ENTERIC FEVER IN SULAIMANI PEDIATRIC TEACHING HOSPITAL: RISK FACTORS, PRESENTATION, AND DRUG SUSCEPTIBILITY

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ABSTRACT

Background

Enteric fever is a severe systemic illness characterized by fever and abdominal pain that is caused by dissemination of typhoid *Salmonella* serovar, Typhi and Paratyphi. These organisms have no known hosts other than humans. Most commonly, foodborne or waterborne transmission occurs as a result of faecal contamination by ill or asymptomatic chronic carriers.

Objectives

The aim of this study was to determine the risk factors, clinical features in paediatric enteric fever infections along with the antimicrobial susceptibility pattern of the causative agents.

Patients and methods

This is a prospective-hospital based study, done in Sulaimani Paediatric Teaching Hospital. During the study period 250 cases suspected to have typhoid fever were admitted over a period of 3 month from 1st May-1st Augusts 2008; 95 cases with positive blood culture for typhoid were studied for clinical presentation, risk factors and drug susceptibility of isolates in comparison with a control group. *Salmonella* strains were identified based on their biochemical properties and antimicrobial susceptibility was determined with Kirby-Bauer disk diffusion method.

Results

Out of 250 clinically suspected cases of enteric fever, only 95 (38%) were culture positive for Salmonella. The antimicrobial susceptibility of isolate showed that more than 97% of the isolates were resistant to chloramphenicol, ampicillin and co-trimoxazole. Significant risk factors were eating food outside home (P=0.001, OR, 10.788; 95%, CI: 4.292 -27.112), low socioeconomic status (P=0.017, OR 0.437, 95%, CI: 0.229 -0.832), and household contact (P=0.001, OR=15.864, 95% CI: 6.648 -37.854).

Conclusion

Enteric fever remains one of the endemic febrile illnesses among paediatric age in our community and mainly caused by multi drug resistant *Salmonella* sereovar Typhi. The most common symptoms indicating infection were fever, headache, vomiting and abdominal pain. Risk factors were eating food outside home, low socioeconomic status and household contact with index cases.

Keywords: *Enteric Fever, Salmonella, Risk factor, paediatric infection, Sulaimani*

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INTRODUCTION

Enteric fever is a severe systemic illness characterized by fever and abdominal pain that is caused by dissemination of *Salmonella* Typhi and *S.* Paratyphi [1]. Enteric fever continues to be a global health problem, with an estimated 21.6 million cases caused by *S.* Typhi and 5.5 million cases caused by *S.* Paratyphi A, B, or C annually and an incidence ranging from 25 to 1000 cases per 100,000 population in endemic regions [2, 3]. An estimated 200,000 to 600,000 deaths occur annually, based on extrapolation from endemic regions [2]. In endemic regions, typhoid fever is more common in urban than rural areas and among young children and adolescents (aged 1 to 15years). Reported risk factors include contaminated water or ice, flooding, food and drinks purchased from street vendors, raw fruits and vegetables grown in fields fertilized with sewage, ill contacts in the household, lack of hand washing and toilets, and evidence of prior *Helicobacter pylori* infection, likely related to chronic reduced gastric acidity [1].

Typhoid fever is usually contracted by ingestion of food or water contaminated by faecal or urinary carriers excreting *S.* Typhi. The incubation period is usually 7 to 14 days. The disease classically begins with an intermittent fever pattern which becomes more sustained over the first few days of the disease. Most patients report fever or rigors and headache; smaller proportion report nausea, vomiting, abdominal cramps and cough. Patients can present paradoxically with either diarrhoea [more common in young children and HIV patients] or constipation [4]. On examination fever is usually present, and careful recording may demonstrate the stepwise progression characteristics of this syndrome. The abdomen may be tender, and approximately half of patients will have a palpable liver and/or spleen, paratyphoid fever shares many of these clinical features [5]. Complications occur in 10–15% of patients and are particularly probable in patients who have been ill for more than 2 weeks [4]. The case fatality rate with antimicrobial chemotherapy is less than 5% but is higher in children under the age of 1 year and older adults [6]. In young children, seizures may occur as a result of fever, hypoglycaemia or electrolyte imbalance. The most important complications are intestinal perforation or haemorrhage. Intestinal perforation results in release of colonic bacteria into the peritoneum with consequent peritonitis [5].

Multidrug-resistant (MDR) typhoid fever is defined as typhoid fever caused by *Salmonella enteric* serovar Typhi strains (*S.* Typhi), which are resistant to the first-line recommended drugs for treatment such as chloramphenicol, ampicillin and trimethoprim-sulfamethoxazole. Since the mid-1980s, MDR typhoid fever has caused outbreaks in several countries in the developing world, resulting in increased morbidity and mortality, especially in affected children below five years of age and those who are malnourished [7]. The optimal diagnostic approach for enteric fever in both children and adults is to culture blood, bone marrow, urine and intestinal secretions, using this approach, the diagnosis can be established in more than 90% of patients [8].

The aim of this study was to determine the clinical presentation, risk factors, and drug susceptibility in paediatric enteric fever infections.

PATIENTS AND METHODS

This is a prospective-hospital based case control study done in Sulaimani Pediatrics Teaching Hospital during the period from May 1st 2008 to August 1st 2008. The hospital serves Sulaimani city and the surrounding district hospitals with an estimated population of around 1.800.000 inhabitants. During the study period 250 cases suspected to have typhoid fever were admitted; 95 cases were blood culture positive for typhoid; they were studied for clinical presentation, physical examination, risk factors, and drug susceptibility of isolates in comparison to 95 control cases non-typhoid febrile illness.

Information were collected from both groups included: age, gender, residence, source of water supply, eating food outside home including ice cream and food from street vendors, having household contact with the disease, socioeconomic state, and associated features with fever including headache, abdominal pain, diarrhoea or constipation and dry cough. Physical examination was performed for temperature, splenomegaly, hepatomegaly, and lymphadenopathy.

Laboratory diagnosis of enteric fever was confirmed using blood culture [9]. Five mL of venous blood was collected and inoculated into blood culture medium (Pad Tan Teb Ltd.) and incubated at 37°C and monitored daily for growth

[10, 11]. Subcultures were performed on blood agar, MacConkey's agar (HiMedia Laboratories) after 24, 48, and 72 hours and on the seventh day of incubation, subcultures were incubated at 37°C for 8-24 hours and *Salmonella* growth was confirmed as from lactose non fermenting colonies and Kligler's Iron Agar (HiMedia Laboratories). *Salmonella* Typhi or *S.* Paratyphi identification was based on their biochemical properties on Kligler's Iron Agar [9]. Antimicrobial susceptibility of *Salmonella* isolates were determined with Kirby-Bauer disk diffusion method [12] using the following antimicrobial discs (Bioanalyse ®, Turkey); chloramphenicol 30 mcg/disc, Ampicillin 10 mcg/disc, co-trimoxazole 25 mcg/disc (trimethoprim/ sulphamethoxazole, 1.25/23.75 mcg/disc), ceftriaxone 30 mcg/disc, ciprofloxacin 5 mcg/disc and azithromycin 15 mcg/disc. The results of antimicrobial susceptibility were recorded according to the standard values provided by Clinical and Laboratory Standards Institute [13].

Data analyzed using SPSS software version 15 [14], Chi square test was used to assess significant difference between variable of contingency table and Odd's ratio for finding relative risk. *P* value <0.05 was regarded as significant.

RESULTS

Cultivation and antimicrobial susceptibility

Figure 1 shows the result of blood culture for *Salmonella* and percentage of isolation of *S.* Typhi, *S.* Paratyphi and negative cultures. Figure 2 shows that more than 97% of the isolates were resistant to Chloramphenicol, Ampicillin, Co-Trimoxazole while most of isolates were susceptible to other agents such as Ceftriaxone, Ciprofloxacin and Azithromycin. Blood culture from the control group (95 patients) used for determination of risk factors all failed to recover a positive culture for *Salmonella.*

Clinical features

To determine the clinical features of enteric fever in paediatric age group, symptoms and signs of enteric fever group were compared with that of the control group. Table 1 shows the comparison between both groups and the *P* value for each parameter.

Risk factors of enteric fever

Table 2 shows comparison of demographic data from both enteric fever group and control group and the statistically significant factors were food intake outside home, low socioeconomic status and household contact with ill patients with typhoid fever.

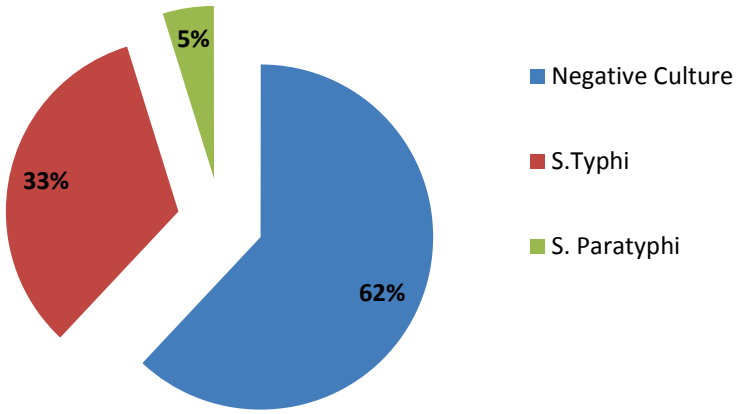

Figure 1. The result of blood culture and confirmation for Salmonella among 250 cases suspected for enteric fever.

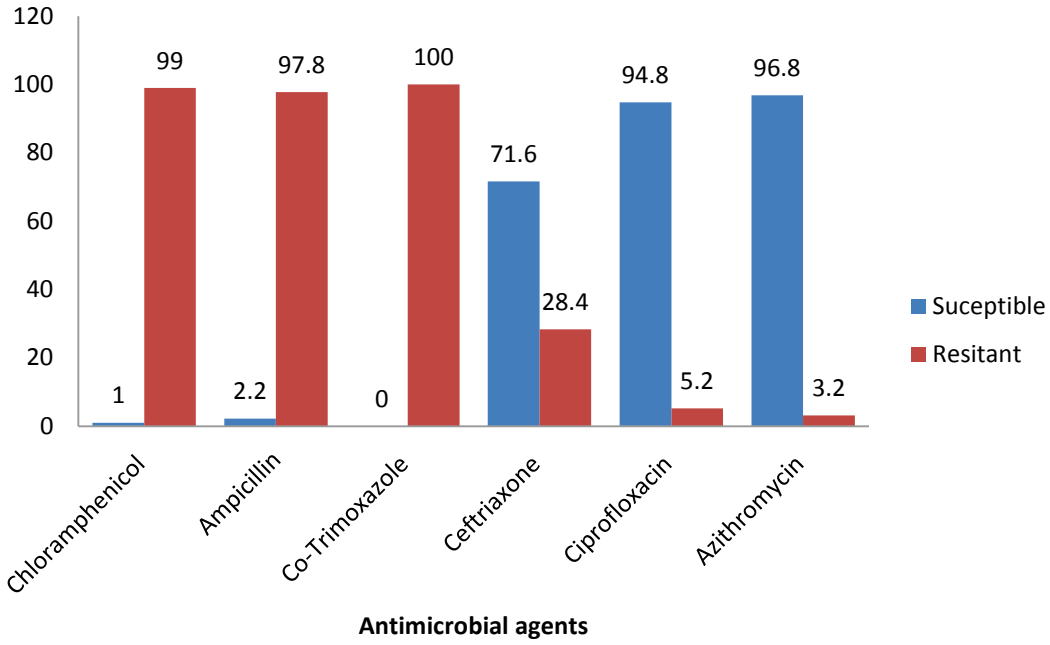

Figure 2. Antimicrobial susceptibility profile using Kirby- Bauer method for 95 Salmonella isolates using six antimicrobial agents. Data represent percentage of susceptible and resistance response respectively.

Table 1. Symptom and signs among both enteric fever group and control group.

Symptoms and signs	Enteric fever group		Control group		*P* value
	Present No (%)	Absent No (%)	Present No (%)	Absent No (%)	
Fever	95 (100)	0	95 (100)	0	**1.0**
Headache	56 (59.5)	39 (39.5)	38 (40)	57 (60)	**0.26**
Diarrhea	41 (43)	54 (57)	63 (66)	32 (34)	**0.18**
Vomiting	55(58)	40 (42)	30 (31)	65 (69)	**0.15**
Dry cough	42 (44)	53 (66)	23 (24)	72 (76)	**0.09**
Abdominal pain	48 (50.5)	47 (49.5)	25 (26)	70 (74)	**0.08**
Constipation	20 (21)	75 (79)	13 (13.5)	82 (86.5)	**0.46**
Splenomegaly	38(40)	57 (60)	8 (8.5)	87 (91.5)	**0.000***
Hepatomegaly	32 (34)	63 (66)	5 (5)	90 (95)	**0.011***

*** *P* value < 0.5**

Note: Some patients had more than one sign and symptom.

Table 2. Comparison of demographic data and risk factors of enteric fever group (95 cases) and control group (95 cases).

Characteristic	Enteric fever group No. (%)	Control group No. (%)	*P* value	Odd ratio	95% Confidence interval	
					Lower	Upper
Age			**0.355**	0.716	0.390	1.314
<5year	28(29.5)	35(36.8)				
>5year	67(70.5)	60 (63.2)				
Gender			**0.310**	0.713	0.403	1.263
Male	42 (44)	50 (52.5)				
Female	53 (56)	45 (47.5)				
Residence			**0.455**	0.764	0.425	1.376
Urban	56 (59)	62 (65)				
Rural	39(41)	33 (35)				
Water supply			**0.298**	0.701	0.390	1.259
Pipe	54 (56)	62 (65)				
No pipe	41 (44)	33 (35)				
Food			**0.001***	17.938	7.148	45.017
Outside home	89 (93.5)	43 (45)				
Inside home	6 (6.5)	52 (55)				
Socioeconomic status			**0.017***	0.437	0.229	0.832
Low	59 (62)	75 (79)				
Moderate to high	36 (38)	20 (21)				
House hold contact			**0.001***	15.864	6.648	37.854
Contact	53 (55)	7 (7)				
No contact	42 (45)	88 (93)				

*** *P* value < 0.5**

DISCUSSION

The optimal diagnostic approach for enteric fever in both children and adults is to culture blood, bone marrow, urine and intestinal secretions. Using this approach, the diagnosis can be established in more than 90% of patients [8]. The true prevalence of enteric fever was beyond the aims of this study but the study showed that 38% of participants with clinically suspected typhoid fever had a positive blood culture; of the *Salmonella* isolates 83 (87%) were *S.* Typhi while the other 12 (13%) were *S.* Paratyphi. These figures were similar to studies in endemic area of India and Indonesia [15, 16].

From the susceptibility pattern of *Salmonella* isolates it is shown that resistance to chloramphenicol, ampicillin and trimethoprim-sulfamethoxazole were exceeding 97% of isolates and indicating the multi-drug resistance pattern of these isolates to recommended first line antimicrobial treatment [17, 18]. On other hand our results showed the development of resistance against the currently recommended agents such as ceftriaxone and ciprofloxacin and this emphasize the role of rational antimicrobial prescription and considering antimicrobial susceptibility prior to prescription [1].

Concerning the symptoms and signs of enteric fever; the predominance of headache, abdominal pain, splenomegaly and hepatomegaly were similar to the findings of literature elsewhere in Iraq and worldwide [19, 20]; while it was different from Ras Al-Kaimah study where the incidence of splenomegaly and hepatomegaly (17.6% and 19.6% respectively) were less than our findings (40% and 34% respectively) [21].

The following demographic characters were selected to compare for risk factors between the two groups:

Age was not a statistically significant risk factor. This is similar to a study done in Karachi, Pakistan [22], while in another study in Jakarta, Indonesia, typhoid fever was associated risk in young age children (OR,0.96;95%CI,0.94 -0.98) [15].

Gender was not regarded as a statistically significant risk factor similar to the study done in in Jakarta Indonesia [15]. Residency also was not counting as a major risk factor , which is similar to both Pakistani and Indonesian studies [15, 22], while in the study from Vietnam, typhoid fever was more in rural agricultural areas as the majority of cases (75%) and highest rates were found in the Southern Mekong river delta, in comparison with the big cities [23].

Water supply was not regarded as a risk factor statistically and this was similar to the study done in Karachi, Pakistan on risk factors for typhoid fever in an endemic setting [22]. Eating food outside home was significant statistically and this was similar to Pakistan study, in which typhoid fever was associated with eating ice-cream and eating food from the roadside cabins during summer months [22].

Low socioeconomic status of the patient was a significant risk factor; this is similar to a study done in India on comparisons of predictors for typhoid and paratyphoid fever in Kolkata, India, poverty carries high risk for enteric fever [16].

Household contact was significant risk factors for enteric fever this may be due sharing food plate or using same contaminated food or drink and this was found in studies done elsewhere [15, 22].

MDR enteric fever is emerging, and empiric treatment should be according to local antibiotics sensitivity. The most common symptoms indicating infection were fever, headache, vomiting and abdominal pain. Risk factors were eating food outside home, low socioeconomic status and household contact with index case.

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