between Monotherapy and Dual Therapy Groups

Widal test	Treatment		Total	P value
	Monotherapy No. (%)	Dual therapy No. (%)		
Negative	16 (31.4)	12 (24.5)	28	0.443
Positive	35 (68.8)	37 (75.5)	72	
Total	51	49	100	

- The table and bar chart show the results of the Widal test on Day 1 for two treatment groups: Monotherapy and Dual therapy.
- 31.4% of the Monotherapy group tested negative, compared to 24.5% in the Dual therapy group
- 68.8% of the Monotherapy group tested positive, compared to 75.5% in the Dual therapy group.
- With a p-value of just 0.443, the Widal test positive rates in the groups receiving monotherapy and dual treatment are not significantly different. On the first day, the results of the Widal test did not seem to be affected by the treatment type.
- **TABLE-7: Comparison of Fever Trends Over Three Days in Monotherapy and Dual Therapy Groups**

	Treatment	Mean	Std. Deviation	P value
Fever Day 1 (°F)	Monotherapy	102.247	.9754	0.100
	Dualtherapy	102.569	.9633	
Fever Day 2 (°F)	Monotherapy	101.122	1.0323	0.001
	Dualtherapy	100.498	.7273	
Fever Day 3 (°F)	Monotherapy	100.090	.8750	<0.001
	Dualtherapy	99.218	.5696	

The table and bar graph present data on fever (in °F) for two treatment groups—Monotherapy and Dualtherapy-over three days. The first day fever temperatures in the groups treated with monotherapy and combination treatment were 102.247°F and 102.569°F, respectively, with a standard deviation of 0.9754 and 0.9633, respectively.

With a p-value of 0.100, the first day fever levels did not differ significantly between the two regimens. This suggests that at the beginning of treatment, both approaches had a similar impact on body temperature**.**

On Day 2, the mean fever temperature decreased in both groups.The monotherapy group had a mean temperature of 101.122°F (Standard deviation : 1.0323), while the dual therapy group had a lower mean temperature of 100.498°F (Standard deviation: 0.7273). The p-value was 0.001, indicating a statistically significant difference. This suggests that by the second day, dual therapy was more effective in reducing fever compared to monotherapy.

- On Day 3, fever levels continued to decline further. The monotherapy group had a mean temperature of 100.090°F (Standard deviation : 0.8750), whereas the dual therapy group showed an even greater reduction with a mean temperature of 99.218°F (Standard deviation : 0.5696). The p-value was <0.001, highlighting a highly significant difference between the two treatments.
- This result indicates that dual therapy consistently led to a faster and more substantial reduction in fever over time compared to monotherapy

- There is significant difference in both treatment approaches initially show similar effects on fever, dual therapy leads to a significantly faster and more effective reduction in fever over time compared to monotherapy. By Day 2 and Day 3, the fever reduction in the dual therapy group was significantly greater, as indicated by the low p-values (0.001 on Day 2 and <0.001 on Day 3). This implies that dual therapy may be a more efficient approach in managing fever, potentially providing faster symptom relief than monotherapy.

ABBREVIATIONS:

EF	Enteric Fever
S	Salmonella
NTS	Non typhoidal salmonella
iNTS	Invasive non typhoidal serovars
CBC	Complete blood count
IV	Intravenous
IPNO	In -patient number

OP NO	Out –patient number
DOA	Date of admission
DOD	Date of discharge

REFERENCES

1. Virginie Pommelet, Patricia Mariani, Romain Basmaci, Enteric fever among children: 50 cases in a French tertiary care centre, Journal of Travel Medicine, Volume 25, Issue 1, 2018, tay,05 https://academic.oup.com/jtm/article/25/1/tay059/5061326
2. Azmatullah A, Qamar FN, Thaver D, Zaidi AK, Bhutta ZA. Systematic review of the global epidemiology, clinical and laboratory profile of enteric fever. J Glob Health. 2015 Dec;5(2):020407. PMID: 26649174; PMCID: PMC4672836https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4672836/
3. Waddington, Claire S., Thomas C. Darton, and Andrew J. Pollard. "The challenge of enteric fever." Journal of Infection 68 (2014): S3 https://www.sciencedirect.com/science/article/abs/pii/S0163445313002806
4. Bhandari J, Thada PK, Hashmi MF, et al. Typhoid Fever. [Updated 2024 Apr 19]. In: Stat Pearls [Internet]. Treasure Island (FL): Stat Pearls Publishing; 2024 Jan. https://www.ncbi.nlm.nih.gov/books/NBK557513/
5. Nusrat N, Islam MR, Paul N, Rahman N. Clinical and Laboratory Features of Enteric Fever in Children and Antibiotic Sensitivity Pattern in a Tertiary Care Hospital of a Low- and Middle-Income Country. Cureus. 2022 Oct 27;14(10):e30784. doi: 10.7759/cureus.30784. PMID: 36320797; PMCID:https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9614183/
6. https://resources.wfsahq.org/atotw/typhoid-enteric-fever-part-1/#:~:text=Typhoid%20fever%2C%20otherwise%20known%20as,%2C%20and%20non%2D spore%20forming
7. Crump JA, Sjölund-Karlsson M, Gordon MA, Parry CM. Epidemiology, Clinical Presentation, Laboratory Diagnosis, Antimicrobial Resistance, and Antimicrobial Management of Invasive Salmonella Infections. Clin Microbiol Rev. 2015 Oct. PMID: 26180063; PMCID: PMC4503790https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4503790/
8. National Center for Biotechnology Information. PubChem Compound Summary for CID 5479530, Ceftriaxone. https://pubchem.ncbi.nlm.nih.gov/compound/Ceftriaxone
9. https://www.drugs.com/search.php?searchterm=inj+ceftriaxone+brand+name
10. National Center for Biotechnology Information (2024). PubChem Compound Summary for CID 447043, Azithromycin. Retrieved September 16, 2024 from https://pubchem.ncbi.nlm.nih.gov/compound/Azithromycin
11. https://www.drugs.com/ingredient/azithromycin.html
12. https://www.researchgate.net/publication/357316306_Study_on_the_efficacy_of_ceftriaxoneversus_azithromycin_for_the_treatment_of

_uncomplicated_enteric_fever_among_the_patien ts_admitted_in_a_tertiary_level_hospital

13. Frenck RW Jr, Nakhla I, Sultan Y, Bassily SB, Girgis YF, David J, Butler TC, Girgis NI, Morsy M. Azithromycin versus ceftriaxone for the treatment of uncomplicated typhoid fever in children. Clin Infect Dis. 2000 Nov;31(PMID): https://pubmed.ncbi.nlm.nih.gov/11073741/
14. Sur D, Ali M, von Seidlein L, Manna B, Deen JL, Acosta CJ, Clemens JD, Bhattacharya SK. Comparisons of predictors for typhoid and paratyphoid fever in Kolkata, India. BMC Public Health. 2007 Oct 12 (PMID). https://pubmed.ncbi.nlm.nih.gov/17935611/
15. Adhikari A, Rauniyar R, Raut PP, Manandhar KD, Gupta BP. Evaluation of sensitivity and specificity of ELISA against Widal test for typhoid diagnosis in endemic population of Kathmandu. BMC Infect Dis. 2015 Nov 14 (PMC). https://pubmed.ncbi.nlm.nih.gov/26573629/
16. Andualem G, Abebe T, Kebede N, Gebre-Selassie S, Mihret A, Alemayehu H. A comparative study of Widal test with blood culture in the diagnosis of typhoid fever in febrile patients. BMC Res Notes. 2014 Sep 17(PMID). https://pubmed.ncbi.nlm.nih.gov/25231649/
17. Sinha B, Rongsen-Chandola T, Goyal N, Arya A. Incidence of Enteric Fever in a Paediatric Cohort in North India: Comparison with Estimates from 20 Years Earlier. J Infect Dis. 2021 Nov 23 (PMCID) https://pubmed.ncbi.nlm.nih.gov/35238363/
18. Khan M, Khattak MT, Gul A, Riaz M, Zahra FT. A comparable risk of extensively drug-resistant typhoid fever in the paediatric cohort during the COVID-19 pandemic. Int J Health Sci (Qassim). 2024 Jan-Feb;18 (PMCID). https://pubmed.ncbi.nlm.nih.gov/38188899/

HOW TO CITE: Swathi Boddupally*, Goreti Shivani, DR.Gangadhara Rao, Jetram Omprakash Reddy, Jakkula Vagdevi, To Study The Safety And Efficacy Of Injection Ceftriaxone Monotherapy Versus Injection Ceftriaxone Plus Oral Azithromycin Dual Therapy In Enteric Fever, Int. J. of Pharm. Sci., 2026, Vol 4, Issue 7, 3214-3224. https://doi.org/ 10.5281/zenodo.21390541