Outbreak of Multi-drug Resistant *Salmonella* Typhi Enteric Fever in Mumbai Garrison

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Abstract

Background: There was an epidemic of enteric fever in Mumbai garrison during Nov-Dec 2000 with more than 150 cases admitted to a tertiary care service hospital.

Methods: All the cases presented with fever and some had splenomegaly, bradycardia, abdominal pain and diarrhoea. The epidemic was investigated by the station health organization (SHO) and the case and bacteriological study was carried out in pathology laboratory of the service hospital. The serological study was carried out at Armed Forces Medical College (AFMC), Pune and the Phage typing was carried out at Lady Harding Medical College, New Delhi.

Results: Blood cultures were positive in 92(63%) for *Salmonella typhi* and Widal test was positive in 83(55%). All strains were resistant to four primary drugs i.e. ampicillin, chloramphenicol, co-trimoxazole and tetracycline. All but two were treated successfully with ceftriaxone. The *Salmonella typhi* belonged to phage group E1 and biotype I.

Conclusion : Extensive epidemiological investigation of cases and water sources of cantonment area pointed to a common source of the epidemic i.e. the well near 'Gurudwara'.

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Key Words : Enteric fever; Multi-drug resistant; Phage type; *Salmonella typhi*

Introduction

Enteric fever is common amongst children and young adults in developing countries, particularly in India [1]. Though sporadic cases occur throughout the year, epidemics break out whenever there is a break-down in sanitary practices. In India more than 3,00,000 cases are reported every year and is associated with significant morbidity and mortality [2]. Drug resistant *Salmonella typhi* has been reported in India since 1960 and outbreaks by these strains occur at intervals in various parts of India [3]. There was an epidemic in Mumbai military garrison by drug resistant *S typhi* during Nov-Dec 2000.

Material and Methods

A total of 150 cases with features of enteric fever were admitted to a service hospital at Mumbai between 01 November 2000 and 15 Dec 2000. Most of the patients had continuous fever, abdominal pain with or without diarrhoea, hepato-splenomegaly, bradycardia, neutropenia and some with rose spots. The laboratory investigation including haematological parameters, blood culture and Widal test were carried out. Blood cultures were carried out in brain heart infusion broth (BHI). Widal tests were carried out in most of the cases on admission and 7-10 days there after. Though four fold rise in titre was found in many cases but single

Widal tests with TO > 160 and TH with > 200 titre was also taken as positive. *S typhi* was isolated and identified by morphology, biochemical and serological methods [4]. The antibiogram was carried out by Stokes' disc diffusion tests [5]. Minimum inhibitory concentration(MIC) to various antibiotics including the four primary drugs i.e. ampicillin, chloramphenicol, co-trimoxazole and tetracycline (ACCoT) were carried out. Serotyping with monospecific antisera was carried out at AFMC, Pune and phage typing was carried out at the National *Salmonella* phage typing Center (NSPTC), Lady Harding Medical College, New Delhi. Epidemiological investigation of all fever cases were carried out by a questionnaire to all patients and participants. Besides this, the water quality in all sources inside the cantonment and health status of food handlers, eateries and mess staff were investigated. Liaison with Mumbai Municipal Corporation was done by Station Health Organization (Mumbai).

Results

A total of 150 cases with typical clinical presentation were investigated. The age of the patients varied from 2½ to 72 years. There was male preponderance (58%). The children and young adults (5-20 years) were 74%, wives of serving personnel 13%, 11% were sailors & ORs and 2% were serving officers. All cases had more than 8 days duration of fever. Other presenting features were as shown in Table-1. Blood

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Table 1

Clinical presentation of the patients

Type	No	Percentage
Fever	150	100
Abdominal pain	60	40
Splenomegaly	123	82
Diarrhea	72	48
Hepatomegaly	24	16
Bradycardia	54	36
Neutropenia	48	32
Rose spots	18	12

culture was positive in 93 (62%) cases and in 83 (55%) cases Widal test was positive. Both were negative in 27 (18%). These were diagnosed as enteric fever as per the clinical and hematological criteria [6]. Diagnosis was confirmed in 3 cases by bone marrow culture. The isolates were resistant to ampicillin, chloramphenicol, co-trimoxazole and tetracycline by Stokes' disc diffusion method. MIC of primary drugs including ampicillin, chloramphenicol, co-trimoxazole and tetracycline were carried out and resistance was confirmed. The MIC to chloramphenicol was 12.5 g/ml and to ciprofloxacin was 0.5 g/ml. All the strains were sensitive to amikacin and ceftriaxone, which were used successfully in all but two cases. The strains were subjected to plasmid analysis. Conjugative plasmids were demonstrated in twelve strains. Two cases died in the hospital, one with septicemic shock, thrombocytopenia and ARDS and another was a child with thalassemia major. The phage typing of the Vi antigens was shown to belong to E1 and biotype I. Epidemiological investigation lead to a common source i.e. the well water of Gurudwara. Further investigation revealed that the water from the well was the source which was mixed with "khir" to serve the excess number of devotees during the day of 'langar' on 12 Nov 2000. Maximum number i.e. 75(50%) cases belonged to the category who attended this function. The water used by the community even before the 'langar' was the source of the typhoid outbreak which could account for the cases from 1 Nov 2000. The well water was in the vicinity of the septic tank of the residential flats and probably got contaminated from the sewerage.

Discussion

The most typical presentations were fever, hepatosplenomegaly and abdominal pain with or without diarrhoea (Table 1). Though bradycardia is a classical feature of enteric fever but this was not seen in all cases. Low or normal leucocyte count with neutropenia, a classical feature was not seen in all cases. The 27 patients who were culture negative and Widal test negative are also included in this study because of their typical clinical picture in a epidemic setting [6] and their response to similar treatments. The blood culture might be negative due to partial treatment received from civil/service OPDs before coming to hospital.

All the strains were resistant to ampicillin,

Table 2

Distribution of Phage groups (%) of *S typhi*

Year	n	E1	A1	Others
1992	74	68.9	5.4	25.7
1993	104	51	7.7	41.3
1994	49	67.3	4	28.7
1995	40	63.1	5	31.9
1996	102	33.3	7.8	58.9
1998	49	43	14.3	42.7
2000	93	100	--	--

chloramphenicol, co-trimoxazole and tetracycline. Antibiotic resistance to first line treatment viz. chloramphenicol was first discovered in the 1960s [3]. Later on, this spread to many parts of the country in subsequent epidemics. ACCoT was the resistance pattern in 89-100% of strains seen in Rohtak, North India [7]. Internationally the multi-drug resistant (MDR) strains have been reported in China and other countries [8-10].

Phage typing of these organisms showed that they belong to phage type E1 and biotype I. Phage type E1 is the most common phage type prevalent in the Indian scenario. 57-70% of the isolates of *S typhi* in various studies were phage type E1 followed by phage type A (4-9%) [7]. From the records at AFMC, it is found that phage type E1 is most prevalent in the military garrison (Table 2). The association of MDR *S typhi* (MDRST) and phage type E1 was recorded in Rohtak between 1989-1991 [7]. Though MDRST strains are increasing since 1991, and prevalent in many parts of India, they are sensitive to fluoroquinolones and third generation cephalosporins. The prevalence of MDRST was 11% at Vellore and 91.3% at Nagpur and Calcutta. However in Calcutta the prevalent phage type is S1 and 0(11-13). In Vellore the multidrug resistance was mediated by plasmid as was found in this study [11]. In the latest report from Rourkela, 16% strains were MDR [14]. During 1991-1995, MDRST was reported from Hyderabad. More than 85% strains were resistant to three or more drugs and 95% were sensitive to fluoroquinolones. most of the strains belonged to phage type E1 and biotype II [15]. In this study the strains were sensitive to ciprofloxacin by disk diffusion method but response to treatment was prolonged apparently due to high MIC. All responded well to ceftriaxone and amikacin.

Extensive epidemiological investigation by SHO pointed to the water from the adjacent well of 'Gurudwara' which was used to dilute the "khir" for a large number of devotees on 12 Nov 2000. This accounted for maximum number of cases i.e. 75 (50%). However the same water source was the cause of other

cases as per the epidemiological investigations.

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