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Original Article

Age distribution of patients presenting with typhoid and paratyphoid fever in Kathmandu, Nepal

Damodar Gajurel*, Rabi Prakash Sharma, Krishna Dhungana, Niranjan Acharya, Prasant Karki and Sudikshya Acharya.

[1]Department of Medicine, Civil Service Hospital, Minbhawan, Kathmandu, Nepal

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Abstract

Background

Enteric fever is a significant cause of morbidity in Nepal. In the past, *Salmonella enterica*serovar Typhi (*S.* Typhi) was the major causative organism of enteric fever. However, more recently, *Salmonella enterica*serovar Paratyphi (*S.*Paratyphi) A has been isolated from most patients presenting with enteric fever in various regions of Nepal. This study aimed to evaluate age differences in patients presenting with typhoid and paratyphoid fever.

Materials & Methods

Between December 2014 and October 2015, 186 patients presented with enteric fever to the Civil Service Hospital in Kathmandu. *S.* Typhi and *S.*Paratyphi A were isolated from blood cultures in 48.4% and 51.6% of the cases, respectively. Age groups of the patients infected with either serovar were compared.

Results

The mean age of patients from whom *S.* Typhi was isolated was 19.3 years, while the mean age of patients from whom *S.* Paratyphi A was isolated was 25.2 years; p=0.025.

Conclusion

Our study shows that age is an important factor in having either typhoid or paratyphoid fever. This will help in the prevention of typhoid and paratyphoid fever in various age groups.

Key words

S. Typhi, S. Paratyphi A

Introduction

Enteric fever is a significant cause of morbidity and mortality worldwide [1]. Typhoid fever and paratyphoid fever fall under the umbrella of enteric fever, caused by the bacteria *Salmonella enterica* serovar Typhi *(S*. Typhi) and *Salmonella enterica* serovar Paratyphi (*S*. Paratyphi) A, B and C [2]. It is estimated that in the year 2000 alone, typhoid fever caused over 21.6 million illnesses and over 200,000 deaths worldwide [1]. In the same year, it was estimated that there were over 5 million illnesses of paratyphoid fever. The incidence of typhoid fever was the highest in south-east Asia and south-central Asia at above 100/100,000 cases per year [1]. These findings are comparable to a systematic review conducted in 2010 which reported an estimated 26.9 million typhoid fever cases that year [3]. While *S.* Typhi is reported to be the more common

Corresponding Author: **Dr. Damodar Gajurel, Senior Consultant | E-mail: drdg188@gmail.com*

cause of enteric fever, *S.* Paratyphi A has also emerged as a significant cause of illness in Asia [4].

Enteric fever thrives in overcrowded and unsanitary environments across the developing world [5]. *Salmonella* spp. are shed in urine and faeces and are mainly transmitted through ingestion of contaminated food or water [5]. In less industrialized countries such as Nepal, where unsafe drinking water, inadequate disposal of sewage, and flooding are common, these organisms are transmitted through the ingestion of contaminated water [6]. *S.* Typhi and *S.* Paratyphi A cause systemic infections and upon the onset of bacteremia, patients present to the hospital with fever and malaise [5]. In Nepal, *Salmonella* infection is a common cause of fever. In this study, the rates of *S*. Typhi and *S*. Paratyphi A infections in Kathmandu are compared, and the age distribution of patients infected with either serovar is evaluated.

Materials & Methods

The Widal agglutination test continues to be a popular method for detection of typhoid fever; however, it has low specificity and sensitivity [7]. Isolation of the organism provides more accurate detection and remains the gold standard for diagnosis of enteric fever [7,8]. The Civil Service Hospital in Kathmandu is one of the few locations in Nepal where affordable culture facilities are available for the diagnosis of bacterial infections. The isolation of specific *Salmonella* spp. from blood cultures provides a clearer picture of the prevalence of typhoid and paratyphoid fever in the community. Furthermore, easy and affordable access to medical services at this location attracts many patients from various ethnic and economic backgrounds. As such, patients presenting to this facility are representative of the general Nepalese population.

Between December 16, 2014 and October 17, 2015 (Poush, 2071 to Ashwin, 2072) 5151 blood samples were collected and cultured at the Civil Service Hospital. Microbial growth was first detected using the automated BACTEC™ FX blood culture system. Positive samples were then cultured in MacConkey agar and blood agar for detection of specific bacteria. For the purpose of this study, 186 culture positive cases of *S.* Typhi and *S.* Paratyphi A were retrospectively evaluated. All medical data were obtained from the electronic medical records software, MiDAS. Data analysis was performed with Excel 2013 for Windows and IBM SPSS Statistics 20 for Windows. Student's t test was used to obtain the mean ages, standard deviations and the significance of the difference in the mean ages between the *S*. Typhi group and the *S*. Paratyphi A group. The level of significance was $p = 0.025$.

Results

Among the 5151 total blood samples that were cultured in 10 months, there were 186 positive cases of enteric fever (3.6%). *S.* Typhi was isolated from 90 patients (48.4%) and *S*. Paratyphi A was isolated from 96 patients (51.6%). The male to female ratio was 1.4:1 and 1.7:1 for *S.* Typhi and *S.* Paratyphi A, respectively. The mean age of patients from whom *S.* Typhi was isolated was 19.3 years (SD = 9.0), while the mean age of patients from whom *S.* Paratyphi A was isolated was 25.2 years (SD = 12.6). This difference was significant with a p value of 0.025. The 95% confidence interval was 17.4 – 21.2 years and 22.8 – 28.0 years for the S. Typhi and S. Paratyphi A groups, respectively. As shown in figure 1, the frequency of *S.* Typhiwas higher in the younger age groups while the frequency of *S.*Paratyphi A was higher in the older age groups.

*Corresponding Author: **Dr. Damodar Gajurel,** Senior Consultant | E-mail: drdg188@gmail.com

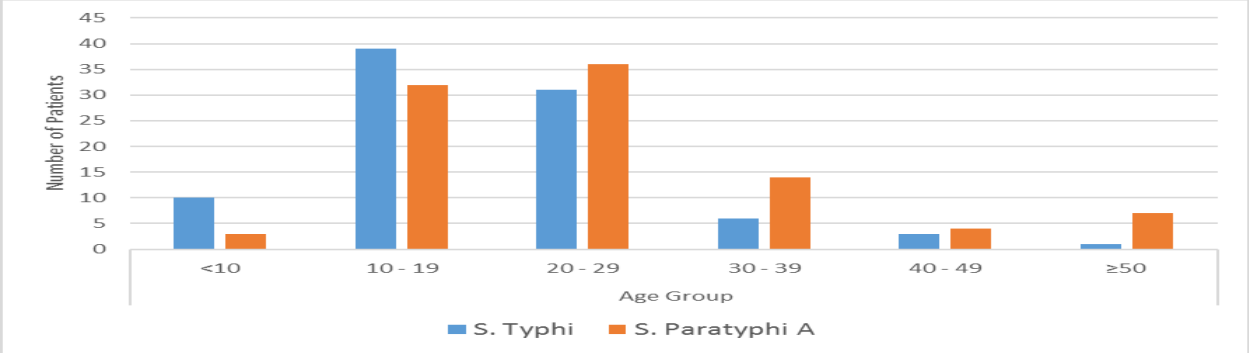

Figure 1. Age distribution of patients infected with S. Typhi versus S. Paratyphi A.

Discussion

S. Typhi has an earlier evolutionary history and has been the more common causative agent of enteric fever in the past [8,9]. However, recent evidence suggests that *S.* Paratyphi A has emerged as a significant cause of enteric fever in Asia [4]. In fact, in south-east China *S.* Paratyphi A is the major causative agent, surpassing *S.* Typhi. *S.*Paratyphi A accounts for a significant proportion of enteric fever cases in India and Pakistan as well [4]. Furthermore, this serovar was isolated from over half of the patients presenting with enteric fever to hospitals in Chitwan and Kathmandu [10,11]. Similarly, in this study, *S.* paratyphi A was the causative organism in 51.6% of the enteric fever cases, corroborating the emerging threat of this organism across south-east Asia. Both typhoid and paratyphoid fever were more common in males than in females. This finding is consistent with other studies performed in Nepal [12,13].

This study demonstrates a significant difference in the mean ages of typhoid patients when compared to paratyphoid patients. Typhoid fever was associated with younger age, while paratyphoid fever was associated with older age. The association of typhoid fever with young age has been validated by numerous national and international studies [12-14]. Immunity against *S.* Typhi lasts approximately one year after the onset of illness in non-endemic areas [15]. However, there is evidence to suggest lifelong immunity in endemic areas where the host receives persistent booster stimulations of *S.* Typhi bacilli from the environment [15]. *S.* Typhi is endemic in Nepal and many adults have suffered from typhoid fever in childhood. As such, it is possible that adults who recovered from *S.* Typhi infections in childhood, and are living in this endemic area, have acquired lifelong immunity against this serovar, resulting in a decreased frequency of typhoid fever in the older population.

With *S.*Paratyphi A becoming increasingly more common in Asia, it is possible that previously unexposed adults are now being exposed to and suffering from paratyphoid infections. *S.* Typhi specific vaccines provide little, if any cross protection against *S.*Paratyphi A [9]. Therefore, it is safe to assume the same is true after natural infection with *S.* Typhi. This may explain the higher number of paratyphoid cases in the older age groups. Other literature also states that paratyphoid fever is more frequently observed in adults [4].

Evidence from Indonesia shows that risk factors for typhoid fever include lack of sanitation facilities, hand-washing without soap, typhoid patients in the household, and sharing food from the same plate (i.e. factors within the household) [14]. Interestingly, paratyphoid fever seems to have different risk factors such as consumption of food from street vendors and flooding (i.e. factors outside the

*Corresponding Author: **Dr. Damodar Gajurel,** Senior Consultant | E-mail: drdg188@gmail.com

household) [14]. Such a clear distinction between the risk factors for typhoid and paratyphoid fever warrants closer investigation into age-related exposure levels to these factors. For instance, children may share food from the same plate more frequently than adults or they may be more likely to practice hand-washing without soap. Such investigations may provide a better understanding of the findings of this study. Furthermore, it will also aid in the design and implementation of effective interventions for the prevention of transmission.

Conclusion

Enteric fever continues to be an important public health concern in Nepal. While *S.* Typhi has been the major causative organism for decades, *S.* Paratyphi A has emerged as an equally significant threat. As humans are the only host of the causative organisms, elimination is possible. Further studies for the identification of age-related typhoid- and paratyphoid-specific risk factors will aid in prevention and elimination efforts.

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*Corresponding Author: **Dr. Damodar Gajurel,** Senior Consultant | E-mail: drdg188@gmail.com