CHARACTERISTIC FEATURES OF CULTURE POSITIVE ENTERIC FEVER IN PEDIATRIC TEACHING HOSPITAL IN SULAIMANI GOVERNORATE

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ABSTRACT

Background

Typhoid fever is still common disease in our country, and at the present time we are facing resistant cases to usual antibiotics.

Objectives

This study has been carried out to identify the clinical and laboratory characteristics of these microorganisms.

Materials and Methods

This is a prospective study done from October 2008 to October 2009, in Sulaimani Pediatric Teaching hospital. Blood cultures were taken from patients suspected of having Typhoid fever ,only patients with positive cultures were included in this study. Data regarding age, sex, residency, clinical presentation, duration of fever at presentation, response to treatment and antibiotic susceptibility were all analyzed by SPSS version 16.0.

Results

Ninety six patients whom with culture proved cases of Enteric fever, 55 males and 41 females. The age of the patients were from 1 month -14 years with an average of 6.8 years. The duration of fever before attendance to medical care was (2-19) days with a mean of 7 days. Mean days needed for subsidence of fever was 5 days ranging from 2-10 days. Mean duration of admission was about 8.5 days, while mean duration of treatment was 14 days. Headache was the most common symptom (67.7%) followed by abdominal pain in 56.6%, diarrhea in 31.2%, While the symptoms least encountered were confusion 5.2% and constipation 1%. Splenomeagly was the commonest sign (56.2%) followed by hepatomegaly (35.4%) and neck stiffness was positive in (3.1%) of the patients whom had normal CSF examination. The mean WBC count was 5.378 10^9/l, with 61% of the patients having neutrophilia and 20.7% having lymphocytosis and 18.3% having equal distribution. Most of the isolates were sensitive to amikacin 87%, followed by doxycycline 85.7%, ciprofloxacin 81.5%, azithromycin 60%. Cefotaxime and ceftriaxone had sensitivities of about 52-54%, while there was 75% resistance to chloramphenicol and nearly 99% resistance to ampicillin. All cases were culture positive; 99% for Salmonella typhi and only 1% grew Salmonella para typhi A and B. The incidence of complications was about 10.4%,GIT bleeding being the most common 4.2% followed by renal failure and hepatitis 2% and ataxia 1.1%. Mortality rate was (1.1%).

Conclusion

Typhoid fever has different presentations according to the locality and also may change its presentation in form of outbreaks in a specific locality. The disease was multidrug resistant, this may be due to previous misuse of antibiotics.

Keywords: *Typhoid fever, Enteric fever, Culture positive, Salmonella.*

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INTRODUCTION

Salmonellosis constitutes a major public health burden and represents a significant cost to society in many countries. It is estimated that, in the United States alone, an estimated 1.4 million non-typhoidal Salmonella infections results in 168,000 physician visits, 15,000 hospitalizations, and 580 deaths annually. The total cost associated with Salmonella infections is estimated at $3 billion annually in the United States. While there is little information on its epidemiology and the burden of Salmonella gastroenteritis from developing countries, Salmonella infections are recognized as major causes of childhood diarrheal illness[1] .

Salmonella typhi infection remains a serious problem in developing countries. It has been estimated that approximately 12.5 million cases of typhoid fever occur annually in the developing world (excluding China) with 7.7 million cases in Asia alone. The disease is predominantly a disease of school age children and young adults and is reported to be milder in infants and young children [2, 3].

The disease occurs by the ingestion of the organism, and a variety of sources of fecal contamination have been reported, including street foods and contamination of water reservoirs. In addition to the virulence of the infecting organisms, host factors and immunity may also play an important role in predisposition to infection [1].

Salmonella typhi is that not killed by gastric acid enters the ileum, invades and multiplys in the reticulo-endothelial system with subsequent bacteraemia. The initial bacteraemic phase, lasting about one week, is characterized by stepwise in fever, relative bradycardia , constipation or diarrhea, splenomegaly , increasing confusion , dry cough , and less commonly a pink macular (rose spot) truncal rash. Recovery commences in the third week but intestinal perforation or hemorrhage may occur.

Diagnosis is confirmed by blood and stool cultures or by bone marrow culture or other recent procedures [4] .

There are general principles of management of typhoid. Adequate rest, hydration, and close observation are important to correct fluid-electrolyte imbalance. Antipyretic therapy (acetaminophen 120-750 mg every 4-6 hr PO) should be provided as required. A soft, easily digestible diet should be continued unless the patient has abdominal distention or ileus. Antibiotic therapy is critical to minimize complications. It has been suggested that empirical therapy with either chloramphenicol or amoxicillin is associated with relapse rates of 5-15% and 4-8%, respectively, whereas the quinolones and 3rd generation cephalosporins are associated with higher cure rates. The antibiotic treatment of typhoid fever in children is also influenced by the prevalence of antimicrobial resistance. Over the past 2 decades, emergence of multidrug-resistant strains of S. Typhi (i.e., isolates fully resistant to amoxicillin, trimethoprim-sulfaniethoxazole, and chloramphenicol) has necessitated treatment with fluoroquinolone (which are the antimicrobial drug of choice for treatment of salmonellosis in adults), or cephalosporins [1].

In this study our plan was to identify the epidemiological criteria of culture positive and resistant strains of *S. typhi* which has been emerged in our community.

The aim of the study

1. To find the common clinical presentation of culture positive typhoid fever in Sulaimani Governorate.
2. To find the incidence of complications.
3. To analyze the response to treatment.

MATERIALS AND METHODS

This is a prospective descriptive study of 1 year duration done in pediatric teaching hospital in Sulaimania.from October 2008 to October 2009. The two researchers had collected data from a number of patients whom had been admitted during this period presenting mainly with fever. Blood cultures were taken from patients clinically suspected to have typhoid Fever. Only patients with a positive blood culture for Salmonella *typhi* or paratyphi were included in this study. CBC, WBC differential and platelet count and ESR were also included.

Data regarding the age, sex, residency, signs and symptoms on presentation, the water supply, and the presence of domestic animals were noted. Patients were examined thoroughly recording palpable spleen or liver or both, any rash, limitation of joint movement or abnormal gait.

The patients were treated first with empirical antibiotics according to the clinician's preference, which may have been changed if needed according to the results of culture and sensitivity. The patients were followed up for their improvement in general condition, the

duration of treatment needed for the disappearance of fever, any complications , and also the total duration of hospitalization and the total duration of treatment including the duration of treatment taken as outpatient were recorded.

The drugs used for culture and sensitivity were; ampicillin, chloramphenicol, ceftriaxone, cefotaxime, gentamycin, amikacin, azithromycin, ciprofloxacin, tetracycline and doxycycline. Any complication during the course of hospitalization was noted. Relapses that had occurred also had been noted although some were difficult to prove by blood culture and may have been missed.

Ethical approval

Verbal concent had been taken from patient and/ or care givers before enrollment in the study.

Data entry and analysis

Prior to data entry and analysis, the questions of study were coded. The data was entered into a Microsoft Excel Spreadsheet, after data cleaning; it was transported into SPSS (Statistical Package for the Social Sciences-verstion16.0). Descriptive statistics (numbers, percentage, mean and standard deviation) were calculated for all variables, as well as analytical statistics done to find the relations between variables.

RESULTS

Ninty six patients with culture proved typhoid fever, 55 males and 41 females, about 73 % of them were from urban and 27% from rural area, as shown in the table 1.

In regard to water supply, 39% of the patients had tap water supply followed by 30% had water, 20 % used both, while Tanker and spring supply were 8.5% and 2.1% respectfully. The age of the patients enrolled in this study were from 1 month -14 years with an average of 6.8 years.

The duration of fever before attendance to medical care was (2-19) days with a mean of about 7 days. Mean days needed for subsidence of fever was about 5 days ranging from 2-10 days. Mean duration of admission was about 8.5 days, while mean duration of treatment was about 14 day, table 2.

In Table 3 analyses the signs and symptoms of the patient who were enrolled in the study. All of the patients should have had fever to be enrolled in the study , aside from that symptom, headache was the most common symptom (67.7%) followed by abdominal pain in(56.2%) then diarrhea in 31%. While the symptoms least encountered were confusion 5% and constipation 1%. Regarding the signs; splenomeagly was the commonest (56.2) followed by hepatomegaly (35.4) and neck stiffness was positive in 3% of the patients whom had normal CSF examinations.

Table. 1 Socio-demographic distribution of the patients.

Socio-demographics	Frequency	Percent
Sex		
Male	55	57.3
Female	42	42.7
Residency		
Urban	70	72.9
Rural	26	27.1
Source of water		
Tap	37	39.4
Well	28	29.8
Both	19	20.2
Tanker	8	8.5
Spring	2	2.1

Table 2. Descriptive features of the patients.

Variables	Mean
Age (Years)	6.8
Duration of fever (Days)	6.9
Duration of fever subsidence	5.16
Duration of admission (Days)	8.53
Duration of treatment(Days)	14.35

Table 3. Frequency of signs and symptoms.

Signs and symptoms	Frequency	Percent
Headache		
Yes	65	67.7
No	31	32.3
Abdominal pain		
Yes	54	56.2
No	42	43.8
Splenomeagly		
Yes	54	56.2
No	42	43.8
Hepatomegaly		
Yes	34	35.4
No	62	64.6
Diarrhea		
Yes	30	31.2
No	66	68.8
Vomiting		
Yes	28	29.2
No	68	70.8
Joint pain		
Yes	16	16.7
No	80	83.3
Confusion		
Yes	5	5.2
No	91	94.8
Neck stiffness		
Yes	3	3.1
no	93	96.9
Skin rash		
Yes	2	2.1
No	94	97.9
Constipation		
Yes	1	1
No	95	99

The mean WBC count was about 5378, with 50% of the patients having neutrophilia, 17% having lymphocytosis and 15% having equal distribution. Most of the patients (87%) had a normal platelet count, about 12% had thrombocytopenia and only 1 case had thrombocytosis. All our cases were culture positive; 99% for *Salmonella typhi* and only 1% grew *Salmonella paratyphi*, Table 4 and 5.

Table 6 shows that most of the isolates were sensitive to Amikacin 86.7%, followed by Doxycycline 85.7%, Ciprofloxacin 81.5%, Azithromycin 60%, cefotaxime and ceftriaxone had sensitivities of about 52-54%, While there were 75% resistance to chloramphenicol and nearly 99% resistance to Ampicillin, it also shows that the antibiotics have not been tested regularly for all the cases due to the intermittent unavailability of the antibiotic discs in the hospital.

The incidence of complications was about 10.4%, GIT bleeding being the most common 4.2% followed by renal failure and hepatitis. Ataxia being the least common1.1%. Mortality rate was (1.1%), table 7.

Table 4. Investigation done for the patients.

Variables	Mean	Minimum	Maximum
WBC	5378.3	1400	18500
PCV	32.3	18.3	49.0
ESR	37.17	8	72

Table 5. Differential count, platelet count and culture results.

Investigations	Frequency	Percent	Missed Data
Differential count			
Lymphocytosis	17	20.7	14 cases
Neutrophilia	50	61	
Equal	15	18.3	
Platelet count			
Normal	74	87	10 cases
Decrease	10	11.8	
Increase	1	1.2	
Culture			
Salmonela. Typhi	95	99	Non
Salmonela para typhi	1	1	

Table 6. Sensitivity of organisms as shown by culture.

Antibiotic sensitivity	Frequency	Percent	Not tested for the antibiotic
Amikacin			
Sensitive	78	86.7	6
Resistance	12	13.3	
Doxycyclin			
Sensitive	72	85.7	10
Resistance	12	14.3	
Ciprofloxacin			
Sensitive	66	81.5	15
Resistance	15	18.5	
Azithromycin			
Sensitive	53	60.2	8
Resistance	35	39.8	
Cefotaxim			
Sensitive	47	54.7	10
Resistance	39	45.3	
Ceftriaxon			
Sensitive	44	52,4	12
Resistance	40	47.6	
Tetracyclin			
Sensitive	24	51.1	49
Resistance	23	48.9	
Gentamycine			
Sensitive	33	39.8	13
Resistance	50	60.2	
Chloramphenicol			
Sensitive	14	24.6	39
Resistance	43	75.4	
Ampicillin			
Sensitive	1	1.1	9
Resistance	86	98.9	

Table 7. Incidence of Complications.

Complications	Frequency	Percent
Non	86	89.6
GIT bleeding	4	4.2
Renal failure and hepatitis	2	2
Ataxia	2	2
Death	1	1.1

DISCUSSION

Enteric fever is one of common infectious problem in our country, and the epidemiological characteristics are quite different from other areas and this could be due to many reasons like deficiency of proper materials for diagnosis, deficiency of medications, and other reasons like poor medical knowledge in of public.

The first table shows that the rate of infections are more among males than females (57.3% males and 42.7% females), this result in agreement with other studies done in Diwaniyah city (43 males , 22 females) [5], Najaf city (65.5% males and 34.5% females) [6] and a study done in Malaysia [7], but other studies show a different results like a study done in Al-Kadhimiya hospital for children (female 63.7% and male 36.3%) [8], and in Al Musaib (female 60.4% and male 39.6%) [9]. The different results also seen in studies done for adult patients like studies done in Salah-Aldin and Thi-Qar [10, 11], a similar study done in Sulaimani (by Mohammad S, Rashid B) showing the same difference but it was insignificant [12]

The table also shows that the rate is more in urban than rural areas which may be considered as unexpected but a similar result seen in Najaf, Musaiband a previous study done in Sulaimani [6,9,12] and not the same with a study done in Baghdad, Salah-Aldin and Thi-Qar cities [8, 10, 11]. These differences in results can be explained due to differences in epidemiological characteristics of typhoid fever in these cities, and it is obvious that there are similarities between the result of Najaf and Sulaimani. Another possible explanation is the differences in the quality of medical services and access of these services.

In our study we found a high percent of patients who had typhoid fever depended on tap water, and well water and some on both. It may indicate that these sources may be contaminated with the sewage system, or that water supply in the city is limmited in its quality and supply, and this agree with the similar study of Sulaimani [12].

Table two showing that the common presentation of typhoid fever in patients included in this study are headache 67.7%, abdominal pain 56.2%, splenomegaly 56.2% and hepatomegaly 35.4%. While diarrhea 31.2% vomiting 29.2%% and joint pain 16.7% were less common. Neck stiffness 3.1%, confusion 5.2%, skin rash 2.1% and constipation 1% were quite uncommon presentation.

A study done among adult patients in Najaf, Babylon city and Diwaniyah show a similar result [6, 13, 15]. A study done in Africa also showed similar results [14]. This could mean that the presentation of typhoid fever in our country and in Middle East or developing countries in general share the same pattern of presentation, whether in adult or in children.

In Table three the patients age in our study was from 1 month-14 years old with a mean 6.8 years and duration of fever was 2-21 day with a mean of 6.9 days. The results have no great differences from Najaf (5-9 days fever) and Diwaniyah (3-14 days) [5, 6], while duration of subsidence of fever give a mean about 5 days and is in agreement with a study done in Diwaniyah for adults in which the majority of patients had no fever by day 5-7 [15].

Table 4 and 5 shows that most of the WBC count in our study was within normal range and, and that WBC differential count was mostly neutrophilia (61.0%) which is an unexpected result, but it may be related to minor undetected complications that they may had, or that this strain of bacteria mainly provoked such a response, the same result was found in Diwaniyah study [15]. The majority of the patients in our study have normal platelets count and 11.8% og the patients presented with thrombocytopenia, while only 1.2% presented with thrombocytosis.

Ninety nine percent of our patients are infected with Salmonela typhi, while 1% only infected with Salmonela para typhi (table 5). This study agrees with other studies in that most of patients included are infected with *Salmonela typhi* although the percentage is different,because other study gave a lower rate with *S. typhi* like Diwaniyah (45 patients with *S. typhi* and 20 patients with *S. paratyphi*), in Kadhimiyah (54.9%, 45.1% respectively), in Aben Alkateeb (19 patients with 8 patients respectively), in Hong Kong study (59% to 41% respectively) and in India, Salem study (51% to 49% respectively) [5, 8, 18, 19], while a simillar study in Sulaimani showing (62% negative culture, 33% *S. typhi* and 5% *S. paratyhpi* [12]. The only study that give a closer result to our study and to the previous study of Sulaimani is Salahdin study (91.4% with *Salmonela typhi* and 8.6% with *Salmonela paratyphi*) [10]. This could be due to a quite simillar environments and simillar laboratory facilities in Sulaymaniyah and Salahdin that lead to a simillar results.

Table six shows that most of the isolates were sensitive to amikacin 87%, followed by doxycyclin 85.7%, ciprofloxacillin 81.5%, azithromycine 60%, while cefotaxim and ceftriaxon had sensitivities of about 52-54%, s 75% resistance to chloramphenicol and nearly 99% resistance to ampicillin.

These results differ from results of Musaib study which shows that the isolates were sensetive to amoxiclav (74.4%) followed by ciprofloxacin (61.2%) then amoxicillin (51.4%) respectively , but shows similar result regarding the resistance to chloramphenicol (only 37.4% sensitive) [9]. This result is due to development of new strains in the last years that are resistant to antibiotics and this may result from abuse of antibiotics in our society.

The previous study in Sulaimani showing that azithromycin was the most sensitive drug , followed by ciprofloxacilin then ceftriaxon, and the resistance is greater among chloramphenicol , then ampicillin and cotrimoxazole [12]. This indicate that sensitivity and resistance may change from time to time in the same area or population.

Table seven shows that we have 12.5% complications among the patients included in this study (GIT bleeding being the most common 4.2% followed by renal failure and hepatitis and we had 1 death 1.1%) in comparison with other study like study done in Babylon they have an incidence of complications around 32.3% with majority of GIT complications (12.3%) followed by hepatitis (6.1%) then CNS complications (4.6%), then renal (3.1%) [13].

From this study we can conclude that most common symptoms were headache followed by abdominal pain, while the most common signs were splenomeagly followed by hepatomegaly. The strain that was isolated was a multiple drug resistant strain, highly resistant to ampicillin and chloramphenicol, and only moderately sensitive to cefotaxime and ceftriaxone, and were mostly sensitive to amikacin, doxycycline and ciprofloxacin, this resistance may have been related to previous misuse of antibiotics in our community.

We recommend routine examination of water supply and the sewage disposal in the community to prevent a such outbreaks in the future, also it is essential to put antibiotic use under specific guidelines to decrease the rate of resistance in microorganisms. In addition to that it is better to start empirical treatment for typhoid fever in highly suspected tired patient with drugs that are most likely to be effective in our locality such as amikacin or doxycycline.

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