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Trends in antibiotic susceptibility of enteric fever isolates in East London

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Summary *Background:* The study sought evidence for changes in the proportions of antibiotic resistant strains among isolates of *Salmonella enterica* serovar Typhi (*S. typhi*) and *Salmonella enterica* serovar Paratyphi (*S. paratyphi*) between 2005 and 2012.
Methods: Blood culture isolates of *S. typhi* and *S. paratyphi* from patients attending Newham and The Royal London Hospitals were included in the study. The organisms were cultured on selective media and identified by Maldi-ToF, API 20E and serology. Minimum inhibitory concentrations (MICs) of augmentin, chloramphenicol, co-trimoxazole, ceftriaxone, ciprofloxacin and azithromycin were determined by E tests for 194 isolates.
Results: Median MICs of ciprofloxacin and ceftriaxone were stable at 0.5 mg/L and 0.125 mg/L, respectively. Chloramphenicol, azithromycin, co-trimoxazole and augmentin median MICs were 4 mg/L, 8 mg/L, 0.064 mg/L and 0.5 mg/L, respectively.
MIC_{90} values were lower than the resistant breakpoint for ceftriaxone, azithromycin and augmentin, but were >256 mg/L for chloramphenicol, 32 mg/L for co-trimoxazole and 1 mg/L for ciprofloxacin.
Conclusions: Antibiotic resistance remained stable for enteric fever isolates between 2005 and 2012. The isolates remained susceptible to augmentin, ceftriaxone and azithromycin over this

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period, but the MIC_{90} was greater than the resistant breakpoint for chloramphenicol, cotrimoxazole and ciprofloxacin. The implications for clinical practice are that isolates of *S. typhi* and *S. paratyphi* from East London remain sensitive to ceftriaxone and azithromycin.

1. Introduction

Antibiotic resistance to many antibiotics has been reported in strains of *S. typhi* and *S. paratyphi* isolated from travellers returning from South Asia and South East Asia with enteric fever [1–4]. In the UK, ceftriaxone or azithromycin are used for empirical treatment of hospitalised cases, and ciprofloxacin is considered once antibiotic susceptibility results are available; cefixime is not used in the treatment algorithm as it has been described to have poor activity against the intracellular bacilli [5]. Imported cases of enteric fever in returning travellers are a common occurrence in East London, whose population has frequent travel to Bangladesh [2].

This previous study reported increasing antibiotic resistance amongst isolates from East London [2]. Antibiotic resistance has implications both for individuals and public health. In this study, we therefore extended the range of antibiotics investigated using minimum inhibitory concentrations (MICs), in a collaboration with the Public Health England Gastrointestinal Bacteria Reference Unit, to determine whether there were any changes in antibiotic resistance between 2005 and 2012.

2. Methods

2.1. Inclusion criteria

Blood culture isolates of *S. typhi* or *S. paratyphi* from patients seen in emergency medicine at Newham Hospital and the Royal London Hospital or admitted to these hospitals during the period 2005–2012 were included in this study. The clinical presentation and demographic data are the subject of a separate report.

2.2. Laboratory methods

One-hundred and ninety-four organisms were cultured on selective media and identified by Maldi-ToF (Bruker Daltonics), API 20E (bioMérieux) and serology. Minimum inhibitory concentrations (MICs) of augmentin, chloramphenicol, co-trimoxazole, ceftriaxone, ciprofloxacin and azithromycin were determined by E test (bioMérieux Basingstoke UK) and interpreted using BSAC criteria [6]. For augmentin and chloramphenicol the MIC breakpoint is 8 mg/L: resistant at MICs >8 mg/L, sensitive at MICs ≤8 mg/L. For co-trimoxazole, the MIC breakpoint for resistance is >4 mg/L, intermediate at 4 mg/L and sensitive at MICs ≤2 mg/L. For ceftriaxone, the MIC breakpoint for resistance is >2 mg/L, intermediate at 2 mg/L and sensitive at MICs ≤1 mg/L. The organism was considered resistant at an MIC >0.06 mg/L for ciprofloxacin, and >16 mg/L for azithromycin [6]. Prior to May 2013, BSAC MIC breakpoints (mg/L) for ciprofloxacin resistance was >1 mg/L, intermediate was 0.125–1 mg/L and the sensitive breakpoint was <0.125 mg/L (old breakpoint). After May 2013, the new breakpoint for ciprofloxacin resistance was >0.06 mg/L.

3. Results

The E test MICs were rounded up to the nearest concentration from a doubling dilution series for the values shown in Tables 1 and 2. None of the isolates were resistant to augmentin (MICs ≤8 mg/L) or azithromycin (MICs ≤16 mg/L). Fifty-one (26%) isolates were resistant to chloramphenicol and forty-nine (25%) isolates were resistant with MICs >32 mg/L but <256 mg/L for co-trimoxazole. There was one isolate with intermediate resistance to ceftriaxone (MIC of 2 mg/L). The majority of the isolates (169/194, 87%)

Table 1 MIC distributions for isolates causing enteric fever.

	MIC Breakpoint (mg/L)			MIC (mg/L)													
Antibiotic (range tested, mg/L)	R>	I	S ≤	**0.008**	**0.016**	**0.032**	**0.064**	**0.125**	**0.25**	**0.5**	**1**	**2**	**4**	**8**	**16**	**>32**	**>256**	Total
Ciprofloxacin (0.006-32)	0.06	N/A	N/A		9	8	8	**1**	**34**	**70**	**52**	**6**	**2**		**1**	**3**		194
Ceftriaxone (0.002-32)	2	2	1			3	56	126	5	1	2	1						194
Chloramphenicol (0.016-256)	8	N/A	8						1		9	68	60	5	**1**		**50**	194
Co-trimoxazole (0.002-32)	4	4	2	1	28	46	23	43	3	1						**49**		194
Azithromycin (0.016-256)	N/A	N/A	16								1	11	75	98	9			194
Augmentin (0.016-256)	8	N/A	8					1	43	66	32	17	34					193

Resistant isolates