Frequency of Complications in Paediatric Patients Presented with Enteric Fever in a Public Sector Hospital.

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ABSTRACT

OBJECTIVE: To assess the frequency of complications of enteric fever in paediatric patients in a public sector hospital.
STUDY DESIGN: A prospective observational study
PLACE AND DURATION: At Children Department, Pakistan Institute of Medical Sciences form 1st July 2016 to 31st July 2017.
METHODOLOGY: Children (newborns to 12 year) having positive Salmonella typhi on bacteriological culture/Typhi dot were included in study. All complications like hepatitis, perforation, bone marrow suppression, pneumonia and encephalitis were categorized according to clinical symptoms and diagnostic test reports.
RESULTS: Out of 65 patients, 47.69% developed complications. Mean age for disease was 6.7 ± 4.31 years with male preponderance (61.5%). Hepatitis was the most common (21.53%) complication followed by bone marrow suppression (12.3%), pneumonia (10.7%), encephalitis (6.1%) and perforation (4.6%). Rate of complication was higher (61.9%) for those not receiving any treatment (40.9%) at time of presentation than those receiving antibiotic treatment. No significant difference (OR=1.0, P-value 0.9) was found between the patients treated with ceftriaxone and quinolone.
CONCLUSIONS: Complications in enteric fever were found to be major health problem in children.
KEYWORDS: Enteric Fever, Complications, Frequency, Hepatitis, Pneumonia, Perforation, Bone Marrow Suppression, Encephalitis

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INTRODUCTION

Enteric fever or typhoid fever is caused by a gram negative bacterium, Salmonella typhi[1]. The organism usually attacks reticuloendothelial system i.e. liver, spleen and bone marrow[2]. Worldwide incidence rate of typhoid is between 11.9 million to 26.9 million per year with mortality rate of 129,000 to 161,000 annually[3]. The incidence rates have been substantially decreased in developed countries. However it still causes overwhelming burden in middle and low income countries. South-east Asian countries, have third highest incidence rate of enteric fever[4]. Annually 451.7 per 100,000 children (2-15 years) are affected by typhoid in Pakistan[5].

One-Third of the patients affected with typhoid develop complications. These includes hepatitis, cholecystitis, peritonitis, bone marrow suppression, pneumonia, psychosis, myocarditis, paralytic ileus and syndrome of inappropriate release of antidiuretic hormone (SIADH)[6]. Most fatal of these complications is peritonitis due to perforation with mortality rate varying between 5 to 80% depending upon surgical facilities available[7]. Flouro-quinolones are regarded as first line therapy for treating thyroid fever[8,9].

Typhoid fever is still a deadly disease in developing countries. Pakistan, India and Bangladesh accounts for the 85% of the cases occurring worldwide. Death in typhoid fever usually occurs when its complication go unchecked. With advent of

multidrug resistant bacteria, rate of complicated fever has grown higher[10]. Very few studies have been reported on typhoid in Pakistan especially in federal capital. Till now no study has been reported on rate of complications of typhoid fever within Pakistan. The study was conducted to fill this gap. The objective of current study was to assess the frequency of complications of enteric fever in paediatric patients in a public sector hospital.

METHODOLOGY

This prospective observational study was conducted in the Children Department, Pakistan Institute of Medical Sciences, Islamabad from 1st July 2016 to 31st July 2017. Children (newborns to 12 year) having positive Salmonella typhi on bacteriological culture/Typhi dot were included in study. Total 65 patients met the inclusion criterion. Patients having other associated illnesses like malaria, hepatitis A and other chronic illnesses with concomitant enteric fever were excluded from study. All patients had undergone routine investigations and were treated with either quinolone or ceftriaxone depending upon previous treatment they received. Tests include complete blood picture, blood CS, typhi Dot, liver function tests, ultrasound abdomen, chest X rays, abdomen X-rays, and routine urinary analysis.

Complications were categorized according to clinical symptoms and diagnostic test reports. Hepatitis was confirmed on the basis of clinical features and two times raised ALT levels. Perforation was confirmed upon strong clinical suspicion with abdominal x-ray and sonographic findings. Bone marrow suppression was confirmed on the basis of confirmation of pancytopenia on blood test reports. Pneumonia was characterized on its clinical features and chest X-ray findings. Encephalitis was diagnosed on the basis of clinical features, CSF analysis and CT scans. All the complications were assessed by the consultant and data was recorded on the form for further analysis.

Data Analysis: Data was analyzed by applying appropriate statistical tests via SPSS v 20. Firstly data was arranged and values label were given. Frequencies and percentages were calculated. Dispersion in quantitative data was analyzed by standard deviation. ODDs ratio was applied to check associations. Statistical significance was checked by P>0.05 values.

RESULTS

Total 65 patients were included in the study. Mean age for disease was 6.7 ± 4.31 years with male preponderance (61.5%). Mean duration for presentation to hospital was 14.9 ± 9.18 days. Most common symptom at time of presentation was fever (70.3%) followed by chills, vomiting, abdominal pain, rigors, anorexia, diarrhea and headache. Out of 65 patients, 31 patients developed complications. Rate of complication was 47.69%. Among complicated cases, 6 developed multi organ complications. Hepatitis was the most common (n=14, 21.53%) complication followed by bone marrow suppression (n=8, 12.3%), pneumonia (n=7, 10.7%), encephalitis (n=4, 6.1%) and perforation (n=3, 4.6%) (Fig-1).

Rate of complication was higher (61.9%) for those not receiving any treatment (40.9%) at time of presentation than those receiving antibiotic treatment. Among patients receiving treatment rate of complication was higher for those having previous treatment with ceftriaxone than for quinolone (Table-I). 46.2% of the patients treated only with ceftriaxone developed complication while rate for complication with patients treated with quinolone was 13.63%.

Majority of the patient (66.2%) had hepato-spleenomegaly at time of presentation. 58.5% had raised ALP levels. 30.8% (i.e. 20 patients) had raised ALT levels whereas bilirubin was raised in 18.5% patients. No association was found between hepato-spleenomegaly (OR=1.5, P-value = 0.2) and raised alkaline phosphatase ALP (OR=1.61, P-value = 0.2) levels with risk of complication. Both were independent findings present in patients of enteric fever. No association was found between raised ALT levels (OR=2.05, P-value = 0.14) and overall risk of complications. However among 20 (30.8%) with raised ALT levels, 14 (21.53%) patients had ALT level two time raised than normal value. These patients also had hepato-spleenomegaly, persistent vomiting and jaundice, that's why diagnosed as hepatitis. Bilirubin was found to be raised in 12 (18.5%) patients with hepatitis, only two patients (3.07%) with hepatitis did not have raised bilirubin levels.

All cases were treated successfully with antibiotic treatment. Only patients with perforation underwent surgery. No death was reported. 34 (52.30%) patients were given quinolone, while 31 (47.69%) were given ceftriaxone. Ceftriaxone was given to those patients who were already taking antibiotic but were not responding to it. No significant difference (OR=1.0, P-value 0.9) was found between the patients treated with ceftriaxone and quinolone. Majority of patients 38 (58.5%) recovered in 3-5 days of antibiotic treatment. 23 patients (35.4%) took 5-10 days in recovery while 4 patients (6.2%) took 10-20 days for complete recovery.

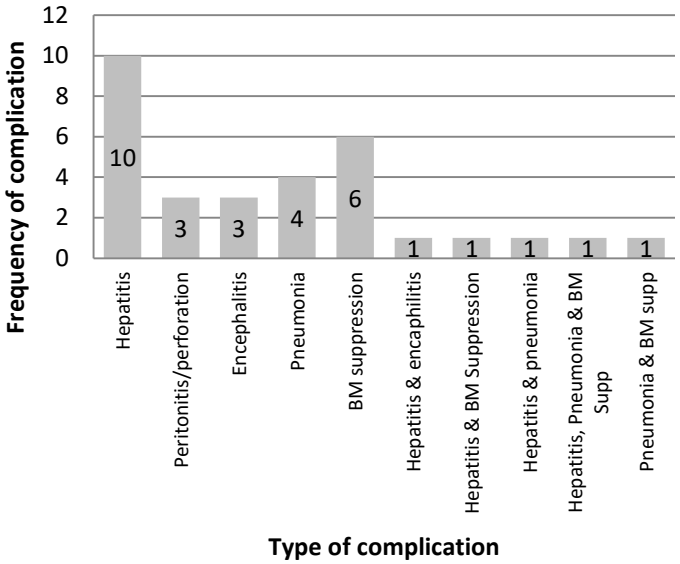

Fig-1: Frequency of Complications (N=31).

Table-I: Types and Frequency of complications in enteric patients with or without prior treatment prior treatment (N=65)

Complications	Ceftriaxone	Quinolone	Antibiotic+ antimalarial	No treatment	Total (N = 65)
Nil	15	6	5	8	34 (52.3%)
Hepatitis	3	0	3	4	10 (15.3%)
Peritonitis / perforation	0	0	0	3	3 (4.6%)
Encephalitis	2	0	0	1	3 (4.6%)
Pneumonia	2	0	0	2	4 (6.1%)
BM suppression	4	1	0	1	6 (9.2%)
Hepatitis & encephalitis	0	0	0	1	1 (1.5%)
Hepatitis & BM suppression	1	0	0	0	1 (1.5%)
Hepatitis & pneumonia	1	0	0	0	1 (1.5%)
Hepatitis, pneumonia & BM supp	0	0	0	1	1 (1.5%)
Pneumonia &BM supp	0	0	0	1	1 (1.5%)

DISCUSSION

In our study mean age of disease 6.7 ± 4.31 years which shows high prevalence of disease among school aged children. Usually 15% of the patients affected with enteric fever develop complications[11].However rate of complicated typhoid fever is higher in developing countries. Ninety percent of the deaths due to complicated fever occur in Asia[12]. In our study rate of complications was 47.7%, which was quite high. Such a high rate of complication could be due to late presentation at hospital as majority of our patients presented after 14.9 days of disease. Also the rate of complications was quite high for those taking no antibiotic medications. Moreover our hospital is the largest tertiary care hospital in the area which also receives number of referrals from the neighboring areas. Most of these patients include those who had not received successful treatment at their local setups.

Extra-intestinal complications of typhoid occur due to systemic involvement. These complications include hepatitis, acalculous cholecystitis, pneumonia, myocarditis and neurological complications[13].Among neurological complications, most of the children suffer from meningitis, encephalopathy, convulsions, sensory motor neuropathies and schizophrenic psychosis. Surgical complications of thyroid fever usually involve intestines. Intestinal perforation is the most fatal complication of typhoid fever[13]. In our study, extra intestinal complications also included hepatitis, bone marrow suppression, pneumonia, encephalitis and perforation.

Hepatitis is usually most common complication encountered by patients infected with Salmonella typhii[6].Our results were also similar. Bone marrow suppression was second common complication in current study population. This is also incongruent with other studies conducted in other parts of world. Study conducted on complications of typhoid fever in Malaysia showed hepatitis to be most common complication followed by bone marrow suppression[14]. Rate of neurological manifestation varies between 5-35% of the complicated cases. Our results were also in concord with it[9]. In current study, 10.76% of the patients developed pneumonia. There was no case of acute cholecystitis and myocarditis in our study. Typhoid perforation is less frequent (0.6-4%) but lethal complication of enteric fever. Majority of the deaths are attributed to perforation[10].In current study 3 patients (4.61%) developed perforation but all were successfully managed by immediate surgical intervention.

In our study, majority of the patients had hepato-spleenomegaly, raised alkaline phosphatase levels not necessarily linked with hepatitis. This finding was in concord with studies conducted with other parts of the world which shows that liver involvement is invariably present in enteric fever and should not be mixed with complication of hepatitis[15,16]. Study by Mirsadraee also showed that ALT is usually raised in typhoid due to typhoid myopathy not due to typhoid hepatitis[17]. In current study raised serum ALT levels were not associated with rate of complication. Patients with enteric hepatitis's had two or more times raised ALT levels. Rest of the patients with raised ALTs had minimally raised level. This may be due to general liver involvement with enteric fever. When jaundice is present in typhoid fever, it is usually due to hepatitis or cholecystitis[18,19]. In our study raised bilirubin levels were found to be strongly linked with hepatitis. Out of 14 patients with hepatitis, 12 had raised bilirubin levels.

According to WHO guidelines, fluro-quinolones must be used as first line therapy for treating enteric fever while third generation cephalosporins must be reserved for the drug resistant cases[8,20]. We used similar protocol. Study conducted in Rawalpindi showed ceftriaxone to be more effective than ciprofloxacin in treating typhoid fever[9]. However, our results showed both drugs to be equally effective (OR=1.0, P-value 0.9) in treating disease.

CONCLUSION

Complications in enteric fever were found to be major health problem in children.

CONTRIBUTION OF AUTHORS

Waris R: Conceived Idea, Designed, Supervision, Data Collection, Critical Review of manuscript

Riaz R: Analysis, Literature Review, Manuscript writing, Critical Review of manuscript

Waris A: Conceived Idea, Designed

Akhtar S: Data Collection

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