

# Treatment Outcome of Enteric Fever in Children at Tertiary Care Hospital Sukkur Pakistan

1. Bahwaluddin Jamro 2. Noor Ahmed Shaikh 3. Khush Muhammad Sohu 4. Aftab Ahmed Soomro 5. Shankar Lal 6. Saifullah Jamro

1. Assoc. Prof. of Paediatrics, GMMC, Sukkur 2. Sr. Registrar of Paediatric Surgery, GMMC, Sukkur  
3. Sr. Registrar of Surgery, GMMC, Sukkur 4. Asstt. Prof. of Hematology, GMMC, Sukkur 5. Sr. Registrar of Paediatrics, CMC, Larkana 6. Prof. & Chairman of Paediatrics, CMC, Larkana

## ABSTRACT

**Background:** Enteric fever (Typhoid fever) is widely recognized as a major public health problem in developing countries.

**Objective:** To evaluate the treatment outcome of enteric fever in children

**Study Design:** Retrospective descriptive study.

**Place and Duration of Study:** This study was conducted at the Paediatric department, Ghulam Muhammad Mahar Medical College Hospital Sukkur from January 2009 to December 2011.

**Patients and Methods:** This was a retrospective study, included all patients of enteric fever, of both sex and age ranged from 6m to 13 years. All enteric patients were confirmed by serological test Typhidot IgM or IgM and IgG positive. The data was collected from case record for demography and treatment outcome.

**Results:** A total of 360 patients were diagnosed to have enteric fever during this period. Mean age of presentation was 6.47 years and 166 (46.12%) patients were <5 years whereas 194 (53.88%) were > 5 years of age. Male:Female ratio was 2:1. Serological test typhidot IgM was positive in 290 (80.5%) and both (IgM + IgG) were positive in 70 (19.45%) of cases. Raised ALT was seen in 90(25%) of cases. Complications were seen in 52 (14.4%) of cases, hepatitis 10 (2.77%), hepatic abscess 3 (0.83%) intestinal hemorrhage 8 (2.22%), peritonitis 4 (1.11%) intestinal perforation 4 (1.11%), cholecystitis 6 (1.66%), paralytic ileus 3 (0.83%) enteric encephalopathy 3 (0.83%), meningitis 1(0.27%) osteomyelitis 3 (0.83%), septic arthritis 2 (0.55%) pancytopenia 3 (0.83%), pneumonia 1 (0.27%) and renal abscess 1(0.27%). Two patients expired (0.55%), one was enteric encephalopathy and other intestinal perforation with peritonitis.

**Conclusion:** Enteric fever remains a major cause of morbidity and mortality in our part of country. Major complications found in our cases were hepatitis, hepatic abscess, intestinal hemorrhage, intestinal perforation, peritonitis, cholecystitis, enteric encephalopathy, meningitis, osteomyelitis, septic arthritis.

**Key Words:** Enteric fever, complications, children.

## INTRODUCTION

Enteric fever (Typhoid fever) is widely recognized as a major public health problem in developing countries. It is a severe systemic infection caused by *Salmonella typhi*. The disease is endemic in the Indian sub-continent, South-East Asia, Africa, the Middle East, South and Central America, where provision of pure water supplies and sewage control are inadequate<sup>1</sup>. World wide incidence of enteric fever is estimated that more than 21.7 million cases and more than 200,000 deaths occur annually, the vast majority in Asia<sup>2</sup> The incidence may vary considerably in the developing world, with estimated rates ranging from 100 to 1,000 cases/100,000 population<sup>2</sup>. Ochiai LR et al, in their review of disease burden due to enteric fever from five Asian countries, reported a higher incidence of enteric fever from India, Indonesia and Pakistan<sup>3</sup>. Enteric fever represents the 4<sup>th</sup> most common cause of death in Pakistan<sup>4</sup>. The disease may occur in all ages, with the highest incidence found particularly in children<sup>5</sup> Young age was seen in a study from Bangladesh, that the 57% of *Salmonella typhi* isolates were in children less than

5 years of age and 27% less than 2 years<sup>6</sup> Various organs have been involved in the course of enteric fever resulting in a wide array of presentation<sup>2</sup> Enteric fever is associated with significant morbidity and mortality due to emerging multidrug-resistant strains of salmonella and delay in diagnosis<sup>7</sup>. In a local study of 1100 hospitalized children, the mortality rate of 1.6% was found to be related to young age and multidrug-resistant infection<sup>7</sup>. Complications occur in 10-15% of patients and gastrointestinal bleeding (10%), intestinal perforation (1-3%) and neuropsychiatric manifestations (2-40%) are the most important ones reported<sup>8</sup>.

The extraintestinal complication of enteric fever reported prevalence 3-35% central nervous system, 1-5%, cardiovascular system, 1-6% pulmonary, 1-26% hepatobiliary system, less than 1% bone and joint and genitourinary system respectively<sup>9</sup>. Death due to enteric fever ranges from 12.1% to 19.4% of cases reported from Nigeria<sup>10</sup>. Despite appropriate therapy, 2-4% of infected children may experience relapse after initial clinical response to treatment<sup>2</sup>. We conducted retrospective study to evaluate treatment outcome of our treated patients in tertiary care hospital, caring for

large number of sick children from rural areas of Sukkur and surroundings.

## PATIENTS AND METHODS

**Place and duration of study:** Paediatric department of Ghulam Muhammad Mahar Medical College Hospital Sukkur Pakistan, from January 2009 to December 2011. This was a retrospective study, included all patients of enteric fever, of both sex and age ranged from 6 months to 13years. All enteric patients were confirmed by serological test Typhidot IgM, or both IgM and IgG positive antibodies. Blood culture was not done Data was collected from case records for demography, laboratory parameters and treatment outcome. All patients underwent investigations such as hemogram, liver and renal function tests. Additional investigation like X-Ray chest and erect posture abdomen, ultrasound abdomen, CSF, MP, serum electrolytes, blood sugar, were done where it was indicated.

All patients initially were treated with Ceftriaxone .The clinical course was closely monitored and looked for complications of enteric fever. Persistence of fever for more than 7 days after antibiotics treatment was taken as a sign to start second line antibiotics. Patients who developed surgical complication treated by paediatric surgeon and all others were conservatively managed with all possible supportive care.

## RESULTS

A total of 360 patients were diagnosed to have enteric fever during this period. Mean age of presentation was 6.47 years and 166 (46.12%) patients were < 5 years whereas 194 (53.88%) were > 5 years of age shown in table 1. M:F ratio was 2:1. Serological test Typhidot IgM was positive in 290 (80.5%) and both (IgM +IgG) were positive in 70 (19.45%) of cases. Majority of children were treated with Ceftriaxone 316 (87.77%) for 10-14 days and only 26 (7.23%) of the children received Cefotaxime and 18 (5%) received Ciprofloxacin. Raised ALT was found in 90 (25%) of cases and anemia in 278 (77.23%), and thrombocytopenia in 78 (21.66%) of cases. Complications were seen in 52 (14.4%) of cases, hepatitis 10 (2.77%), hepatic abscess 3 (0.83%), cholecystitis 6 (1.66%), intestinal hemorrhage 8 (2.22%), peritonitis 4 (1.11%), intestinal perforation 4 (1.11%), paralytic ileus 3 (0.83%), enteric encephalopathy 3 (0.83%), meningitis 1 (0.27%), osteomyelitis 3 (0.83%), septic arthritis 2 (0.55%), pancytopenia 3 (0.83%), pneumonia 1 (0.27%), and renal abscess 1(0.27%) as shown in table 2. Relapse of enteric fever was found in 5 (1.38%) of cases after 3 weeks of treatment. Two patients expired (0.55%), one was enteric encephalopathy and other intestinal perforation with peritonitis.

**Table No.1: Age, Sex and Typhidot antibodies positive.**

Age	%age	Male	Female	Typhidot IgM	Typhidot IgM +IgG
6m to 12m No;20	5.56%	12	8	10	10
1y to 2y No: 56	15.56%	39	17	36	20
2y to 5y No 90	25%	60	30	56	34
6y to 10y No:144	40%	94	50	121	23
11y to 13y No:50	13.88%	35	15	47	03

**Table No.2: Complications of enteric fever in 52 (14.4%) of children**

Complication	Number of patients	Percentage
Hepatitis	10	2.77%
Hepatic abscess	03	0.83%
Cholecystitis	06	1.66%
Intestinal hemorrhage	08	2.22%
Peritonitis	04	1.11%
Intestinal perforation	04	1.11%
Paralytic ileus	03	0.83%
Enteric encephalopathy	03	0.83%
Meningitis	01	0.27%
Osteomyelitis	03	0.83%
Septic arthritis	02	0.55%
Pancytopenia	03	0.83%
Pneumonia	01	0.27%
Renal abscess	01	0.27%
Death of patients	02	0.55%

## DISCUSSION

Enteric fever still remains a major endemic public health problem in Pakistan especially in areas where healthcare facilities being limited and peoples are illiterate, living in unhygienic surroundings, drinking raw-water from canals and especially in rural areas or kachiabadies. Enteric fever accounts for significant cause of morbidity in children, in developing countries. In our study 46.12% of patients were under 5 years, similar to the reported by Shah I, et al<sup>11</sup> from India. Most of 53.88% our cases were old than 5 years as reported in most of studies<sup>12, 13, 14</sup> in children. Also in our patients males were 66.66% more common affected as compared to females, similar to the reported from India by Shah I et al <sup>11, 13</sup> whereas Abdel Wahab et al <sup>15</sup> found equal distribution between the boys and girls. Typhidot IgM was positive in 290 (80.5%) of cases similar to the results of locally reported by Hayat AS et al<sup>16</sup>.Majority of children were treated with Ceftriaxone 316 (87.77% , similar to the reported by Ganesh R et al from India<sup>12</sup>.Raised serum ALT was found in 90 (25%) cases in our cases which is lower when compared to

earlier studies by Ganesh R et al<sup>12</sup> where hepatic dysfunction was seen in 57% of cases, and 60% of cases<sup>17</sup>. In majority 278 (77.23%) of our children anemia was seen and only (21.66%) of cases thrombocytopenia was seen, while Shah I et al<sup>11</sup> from India reported in his series 87.9% anemia and 33.33% thrombocytopenia.

Complications of enteric fever were seen in 52 (14.4%) of patients, similar to previously reported in other studies<sup>2,8,11</sup> whereas complications seen by others in over 30% of the patients<sup>18,19,20</sup>.

Hepatitis was the most common complication seen in our children 10 (2.77%) which is very low than reported by Ahmed A et al<sup>10</sup> from Nigeria 31 (12.2%) of patients. Hepatic abscess was seen in 3 (0.83%) of children, similar to previously reported by Chaudhary R et al<sup>21</sup> in his series of enteric cases. Cholecystitis was seen in 6 (1.66%) children in our study as reported by others<sup>2,9,22</sup>. The second most common complication was seen intestinal hemorrhage in 8 (2.22%) children, which is less than reported in other study from India 10% gastrointestinal bleeding<sup>8</sup>, but very low results are also reported <1%<sup>2</sup>. Perforation and peritonitis was seen in 4 (1.11%) our children respectively, similar to the other studies<sup>2,8</sup> but unlike to the Nigerian study where intestinal perforation was seen 17.8%-to 29% of enteric patients<sup>10</sup>. Enteric encephalopathy and psychosis were seen in 3 (0.83%) in our children which is very low than (3-35%) reported in other studies<sup>8,9,10</sup>. Paralytic ileus was seen in 3 (0.83%) in our patients as reported by Malik AS et al from Malaysia<sup>18</sup>. Common complication of enteric fever has been reported by Malik AS et al<sup>18</sup> as bone marrow suppression, we had seen pancytopenia in our 3(0.835). Osteomyelitis was seen in 3 (0.83%) children in our study, similar to the reported by Huang BD<sup>8</sup>.

The other less common complication seen in our children were septic arthritis 2 (0.55%), meningitis, pneumonia and renal abscess 1(0.27%) in each respectively as reported in many other studies<sup>2,7,8,12</sup>. Relapse of enteric fever was seen in 5 (1.38%) of cases within 2-3 weeks after treatment, similar relapse of enteric fever was seen in 4 (1%) by Ganesh R et al from India<sup>12</sup>, unlike to our results high relapse was seen in 6 (19.4%) patients in Nigeria by Ahmed A et al<sup>10</sup>.

Mortality was minimal in our study as has been reported by others studies<sup>11,22</sup>. Only two patients expired in our study 2 (0.55%), one was enteric encephalopathy and an other intestinal perforation with peritonitis. Higher mortality was reported from Nigeria by Ahmed A et al<sup>10</sup> that 12.1% to 19.4%. The high mortality was associated with the presence of jaundice, anemia or malnutrition<sup>23</sup>.

## CONCLUSION

Enteric fever remains a major cause of morbidity and mortality in our part of country. Major complications

seen in our children were hepatitis, hepatic abscess, cholecystitis, intestinal hemorrhage, intestinal perforation, peritonitis, enteric encephalopathy, meningitis osteomyelitis, septic arthritis, pancytopenia and renal abscess. Relapse rate was seen 1.38% patients.

## Recommendations:

1. Enteric fever should be suspected in young children and infants with fevers of unknown origins in our settings.
2. The preventive strategies for enteric fever include safe water, hygiene and appropriate vaccination strategies.
3. Mass immunization programs using Vi and Ty21a vaccines for more than 2 years of children.
4. Early diagnosis (Typhidot IgM) and referral to prevent complications is essential.
5. Third generation cephalosporins is associated with higher cure rates and can be used empirical in absence of culture and sensitivity facilities.

## REFERENCES

- 1 Gillespie S. Salmonella infection. In: Cook GC, Zumla A, editors. *Manson's Tropical Diseases*. 21<sup>st</sup> ed. London: UK Elsevier Science, Health Science Division; 2003.p.937-947.
- 2 Bhutta ZA. Enteric Fever. In: Kliegman RM, Stanton BF, Geme 111 JW, Schor NF, Behrman RE, editors. *Nelson Textbook of Pediatrics*. 19<sup>th</sup> ed. Elsevier Saunders; 2011.p.954-958.
- 3 Ochiai LR, Acosta CJ, Danovaro-Holliday MC, Baiqing D Bhattcharya SK, et al. A study of Typhoid fever in five Asian counties; disease burden and implications for control. *Bull World Health Organ* 2008;86(4):260-8.
- 4 World Health Organization 6<sup>th</sup> International Conference on Typhoid Fever and other Salmonellosis. Geneva WHO 2006. Ref Type; Pamphlet.
- 5 Anggraini R, Handoyo I, Aryati. DOT-EIA typhoid test using Omp Salmonella typhi local phage type antigen to support the diagnosis of typhoid fever. *Folia Medica Indonesiana* 2004;40:10-20.
- 6 Saha SK, Baqui AH, Hanif M, Darmstadt GL, Ruhulamin M, Nagatake T, et al. Typhoid fever in Bangladesh: implications for vaccination policy *Pediatric Infectious Disease J* 2001;20(5):521-524.
- 7 Bhutta ZA. Impact of age and drug resistance on mortality in typhoid fever. *Arch Disease Child* 1996;75(3):214-217.
- 8 IAP task force report. Management of enteric fever in children *Indian pediatr* 2006;43:884-7.
- 9 Huang DB, DuPont HL. Problem pathogens; extra-intestinal complications of Salmonella enterica serotype Typhi infection, *Lancet infect Dis* 2005; 5(6):341-348

- 10 Ahmed A, Ahmed B. Jaundice in typhoid fever patients: Differentiation from other common causes of fever and jaundice in the tropics. *Annals of African Medicine* 2010;9(3):135-140.
- 11 Shah I, Patankar N. Age Related Clinical and Laboratories Manifestations of Enteric Fever in Children. *JK Science* 2009;11(3):119-122.
- 12 Ganesh R, Janakiraman L, Vasanthi T, Sathiyasekeran M. Profile of Typhoid Fever in Children from a Tertiary Care Hospital in Chennai-South India. *Indian J Pediatr* 2010;77:1089-1092.
- 13 Rafiq H, Zia R, Naeem S. Typhoid Fever-Continues as a major threat in Children. *Biomedica* 2009;25:1-2.
- 14 Walia M, Gaiind R, Paul P, Mehta R, Aggarwal P, Kalaivani M. Age-related clinical and microbiological characteristics of enteric fever in India *Trans R Soc Trop Med Hyg* 2006;100(10): 942-48.
- 15 Abdel Wahab MF, el -Gindy IM, Sultan Y, el-Naby HM. Comparative study on different recent diagnostic and therapeutic regimens in acute typhoid fever *J Egypt Public Health Assoc* 1999; 74(1-2):193-205.
- 16 Hayat AS, Shah IA, Shaikh N. Typhoid Fever Evaluation of Typhidot (IGM) in Early and Rapid Diagnosis of Typhoid Fever. *Professional Med J* 2011;18(2):259-264.
- 17 Khosla SN, Singh R, Singh GP, Trehan VK. The spectrum of hepatic injury in enteric fever. *Am J Gastroenterol* 1988;83:413-6.
- 18 Malik AS, Malik RH. Typhoid fever in Malaysian children. *Med J Malaysian* 2001;56(4):478-90.
- 19 Tohme A, Zein E, Nasnas R. Typhoid fever. Clinical and therapeutic study in 70 patients. *J Med Liban* 2004;52(2):71-77.
- 20 Kumar R, Gupta NS. Multidrug-resistant typhoid fever. *Indian J Pediatr* 2007 ; 74 (1) :39-42
- 21 Chaudhry R, Mahajan RK, Diwan A, Khan S, Singhal R, Chandel DS, et al. Unusual presentation of enteric fever; three cases of splenic and liver abscesses due to *Salmonella typhi* and *Salmonella paratyphi A*. *Tropical Gastroenterology* 2003; 24(4):198-199.(12kb) Abstract only.
- 22 Lefebvre N, Gning SB, Nabeth P, et al. Clinical and laboratory features of typhoid fever in Senegal. A 70- case study. *Med Trop (Mars)* 2005;65(6): 543-48.
- 23 Uba AF, Chirdan LB, Ituem AM, Mohammed AM. Typhoid intestinal perforation in children; A continuing scourge in a developing country. *Pediatr Surg Int* 2007; 23:33-9.

**Address for corresponding author:****Dr. Bahawaluddin Jamro,**

Associate Professor of Paediatrics,

Ghulam Muhammad Mahar Medical College Sukkur

Email address: drbahawaljamro@gmail.com

Cell No: 03363861772

Office No: 07193107