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Brief Communication

Bacterial aetiology and antimicrobial resistance pattern in culture positive enteric fever at a private hospital in Sri Lanka

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Abstract

There is a paucity of information on enteric fever in Sri Lanka. This laboratory-based study aimed to identify the causative agent and demographic profile of patients with blood culture confirmed enteric fever at a private hospital in Colombo between February 2011 and November 2012. There were 100 isolates, S. Paratyphi A (n=92) and S. Typhi (n=8). Eighty-three patients were below 40 years. Antimicrobial resistance was seen to ciprofloxacin and azithromycin. If the emergence of S. Paratyphi A as an important cause of enteric fever is confirmed by further studies, the development of a bivalent vaccine effective against both typhoid and paratyphoid fever will be required for prevention of enteric fever.

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Introduction

Enteric fever is endemic in most developing countries and includes typhoid and paratyphoid fevers caused by *Salmonella* Typhi (S. Typhi) and *Salmonella* Paratyphi (A, B and C) (*S.* Paratyphi A, B, C), respectively. The global estimated cases of typhoid fever in 2000 was 22 million with 2.2 million deaths while that of paratyphoid fever was 5.5 million with no deaths [1]. In some regions, notably Asia and South Asia, the proportion of cases due to *S.* Paratyphi A are increasing [2,3].

Timely administration of effective antibiotics is very important to prevent deaths due to enteric fever. However, *S.* Typhi isolates from different parts of the world have been found to be resistant to ampicillin, co-trimoxazole, ciprofloxacin and azithromycin [4,5] Similarly, antibiotic resistance has also emerged in *S.* Paratyphi A [6,7] Resistance to commonly used antibiotics in *S.* Typhi and *S.* Paratyphi A has also emerged in Sri Lanka [8,9,10]. Therefore, antibiotic sensitivity testing of isolates is important in surveillance and for the development of empiric guidelines.

According to the Weekly Epidemiological Reports of the Epidemiological Unit, Sri Lanka, about 1300-3000 clinically suspected cases of enteric fever are notified annually and a shift

from *S.* Typhi to *S.* Paratyphi A as the predominant causative agent in certain provinces was noted.

There is a dearth of knowledge on the prevalent serotypes, antibiotic sensitivity patterns and affected age groups in Sri Lanka. The aim of the study was to identify the aetiological agent responsible for enteric fever in laboratory confirmed enteric fever patients, to determine the antibiotic sensitivity patterns of the isolated pathogen, describe the demographic profile of patients and ascertain the notification rate.

Materials and Methods

A descriptive, cross sectional, laboratory-based, retrospective study was carried out at a 280 bed, tertiary care, private hospital in the Colombo Municipality area. Blood culture positive enteric fever patients presenting to the hospital between February 2011 and November 2012 were identified from laboratory records and patient records were retrieved for analysis.

The causative agent, antibiotic sensitivity pattern, patient's address, gender, age and ethnicity, date of admission and date of discharge were recorded using a data collection sheet. Antibiotic sensitivity of the isolate for amoxicillin, chloramphenicol, co-trimoxazole, ciprofloxacin, co-amoxiclav, azithromycin, ceftriaxone and timentin was determined using the CLSI method. Evidence of notification to the Epidemiology Unit were obtained using the notification register of the hospital.

The proportion of enteric fever caused by *S.* Typhi and *S.* Paratyphi A was determined. Demographic profile of the cases was described using descriptive statistics and distribution by age, sex, residence and ethnicity were determined. The percentage of strains resistant to commonly used antibiotics was calculated for both *S.*Typhi and *S.* Paratyphi A.

Results

A total of 100 blood culture positive enteric fever patients were included in the study, 92 patients with paratyphoid fever and 8 patients with typhoid fever. There were 57 males and 43 females. Gender was not significantly associated with acquiring enteric fever. The age range of the patients was 2½ - 76 years, with a median age of 28 years (Figure 1). Patients were significantly more likely to be below the age of 40 (p <0.005) and more than half (53%) the patients were in the 21-40 age group. Of the patients, ethnicity was available only for 89 patients. There were 59 Sinhalese (66.3%), 11 Tamils (12.4%) 16 Moors (18%) and 3 other ethnicities (3.4%).

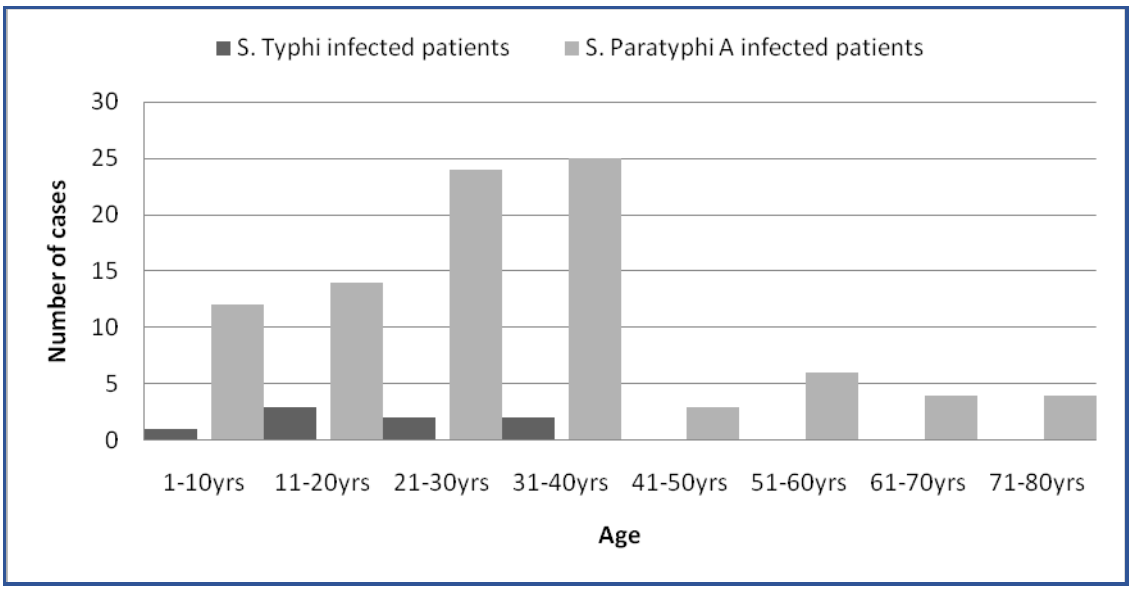

Figure 1: Age range of patients with enteric fever according to causative agent

Geographical location was available for only 65 patients. Twenty four (36.9%) patients lived within the Colombo Municipality Council (CMC) limits, 28 (43.1%) were from Medical Officer of Health (MOH) areas within the Colombo District and 13 (20%) were from outside the Colombo District. The location of cases of paratyphoid A fever (n=58) is shown in Figure 2.

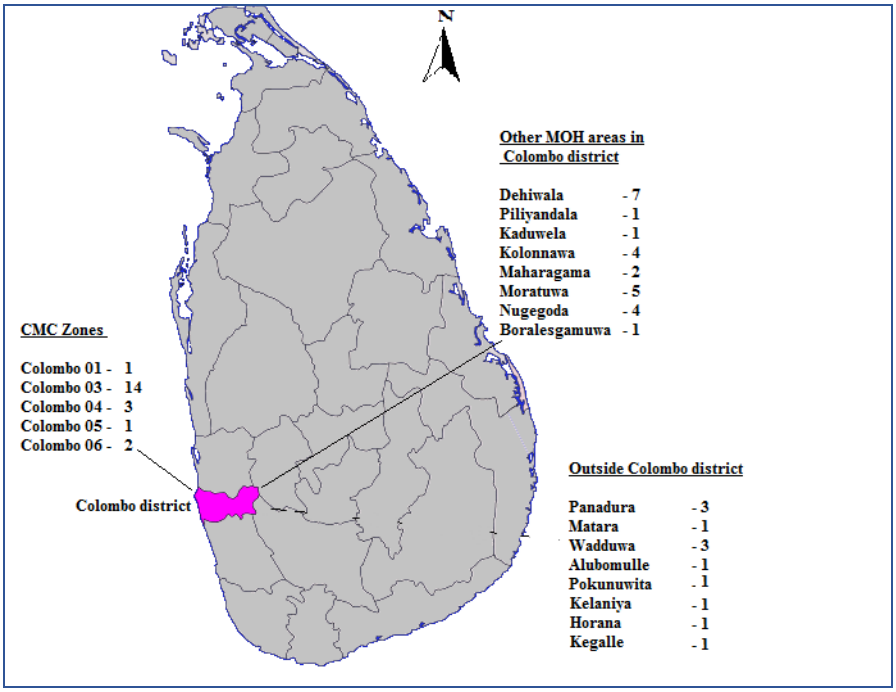

Figure 2: Geographical location of patients infected with Salmonella Paratyphi A

Antimicrobial susceptibility patterns

Resistance was seen only to ciprofloxacin and azithromycin, in a proportion of strains (Table 1). Among the isolates of *S.* Paratyphi (59/80) 73.8% were resistant to ciprofloxacin and 18/62 (29.0%) were resistant to azithromycin. Sixteen strains of 62 isolates tested (25.8%) were resistant to both antibiotics.

Table 1: Antimicrobial susceptibilities of S. Paratyphi A and S. Typhi isolates.

Antimicrobial agent	*S. Typhi* R No./Total no. tested	% R	S. *Paratyphi* A R No./Total no. tested	% R
Amoxicillin	0/8	0	0/80	0
Chloramphenicol	0/8	0	0/80	0
Co-trimoxazole	0/5	0	0/80	0
Ciprofloxacin	2/8	25	59/80	73.8
Co-amoxiclav	0/5	0	0/23	0
Azithromycin	1/4	25	18/62	29.0
Ceftriaxone	0/8	0	0/80	0
Timentin	0/5	0	0/18	0

R – Resistant

Only 48 of these culture positive confirmed cases of enteric fever had been notified to the Epidemiology Unit.

Discussion

This study confirms that the predominant cause of enteric fever in Colombo in 2011/12 was *S.* Paratyphi A. The risk of acquiring *S.* Paratyphi A has been associated with increased consumption of food outside homes, mainly from street vendors [11] and this could be a reason for the emergence of paratyphoid fever in this urban setting. The ability of *S.* Paratyphi A to multiply in food may have contributed to transmission. In contrast, the risk of typhoid fever has been found to be associated with poor hygienic practices, such as washing hands without soap, sharing food from the same plate and not having a toilet in the house [11] and the low incidence of typhoid fever could be related to improved hygiene and sanitation in this setting.

S. Paratyphi A infection was seen in both males (55%) and females (45%) indicating that sex was not a significant factor. This contrasts to studies carried out in Indonesia [11] and in China [12] where a male predominance was seen. This may be due to differences in female employment rates as working women would be more exposed to risk factors for paratyphoid fever such as eating food from street vendors.

The youngest patient in this study was 2½ years of age and the oldest was 76, showing that no age is exempt from infection. However, similar to a previous study from China [13], about 81% (75/92) of the paratyphoid A patients were in the 10-40 years age group, with the majority (53.0%) between 21-40 years. In contrast, in areas where typhoid fever still predominates,

such as Jaffna [14] and Nepal [7] the majority of patients are children. This is consistent with the risk factors for typhoid fever, such as hand washing without soap and sharing the same plate, being found within households, putting the younger age groups at risk while the working/ student group is more at risk for paratyphoid fever that is transmitted through street food [11].

Resistance to antibiotics is well described in *S.* Typhi and *S.* Paratyphi A isolates from Sri Lanka [15]. The present study showed that resistance has developed against ciprofloxacin and azithromycin which could be as a result of irrational use of these antibiotics, particularly in upper respiratory infections. A high resistance of *S.* Paratyphi A to ciprofloxacin (75%) was seen, similar to the findings of Jayathilake *et al.* (2011)[8] and Chandrasiri *et al.* (2010) [10]. Therefore, ciprofloxacin should not be used in empiric therapy for the treatment of enteric fever in Sri Lanka without an antibiotic susceptibility test report. Azithromycin has been used as an effective drug in the treatment of enteric fever resistant to ciprofloxacin. The 29% resistance to azithromycin in *S.* Paratyphi A isolates in our study is alarming because it is one of the most effective drugs in the treatment of enteric fever.

However, it appears that the first line drugs for enteric fever such as amoxicillin, chloramphenicol and cotrimoxazole are effective in the empiric treatment of paratyphoid fever in Colombo. Re-emergence of sensitivity to these antibiotics in *S.* Typhi and *S.*Paratyphi A isolates could be because they have not been used as first line drugs in the recent past while increasing ciprofloxacin and azithromycin resistance may be a result of widespread use of these antibiotics in general practice.

It was surprising to note that only half of the culture confirmed cases had been notified to the relevant health authorities. Corea *et al*. (2010) [16] have previously reported that only about 29% of the culture positive cases were notified to the health authorities by three government hospitals and two private hospitals in Colombo and Ragama.

Conclusions and recommendations

There is a shift from typhoid fever to paratyphoid fever in this hospital. Further studies are required to confirm this shift in other parts of the Colombo District and Western Province. If the emergence of *S*. Paratyphi A as an important cause of enteric fever, is confirmed in wider studies (a trend seen in many other Asian countries), this may warrant the development of a bivalent vaccine effective against both *S.* Typhi and *S.* Paratyphi A. The majority of isolates were resistant to ciprofloxacin and show emerging resistance to azithromycin. Preventive measures should address the high-risk groups between 20-40 years. Laboratory notification of culture positive enteric fever should be strengthened.

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Conflicts of interest

The authors declare that there are no conflicts of interests.

Ethics statement

Ethics clearance for this study was obtained from the Ethics Review Committee of the Faculty of Medicine, University of Colombo, Sri Lanka. Protocol No EC-11-028.

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