

Review

Challenges in measuring complications and death due to invasive *Salmonella* infections

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ABSTRACT

Despite the highest burden of Typhoid fever in children globally, exact estimates of morbidity and mortality are lacking due to scarcity of published data. Despite a high prevalence and a socioeconomic burden in developing countries, published data with morbidity and mortality figures are limited especially Africa and South American regions. Data from the community is insufficient and most case fatality estimates are extrapolations from hospital based studies that do not cover all geographical regions, and include cases which may or not be culture confirmed, MDR resistant or sensitive cases, or from mixed populations of age (adults and children).

Complications of typhoid such as intestinal perforation, bone marrow suppression, and encephalopathy are dependent on MDR/Fluoroquinolone resistant *Salmonella* infection, comorbidities such as malnutrition, and health-care access. Data is again insufficient to estimate the true burden of Typhoid Fever in different regions and groups of populations. Although there has been a rapid decline in cases in developed countries with the advent of improved sanitization, timely and easy access to health care and laboratories, this is still not the case in the developing countries where Typhoid deaths are still occurring. The way forward is to develop rapid and cost effective point of care diagnostic tests, put in place validated clinical algorithms for suspected clinical cases, and design prospective, and community based studies in different groups, implement maintenance of electronic health records in large public sector hospitals and regions to identify populations that will benefit most from the implementation of vaccine. Policies on public health education and typhoid vaccine may help to reduce morbidity and mortality due to the disease.

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1. Background and epidemiology

Populations in South Asia, particularly children are considered to have the highest burden of typhoid fever globally. The true burden of the disease is however difficult to ascertain. In the year 2000, typhoid reportedly caused almost 22 million episodes of enteric fever and more than 200,000 deaths, with the majority of disease burden being borne by children and adolescents in South and South-eastern Asia [1]. Most data for enteric fever comes from vaccine or drug trials and trials, or hospital based studies. Data from community-based studies are rare and data on mortality due to enteric fever are even more limited.

Typhoid is mainly a problem of developing countries; the disease is rare in developed countries where there is access to basic sanitation and clean water. High annual incidence rates of blood culture-confirmed typhoid fever are reported from disadvantaged populations with poor access to water and sanitation such as the slums of North Jakarta, Indonesia; Kolkata, India and Karachi, Pakistan with incidence ranging from 180–494/100,000 among 5–15 year olds [1,2]. However, it is recognized that the assessment of disease burden from Africa remains uncertain. Recent reports suggest that there is an increasing problem, requiring further prevalence studies [2]. Prevalence of 0% to 4.23% in febrile subjects based on cultures, have been reported from Africa in predominantly outpatient settings [3]. Blood culture positivity in samples collected from 2007 to 2009 in febrile subjects in Kenya, ranged from 137 (6.4%) of 2142 blood cultures processed from Kibera and 22 (0.6%) of 3577 blood cultures from rural Lwak [4].

Data by Institute for Health Metrics and Evaluation (IHME) on typhoid and paratyphoid for the year 2010 [5,6] estimated the burden of death as 190,200 deaths from typhoid and paratyphoid

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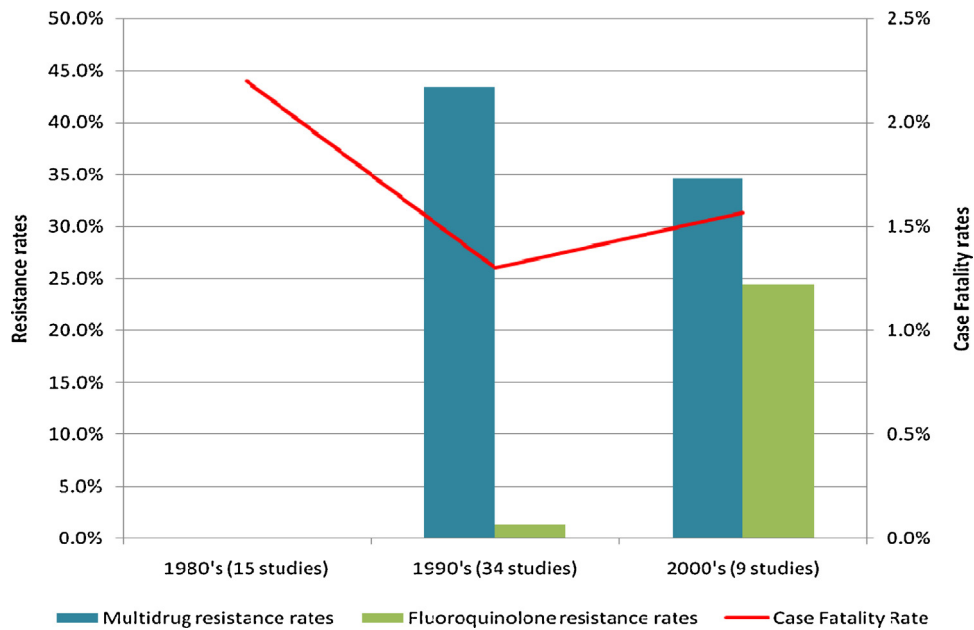


Fig. 1. Studies reporting Case fatality rates in the last 3 decades with MDR and FQ resistance.** Studies retrieved as a subset of a larger ongoing review on enteric fever. Inclusion criteria of studies in children and adults with – reporting of outcomes on clinical features and mortality, all cases either culture positive or culture + serology proven typhoid with $\geq 50\%$ culture positivity; $N > 5$, no case series, no specific subsets (pregnant/neonates/HIV/travelers/uncomplicated, no mixed age groups, lab studies or diagnostic studies) *Salmonella Paratyphi* not included unless data unable to be separated from *Salmonella Typhi*.

fevers, with 12,239,000 DALYs lost. GBD [5] placed typhoid and paratyphoid together as the 35th leading cause of years of life lost, with the highest burden in Asia and sub-Saharan Africa. However, this data is not disaggregated for typhoid and paratyphoid fever, and the estimates have been criticized for utilizing liver abscesses and cysts as the prime disease complications of interest [7]. Other burden estimates of typhoid have also used a CFR (case fatality rate) approximation of 1.0% and extrapolated to incidence data

[8–10]. Despite the high burden of disease, challenges in collection and reporting of data on morbidity and mortality of typhoid remain.

2. Factors determining severity of typhoid

Enteric fever is known to cause prolonged illness with a range of complications, from bone marrow suppression, abscesses at

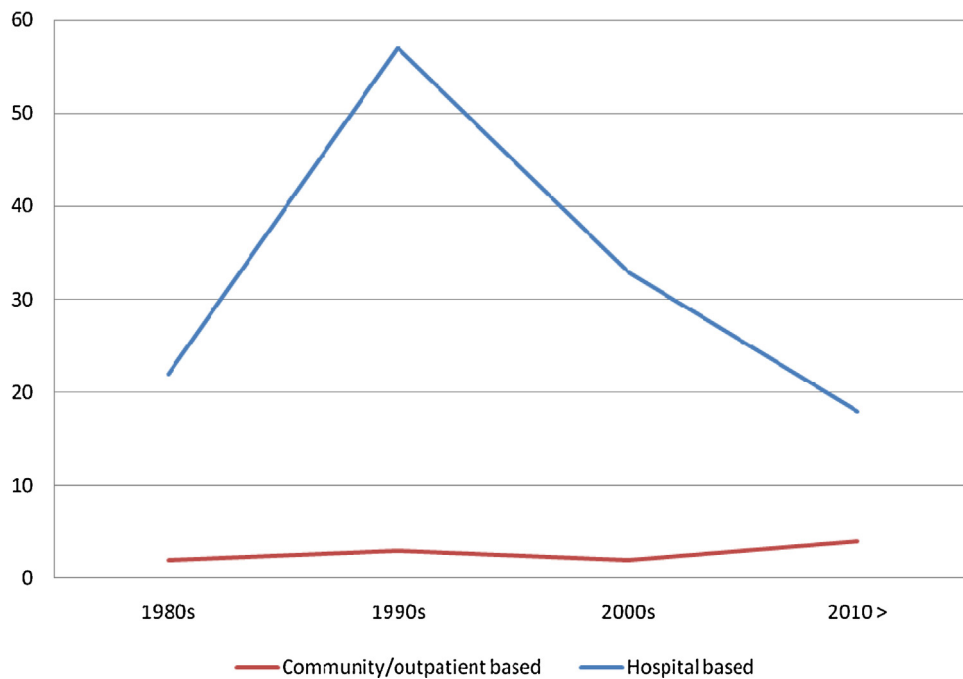


Fig. 2. Publications on children and adults with Typhoid fever according to setting.* Studies retrieved as a subset of a larger ongoing review on enteric fever. Inclusion criteria of studies in children and adults with—reporting of outcomes on clinical features and mortality, all cases either culture positive or culture + serology proven typhoid with $\geq 50\%$ culture positivity; $N > 5$, no case series, no specific subsets (pregnant/neonates/HIV/travelers/uncomplicated, no mixed age groups, lab studies or diagnostic studies) *Salmonella Paratyphi* not included unless data unable to be separated from *Salmonella Typhi*.

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