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A study of Atypical Manifestations of Enteric Fever in Children

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ABSTRACT

Background: Enteric fever is an important pediatric problem in Nepal. Its characteristic features like high fever, pain abdomen and constipation with coated tongue,relative bradycardia, hepatosplenomegaly and leucopenia are not always present in children. Atypical manifestations are frequently present which may elude or delay diagnosis. Published data on these are scarce or nonexitstent in Nepali children.This study was undertaken to observe the atypical manifestations of enteric fever in children in Kathmandu and to study the antibiotic susceptibility profile of the isolates as well as the outcome of the treatment.

Methods: High fever cases without clinical diagnosis of enteric fever, with positive blood culture, attending the Pediatrc outpatient department of Kathmandu Medical College, Sinamangal were excluded for other co-morbid conditions and then included in the study.Atypical cinical and laboratory features, along with antibiotic susceptibility pattern were recorded and treatment followed up. The duration of the study was April 2006 to October 2007 (ie. 18 months)

Results: Of a total 212 patients with high fever without clinical diagnosis of enteric fever 58 cases (27.3%) had positive blood culture and included in the study .There were 36 males and 22 females and the M:F ratio was 1.6:1. Six to ten years old (36) formed the predominant group (58.6%). Atypical Fever (13 cases) or atypical Gastrointestinal (GI) features (12 cases) were observed in nearly half (25/58, 43.1%) the cases. Six cases of hepatomegaly without splenomegaly were recorded (10.3%). Ratio of clinical: laboratory atypical features was 3:0 in 0-5 year age group and 2:1 in 10-15 year age group. Most Salmonella isolates (93.3%) were sensitive to Ofloxacin, Ciprofloxacin (83.3%) and Amikacin (80%) ranked second and third most sensitive. Amoxycillin (80%) *in vitro* sensitivity did not match with clinical response. Ceftriaxone (70.3%) was less sensitive than expected from its parenteral use, whereas resurgence of Chloramphenicol (60%) sensitivity was observed.

Conclusions: Both, clinical and laboratory atypical manifestations were common in enteric fever in children. Enteric fever should be suspected in children with high fever in endemic areas although presenting features differ from the typical. Atypical features do not worsen prognosis in enteric fever. Drug sensitivity surveillance is a key step to delay resistant strain emergence.

Key words: Enteric fever, Atypical features, Susceptibility pattern.

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INTRODUCTION

Enteric Fever is an important health problem in Nepal. It is common in children and adolescents.[1] Its presenting manifestations may be frequently atypical and diagnosis elusive. Knowledge about its mimicry facilitates investigation and contributes to diagnostic accuracy. Appropriate treatment based on sensitivity study rapidly decreases infectivity, shortens convalescence and prevents complications. Characteristic features like high fever, pain abdomen and constipation with coated tongue, relative bradycardia, hepatosplenomegaly and leucopenia are not always present in children with enteric fever. So, clinicians benefit from familiarity with its atypical manifestations. Published data on atypical features in enteric fever in children are scarce or nonexistent in Nepal. So, this study was undertaken to observe atypical manifestations of enteric fever in children in Kathmandu and to study antibiotic susceptibility profile of the isolates as well as the outcome of the treatment.

METHODS

Patients with high fever attending pediatric outpatient department of Kathmandu Medical College, Sinamangal and without clinical diagnosis of enteric fever were included in the study. After history-taking and physical examination recordings, blood samples were taken for culture of Salmonella typhi along with other routine investigations. Cases with positive blood culture were further investigated to exclude other associated conditions. Only enteric fever cases without co-morbid condition were included in the study. Antibiotic sensitivity of positive cultures were obtained to select appropriate drug treatment. Cases follow up were done on the basis of response to antibiotics. The results were compiled, tabulated and analysed for interpretation and conclusion using appropriate statistical tools. The duration of study was from April, 2006 to October, 2007 (i.e. 18 months).

RESULTS

Total number of patients with high fever but without a clinical diagnosis of enteric fever registered within the study period was 212. Of those, having positive blood culture 58 cases (27.3%) met the inclusion criteria. All those patients recovered fully with treatment for enteric fever and had complete resolution of all abnormal features. The sex distribution was as per given in Table-1 and the age distribution in Table-2. There were 36 males and 22 females and the M:F ratio was 1.6:1. Maximum number of patients (34)were of 6-10 years age group (58.6%). The type of atypical features recorded were categorized in Table -3 and the various features observed were listed in Table-4. Atypical fever (13 cases), together with atypical Gastrointestinal (GI) features (12 cases) constituted nearly half (25/58, 43.1%) of the total. Among laboratory features (16 cases), hematological (8 cases) was the predominant (13.7%) atypical feature. Six cases of hepatomegaly without splenomegaly (6/58, 10.3%) were recorded in the series . A comparision between clinical and laboratory features (ratio 42:16 or 2.6:1) the ratio to be 3:1 at age group 0-5 years changing to 2:1 at 10-15 years age group (Figure 1).

Sensitivity of the isolated organism (Salmonella typhi) to various commonly used antibiotics is shown in Table -5. Almost all (93.3%) isolates were sensitive to Ofloxacin, whereas Ciprofloxacin (83.3%) and Amikacin (80%), ranked second and third most sensitive. Amoxycillin (80%) although equally sensitive in *in vitro* did not match in the clinical response. Three out of five patients initially started on Amoxycillin, despite *in vitro* sensitivity had to be changed to Ofloxacin due to poor response. Similarly, sensitivity to Ceftriaxone (70.3%) was much less than expected from its parenteral use, whereas, Chloramphenicol sensitive Salmonella typhi (60%) was showing resurgence although, one fifth (19.8%) continue to be fully resistant.

Table 1. Sex distribution (n=58)

Total number of patients included in the study (n)	Male		Female		M:F Ratio
	No.	%	No.	%	
58	36	62	22	38	1.6:1

Table 2. Age distribution (n=58)

Age group (yrs):	0-5	6-10	11-15	Total
Number of patients	3	34	21	58
%	5.2	58.6	36.2	100.00

Table 3. Type of atypical cases (n=58)

S.N.	Clinical:	no	%
1	Atypical Fever	13	22.4
2.	General symptoms	7	12.1
3.	Respiratory symptoms	3	5.2
4.	Gastro-intestinal symptoms	12	20.7
5.	Urinary symptoms	2	3.4
6.	Musculo-skeletal symptoms	5	8.6
	Total	42	72.4

S.N.	Laboratory:	no	%
1	Hematological	8	13.8
2.	Urinary	5	8.6
3.	Biochemical	3	5.2
	Total	16	27.6

Table 4. List of atypical cases (n=58)

S.N.	Clinical :	no	%
1.	Irregular fever	9	15.5
2.	Fever with rigors	2	3.4
3.	Fever with sweating	1	1.7
4.	Fever with evening rise	1	1.7
5.	Fever with rapid pulse	5	8.6
6.	Fever with epistaxis	1	1.7
7.	Fever with cough	3	5.2
8.	Fever with chest pain	2	3.4
9.	Fever with calf muscle pain	2	3.4
10.	Fever with knee joint pain	1	1.7
11.	Fever with diarrhea, vomiting	6	10.3
12.	Fever with urticaria	1	1.7
13.	Fever with urinary frequency	2	3.4
14.	Fever with hepatomegaly without splenomegaly	6	10.3
	Total	42	72.4

S.N.	Laboratory :	no	%
1.	Leucocytosis	4	6.9
2.	Polycythemia	1	1.7
3.	Thrombocytopenia	1	1.7
4.	Eosinophilia	2	3.5
5.	Raised blood urea	1	1.7
6.	Pyuria with negative urine culture	2	3.5
7.	Proteinuria	1	1.7
8.	Hematuria	2	3.5
9.	Raised serum bilirubin	1	1.7
10.	Raised SGPT	1	1.7
	Total	16	27.6

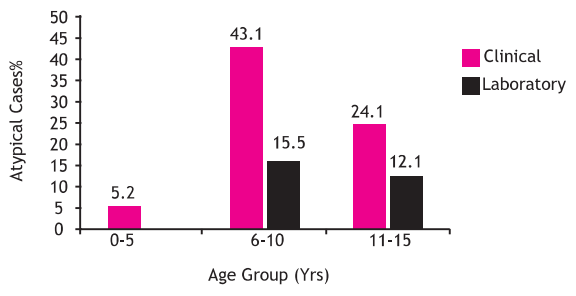

Figure 1. Atypical cases: Comparison of Clinical vs Laboratory features

Table 5. Sensitivity pattern* (n=58)

S.N.	Antibiotics	Sensitive %	Partially sensitive%	Resistant %
1.	Amikacin	80	-	-
2.	Amoxycillin	80	-	19.8
3.	Ceftazidime	3.3	-	-
4.	Ceftriaxone	70.3	3.3	
5.	Cephalexin	50	9.9	
6.	Cephotaxime	6.5	-	-
7.	Chloramphenicol	60	-	19.8
8.	Ciprofloxacin	83.3	9.9	-
9.	Cotrimoxazole	3.3	-	50
10.	Gentamicin	3.3	-	-
11.	Nalidixic acid	13.2	-	70
12.	Nitrofurantoin	6.6	-	-
13.	Norfloxacin	6.6	-	-
14.	Ofloxacin	93.3	3.3	-

* Figures given here are percentages of the total

DISCUSSION

In the present series 58 out of 212 high fever cases without clinical diagnosis of enteric fever were bacteriologically confirmed by blood culture. This diagnostic yield (27.3%) could be improved by simultaneous culture of bonemarrow aspirate and blood culture as was done in other studies. [2-6] Moreover, blood culture might be negative due to partial treatment received elsewhere, before coming to hospital. Widal agglutination test although included by some researchers is appropriate only one week after the onset of fever, whereas all our patients presented within the first week.[3-7] This early reporting trend which may be indicative of increasing parental concern, may have accounted for the apparent lack of complications. This situation however, is not representative of elsewhere in the country. Features due to complications when present, may dominate the presenting symptoms and signs and increase atypical manifestations.

Atypical features: Atypical fever, although can lead to misdiagnosis, atypical Gastrointestinal (GI) features may be taken as clues. Of laboratory features, hematological investigations being the commonly requested along with blood culture, may account for being the predominant laboratory atypical feature. All patients responded to treatment of enteric fever in spite of atypical manifestations. Similar conclusions were made in a study reported from Pondicherry, India. In another comparative study, no significant difference in clinical presentation, laboratory findings and outcome observed in those infected by susceptible or multidrug- resistant (MDR) strains of Salmonella typhi.[2,8] Atypical manifestations, when present, do not mean a worse prognosis in enteric

fever and patients with high fever in enteric fever endemic area should be suspected of this disease even though the presenting features differ from the typical.[2]

Drug susceptibility profile: Drug resistance (including MDR) although is a recognised problem in enteric fever treatment, good response was observed in the present series.[9] However, surveillance is the key to delaying such an occurrence. Ofloxacin was observed to have highest sensitivity rate (93.3%) and Amoxicillin (80%) maintained its *in vitro* efficacy. Resurgence of Chloramphenicol sensitivity (60%) was noteworthy as also reported by others.[11]

CONCLUSIONS

Enteric fever with atypical features comprised of more than a quarter (27.3%) of high fever cases without a clinical diagnosis of enteric fever. Nearly half (43.1%) of those had either atypicality of fever (13/58, 22.4%) or atypical Gastrointestinal (GI) features (12/58, 20.6%). Atypical Laboratory features which were fewer than clinical (ratio 1:2.6) were commonly hematological (8/16, 50%). Enteric fever with atypical features should be suspected in children having high fever in endemic areas even if the presenting features differ from the typical. Atypical features do not mean a worse prognosis in enteric fever. Surveillance is a key step to delay emergence of resistant strain.

REFERENCES

1. Shrestha YB. Disease pattern in Nepalese children. J Nep Med Assoc. 1984; 9(1): 35-41.
2. Dutta TK, Beeresha, Ghotekar LH. Atypical manifestations of typhoid fever. J Postgrad Med. 2001; 47(4): 248 – 51.
3. Arora RK, Gupta A, Joshi NM, Kataria VK, Lall P, Anand AC. Multidrug resistant typhoid fever: study of an outbreak in Calcutta. Indian Pediatr. 1992; 29:61-66.
4. Buch NA, Hassan MU, Kakroo DK. Enteric fever: A changing sensitivity pattern, clinical profile and outcome. Indian Pediatr. 1994; 31:981-85.
5. Sharma A, Gathwala G. Clinical profile and outcome in Enteric fever. Indian Pediatr. 1993; 20:47-50.
6. Raghuraman TS, Krishnamurthy L, Menon PK, Singh D, Jayaprakash DG. Clinical profile and therapy in Enteric fever. Indian Pediatr. 1994; 31: 196-99
7. Mishra RN, Bawa KS, Magu SK, Bhandari S, Nagendra A, Memon PK. Outbreak of Multidrug Resistant Salmonella typhi Enteric fever in Mumbai Garrison. MJAFI 2005; 61:148-50.
8. Alsoub H, Uwaydah AK, Matar I, Zebeib M, Elhag KM. A clinical comparison of typhoid fever caused by susceptible and multidrug – resistant strains of salmonella typhi. Br J clin Pract. 1997; 51 (1): 8-10
9. WHO Drug – resistant Salmonella. 2007. http://www.who.int/mediacentre/factsheets/fs139/en.
10. Ackers ML, Puhr ND, Tauxe RV, Mintz ED. Laboratory – based surveillance of Salmonella serotype typhi Infections in the United states: Antimicrobial resistance on the rise. JAMA. 2006; 283(20): 2668 – 73.
11. Takkar VP, Raikumar, Takkar R, Khurana S. Resurgence of chloramphenicol sensitive Salmonella typhi. Indian Pediatr. 1995; 32:586-87.