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Short Communication

Salmonella Typhi and Paratyphi A infections in Cambodian children, 2012–2016

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ABSTRACT

Objectives: Enteric fever remains an important diagnostic and treatment challenge in febrile children living in the tropics. In the context of a national *Salmonella enterica* serovar Paratyphi A outbreak, the objective of this retrospective study was to compare features of *S.* Typhi and *S.* Paratyphi A infections in Cambodian children.
Methods: Clinical and laboratory features were reviewed for 192 blood culture-confirmed children with *S.* Typhi and *S.* Paratyphi A infections presenting to a paediatric referral hospital in Siem Reap, 2012–2016.
Results: Children with *S.* Typhi infections were younger, were more likely to have chills and/or diarrhoea, and were more frequently hospitalized than those with *S.* Paratyphi A infections. Over three quarters (88.3%) of *S.* Typhi isolates were multidrug-resistant, compared to none of the *S.* Paratyphi A.
Conclusions: In this small study of Cambodian children, *S.* Typhi infections were more severe than *S.* Paratyphi A infections. Antibiotic resistance limits treatment options for enteric fever in this population.

Enteric fever, caused by infection with *Salmonella enterica* serovar Typhi (*S.* Typhi) or serovar Paratyphi A/B/C (*S.* Paratyphi), remains a significant cause of morbidity and mortality globally (GBD, 2017 Typhoid and Paratyphoid Collaborators, 2019). The non-specific clinical presentation and rising rates of antimicrobial resistance make empiric treatment challenging (Gibani et al., 2018). In Cambodia, a recent national outbreak of *S.* Paratyphi A was identified initially in returning European tourists (Vlieghe et al., 2013; Kuijpers et al., 2017). Since comparative data on *S.* Typhi and *S.* Paratyphi A infections in paediatrics are scarce, this outbreak afforded a review of clinical presentation, treatment, and outcomes in Cambodian children.

Clinical and laboratory data were reviewed from blood culture-confirmed cases of *S.* Typhi and *S.* Paratyphi A infection at Angkor Hospital for Children, a paediatric referral hospital in Siem Reap, between January 1, 2012 and December 31, 2016. Over this time period, it was normal clinical practice for febrile children to have blood cultures on hospital admission, as described previously (Fox-Lewis et al., 2018). Data were analysed using R (v3.4.0); comparisons between groups were made using the Wilcoxon rank sum test, Chi-square test, or Fisher's exact test, as appropriate.

Clinical notes from 192/224 (85.7%) cases could be reviewed. *S.* Typhi predominated in 2012–2013 (100/106; 94.3%) and 2015–2016 (38/45; 84.4%). In 2014, almost 61.0% of infections (25/41) were caused by *S.* Paratyphi A (Fig. 1). Relevant clinical features are summarized in Table 1.

On univariable analysis, *S.* Paratyphi A infected older children compared to *S.* Typhi: median age 10.2 years (range 2.7–15.5 years) and 7.2 years (range 1.2–15.2 years), respectively ($p < 0.001$). Chills (20.8% vs. 0%; $p < 0.001$) and diarrhoea (24.0% vs. 7.9%; $p = 0.03$) were more common in children with *S.* Typhi infection, whereas headache was more common in those with *S.* Paratyphi A (30.5% vs. 50.0%; $p = 0.04$). There were no significant differences in clinical examination or white blood cell count results between the two groups. Children with *S.* Typhi infection had slightly lower haemoglobin values than those with *S.* Paratyphi A: median 105 g/l versus 115 g/l ($p < 0.001$). Children with *S.* Typhi were more likely to be admitted than those with *S.* Paratyphi A: 61.0% versus 42.1% ($p = 0.05$); they also had longer hospitalization duration and fever clearance times (Table 1).

In a multivariable logistic regression model, younger age (odds ratio 0.79, 95% confidence interval 0.67–0.91; $p = 0.002$) and longer

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