

Factors Associated with Presence of Pneumonia and Meningitis Among Pediatric Patients Presenting with Enteric Fever

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ABSTRACT

Objective: To study association of various factors with presence of complications like pneumonia and meningitis in children presenting with enteric fever.

Study Design: Comparative cross-sectional study.

Place and Duration of Study: Pediatrics Department Pak Emirates Military Hospital, Rawalpindi Pakistan, Mar 2021 Feb 2022.

Methodology: A total 200 pediatric patients with confirmed diagnosis of enteric fever presenting at pediatric department were recruited in this analysis. Detailed systemic examination was conducted followed by relevant investigations to look for complications like pneumonia and meningitis in study participants. All baseline blood investigations including liver function tests were carried out at time of clinical evaluation. Age, gender, residential area and salmonella typhi vaccination status were associated with presence of pneumonia and meningitis in children with enteric fever.

Results: Out of 200 children with enteric fever included in the study 112(56%) were male while 88(44%) were female. Mean age of the children in our study was 9.56 ± 5.63 years. 24(12%) children were having pneumonia while 6(3%) children had meningitis. Fever was the commonest symptom reported by our study participants. Statistical analysis revealed that not being vaccinated for salmonella typhi and being from rural area had statistically significant relationship with presence of pneumonia and/or meningitis in our target population (p -value <0.005).

Conclusion: Complications were not uncommon in children suffering from enteric fever presenting to our hospital. Children who were not vaccinated or were coming from rural area were found more at risk of having complications like pneumonia and meningitis in our study.

Keywords: Complications; Enteric fever; Pneumonia; Meningitis.

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INTRODUCTION

Lower- and middle-income countries bear big burden of infectious diseases and still a lot of children each year fall prey to infections which may range from asymptomatic disease to life threatening complications. Salmonella typhi is one of these infections causing significant mortality and morbidity in patients of all age group especially children.¹ People in developed world may get affected when they travel in developing countries or countries with high disease burden.² Abdominal symptoms still remain common form of presentation but any system of body can get affected or complicated in enteric fever.³ Diagnosis of enteric fever is usually clinical strengthened by investigations like blood culture and sensitivity.⁴ Culture and sensitivity result come after few days and clinical condition may get worse leading to multi-system complications.⁵

Typhoid fever spreads from drinking water contaminated with urine or feces of infected people. Poor sanitation, low socioeconomic status, and inadequate hygiene are the most common found culprits.⁶

Complications may arise due to inadequate treatment or due to delay in diagnosis and include typhoid intestinal perforation leading to gastrointestinal hemorrhage, hepatitis, cholecystitis, myocarditis, shock, encephalopathy, pneumonia, and anemia.⁷ Duhil *et al.*, in 2018 studied an immunocompetent child with enteric fever who suffered from pneumonia further complicated by pleural empyema. They emphasize on atypical presentation and complications of enteric fever in children without any apparent risk factors.⁸ Mshana *et al.*, in 2015 studied an interesting case of a child with meningitis who suffered from Salmonella typhi. Child under observation also had urinary schistosomiasis suggesting that enteric fever may not always have routine presentation and clinicians should be aware of all the complications that may occur in such patients.⁹

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Pakistan bears huge burden of infectious diseases including enteric fever. Local study had revealed that treatment resistant strain occurs in our set up and considerable number of patients may suffer from various systemic complications.¹⁰ Limited local has been available regarding complications such as pneumonia and meningitis in children suffering from enteric fever. We therefore planned this study with the rationale to study association of various factors with presence of complications like pneumonia and meningitis in children presenting with enteric fever.

METHODOLOGY

This comparative cross-sectional study was conducted in the Departments of Pediatrics and microbiology, Combined Military Hospital (CMH), Rawalpindi Pakistan, from March 2021 to February 2022. Research evaluation and the ethical committee approved (letter no 32950) the study and informed consents in written form was taken from the patient's parents. Sample size was calculated by using the WHO sample size calculator by keeping population prevalence proportion of lungs involvement in enteric fever as 6.1% and margin of error as 10%.¹¹ Primary data was collected via non probability purposive sampling technique.

Inclusion Criteria: The study included all pediatrics patients (1 to 12 years) who were confirmed to have typhoid fever. The inclusion criterion was patients having fever of (temperature $>38^{\circ}\text{C}$) for the last 5 days, abdominal pain, nausea and vomiting with positive blood culture test for salmonella typhi.

Exclusion Criteria: Patients who had neurological or pulmonary symptoms before onset of typical symptoms of enteric fever or those were with chronic diseases or those who were severely dehydrated were excluded from the study. Those who refused to detailed clinical and laboratory evaluation were also not included in the study. Children with syndromes or chronic auto-immune or metabolic disorder were not made part of the study.

After written informed consent of parents, pediatric patients who fulfilled above mentioned inclusion/exclusion criteria were included in the study. Typhoid fever was diagnosed by using relevant clinical and laboratory parameters as per hospital protocol by consultant pediatrician.¹² All of these patients underwent tests such as complete blood count, chest x-ray and relevant neuroimaging as advised by consultant managing the individual patient. Pneumonia,¹³ and meningitis,¹⁴ were

diagnosed by treating team as per set criteria on the basis of clinical symptoms, examination findings and relevant investigations. Typhoid vaccine has been added in expanded program of immunization and children were considered vaccinated if mentioned on vaccination card or accurately remembered by parents. All relevant socio-demographic, clinical and laboratory information was entered in a proforma designed for this study.

This was a descriptive statistical analysis was carried out with Statistical Package for the Social Sciences (SPSS) version 23:00. Mean \pm SD was calculated for age of patients. Frequency along with percentage was calculated for gender, clinical characteristics and complications occurred in our study participants. Pearson chi-square test was used to assess association between age, gender, area of residence and typhoid vaccination status with presence of pneumonia and/or meningitis by keeping the *p*-value less than or equal to 0.05 as significant.

RESULTS

Out of 200 children with enteric fever included in the study 112(56%) were male while 88(44%) were female. Mean age of the children in our study was 9.56 ± 5.63 years. 49(24.5%) patients had any one or more components of liver function tests deranged while 151(75.5%) had normal liver function tests. Table-I revealed the sociodemographic, clinical and biochemical profile of children included in the study. Fever was the commonest symptom reported by our study participants.

Table-II showed the complications suffered by patients in our study. Pneumonia occurred in 24(12%) children while meningitis occurred in 12(6%) patients. Disseminated intravascular coagulation was seen in only 02(1%) patients.

Table-III revealed the results of Statistical analysis. Not being vaccinated for salmonella typhi and being from rural area had statistically significant relationship with presence of pneumonia and/or meningitis in children suffering from enteric fever (*p*-value <0.005).

DISCUSSION

Results of this study showed that pneumonia and meningitis may occur or may be presenting features in children having salmonella typhi infection. Patients from rural area may present late and be more at risk of developing the complications. Enteric fever can be a benign infectious disease settling with due course of

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anti-microbial drugs but sometimes may be complicated and patients may have life threatening consequences of enteric fever. Due to limited data for complications of enteric fever in children in Pakistan we conducted this study with the aim to study association of various factors with presence of complications like pneumonia and meningitis in children presenting with enteric fever.

Table-I: Basic Demographic Profile of Children Suffering From Enteric fever (n=200)

Study Parameters	n(%)
Mean Age	9.56±5.63 years
Gender	
Male	112(56%)
Female	88(44%)
Hemoglobin	
Within range	144(72%)
Deranged	56(28%)
White cell Count	
Within range	42(21%)
Deranged	158(79%)
Platelet Count	
Within range	74(37%)
Deranged	126(63%)
C-reactive Protein	
Within range	136(68%)
Deranged	64(32%)
Clinical Profile	
Fever for >5 days	200(100%)
Constipation	38(19%)
Diarrhea	60(30%)
Vomiting	50(25%)
Headache	18(9%)
Splenomegaly	36(18%)
Hepatomegaly	50(25%)
Oral ulcers	12(6%)
Others	04(2%)

Table-II: Complications Seen in Patients (n=200)

Complications	n(%)
Pneumonia	24(12%)
Meningitis	06(3%)
Bone involvement	03(1.5%)
Disseminated intravascular coagulation	02(1%)
Hepatitis	03(1.5%)
Anemia	08(4%)
Others	2(1%)

Marchello *et al.*,¹⁵ in 2020 worked extensively to find out complications of enteric fever in patients from different cultures and ethnicities. They figured about large number of complications which may occur in patients of enteric fever. Pulmonary and neuropsychiatric complications made a considerable chunk of overall complications that occurred in patients of enteric fever. We also studied

complications but our main emphasis was on pneumonia and meningitis. Meningitis was seen in few children but pneumonia was found in around 12% of children who suffered from enteric fever.

Table-III: Factors Associated with Presence of Pneumonia and Meningitis in Study Participants

Factors Studied	No Pneumonia or Meningitis	Pneumonia and/or Meningitis	p-value
Age			
<8 years	85(49.7%)	10(34.5%)	0.126
8-12 years	86(50.3%)	19(65.5%)	
Gender			
Male	93(54.3%)	19(65.5%)	0.260
Female	78(45.7%)	10(34.5%)	
Area of residence			
Rural	110(64.3%)	11(37.9%)	0.008
Urban	61(35.7%)	18(62.1%)	
Vaccination status			
Vaccinated	120(70.2%)	11(37.9%)	0.001
Not vaccinated	51(29.8%)	18(62.1%)	

Shahid *et al.*,¹⁶ studied patients from Karachi, Pakistan regarding overall clinical and complications profile in patients suffering from drug resistant typhoid fever. They included only resistant cases so complications studied by them may be over representation if we consider all patients suffering from salmonella typhi infection. Still our results supported the findings generated by Shahid *et al.*, as pneumonia, meningitis, bone involvement, DIC, hepatitis and anaemia were seen in our study participants and more in children who belonged to rural areas. Long time for untreated illness due to delay in reaching the health facility may be one of the reasons for this finding.

Ray *et al.*, in 2021 studied this phenomenon from another angle and studies patients of typhoid and enteric fever who were managed at intensive care unit due to various reasons.¹⁷ Encephalopathy, psychosis and pneumonia were seen in patients who required management of enteric fever in critical care settings. We did not follow patients long for observing the admission pattern and course of illness and cannot comment on requirement of critical care settings for management of our patients but our results reflect serious complications like presence of pneumonia and meningitis.

Dange *et al.*,¹⁸ in 2021 published a rare case of Salmonella meningitis and hemophagocytic lymphohistiocytosis. They found it though rare but neurological and haematological complications could

be expected in patients suffering from enteric fever. Our results showed that these complications were not uncommon in children suffering from enteric fever presenting to our hospital. Children who were not vaccinated or were coming from rural area were found more at risk of having complications like pneumonia and meningitis in our study.

Our study added to complications related epidemiological data in our region. Pneumonia and meningitis emerged as complications of enteric fever and children who were from rural background or not vaccinated were more at risk of having complicated illness.

LIMITATIONS OF STUDY

Comparative cross-sectional study design does not establish cause effect relationship and we cannot conclude that pneumonia or meningitis were consequence of enteric fever. Moreover, vaccination cards were not checked in all the patients and memory of parents was relied upon increasing the chances of recall bias in our study. Number of confounding factors could affect the complication rate and studying all of them was not possible in one study.

CONCLUSION

Complications were not uncommon in children suffering from enteric fever presenting to our hospital. Children who were not vaccinated or were coming from rural area were found more at risk of having complications like pneumonia and meningitis in our study.

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RK & ST: Study design, drafting the manuscript, data interpretation, critical review, approval of the final version to be published.

AS: Data acquisition, data analysis, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

REFERENCES

1. Nizamuddin S, Ching C, Kamal R, Zaman MH, Sultan F. Continued Outbreak of Ceftriaxone-Resistant *Salmonella enterica* Serotype Typhi across Pakistan and Assessment of Knowledge and Practices among Healthcare Workers. *Am J Trop Med Hyg* 2021; 104(4): 1265-1270. <https://doi.org/10.4269/ajtmh.20-0783>
2. Jensenius M, Han PV, Schlagenhauf P, Schwartz E, Parola P, Castelli F, et al. Geo Sentinel Surveillance Network Acute and potentially life-threatening tropical diseases in western travelers--a GeoSentinel multicenter study, 1996-2011. *Am J Trop Med Hyg* 2013; 88(1): 397-404. <https://doi.org/10.4269/ajtmh.12-0551>
3. Brooks WA, Hossain A, Goswami D, Nahar K, Alam K, Ahmed N, et al. Bacteremic typhoid fever in children in an urban slum, Bangladesh. *Emerg Infect Dis* 2005; 11(2): 326-329. <https://doi.org/10.3201/eid1102.040422>
4. Sheikh M, Bhat AA, Rather GN, Akhter R, Bhat I, Wani T, et al. Clinical profile of enteric fever in tertiary care hospital of Kashmir. *Int J Contemp Pediatr* 2017; 4(3): 1754-1757.
5. Andrews JR, Ryan ET. Diagnostics for invasive *Salmonella* infections: Current challenges and future directions. *Vaccine* 2015; 33(3): C8-15. <https://doi.org/10.1016/j.vaccine.2015.02.030>
6. Näsström E, Jonsson P, Johansson A, Dongol S, Karkey A, Basnyat B, et al. Diagnostic metabolite biomarkers of chronic typhoid carriage. *PLoS Negl Trop Dis* 2018; 12(1): e0006215. <https://doi.org/10.1371/journal.pntd.0006215>
7. Marchello CS, Birkhold M, Crump JA. Complications and mortality of typhoid fever: A global systematic review and meta-analysis. *J Infect* 2020; 81(6): 902-910. <https://doi.org/10.1016/j.jinf.2020.10.030>
8. Duhil de Bénazé G, Desselas E, Houdouin V, Mariani-Kurkdjian P, Kheniche A, Dauger S, et al. Pneumonia with pleural empyema caused by *Salmonella* Typhi in an immunocompetent child living in a non-endemic country. *Paediatr Int Child Health* 2018; 38(3): 227-230. <https://doi.org/10.1080/20469047.2017.1316938>
9. Chacha F, Mshana SE, Mirambo MM, Mushi MF, Kabymera R, Grwing L, et al. *Salmonella* Typhi meningitis in a 9-year old boy with urinary schistosomiasis: a case report. *BMC Res Notes* 2015; 8(3): 64-68. <https://doi.org/10.1186/s13104-015-1030-2>
10. Akram J, Khan AS, Khan HA, Gilani SA, Akram SJ, Ahmad FJ, et al. Extensively Drug-Resistant (XDR) Typhoid: Evolution, Prevention, and Its Management. *Biomed Res Int* 2020; 2020(3): 6432580. <https://doi.org/10.1155/2020/6432580>
11. Iftikhar A, Bari A, Jabeen U, Bano I. Spectrum of complications in childhood Enteric Fever as reported in a Tertiary Care Hospital. *Pak J Med Sci* 2018; 34(5): 1115-1119. <https://doi.org/10.12669/pjms.345.15262>
12. Neupane DP, Dulal HP, Song J. Enteric Fever Diagnosis: Current Challenges and Future Directions. *Pathogens* 2021; 10(4): 410. <https://doi.org/10.3390/pathogens10040410>
13. Rodrigues CMC, Groves H. Community-Acquired Pneumonia in Children: the Challenges of Microbiological Diagnosis. *J Clin Microbiol* 2018; 56(3): e01318-17. <https://doi.org/10.1128/JCM.01318-17>
14. Zainel A, Mitchell H, Sadarangani M. Bacterial Meningitis in Children: Neurological Complications, Associated Risk Factors, and Prevention. *Microorganisms* 2021; 9(3): 535. <https://doi.org/10.3390/microorganisms9030535>
15. Marchello CS, Birkhold M, Crump JA. Complications and mortality of typhoid fever: A global systematic review and meta-analysis. *J Infect* 2020; 81(6): 902-910. <https://doi.org/10.1016/j.jinf.2020.10.030>
16. Shahid S, Mahesar M, Ghouri N, Noreen S. A review of clinical profile, complications and antibiotic susceptibility pattern of extensively drug-resistant (XDR) *Salmonella* Typhi isolates in children in Karachi. *BMC Infect Dis* 2021; 21(1): 900. <https://doi.org/10.1186/s12879-021-06599-2>
17. Ray B, Raha A. Typhoid and Enteric Fevers in Intensive Care Unit. *Indian J Crit Care Med* 2021; 25(Suppl 2): S144-S149. <https://doi.org/10.5005/jp-journals-10071-23842>
18. Dange NS, Sawant V, Dash L, Kondekar AS. A Rare Case of *Salmonella* meningitis and Hemophagocytic Lymphohistiocytosis. *J Glob Infect Dis* 2021; 13(2): 100-102. https://doi.org/10.4103/jgid.jgid.224_20