Typhoid fever in children: some epidemiological considerations from Karachi, Pakistan

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Summary

Background: The morbidity of typhoid fever is highest in Asia with 93% of global episodes occurring in this region. Southeast Asia has an estimated incidence of 110 cases/100 000 population, which is the third highest incidence rate for any region. Pakistan falls into this region. There is also a considerable seasonal variation of typhoid fever, carrying significant public health importance. Children are worst affected. Population-based data from Pakistan are scarce.

Methods: From June 1999 to December 2001 a fortnightly surveillance system was established in two squatter settlements in Karachi, Pakistan, with two study centers, each staffed by a doctor and five community health workers. Cases of continuous high-grade fever for three or more days were referred to these centers and screened clinically. Blood culture and Typhidot tests were done.

Results: One-third of the 4198 cases with febrile episodes of three or more days detected in the community were screened at the centers; 341 were clinically suspected of having typhoid fever. Forty-nine were positive by culture whereas 161 were positive by serology. Ten cases were multi-drug resistant. Incidence of culture-proven typhoid was estimated to be 170 (95% CI: 120, 220)/100 000 population, whereas serology-based incidence was 710 (95% CI: 620, 810)/100 000 population. Peak incidence was noted in October followed by May and June.

Conclusion: Passive surveillance, even when augmented by household visits, misses a significant portion of suspected cases. Morbidity of typhoid is quite high in Pakistan and needs public health intervention. Hot months have higher incidence of typhoid. Healthcare behavior studies will help to develop a better surveillance system.

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Introduction

The epidemiology of typhoid fever can be traced back to the classic study by Austin Flint in 1843. Typhoid fever is an acute systemic illness caused by Salmonella enterica serovar Typhi. It is characterized by sustained fever, headache, malaise, anorexia, relative bradycardia, constipation or diarrhea, and nonproductive cough. The disease continues to be a worldwide health problem. Recent data show the annual burden of disease to be 21 million cases globally with over 200,000 deaths due to typhoid fever. Earlier it was estimated to be 16 million with over 600,000 deaths. This clearly shows an increase in morbidity with a decrease in mortality.

The morbidity of typhoid fever is highest in Asia with 93% of the global episodes occurring in this region. It also has the highest regional incidence rate of 274 cases per 100,000 population, over five times higher than the second highest, Latin America. Southeast Asia has an incidence of 110 cases/100,000 population, which is the third highest incidence rate for any region. Pakistan falls into this region.

Although population-based data from Pakistan are scarce, several hospital-based studies from different parts of the country have consistently shown a very high incidence of typhoid fever, especially in the younger age groups. More recent information from Delhi has indicated that the relative incidence of typhoid fever is considerably greater in preschool children. Not only is the morbidity quite high but the emergence of multidrug-resistant isolates has made effective therapy of typhoid very difficult as first-line drugs are losing their efficacy against the organism.

There is also considerable epidemiological interest in the seasonal variation of pediatric typhoid fever. The impact of climatic factors is substantial and prophylactic measures for the summer months are advocated. There are however considerable regional differences in seasonality. There is no clear relationship with rainfall in Vietnam in contrast to a temporal relationship with rainfall patterns in Karachi, with cases peaking after the monsoon rains (Mr Abdul Qayoom, Computerized Data Processing Center, Meteorology Department, Government of Pakistan, Karachi, Personal Communication). This consistent relationship may indicate the importance of contamination of water supply by an overwhelmed and inadequate drainage system. This evidence is fairly similar to the recent experience of the risk factors for acquisition of typhoid in Tajikistan, indicating the importance of public health measures and potential interventions that can be instituted only on the information obtained through community-based longitudinal studies. As humans are the only known reservoir of infection, it is very difficult to break the transmission chain.

With this background of scarce population-based data we designed one of the first studies in Pakistan to obtain estimates of typhoid fever in under-16-year-olds in the population.

Materials and methods

Study site

Sultanabad and Hijrat Colony are squatter settlements in districts west and south of Karachi, the largest city of Pakistan, and represent field sites of the Urban Health Program (UHP), Department of Community Health Sciences (CHS), Aga Khan University (AKU). In addition to four government-supported dispensaries and 24 drug outlet stores (pharmacies) in this area, there are two primary care health centers served by the UHP. The majority of the population accesses the private sector for medical care, comprising approximately 40 qualified and 26 non-qualified healthcare providers with questionable standards of care.

The local climate has three distinct seasons: a hot humid summer (May and June), a monsoon season (July and August), and following on from the monsoon season, a second 'summer' (September and October). During the rest of the year the weather remains mild.

Institutional ethical approval for this study was obtained from the AKU Ethical Review Committee.

Inclusion criteria

All residents under 16 years of age reporting to the community clinics with fever of over 72 hours with no localizing signs were recruited in the study.

Identification of febrile illnesses

Domiciliary surveillance

The research team comprised faculty investigators from the Departments of Pediatrics and CHS, AKU along with a research officer and two field medical officers. Domiciliary surveillance was started in June 1999 and continued until December 2001. Ten community health workers were trained in household surveillance of febrile episodes and clinical case recognition. They visited each household every fortnight. A structured format was used to keep records of febrile illnesses in the previous 15 days. Duration of fever in children was determined by parental assessment. Patients were referred to the centre for further evaluation if fever of 72-hour duration or above was reported. People reported to be ill but not available at the visit were revisited in the evening, as were those households that were found locked. If the residents could not be contacted, we recorded them as 'not available' until the next scheduled visit.

Community clinics

As part of a larger study, two typhoid diagnostic and therapeutic centers were established in premises donated by the communities or rented on subsidized rates by the already functional primary healthcare program of CHS. These centers were staffed with a doctor and nurse at all times and received an average of between 30 and 40 children with febrile episodes daily, who were either self-referred or referred by the surveillance team or community physicians. These centers operated between 0900 and 2200 hours, six days a week. One side room per site was reserved for sample collection and storage. A system of twice-daily transportation of specimens to and from the neighboring sentinel AKU laboratory pickup point was developed.

Initially, those patients who had fever of five days or more, without localizing signs, were selected. Following an interim review of surveillance data after six months the duration of fever was changed to include patients with fever of 3 days or more. This decision was taken to increase the surveillance
sensitivity, however, it did not affect the proportion of the patients screened. This was 29% (79/273) in the first six months whereas it was 27% (262/975) during the rest of the study.

For all suspected typhoid patients a detailed clinical encounter form was completed at the clinic. This recorded form of tongue coating (if any), pallor, jaundice, lymph nodes, dehydration, rose spots, severity of toxicity, edema, symptoms of respiratory distress, cardiovascular examination, central nervous system examination (including focal neurological signs) and detailed abdominal examination. Core body temperature (axillary) was measured by clinical thermometer (Shanghai Medicine and Health Products, Shanghai, China) and recorded. A nutritional assessment was also done. History and duration of presenting complaints, family history and prior use of antibiotics were also recorded. Major socio-demographic variables noted included age, sex and socio-economic status of the family. Information on modes of excreta disposal and source of drinking water were also collected for the ongoing case control study on assessment of risk factors for typhoid.

Referral through community health providers

Private doctors were requested to refer fever cases to the health centre from the beginning of the project. However, there was negligible referral despite best possible efforts to establish a effective liaison. Lack of cooperation resulted mainly from a fear of losing their patients and hence financial loss. Others were reluctant to use chloramphenicol as a first line of treatment due to ‘rampant’ resistance to this drug. Still others were uncomfortable to use oral medicine with which most of their patients were not satisfied.

Case definition

It was necessary to use a combined culture and serology approach for defining typhoid because of the high rates of antibiotic usage at the household level and by healthcare providers in the community. Hence, any patient who grew Salmonellae in her/his blood culture or tested positive with the Typhidot test was considered as having typhoid fever. Every patient was treated according to the lab test results.

Laboratory procedures

Following verbal consent, blood samples were obtained if body temperature was 38°C or more. Patients gave only one sample during a febrile episode. In all cases thus selected, blood was cultured using Bactec system (Becton Dickinson, USA), a complete blood count was taken, malarial film and the Typhidot—ELISA (MBDR, Kuala Lumpur, Malaysia) tests were obtained. The latter test has recently been validated among children with typhoid fever in Karachi and found to be significantly more sensitive than the Widal test.

Statistical analysis

Data were stored and analyzed with Epiinfo version 6.04 (Centers for Disease Control and Prevention, Atlanta, GA, USA). Incidence calculations were made using Microsoft Excel 2000 (Microsoft Corp., Redmond, WA, USA) spreadsheets. We estimated the incidence rate of typhoid fever by dividing the number of clinically suspected, culture- and serology-positive cases by person years of follow-up expressed per 1000. Person years were calculated by multiplying the total number of children, or number of children in each age group, by 2.5 (duration of study in years) assuming a steady state. Confidence intervals for incidence were calculated by treating the numerator as a Poisson variable and then obtaining the 95% CI for the count and then dividing these two values by person-time. Relative risks were calculated by considering the youngest age group as reference category and using Epiinfo relative risks, and their 95% CI were obtained.

Results

A baseline census was conducted in 1996 by UHP complemented by another census in 1999 for the purpose of this study. Thus a detailed demographic sampling frame was established. The 1999 census showed a mixed Punjabi—Pathan population of 29 160 with a pediatric population (under 16 years of age) of 11 668. There were 7743 households in this community. Families lived in houses built from clay with one or two rooms. Thirty percent of households had a piped water supply. The drainage system for sewage and wastewater was inadequate.

Children under 16 years of age in the population were eligible for enrolment in this study. 11 668 children under 16 years of age were visited fortnightly for the period of 30 months, i.e., from June 1999 to December 2001. Of these, 6218 (53%) were under 5 years old and 5450 (47%) were aged 5—15 years. There were no refusals to give the required information.

Distribution of febrile cases

Trained healthcare workers detected a total of 17 485 febrile episodes in the community. Of these 4198 (24%) episodes were of ≥72 hours duration indicating that 36% of the pediatric population suffered from febrile episodes of ≥3 days duration. Four hundred and seventy-eight (11%) were in the age group 0—1 year, 2184 (52%) in age group >1—5 years, 1001 (24%) in age group >5—10 years and 533 (13%) in the age group >10—15 years (Figure 1).
Logically negative but the incidence of clinical typhoid were clinically suspected to be cases of typhoid. Based on the study physicians, about half of those who reported to the clinics were >1–5 years old whereas only 11% were in the age group 0–1 year. As per clinical case definition, 341 (178 male, 163 female) of the 1248 (27%) patients with suspected typhoid were eligible to be sampled for blood culture and serology (Typhidot).

Of the 1248 who reported to the community clinic, 341 were clinically suspected to be cases of typhoid. Based on person-years of observation, the incidence of clinical typhoid was calculated to be 11.69/1000. Table 1 shows overall person-years of observation, the incidence of clinical typhoid were clinically suspected to be cases of typhoid. Based on the study physicians, about half of those who reported to the clinics were >1–5 years old whereas only 11% were in the age group 0–1 year. As per clinical case definition, 341 (178 male, 163 female) of the 1248 (27%) patients with suspected typhoid were eligible to be sampled for blood culture and serology (Typhidot).

Of those clinically suspected of having typhoid fever, *Salmonella enterica* serovar Typhi were isolated in 42 (12.3%) blood cultures whereas seven (2.1%) were *Salmonella paratyphi* A (Figure 2). Fourteen percent (6/42) *Salmonella enterica* serovar Typhi were multi-drug resistant as compared to 57% (4/7) *Salmonella paratyphi*. Three cases were serologically negative but *Salmonella* were detected in their blood. No growth was observed among 221 (64.8%) of the blood cultures while of the remaining 71 (20.8%), one grew *Haemophilus influenzae* while others included nonpathogenic skin and environmental contaminants (mostly *Staphylococcus epidermidis* and *Bacillus* species). Final diagnoses of 341 patients were: 39 (11.4%) were multidrug-sensitive typhoid, 10 (2.9%) were multidrug-resistant typhoid and 161 (47.2%) culture-negative typhoid. The clinical course of six (1.8%) of the patients was indicative of typhoid fever but none of the tests were positive. There were 125 (36.7%) non-typhoidal illnesses. Of these, six were cases of *Plasmodium vivax*, three were cases of UTI, one was a case of pneumonia and there was one case of *Haemophilus influenzae* septicemia; the remaining 114 were undetermined viral illnesses (Figure 3).

In the 341 suspected cases of typhoid found eligible for screening, multiple clinical presentations were noted (Table 2). Fever and abdominal pain were the two most commonly recorded clinical features. Cough was more common in those patients found to be serologically positive.

Seasonal variation was observed. The highest incidence peak was noted in October (second summer in Karachi) and the incidence also increased in the summer months of May and June. The monsoon season (July and August) favored typhoid transmission especially if there was a significant rainfall as in 2001 (Figure 4).

**Discussion**

Studies report that typhoid fever is endemic in Southeast Asia and the Indian subcontinent. However, measuring the incidence of febrile illness caused by various pathogens poses a major public health challenge because hospital-based approaches capture only a fraction of patients, clinical diagnosis is usually unreliable and diagnostic tests are often not available in disease-endemic countries. Consequently, the incidence and relative importance of etiologic agents of the febrile illness remain unknown in many parts of the world. Although conducting surveillance at the tertiary care hospital level is attractive from the perspective of laboratory capacity and infrastructure, such surveillance captures only the most severe illnesses in persons who have access to hospital care and therefore does not accurately represent disease incidence. Thus, public health personnel have insufficient data to estimate disease burden in order to prioritize scarce health resources. To our knowledge, this study is the first of its kind in Pakistan, where surveillance was extended beyond the tertiary hospital into the community to determine incidence of typhoid fever closer to the population level. Introduction of augmented passive surveillance, participation of family physicians, although less than optimal, and provision of treatment facilities closer to the residence, minimized patient selection that interferes with the true incidence estimation.

**Table 1** Incidence rate and relative risk of typhoid fever among children under 16 years of age in Hijrat Colony and Sultanabad, Karachi, Pakistan, June 1999–December 2001

<table>
<thead>
<tr>
<th>Age groups (years)</th>
<th>No. of children</th>
<th>Person years</th>
<th>Typhoid cases positive by blood culture n (%)</th>
<th>IR (95% CI)</th>
<th>RR (95% CI)</th>
<th>Typhoid cases positive by serology n (%)</th>
<th>IR (95% CI)</th>
<th>RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–1</td>
<td>1551</td>
<td>3877.5</td>
<td>0 (0)</td>
<td>—</td>
<td>—</td>
<td>0 (0)</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>&gt;1–5</td>
<td>4667</td>
<td>11668</td>
<td>13 (26.5)</td>
<td>1.1 (0.6, 1.2)</td>
<td>1</td>
<td>58 (28)</td>
<td>5.0 (3.8, 6.43)</td>
<td>1</td>
</tr>
<tr>
<td>&gt;5–10</td>
<td>3838</td>
<td>9595</td>
<td>27 (55.1)</td>
<td>2.8 (1.9, 4.1)</td>
<td>2.5 (1.3, 5.0)</td>
<td>99 (47.8)</td>
<td>10.3 (8.5,12.6)</td>
<td>2.1 (1.5, 2.8)</td>
</tr>
<tr>
<td>&gt;10–15</td>
<td>1612</td>
<td>4030</td>
<td>9 (18.4)</td>
<td>2.2 (1.0, 4.2)</td>
<td>2.0 (1.0, 4.7)</td>
<td>50 (24.1)</td>
<td>12.4 (9.2,16.4)</td>
<td>2.5 (1.7, 3.6)</td>
</tr>
<tr>
<td>Overall</td>
<td>11668</td>
<td>29170</td>
<td>49 (100)</td>
<td>1.7 (1.2, 2.2)</td>
<td>—</td>
<td>207 (100)</td>
<td>7.1 (6.2, 8.1)</td>
<td>—</td>
</tr>
</tbody>
</table>

CI, confidence interval; IR, incidence rate; RR, relative risk.
This study quantifies the incidence of clinical, blood culture and serology positive typhoid fever in two squatter settlements in Karachi, Pakistan during a period of 30 months. Based on person years of observation, the overall incidence of clinical typhoid in this study was 11.69/1000, sero-positive typhoid 7/1000 and culture-positive typhoid 1.68/1000. The latter is close to the culture-positivity rate of 1.98/1000 in Vietnam. Clinical typhoid in our study was 1.67 times more prevalent than serological typhoid and approximately 7 times more than culture-positive typhoid. This again is consistent with population-based studies in Vietnam, where the clinical diagnosis of typhoid fever (febrile illness ≥3 days without localizing signs) was found to be somewhat inconclusive (no significant differences in symptoms amongst culture-positive and -negative cases as in our study) and the incidence of clinical typhoid fever was overestimated. Another study will report on the efficacy of a clinical scoring system to objectively evaluate pediatric typhoid in comparison with blood cultures and serology.

Fifty percent of all febrile episodes in a hospital setting tend to be caused by S. enterica serovar Typhi. This is understandable since patients are admitted to the hospital in the case of prolonged and severe illness or when complications develop. Population-based experience of the incidence of typhoid fever in Vietnam, Delhi and Egypt is, however, different, and blood culture positivity rates among febrile cases have been reported to be only 8.5%, 5% and 4.2% respectively.

It should be borne in mind that the incidence of typhoid fever based upon blood culture is only half of the actual level. Moreover, isolation of the organism is often jeopardized by lack of facilities or inadequate or improper anti-
biotic use before culture. It has been reported that 71% of those participating in the sentinel surveillance system in Egypt were already using an antimicrobial agent at the time they sought treatment by a health provider. This is not surprising. Our study found 14% of typhoid bacilli and 57% of *S. paratyphi* strains to be multidrug resistant, a reflection of injudicious use of antibiotics in the community. Similar multidrug-resistant estimates have been reported from other studies in Bangladesh and Karachi. Additionally, contamination of blood cultures (quite a few contaminants, mostly skin flora reported from our samples) prevents the recovery of pathogens from a proportion of blood cultures.

Despite the above constraints resulting in poor culture yields from febrile episodes, in our study 39/341 (11.4%) tested positive for typhoid and 2% for *S. paratyphi*. Comparing the proportion of *S. enterica* serovar Typhi among *Salmonella* species in the positive cultures, 42 (85%) were positive for *S. enterica* serovar Typhi whereas seven (14%) were other Salmonellae (all *S. paratyphi* A). This spectrum is consistent with the yield from blood cultures across other studies. Taking only one blood sample could have contributed to the low culture yield. In the community setting it was not possible to take multiple blood samples as recommended in ideal conditions. However, it has been reported that the organism can be grown in 91.5% of septic episode first blood cultures and taking a second sample increases the chance to 99%. If we had taken three samples, we would have grown organism in 53 or 54 (~100%) septic episodes.

### Table 2 Presenting signs and symptoms of patients: whole group, typhoid patients positive by serology and positive by culture

<table>
<thead>
<tr>
<th>Sign/symptom</th>
<th>Overall n (%)</th>
<th>Serology-positive n (%)</th>
<th>Culture-positive n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever</td>
<td>338 (99.4)</td>
<td>206 (99.5)</td>
<td>48 (98)</td>
</tr>
<tr>
<td>Abdominal Pain</td>
<td>65 (19.1)</td>
<td>42 (20.4)</td>
<td>10 (20.4)</td>
</tr>
<tr>
<td>Cough</td>
<td>57 (16.8)</td>
<td>31 (15)</td>
<td>3 (6.1)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>43 (12.6)</td>
<td>25 (12.1)</td>
<td>7 (14.3)</td>
</tr>
<tr>
<td>Headache</td>
<td>26 (7.6)</td>
<td>19 (9.2)</td>
<td>1 (2)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>26 (7.6)</td>
<td>12 (5.8)</td>
<td>3 (6.1)</td>
</tr>
<tr>
<td>Myalgia/arthralgia</td>
<td>15 (4.4)</td>
<td>9 (4.4)</td>
<td>—</td>
</tr>
<tr>
<td>Anorexia</td>
<td>11 (3.2)</td>
<td>8 (3.9)</td>
<td>2 (4.1)</td>
</tr>
<tr>
<td>Weakness</td>
<td>6 (1.8)</td>
<td>4 (1.9)</td>
<td>2 (4.1)</td>
</tr>
<tr>
<td>Sore throat</td>
<td>6 (1.8)</td>
<td>3 (1.5)</td>
<td>—</td>
</tr>
<tr>
<td>Nausea</td>
<td>4 (1.2)</td>
<td>2 (1)</td>
<td>—</td>
</tr>
<tr>
<td>Chest discomfort</td>
<td>4 (1.2)</td>
<td>2 (1)</td>
<td>—</td>
</tr>
<tr>
<td>Dizziness</td>
<td>2 (0.6)</td>
<td>1 (0.5)</td>
<td>—</td>
</tr>
<tr>
<td>Constipation</td>
<td>1 (0.3)</td>
<td>1 (0.5)</td>
<td>—</td>
</tr>
<tr>
<td>Melena</td>
<td>1 (0.3)</td>
<td>1 (0.5)</td>
<td>—</td>
</tr>
<tr>
<td>Dysuria</td>
<td>1 (0.3)</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Obtundation</td>
<td>1 (0.3)</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Others</td>
<td>10 (2.9)</td>
<td>4 (1.9)</td>
<td>1 (2)</td>
</tr>
</tbody>
</table>

![Figure 4](image_url) Monthly average temperature, average precipitation and typhoid fever patient registration in Karachi, Pakistan, June 1991—December 2001.
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giving the incidence of 1.8/1000 person years, not far from that estimated. In our sample 37.0% (126/341) were taking antibiotics prior to the taking of a blood sample. This could be yet another factor leading to underestimation of the typhoid incidence. Thus, although an underestimate, our study confirms a high disease burden of typhoid fever in Karachi.

Our study found a significantly higher incidence of culture-positive typhoid fever in the 5–10 years age group. This is consistent with other settings, which show age-specific attack rates reaching a peak between 5 and 12 years. However, a high incidence among serologically positive cases in the >10–15 year age group in our sample should be viewed with caution. It could be a marker of past infection. It is already known that following acute infections patients may continue to excrete typhoid bacilli for several weeks to years. No culture-positive typhoid fever was detected in very young children. It should be noted that very few of the latter were brought to the clinics for screening. Other studies have also noted under-reporting in this age group, especially when case detection is passive. Moreover, there is a natural reluctance to draw 5 ml blood from infants. It has also been confirmed that typhoid fever may be milder or atypical in presentation in the preschool years due to an underdeveloped reticuloendothelial system.

In congruence with seasonality patterns elsewhere, marked seasonality in the incidence of typhoid fever was noted. In Vietnam, the peak occurrence was at the end of the dry season in March and April. In our study a peak occurs in October (second summer) when the temperature rises after rainfall. The same has been observed in Indonesia. Another, but smaller, peak is noted in May and June. Consumption of commercially prepared ice, ice creams and locally-made chilled drinks increases with the increase in temperature and some of these items have been identified as risk factors for typhoid fever in Karachi. Rains also cause flooding leading to mixing of sewage and drinking water. In the later part of the year both factors might play their roles and could be the reason for the highest incidence of typhoid fever in October. However, this needs further study.

Healthcare provider-based surveillance has been used to capture typhoid cases for vaccine studies and to measure typhoid fever incidence. However, such an approach needs consideration of the healthcare-seeking behavior of the population, existing healthcare systems, practices of the healthcare providers and precision of surveillance systems. It could be that we only screened 30% of fever cases identified during household surveillance, therefore cases were missed. Quick remedies for febrile illnesses (even at a high price) are common and acceptable at community level. Most of the providers had an established system for diagnosing and treating fever illnesses. Any alternative system of patient referral requiring further work-up was not a viable option for their market. This resulted in poor referral from community health providers to the study clinic. This raises the need to develop integrated models of syndrome-based management of febrile episodes, especially for primary care physicians lacking the facility of even basic laboratory tests. Local modifications of algorithms for the empiric management of febrile patients, e.g., fever module of the World Health Organization/United Nations Children’s Fund guidelines for the integrated management of childhood diseases, would be helpful.

Our study concludes that typhoid fever is endemic in this community with the highest incidence occurring in children (both girls and boys) of age 5–10 years, especially after rainfall months. Facility-based surveillance missed a significant proportion of potential cases raising the need for even more extensive surveillance systems. There is also a need to conduct studies on the healthcare-seeking behavior of the population, and practices of the healthcare providers, so that more precise studies can be designed to capture true incidence. This will ultimately be required in order to take the decision for the use of mass scale vaccination against typhoid fever in high-risk age groups.

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