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Upsurge of *Salmonella* Paratyphi a infection in and around Puducherry following the torrential rains of December 2015

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Abstract

Introduction: Incidence of *Salmonella* Paratyphi A is on the increasing trend as compared to *S*.Typhi in the past few decades, in India. This upsurge in the incidence of paratyphoid fever is a large financial burden and of great public health concern. Following heavy rain fall, we observed clustering of paratyphoid cases from Puducherry. Hence this study was conducted to evaluate the demographic profile and antimicrobial susceptibility pattern of these *S*.Paratyphi A isolates.

Material & Methods: Retrospective analysis was done among 43 paratyphoid cases, for analysing their demographic profile, clinical profile, antibiogram pattern and treatment given for them.

Results: All 43 *S*.Paratyphi A isolates were from in and around Puducherry within 10 kilometers, with similar clinical profile and showed uniform susceptibility to first line antibiotics, azithromycin and ceftriaxone. All the isolates showed reduced susceptibility to ciprofloxacin. The outbreak lasted for four months, and probably due to good sanitation, water chlorination and good drainage facilities helped to control the outbreak.

Conclusion: *S.Paratyphi A* is replacing *S*.Typhi in Puducherry. Clustering of cases with same antibiogram over a short time period in a geographically restricted area needs to be further evaluated as an outbreak, which has to be tackled precisely and effective preventive measures needs to be undertaken to prevent such outbreaks in future.

Keywords: *Salmonella* Paratyphi A, Paratyphoid Fever, Outbreak, Ciprofloxacin, Rain Fall, Antibiogram, Young Adults, Puducherry.

Background

Enteric fever is a systemic illness, endemic in India and caused mainly by *Salmonella* enterica serovar Typhi (*S*.Typhi) and *Salmonella* Paratyphi A. Every year more than 22 million cases and 6,00,000 deaths occur worldwide from enteric fever.[1] Incidence of *Salmonella* Paratyphi A is on the increasing trend as compared to *S*.Typhi in the past few decades, with a unique antimicrobial susceptibility pattern of being resistant to fluoroquinolones and showing uniform susceptibility to first line antimicrobials like ampicillin, chloramphenicol and cotrimoxazole.[2] This upsurge in the incidence of paratyphoid fever is posing a major public health concern in this part of subcontinent.[3]

Recent reports from various parts of India showed an increase in the incidence of paratyphoid fever in many regions such as the urban slums at New Delhi, Chandigarh, Shimla, Mumbai, Nagpur, Kolkata, Rourkela, Karnataka, Chennai, and Kozhikode.[1,4–6] More recently, a multi-centric surveillance study carried out by Indian Network for Surveillance of Antimicrobial Resistance Group showed that a total of 764 *Salmonella* Paratyphi A strains were isolated between January 2008 to December 2010 from all 15 participating centres throughout India.[6,7]

Outbreaks of enteric fever due to *S*.Typhi have been reported periodically from places in and around Puducherry.[8,9] But this is probably for the first time, clustering of cases due to *S*.Paratyphi A is being reported from Puducherry. Hence this study was conducted to analyse the demographic profile of these paratyphoid fever cases and antimicrobial susceptibility pattern of these *S*.Paratyphi A isolates.

Materials & Methods

A retrospective analysis of forty seven *Salmonella* species isolated from blood of patients suspected with enteric fever, during the period of December 2015 to April 2016, was done after obtaining waiver of consent from the Institute Ethics committee at a tertiary care hospital, Puducherry. The following data were retrieved for analysis from medical records and from the laboratory records: Demographic characteristics of patients, clinical presentation, and serotyping.

Blood samples from clinically suspected enteric fever cases were inoculated on to BacT/ALERT blood culture bottles and incubated, once positive growth signal is obtained, subcultures were made onto standard culture media. Following overnight incubation, the isolates were identified by performing Gram smear, standard biochemical tests and further confirmed by serotyping with specific *Salmonella* polyvalent antisera O and with O2 or O9 antisera.[10]

Total of 43 *Salmonella* Paratyphi A and 4 *Salmonella* Typhi strains were isolated. Out of which only 43 *S*.Paratyphi A isolates were included in the study for further analysis. Isolates were subjected for antimicrobial susceptibility testing for ampicillin 10 µg, cotrimoxazole 25 µg, chloramphenicol 30 µg, cifprofloxacin 5 µg, ceftriaxone 30 µg and azithromycin 15 µg by Kirby Bauer disc diffusion testing using 0.5 Mc Farland bacterial suspension on

Mueller-Hinton agar. Isolates with intermediate levels of resistance to ciprofloxacin by disk diffusion testing were further subjected to estimation of minimum inhibitory concentration (MIC) of ciprofloxacin by epsilometer strip test method (HiMedia, Mumbai India). The antimicrobial agent concentration, at which edge of the inhibition ellipse intersects the side of the E-strip, was taken as MIC value. *Escherichia coli* ATCC 25922 was used as quality control strain for both the disc diffusion and MIC testing. Data entry and analysis was done using Microsoft Excel.

Results

Among the 47 enteric fever isolates during the period of four months, 43 isolates were *S.*Paratyphi A and four were *S.*Typhi. Among the 43 paratyphoid cases, 26 (60.4%) of them were males and 17 (39.6%) were females, with male to female ratio was 1.5:1.

Age of the patients ranged between 5 to 65 years and mean age was 25±5 years with maximum cases between 13 to 30 years (65%). Paediatric cases of less than 12 years accounted for 5 cases (1.2%). Age distribution of paratyphoid cases is shown in Fig. 1.

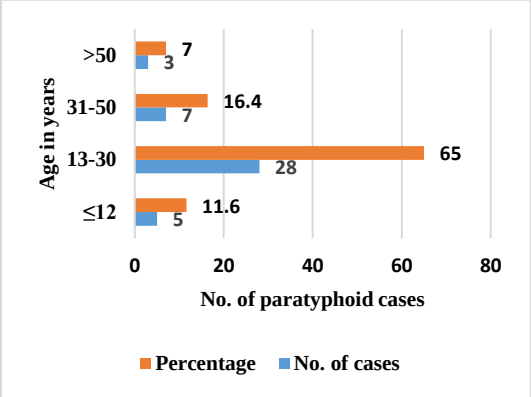

Fig. 1: Age distribution of paratyphoid cases

All of the paratyphoid cases were from in and around the Union Territory of Puducherry within the perimeter of around 10 Kilometers. Majority of the cases were from in and around Kalapet (23.3%), followed by Villianur (16.2%), Chinna Kalapet (9.3%), Kottakuppam (9.3%), Cuddalore (9.3%) and Vanur (7%). The first case to be reported was on 10th of December 2015 from Kalapet. Fig. 2 shows area wise distribution of paratyphoid cases in around Union Territory of Puducherry.

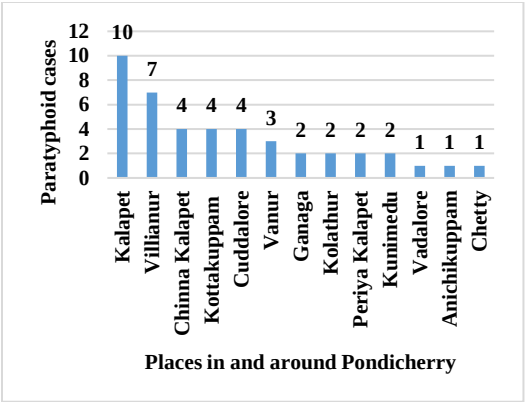

Fig. 2: Area wise distribution of paratyphoid cases.

Total of 43 paratyphoid cases were reported during the short period of four months duration. There was steep rise in the number of cases from last week of December 2015 to March 2016 and maximum number of cases were reported in the month of March 2016, following which there was fall in the cases reported. Paratyphoid fever cases in Puducherry following torrential rain fall in December 2015 is shown in the fig. 3.

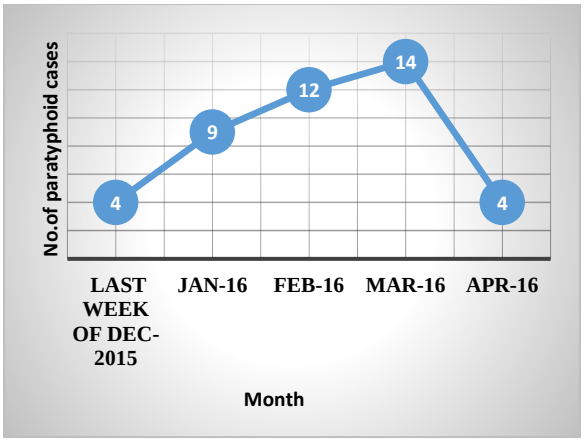

Fig. 3: Paratyphoid fever cases in Puducherry (December 2015 to April 2016)

Among these cases, fever was the chief presenting complaint with the duration ranging from 3- 10 days. Other associated symptoms were abdominal pain, diarrhoea, vomiting and constipation. All the patients were inpatients and were hospitalised for 3 to 6 days. All *S.*Paratyphi A isolates had uniform antibiogram pattern, being susceptible to ampicillin, chloramphenicol, cotrimoxazole, ceftriaxone, azithromycin with reduced susceptibility to ciprofloxacin, by disk diffusion testing, which was further confirmed by MIC testing. Ciprofloxacin MIC ranged between 0.19 µg/mL to 0.5 µg/mL; all were intermediate susceptible to ciprofloxacin. Fig. 4 shows distribution of MIC value of ciprofloxacin among 43 paratyphoid isolates.

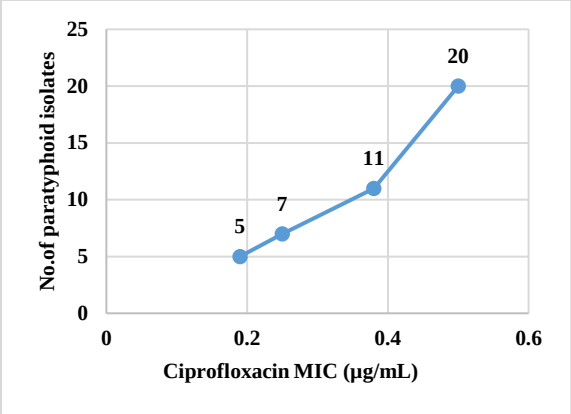

Fig. 4: Distribution of MIC value of ciprofloxacin among 43 paratyphoid isolates

Among the 43 cases, 20 cases (46.4%) were treated with combination of inj. ceftriaxone 2gm I.V. for 1day and tablet cefixime 200mg for 4days, followed by 15 cases (35%) received combination of injection ceftriaxone 2g for 3days and tablet azithromycin 500mg for 10days and eight cases (18.6%) received tablet azithromycin 500mg for 5days. None of them suffered from any complications and improved on discharge. Fig. 5 shows treatment received by 43 paratyphoid cases.

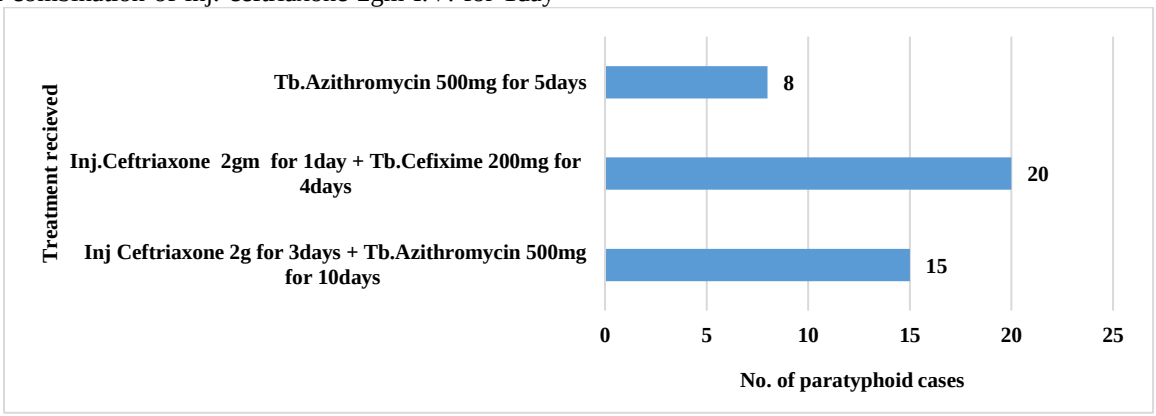

Fig. 5: Treatment received by 43 paratyphoid cases

Discussion

Enteric fever is serious public health problem in India.[2] Main contributing risk factors for prevalence of enteric fever are contaminated food and water, poor sanitation, close contact with cases or carriers, closer location to water bodies, and poor personal hygiene.[11] Climatic variables such as, rainfall, flooding have an important effect on the transmission and distribution of enteric fever infections in human populations.[12,13] The onset of present clustering of enteric fever cases also coincides following a torrential rain fall in Puducherry and Chennai, which has led to the probable contamination of sewage water with drinking water sources.

In India, *Salmonella* Paratyphi A was the less frequent cause of enteric fever in earlier days (3-17%).[8,9] However, over the period of time there is a steady increase in the incidence of *S*.Paratyphi A cases in many parts of the country including Puducherry.[14] During this period of 4 months duration, 47 enteric cases were reported of which only 4 were typhoid fever cases. As enteric fever is endemic in Puducherry[8,9] these cases would be the part of usual occurrence of cases and not part of this epidemic outbreak. From our observation it appears that *S*.Paratyphi A is replacing *Salmonella* Typhi in Puducherry. The disproportionate increase in the numbers of *S*. Paratyphi A cases may be due to the typhoid vaccine effect (Ty21a and Vi vaccines), which protects individuals only from typhoid fever and also reduction strategies which were effectively used against *S*.Typhi control might not be useful against *S*. Paratyphi A.[6,15] Due to this *S*.Typhi infections are getting under control and isolation of *S*.Paratyphi A is becoming more common.

According to WHO definition of a disease outbreak is the occurrence of cases of disease in excess of what would normally be expected in a defined community, geographical area or season. Clustering of cases during this short period of four months in a geographically restricted area may be considered as an outbreak; however further demographic localization of these cases needs to done to declare it as an outbreak of paratyphoid fever.

The incidence of enteric fever varies with age groups and seasons. The incidence of paratyphoid fever is highest among teenagers and young adults; whereas typhoid fever is more common in children.[16] Similar observations were observed in the present study with

majority of cases belonged to the age group of 13-30 years (65%). This is possibly due to a different mode of transmission between *S.* Typhi and *S.* Paratyphi A. *Salmonella* Typhi is mainly transmitted by household contact. In contrast, *S.*Paratyphi A is mainly transmitted by contaminated food from a street vendor.[3,17] Various studies have shown that, during outbreaks of enteric fever, paediatric and young adult population bears the burden of disease.[18]

Various researchers from India and Nepal have reported higher incidence of cases during monsoon season, which can be explained by heavy rain fall or flooding causing a greater risk of water stagnation and contamination.[3,17] We observed a steady rise in the number of paratyphoid cases over a period of 4 months from last week of December 2015 to April 2016 and a steep fall afterwards. The reason for this clustering of cases could be the torrential rain fall, which occurred during the November last week and 1st week of December 2015.

All 43 isolates were reported had similar demographic details. They were from common geographical area in and around 10 kilometres of Union Territory of Puducherry, majority of them were young adults, had similar clinical profile and showed good improvement with adequate anti-enteric fever treatment, all were serotyped as *S.*Paratyphi A and had similar antimicrobial susceptibility pattern with uniform susceptibility to ampicillin, chloramphenicol, ceftriaxone, cotrimoxazole, azithromycin and decreased susceptibility to ciprofloxacin. Earlier reports from Puducherry have shown decline in the number of multidrug resistant *Salmonella* isolates and concurrently increase in the number of isolates sensitive to all antibiotics except nalidixic acid with reduced susceptibility to ciprofloxacin. [8,19] Similar antimicrobial susceptibility pattern we have observed among all 43 isolates. Based on our observation it is very clear that ceftriaxone and azithromycin can be used for effective management of enteric fever cases in our tertiary care centre.

Steady fall in the cases after 4 months could be probably attributed to improvement in access to clean water and improved sanitation and drainage facilities by the Government of Puducherry.

Conclusion

From our observation it appears that *S.Paratyphi A* is replacing *S.* Typhi in Puducherry. Clustering of cases with same antibiogram over a short time period in a geographically restricted area needs to be evaluated further as an outbreak, which has to be tackled meticulously and adequate preventive measures to be planned to avoid such outbreaks in future. Awareness among the residents on importance of use of safe drinking water and good environmental sanitation practices needs to be created.

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