

Epidemiology, antibiotic resistance trends and the cost of enteric fever in East London, 2005–2010

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KEYWORDS S. typhi; S. paratyphi; Cost of enteric fever; Azithromycin; Resistance	Summary Introduction: Enteric fever seen in the UK has usually been acquired abroad. The cost to the NHS of treating enteric fever cases is not known. Data on the epidemiology of enteric fever, inpatient treatment costs and the public health management is needed to make decisions regarding the cost benefit considerations of introducing targeted prevention strategies. <i>Methods:</i> A retrospective study of laboratory confirmed enteric fever cases was conducted to estimate the cost of inpatient treatment and to determine antimicrobial resistance patterns at two hospitals in East London between January 2005 and the end of August 2010. <i>Results:</i> 138 cases of enteric fever were identified during the study period (90 S.ser.Typhi and 48 S. ser. Paratyphi). 92% had a recent history of foreign travel, 57% had travelled to visit friends and relatives (VFRs), 26% sought pre-travel health advice and 26% of patients had received typhoid vaccination. The inpatient treatment cost of 138 cases to the NHS was £272,747. The proportion of isolates with high level ciprofloxacin resistance (MICs>1 mg/L) has increased from 10% in 2006 to 30% in 2010. Our data also shows the emergence of isolates with high azithromycin MICs (>32 mg/L); 60% (six out of ten) isolates tested in July—August 2010. <i>Conclusions:</i> There is a significant direct cost of treating enteric fever cases on the NHS. Cost reduction measures are confined due to the lack of effective oral antibiotics following the emergence of high level resistance to ciprofloxacin and azithromycin. Outpatient parenteral antibiotic therapy service and improved preventative public health measures aimed at VFR travellers in particular may be helpful in reducing costs.

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Introduction

Enteric fever is a systemic infection caused by Salmonella enterica subsp. enterica serovar. Typhi (S.ser.Typhi) or Salmonella enterica subsp. enterica serovar.Paratyphi (S.ser.Paratyphi). These organisms pose a risk to travellers visiting endemic areas. Enhanced surveillance of enteric fever in England, Wales and Northern Ireland from May 2006 to April 2007 reported 457 cases of enteric fever; most cases were from the London area (40% of cases) and 86% had travelled to visit friends and relatives (VFRs) in the Indian subcontinent.^{1,2} The incidence of enteric fever among travellers from UK to India, Pakistan and Bangladesh was 17.32 per 100,000 visits.¹ The risk of enteric fever is six fold higher in VFRs compared to other travellers.¹

The London Boroughs of Tower Hamlets and Newham, which are ethnically diverse, account for sixteen percent of enteric fever cases (121/757) reported for London (2006-2009). Notably the annual rate of S.ser.Paratyphi per 100,000 in Tower Hamlets (2.11) is almost double the rate for London (1.09) and over four times higher than the rate for England (0.46). The annual rate of S.ser.Typhi in Newham (5.58) is over four times the rate for London (1.38) and over eleven times higher than the rate for England (0.48) as shown in Table 1.

Travellers with enteric fever usually present with a nonspecific febrile illness with insidious onset. Death and serious complications are unusual among travellers with enteric fever.^{3,4} There was no significant difference in clinical presentation or outcome between S.ser.Typhi and S.ser.Paratyphi cases.³ Isolates with reduced susceptibility to ciprofloxacin [minimum inhibitory concentration (MIC) – 0.125–1 mg/L] have emerged in recent years.^{4,5} Third generation cephalosporins and azithromycin are increasingly being used as first line antibiotics for the treatment of enteric fever.⁶

The UK enhanced surveillance report recommended studies looking at the length of hospital stay and cost of inpatient treatment of enteric fever cases.¹ To our knowledge, there are no studies from the UK estimating the direct inpatient costs of treating enteric fever cases. The primary objective of our study was to determine the cost associated with inpatient treatment. The secondary objective was to describe local epidemiology and trends in antibiotic resistance among *S.ser.Typhi* and *S.* ser. Paratyphi bacteraemia isolates.

Methods

Study design

We conducted a retrospective laboratory based surveillance study of all patients admitted with *S.ser.Typhi* OR *S.* ser. Paratyphi bacteraemia to the Royal London Hospital and Newham University Hospital between 1 January 2005 and 30 August 2010. The Royal London Hospital is a large tertiary hospital which serves a large Bangladeshi population in the London borough of Tower Hamlets; 33% of the total borough population are of Bangladeshi origin and onehalf of the total UK Bangladeshi population live in Tower Hamlets.⁷ Newham hospital provides an acute medical service to people living in the London Borough of Newham which is the second most ethnically diverse London borough with a large Asian population; 38% of the total borough population (Indians-12.2%, Bangladeshi-10%, Pakistani-8.9%).⁷

Enhanced enteric fever surveillance data from North East and North Central London Health Protection Unit was reviewed for the following data: ethnicity, history of recent foreign travel, reason for travel, pre-travel health advice, and typhoid vaccination. Hospital electronic records were reviewed for patient demographics, length of hospital stay and clinical outcome.

Microbiology

Blood culture isolates were analysed using bioMerieux BacT/ALERT automated blood culture system, identified with API20E biochemical identification kit (bioMerieux, France) and species was confirmed by using polyvalent and monovalent sera. S.ser.Typhi and S.ser.Paratyphi isolates were referred to the Health Protection Agency (HPA) Salmonella Reference unit at Colindale for the confirmation of identification, serotyping and phage typing. Susceptibility of the isolates to ampicillin, chloramphenicol, trimethoprim, ceftriaxone, cefuroxime and nalidixic acid was determined by British Society of Antimicrobial Chemotherapy (BSAC) disc susceptibility method.⁸ Prior to 2006, nalidixic acid resistance was used as a surrogate marker of ciprofloxacin resistance and MICs by E test were not routinely performed. Reduced ciprofloxacin susceptibility was defined as an isolate with Ciprofloxacin MIC of 0.125-1 mg/L by E test.⁹ Isolates with an MIC of >1 mg/L

Table 1Total number of cases of S.ser. Typhi and S.ser. Paratyphi and mean rate/100,000 per year for England, London,Tower Hamlets and Newham (2006–2009).

Area	S.ser. Typhi case	S.ser. Typhi cases		S.ser. Paratyphi cases	
	Total cases	Mean rate & 95% C.Is	Total cases	Mean rate & 95% C.Is	
England ^a	992	0.48 (0.45–0.51)	958	0.47 (0.43–0.49)	
London ^a	423	1.38 (1.25–1.52)	334	1.09 (0.97-1.21)	
Tower hamlets ^b	28	3.11 (2.06-4.49)	19	2.11 (1.26-3.29)	
Newham ^b	54	5.59 (4.10-7.29)	20	2.07 (1.26-3.19)	

^a Travel Health and Migrant Section, Centre for Infections, HPA, Laboratory confirmed cases.

^b North East & Central Health Protection Unit Notifications and ONS (Office of National Statistics) mid year population estimates utilised.

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