

Risk Factors and Outcome of Complicated Typhoid Fever at Dr M R Khan Shishu Hospital

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Abstract

Background: Typhoid fever is caused by salmonella typhi which invades the bloodstream causes systemic involvement & different complications. This study was designed to evaluate the complications of typhoid fever in children admitted to a tertiary care hospital.

Methodology: This retrospective cross-sectional study was conducted at Dr. M R Khan Shishu Hospital & ICH, over twelve months from July 2019 to June 2020 of 100 children aged 6 months to 15 years who were diagnosed with typhoid fever. Complete history, physical examination and investigation were done to reach the complications. Complications were evaluated and data were analyzed.

Background

Typhoid fever, is a severe febrile illness caused by the Gram-negative bacillus salmonella typhi. It is a major public health problem in many developing countries including Bangladesh.¹ Globally about 20 million episodes of illness and over 140,000 deaths are due to salmonella typhi. This burden is high in low and middle income countries including South East Asia.² The reported, prevalence of typhoid fever in Bangladesh is 0.67%.³⁻⁴ Without treatment typhoid fever can be fatal with a case fatality rate of 10-30%.⁵ Even with treatment, multi-drug resistant typhoid fever is more severe with higher rates of toxicity, complications and mortality.⁶

Results: Complications were found in 37% of typhoid fever cases. Among them, hepatitis, UTI, pneumonia, thrombocytopenia were mostly observed. The majority were boys from poor socio-economic backgrounds. Complications were usually found on the third week and significantly associated with male child, young age, poor socio-economic background, poor oral compliance, delay treatment, leukocytosis and thrombocytopenia.

Conclusion: A significant portion of children with typhoid fever can develop complications.

Keywords: Complications, Typhoid Fever, Children

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Salmonella typhi is transmitted by faeco-oral route and in course of time, it can involve various organs of the body.⁷⁻⁸ After oral ingestion of 10^5 - 10^9 numbers of salmonellae typhi; invade the terminal ileum gut mucosa. Then organisms enter the mesenteric lymph node and then pass into the bloodstream via the lymphatics. This primary bacteremia is usually asymptomatic. These blood-borne bacteria are disseminated throughout the body and colonize & replicate within the macrophage of the reticuloendothelial system. Then shed back in the blood causing secondary bacteremia that coincides with the onset of clinical symptoms and causes different complications.⁹

Typhoid fever may manifest from uncomplicated typhoid fever to complicated variety. Classical symptoms include gradual onset of sustained fever, chills, abdominal pain, diarrhea, constipation, anorexia, reduce level of consciousness, hepatosplenomegaly, leukopenia, thrombocytopenia, eosinopenia.^{2,10} Atypical presentations in older children include pneumonia, splenic abscess, liver abscess, meningitis, cholecystitis, chorea, palatal palsy, osteomyelitis, peritonitis, aphasia, and even psychosis.¹¹ The commonly encountered complications are hepatitis, intestinal perforation, hemorrhage, central nervous system manifestations and acute cerebellar ataxia.¹²⁻¹⁴

There are few studies evaluating the complications of typhoid fever in children in Bangladesh and those

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studies were carried out outside of our country. Therefore, this study aimed to evaluate the complications of typhoid fever in children in a tertiary care children's hospital in Dhaka, Bangladesh.

Methodology

This retrospective cross-sectional study was conducted at Dr. M R Khan Shishu Hospital & Institute of Child Health, Mirpur-2, Dhaka from July 2019 to June 2020 among children aged 6 months to 15 years who were diagnosed with typhoid fever. After obtaining ethical clearance and written consent from parents, children were enrolled. For each case, a detail history was taken and thorough general and systemic examination was done. Depending upon clinical feature and examination findings, relevant investigations were sent to find out complications. Blood culture sent at admission after exclusion viral cause and widal test at 7th day of fever. Fever considered significant when it is high grade continued in nature and rising like step ladder pattern. Age 6 months to 15 years of both sex, culture positive for salmonella typhi, widal test: TO > 1:160, TH > 1:320 were included in our study. Patients with co-infection like viral hepatitis, dengue fever, para typhoid and those who did not give consent were excluded. Total 100 cases of diagnosed typhoid fever who meet the inclusion and exclusion criteria, were evaluated further with other investigations to see systemic complications. CBC sent in all cases; SGPT, S bilirubin sent who had anorexia, jaundice, abdominal pain to diagnose hepatitis, CXR sent for cough or tachypnoea to diagnose pneumonia, Urine RME and culture sensitivity sent who had urinary complaints to diagnose UTI; S electrolytes and plain X-ray abdomen sent who had abdominal distension and absent bowel sound to diagnose paralytic ileus; CSF study done who had convulsion, altered consciousness for encephalopathy and to exclude meningitis; X-ray and USG of joint done who had pain and swelling to diagnose septic arthritis; USG of whole abdomen done who had abdominal pain radiating to back and murphys sign positive to diagnose cholecystitis; CXR, ECG and Color doppler echocardiography done who had dyspnea, relative tachycardia, gallop rhythm to diagnose myocarditis. Treatment started empirically and also considering blood culture report with injection

ceftriaxone over a dose 100 mg/kg/day up to afebrile for 5 days followed by oral cefixime for total 14 days. Counseling, supportive treatment and complications managed accordingly. Typhoid fever diagnosed in febrile child with salmonella typhi positive in blood culture or significant rise of widal test (When blood culture negative for salmonella typhi). Monthly income less than 10000, 10000- 50000, more than 50000 thousand are considered poor, middle and rich class respectively. Patient who did not take 14 days treatment before admission defined as substandard duration of treatment. When fever did not touch the baseline within 10 days defined as delay response. When counseling not done/ all information not delivered regarding typhoid fever defined as improper counseling. Delay admission defined when fever duration more than 1 week during admission. Chi square and t test was done where appropriate. A p-value of < 0.05 was considered as significant. Data was collected and analyzed maintaining standard procedure with SPSS.

Results

Among 100 Typhoid fever children, 37(37%) developed complications. (Fig 1)

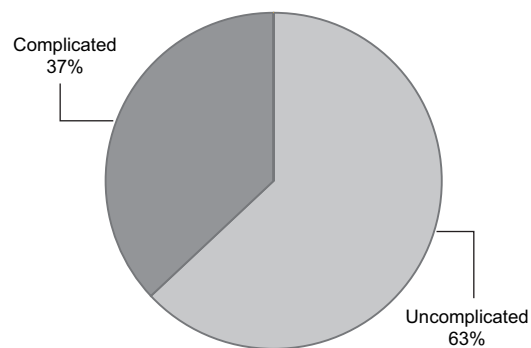


Fig.-1: Frequency of complications of typhoid fever (n =100)

Complications observed were hepatitis (24.3%), followed by UTI (16.2%), pneumonia(13.5%) and thrombocytopenia (13.5%). Others complications were paralytic ileus, encephalopathy, septic arthritis, pneumonia with paralytic ileus, cholecystitis etc. (listed in Table I)

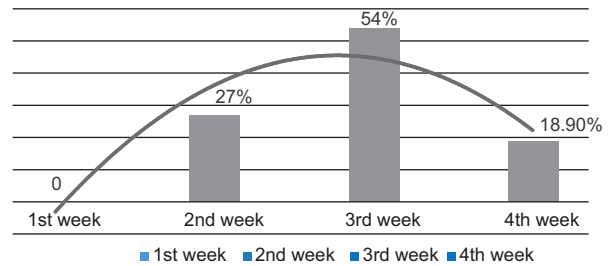
Table-I

<i>Distribution of complications among study population (n=37)</i>		
Complications	Number (n=37)	Percentage
Hepatitis	9	24.3%
UTI	6	16.2%
Pneumonia	5	13.5%
Thrombocytopenia	5	13.5%
Paralytic ileus	2	5.4%
Encephalopathy	2	5.4%
Septic arthritis	2	5.4%
Pneumonia with paralytic ileus	2	2.7%
Cholecystitis	1	2.7%
Myocarditis	1	2.7%
Total	37	100%

Complications mostly observed during third week (54.05%) followed by 2nd week. No complication was found during first week of illness. (Figure 2)

The mean WBC count of the patients with complications (12672.76 ± 6289.633 SD) was higher than patients without complications (8632.26 ± 3091.913 SD). This was statistically significant,

The mean platelet count of the patients without complication (2.3971 ± 1.18248 SD) was higher than

**Fig.-2:** Timing of complications of typhoid fever (n=37)

patients with complication ($2.0008 \pm .73989$ SD) and it was statistically significant (Table II). Thrombocytopenia mostly found in complicated typhoid fever, few uncomplicated cases had thrombocytopenia

The mean age of the patients without complications (5.0639 ± 3.07626 SD) was higher than patients with complications (4.3379 ± 3.07081 SD), which reveals significant difference.

The greater portion of patients (67.56%) with complications were male (Table III).

Regarding risk factor for development of complication, Chi square test shows statistically significant difference was found in poor compliance due to oral route and delay in initiation of treatment due to delay admission, in 60% and 55% respectively. (Table IV)

Clinical outcome of complicated typhoid fever was excellent with 100% complete recovery with conservative management (Table V)

Table-II

<i>Comparison of hematological findings of the patients with and without complications of typhoid fever (n=100)</i>			
Attributes	Without Complications (n=63)	With Complications(n=37)	P- value
WBC count/mm ³	8632.76 ± 3091.633	12672.76 ± 6289.913	0.000*
Haemoglobin (gm/dL)	11.426 ± 1.1633	$11.177 \pm .7279$	0.088
PlateletCount/mm ³	2.3971 ± 1.18248	$2.0008 \pm .73989$	0.02*

*Statistically significant

Table III

<i>Association of demographic features with complications of typhoid fever (n=100)</i>			
	Without Complications(n=63)	With Complications(n=37)	P value
Age	5.0639 ± 3.07626	4.3379 ± 3.07081	0.036*
Sex			
Female	30 (47.6)	12 (32.43)	0.01*
Male	33 (52.3)	25 (67.56)	
Socio-economic Class	0.002*		
Poor	33 (52.38)	22 (59.45)	
Middle	25 (39.68)	12 (32.43)	
Rich	5 (7.93)	3 (8.10)	

*Statistically significant

Table-IV

<i>Association between risk factors and development of complications of Typhoid fever (n=100)</i>			
Factors	Without complications n= 63 (%)	With complications n= 37 (%)	P value
Not taken standard duration of treatment before admission-Yes	5(5.55)	6(60)	0.088
-No	85(94.44)	4(40)	
Taken Substandard dose schedule			0.08
-Yes	5(6.57)	8(33.33)	
- No	71(93.42)	16(66.66)	
Delay response suspected drug resistance			0.075
-Yes	5 (5.26)	3(60)	
-No	90(94.73)	2(40)	
Poor compliance due to oral route			0.033*
-Yes	21 (23.33)	6 (60)	
-No	69(76.66)	4(40)	
Improper counseling done before admission			0.066
-Yes	6(6.74)	6 (54.54)	
-No	83(93.25)	5(45.45)	
Delay in the initiation of treatment due to delay admission			0.02*
-Yes	31(38.75)	11(55)	
- No	49(61.25)	9(45)	

*Statistically significant

Table-V

<i>Clinical outcome of complicated Typhoid fever (n=37)</i>			
	Complete recovery with conservative management	Surgery	Mortality
Study population with complicated typhoid fever	37(100%)	0(0%)	0(0%)

Discussion

In the present study, about one-third of the total patients had complications (37%). Another study found 27% of patients of typhoid fever with complications.¹⁵ So similar observation was found regarding prevalence of complicated typhoid fever in children; having one-third of cases with complications and some patients had multiple complications at a time.¹⁰

Current study revealed that, among 37 complicated children, the majority had hepatitis and other frequent

complications like pneumonia, UTI, thrombocytopenia, paralytic ileus, encephalopathy, septic arthritis, cholecystitis, myocarditis. A documented complication of anicteric hepatitis, bone marrow suppression, paralytic ileus, myocarditis, psychosis, cholecystitis, osteomyelitis, peritonitis, pneumonia, hemolysis and SIADH found in another study.¹² Some other studies showed that maximum cases have abdominal complications (12.4%). In this study, majority of complications appeared in the third week of this study.

A similar study showed that most complications occurred in the second to fourth weeks.¹⁶

Leukocytosis was observed in our study among patients with complications. A similar study showed that typhoid fever is associated with high WBC count and it significantly increased in 70% of cases.¹⁶ Low platelet count was also found in patients with complications in this study which is similar with other study findings. Thrombocytopenia is considered as a sign of severe disease in typhoid fever with a higher risk for the development of complications.¹⁷ This study revealed the majority of patients were within the range of 6 to 9 years of age. A meta-analysis also showed that the highest prevalence is seen in the age group of 5-9 years.¹⁸

In this study, male were predominant which is consistent with another study findings.¹³ The greater portion of patients (59.45%) with complications belonged to poor socio-economic class. A study reported similar to this study that, features like severe abdominal pain, diarrhea, hepatosplenomegaly, leucopenia, thrombocytopenia, severe anemia, poor socioeconomic status, malnutrition were more commonly seen in patients with complicated enteric fever.¹⁹ Poor compliance due to oral route and delay in initiation of treatment due to delay admission significantly associated with complication, other study found the increased incidence of complications and mortality in MDR typhoid fever is high due to delay in instituting effective antibiotic therapy.⁸ In this study 100% cases recovered with conservative management. A study showed that, with appropriate treatment initial clinical response occurs in 96-98% cases and chance of being carrier 2-4%.⁶

Conclusion

Typhoid fever presents with complications in 37% of cases. Hepatitis, UTI, pneumonia, thrombocytopenia and paralytic ileus are the most frequent complications. Majority of complications were found in 3rd week. Male child, younger age, poor socioeconomic background, poor compliance due to oral route, delay treatment, leukocytosis and thrombocytopenia are significantly associated with complications.

Recommendations

Further, nationwide studies are needed with a larger sample size involving different geographical areas, to combat these issues.

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