



## Prevalence of Enteric Fever in the Local Population of Rawalpindi And Islamabad Pakistan

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### Abstract

Enteric fever is the massive bacterial disease in global and caused by *Salmonella typhi*. It is known that humans are the only natural host and reservoir for *S. typhi*. That transmits enteric fever through the fecal-oral route through the ingestion of infected water and food. The prevalence rate is high in South Central and South-East Asian countries recorded as (>100/100,000) cases per year. The aim of designing of the present study, there is no specific epidemiology report present at Rawalpindi and Islamabad. Total of 500 blood samples were collected from patients showing sign and symptoms of enteric fever. Sample collected from different government and private hospitals, medical laboratories, and health organizations from November 2013 to April 2014. Immuno chromatographic technique (ICT) was used for the detection of enteric fever via typhoid test kit. Out of 500 samples, 368 (73.6 %) patients were found serologically negative while 132 (26.4%) were positive. Among the positive samples, 42 (31.8%) were adult samples that included 25 IgM, 12 IgG and 5 both IgM and IgG. Infected children of age 13-15 years were 30 (22.72%) with IgM 19, IgG 8 and both IgM and IgG 3. Thirty-one (31) samples were positive among children of age group 5-12 years with 15 IgM positive, 10 IgG positive and 3 both IgM and IgG positive. Furthermore, 29 (21.96 %) were positive among children of age group 1-4 years. This high incidence of enteric fever among susceptible outdoor patients and laboratories patient show that enteric fever is a serious health problem in Rawalpindi, Islamabad. Preventive measures such as vaccination, maintaining food hygiene and awareness campaign are required in the twin cities of Rawalpindi-Islamabad for the eradication of enteric fever.

**Keywords:** Enteric Fever; Salmonella Paratyphi; Salmonella Typhi; Pakistan;

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## 1. INTRODUCTION

Enteric fever is the massive bacterial disease in the world. Its etiological agent is *Salmonella typhi*. *S. typhi* is a motile facultative anaerobic rod-shaped Gram-negative bacterium, closely related to *Escherichia coli* and belongs to family *Enterobacteriaceae*<sup>1</sup>. This clinical disorder caused by *Salmonella* disease in humans is generally separated into two groups: dissemination of enteric fever is occurred due to infected food and water by both *S. Typhi* and *S. paratyphi*<sup>2</sup>.

In the past outbreak of 424-430 BC, in which some people believed that it is caused by enteric fever, killed one-third of the population of Athens including their leaders and nobles and at the end the power shifted from Athens to Sparta and thus the Golden age of Athens come to end in the ancient world<sup>3</sup>. Enteric fever is the massive bacterial disease in the world that is caused by *Salmonella paratyphi* accounts for 10-20% of all cases of enteric fever caused by *Salmonella*. In Asia the ratio of enteric fever is very high as compared to south-eastern and south-central regions of world. It is estimated that around hundred cases per hundred thousand (100 cases / 100,000 cases) occur due to poor sanitation, however, better sanitation and good health care are thought to reduce the infection of enteric fever<sup>4</sup>. Worldwide, about 21 million people are affected from enteric with mortality of rate of 200,000<sup>5</sup>.

Currently there are 2,463 serotypes of *Salmonella* bacteria. The nomenclature concept proposed by the Kauffmann for the *salmonella* genus, initially has developed from one serotype-one species based on the serologic identification of H (flagellar) and O (osmotic) antigens. Individual serotype was considered a distinct species, for instance (*S. Enteritidis*, *S. Newport*, and *S. Paratyphi A*). Based on the clinical role of a strain further taxonomic classification have been proposed, on biochemical characteristics that classified serotypes into subgenera, and eventually, on genomic similarity. The seven subgenera of *Salmonella* bacteria were referred to as subspecies such as (I, II, IIIa, IIIb, IV, V, and VI), proposed by Le Minor and Popoff in 1987. Because of biochemical reactions and genomic relatedness, the subgenus III was further divided into IIIa and IIIb. In 1979 Rohde integrated all *Arizona* serotypes into the Kauffmann-White<sup>6</sup>.

It is known that humans are the only natural host and reservoir for *S. Typhi*<sup>7</sup>. That transmits enteric fever through the fecal-oral route by the ingestion of contaminated water and food<sup>8</sup>. Therefore, preventive strategies against enteric fever include provision of hygienic water supply; proper sanitary disposal of human urine and feces, sterile manufacture of drinks and foods, maintenance of hygiene and cleanliness while cooking at home and proper hand-washing facilities where food is handled. Furthermore, barring of patients of enteric fever from food handling tasks and awareness of public about appropriate hand washing, consumption of unhygienic foods and drinks are also important for the prevention of enteric fever. Currently, the South Africa Government has adopted procedures for achieving some of the above-mentioned strategies. For instance, authorized and governmental frameworks have been put in place to give all South African residents access to basic water supply and cleanliness. Health education programs have been initiated to make community awareness to consumptions of contaminated foods and drinks<sup>9</sup>. Enteric fever has a major socio-economic impact because a number of months are required for a patient to recover his health and work normally again. Although, the causative agents and transmission of malaria and enteric are different but both share similar sign and symptoms<sup>10</sup>.

The risk factors which are involved in individual level are unhygienic water supply and contaminated food, the utilization of spoil vegetables and fruits, and keep in a contact with other patients or chronic carriers; risk factors on community-level is consist of inhabitants density, rainfall, river level, temperature, and proximity to water sources<sup>11</sup>.

Chronological examination data recommend that enteric fever was prevalent in North America and Western Europe. To continuously minimize with the initiation of municipal water management, dairy products pasteurization, and the excretion of human feces from food production. Currently, enteric fever hindrance focuses on developing proper sanitation; make sure the protection of cuisine and supplies of water, detection, and cure of persistent vectors of *S. typhi* and use of typhoid vaccines to decrease the

vulnerability of hosts to disease<sup>12</sup>. The aim of the current study is to determine the prevalence of enteric fever in the local population of twin cities of Rawalpindi Islamabad to find out the age group at risk towards *S. typhi* bacteria.

## 2. MATERIALS AND METHODS

### 2.1 Study area

A field survey was conducted in District Rawalpindi and Islamabad to get comprehensive information about the causes and prevalence of enteric fever in pre-school aged; school-aged children and adults. Data were collected from different sources like government and private hospitals, clinics, medical laboratories, health organizations, Pakistan Institute of Medical Sciences Islamabad, Polyclinic Hospital Islamabad, Shifa International Hospital Islamabad, National Institute of Health Islamabad, District Head Quarter Hospital Rawalpindi, Hearts International Hospital Rawalpindi, Railway Hospital Rawalpindi, Benazir Bhutto Hospital Rawalpindi, Bilal Hospital Rawalpindi (BH), Combined Military Hospital Rawalpindi, Islamabad Diagnostic Center, Ali Medical Center Islamabad, Bio Care Lab Islamabad and Computerized Innovative Tests and Investigation Lab Rawalpindi.

### 2.2 Data collection and processing

A questionnaire was prepared to collect information from the patients of different hospital, medical laboratories, and various health settings of Rawalpindi and Islamabad, Pakistan. Information was collected through pre-formed questionnaires from suspected patients of different age groups i.e. children of pre-school; school-aged and adults who were showing and symptoms of enteric fever.

### 2.3 Sample collection and storage

Sterilized the area surrounded by the median cubital vein of the arm through alcoholic swab and tourniquet is placed around the upper arm for pressure of the blood. Through the vein puncture technique, about 3 millilitres of blood were drawn from each suspected patient.

### 2.4 Laboratory procedure

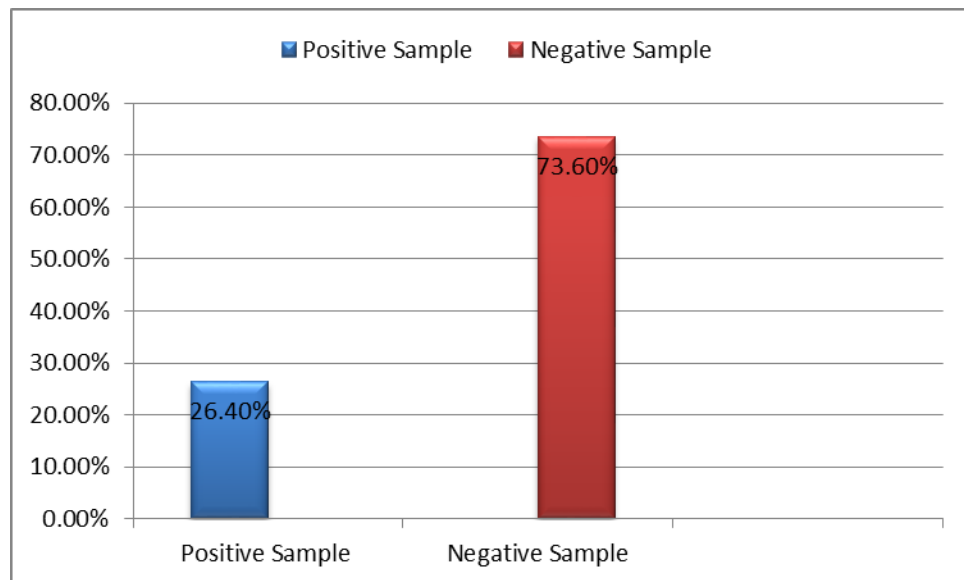
Blood samples were centrifuged at 3000 rpm for 5 minutes for separation of serum and stored at 2-8 °C for up to 3 days. For long term storage the samples were placed at -20°C. The sample was thawed, mixed well and brought to room temperature for performing the test. Orient Gene Biotech ([www.orientgene.com](http://www.orientgene.com)) the Typhoid IgG/IgM Rapid Test Kit was used for diagnosis of enteric fever. Briefly, 50-μL sera loaded on the kit through pipette dropper followed by addition of 1-2 drops of the buffer. Wait for 2-5 minutes for antigen antibody interaction which produces color band ICT strip. In addition to Control band (C), there are bands for the IgG and IgM indicating that the test is whether positive for the IgG or IgM antibody against *S. typhi*. The appearance of band in both IgM/IgG shows positive while no band shows negative result.

### 2.5 Statistical analysis

Data were analyzed by using descriptive statistics test, and percentage. Data were expressed in tabular and charts forms.

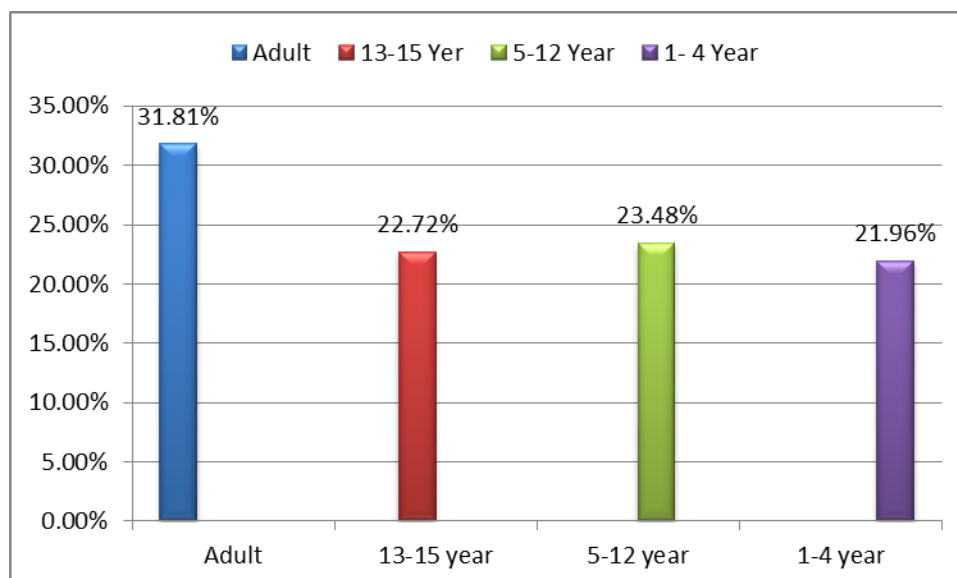
## 3. RESULTS AND DISCUSSIONS

In the current study, 500 samples were selected on clinical basis for diagnosis of enteric fever. Typhidot test was used for all samples for the diagnosis of typhoid in the suspected patients showing signs and symptoms of typhoid. Out of 500 suspected patients, 132 (26.4%) were typhoid positive and 368 (73.6%) were typhoid negative on the ICT strip (Fig. 1).



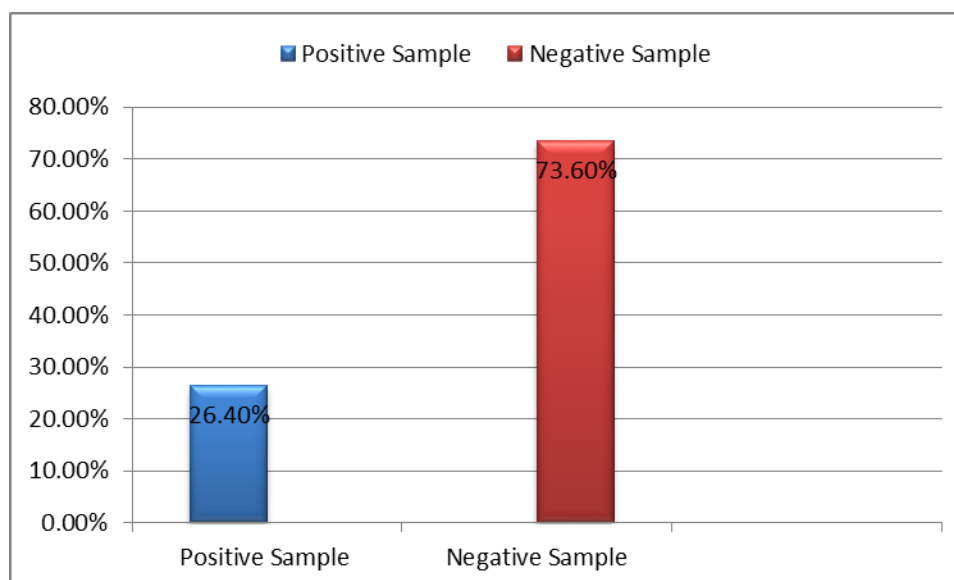
**Fig. 1.** Prevalence of positive sample of enteric fever in various age groups

Among the different age group the incidence of enteric fever was highest among the adults (31.8%) as compared to 13-15 years (22.7%) school-age children, 5-12 years (23.48%) school-age children and pre-school age children (21.96) (Fig. 2).



**Fig. 2.** Prevalence of positive sample of enteric fever in various age groups

Anti-typhoid IgM was found in 25 samples out of total and anti-typhoid IgG was determined in 12 samples whereas 5 samples were positive for both anti-typhoid IgG and IgG antibodies in adult group. In school-age children (13-15 years) group, 19 samples were positive for IgM, 8 samples were positive IgG and 3 samples were positive for IgM/IgG. In school-age Children (5-12 years) age group IgM positive children (1-4) year age group, 29 samples were positive only for IgM, neither sample was found positive for IgM nor for IgG (Fig. 3).



**Fig. 3.** Prevalence of IgM, IgG and IgM/ IgG samples of enteric fever

IgM positive samples indicates early stage or first time infection of enteric fever while IgG positive indicates past infection. The study could not be proceeded for further analysis i.e. ELISA, Polymerase Chain Reaction (PCR) and blood culture because of limited resources. Some earlier studies indicate the same finding<sup>13</sup>. Such outcomes may be because adults were more attracted towards street foods while outing with friends and drink unsafe water during visiting.

Enteric fever is a serious public health issue in the world. The prevalence rate is high in South Central and South-East Asian countries recorded as (>100/100,000) cases per year<sup>4</sup>. In Pakistan, enteric fever is widespread, and the most important causes for the high incidence rate are overpopulation, lack of knowledge, poverty, poor drinking water, and inadequate facilities for sanitary waste. A survey collected from Karachi, Pakistan via serology and blood culture shows prevalence 710 per 100,000 cases<sup>2</sup>. In the recent study, it has been observed that typhoid prevalence is low among preschool-aged children (1-4 years) and school-age children (5-12 years) as compared to adults. Our findings support the observations of Sinha et al, Lin et al and Rafiq et al who reported 11%, 17% 44% enteric cases in adult respectively in Viet-Nam, India and Pakistan,<sup>14,15,16</sup>.

Conversely, enteric fever among preschool-aged children is unusual and subclinical<sup>17, 18</sup>. This might be because of difficulty in taking samples from the infants for the cultured based diagnosis of enteric fever. The current study shows comparable incidence of typhoid in preschool children and school-aged children while in adults it is relatively high. However, Crump et al, report heavy burden of enteric fever in adolescents, children, and infants. The cuisines which are prepared under unhygienic conditions such as cold ice creams and beverages in the streets can play a vital role in the incidence of enteric fever among adolescents and school-aged children<sup>19</sup>.

Typhidot test is a rapid serological test for the detection of enteric fever. Though, its usefulness in terms of Specificity and sensitivity as compared to the Widal test. Typhidot test depends on the detection of antibodies that appear in detectable titers as the onset of 2-3 days of the infection. According to Yadav et al, Typhidot test showed 85 percent of sensitivity and 100 percent specificity in blood culture-confirmed cases of enteric fever as compared to the Widal test which has 45 percent sensitivity and 86 percent specificity. Typhidot test detects IgM and IgG antibodies against the *S. typhi* outer membrane protein (OMP). After the onset of 2-3 days of infection, the Typhidot test is positive and detects IgM and IgG antibodies separately. The Typhidot test is based on the presence of IgM and IgG antibodies specific to 50KD (Kilo Dalton) OMP antigen, which is immobilized on nitrocellulose strips<sup>20</sup>.

Detection of IgM antibody show acute typhoid (early infection phase) while the detection of both IgG and IgM antibodies also indicates acute typhoid (middle infection phase). The detection of specific IgG antibody is high in highly endemic areas with high frequency of typhoid transmission. Since after the infection the anti-typhoid IgG antibodies last for more than two years<sup>21</sup>.

The proportion of infection caused by *S. paratyphi*, as compared to *Salmonella Typhi*, is highly variable depending on the geographical background. It's believed that *S. paratyphi* is responsible for about one-fifth of cases of enteric fever<sup>4</sup>. Increasing prevalence of *S. paratyphi* infection over the past two decades is responsible for increase in the incidence of enteric fever in parts of Asia, including Cambodia<sup>22</sup>, Nepal<sup>23</sup> and China. According to Arndt et al, the maximum burden of paratyphoid fever has been reported from China, with an expected yearly occurrence of 150 cases/100 000 person-years. The existing data for Africa show that *S. Paratyphi* is accountable for less than two percent of enteric fever cases<sup>24</sup>.

In South Central Asian countries, like Pakistan, enteric fever is the major infectious disease; it has been responsible for causing a high rate of mortality and morbidity in South East Asian countries. Numerous periodic or plague cases have been recorded all over the entire year across the country. In rural areas, enteric fever is still widespread due to the lack of pure drinking water supply, less hygiene, and contaminated food. Enteric fever can be a major indicator of the socio-economic situation of inhabitants in other Asian countries. Throughout the world, Pakistan, Nepal, India, Mexico, Egypt, Indonesia, and Peru are the mainly notorious hotspots for enteric fever<sup>25</sup>. This high prevalence of enteric fever in Pakistan is mostly added via continual poverty, less personal cleanliness, and unhygienic sanitary condition<sup>26</sup>.

#### 4. CONCLUSIONS

Enteric fever is endemic in twin cities of Rawalpindi and Islamabad. In the present study, we conclude that; adults are more prone to salmonella infection, due to high exposure to unhygienic environmental factors as compared to school aged and pre-school aged children. Water quality, unhygienic food, unhygienic environment and improper vaccination have great impact on burden of enteric fever in the population. To overcome this, clean drinking water and proper sanitation are required for the community. Educating the community about the prevention policies of enteric fever. But this is not sufficient; we also required good planning and eradication programs to overcome this infection not only in Rawalpindi, Islamabad but also in Pakistan.

#### 5. LIMITATION

Samples were not further proceed for ELISA, blood culture and PCR test, because of limited resources. Medical history was not taken from the patients such as their response towards various antibiotics and their treatment duration.

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#### CONFLICT OF INTEREST

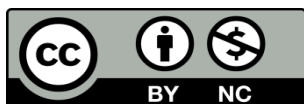
All authors declare no conflict of interest regarding this article.

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