

Letter to the Editor

Ongoing outbreak of *Salmonella enterica* serovar Paratyphi A infections, Phnom Penh, Cambodia

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Dear Editor,

Salmonella enterica serovar Paratyphi A (*Salmonella* Paratyphi A) is an emerging pathogen in Asia accounting for 14% (Indonesia) to 64% (southeastern China) of enteric fever cases in this continent [1]. Between January and September 2013, an unusual increase in the number of *Salmonella* Paratyphi A infections was registered in adult patients attending Sihanouk Hospital Centre of HOPE (SHCH), in Phnom Penh, Cambodia [2]. A similar trend was noted in travellers returning from Cambodia [3]. These findings were shared with the national health authorities and an epidemiological investigation was initiated; up to now, no common source or specific transmission route has been identified. After a temporary decrease in the number of infections by the end of 2013, we presently report another upsurge of infections in Phnom Penh, observed in the period between September 1st 2013 and September 1st 2014.

The study

Blood cultures were systematically sampled in all adult patients presenting at SHCH with signs of the Systemic Inflammatory Response Syndrome (SIRS). Children were not included as they are admitted in other, specialized, pediatric hospitals in the city. Blood cultures were incubated using 2×10 mL, BacT/ALERT (bioMérieux, Marcy l’Etoile, France) and processed as previously described [2].

Between 1st September 2013 and 1st September 2014, 7 cases of typhoid fever and 69 cases of

paratyphoid fever (caused by *Salmonella* Paratyphi A) were diagnosed at SHCH (Figure 1).

Of these 69 cases of paratyphoid fever, 32 were male patients (46.4%) and the median age was 27 years (range 16-86). Similar to the cases described in the initial outbreak report, most patients (55/67, 82.1%) were from Phnom Penh province.

All patients presented with a history of fever; other frequent symptoms included abdominal pain (56.9%) and diarrhea (22.4%). Six patients had underlying diseases, including HIV, hepatitis B and diabetes mellitus. Only four patients required hospital admission. Preliminary antibiotic susceptibility data showed that one isolate was resistant to amoxicillin and one to co-trimoxazole. Twenty-nine isolates were considered to be intermediate susceptible to ciprofloxacin by disc diffusion (5 µg disk content, Rosco, Taastrup, Denmark), but were susceptible when tested with the E-test macromethod with minimal inhibitory concentration < 0.064 mg/L (bioMérieux, Marcy-L’Etoile, France) [4]. The empirical treatment included mainly ceftriaxone (65.6%; 40/61 cases) which was given on average for 7 days and which was often de-escalated to ciprofloxacin after a few days. The mean duration of antibiotic therapy was 11 days. In 67 patients for whom follow-up information was available, no clinical or microbiological relapse was reported.

Historically, infections with *Salmonella* Paratyphi A are considered less severe than those caused by *Salmonella enterica* serovar Typhi (*Salmonella*

Typhi), the organism causing classic enteric (or typhoid) fever. Recent evidence suggests however, that both serovars cause a similar clinical syndrome [5,6]. In our setting, *Salmonella* Paratyphi A caused a relatively mild disease as only four patients required hospitalization and all patients were cured. Although increasing multidrug resistance of *Salmonella* is a global health concern, almost all *Salmonella* Paratyphi A isolates at SHCH were fully susceptible to all antibiotics routinely tested for. As it has been suggested that *Salmonella* Paratyphi A might have a greater tendency to acquire resistance than does *Salmonella* Typhi, continued surveillance of antibiotic susceptibility is essential [7].

Although *Salmonella* Paratyphi A is causing an increasing proportion of enteric fever cases in Asia, there has been no clear explanation for its successful spread. It has been suggested that large scale vaccination against *Salmonella* Typhi may play a role. However, the increase has also occurred in countries, including Cambodia, where these vaccinations are not routinely administered. A change in virulence has also been proposed to play a role. However, preliminary data on the evolution of *Salmonella* Paratyphi A suggests that the recent increase in infections is due to changes in environmental factors rather than the progression of a particularly virulent strain [8]. Environmental factors could include changes in climate and transmissions to naïve hosts [8,9]. Likewise, in Cambodia no apparent reason for the increase in *Salmonella* Paratyphi A infections has been identified so far. There could be a link with festivities and national holidays. As can be observed from Figure 1, peaks in the number of infections occur around

February/March, the period following Chinese New Year and May/June, the period following three other national holidays in Cambodia, including Khmer New Year. Apart from increased migration of people, these events have recently been associated with strikes from garbage collectors, resulting in an accumulation of waste which is known to facilitate enteric disease transmission [10]. In addition, recent years have shown increased popularity of street food consumption that is also a known risk factor for acquisition of *Salmonella* Paratyphi A [9]. A case-control study could increase our understanding of these factors. In addition, studies are needed on *Salmonella* Paratyphi A rates from neighboring countries to confirm that this increase was not confined to Phnom Penh.

Conclusions

This ongoing outbreak of *Salmonella* Paratyphi A in Phnom Penh underlines the importance of sound epidemiological investigation and public health measures being taken in due time. Further investigations to identify context specific risk factors for the spread and acquisition of *Salmonella* Paratyphi A, including cultural and climate related factors, are urgently needed and its antibiotic susceptibility should be monitored. Further study of the genetic relationship of these outbreak isolates is underway to look into the possibility of a particular genetic lineage that could be responsible for the recent and successful spread of *Salmonella* Paratyphi A in Asia.

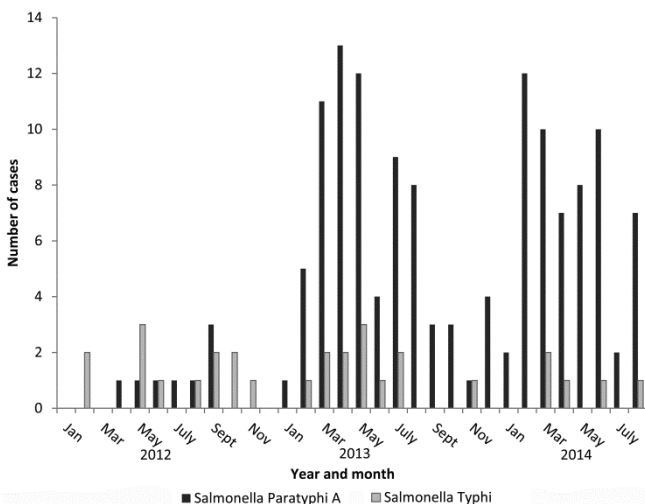
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Figure 1. Number of blood culture confirmed (para)typhoid fever cases during the period January 2012 – September 2014 at Sihanouk Hospital Centre of Hope, Phnom Penh, Cambodia



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