IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 18, Issue 4 Ser. 15 (April. 2019), PP 73-83
www.iosrjournals.org

"Identification of Increased Antimicrobial Resistance of Salmonella Typhi& S. Para Typhi and Its Pattern: A Study in a Tertiary Care Paediatric Hospital, Dhaka, Bangladesh"

Dr. Nurun Nahar[1], Dr. Mohammad Ahmed Ahsan[2], Dr. Atiqul Islam[3], Dr. A. K. M. Khairul Islam[4]

[1.] *Registrar, Emergency, Observation &Referral Unit, Dhaka Shishu (Children) Hospital, Dhaka, Bangladesh*
[2.] *Classified Specialist in Aerospace Medicine, Central Medical Board, Bangladesh Air Force*
[3.] *Assistant Professor, Department of Paediatric Infectious Diseases and Community Paediatrics, Dhaka Shishu (Children) Hospital. Dhaka, Bangladesh.*
[4.] *MRO, Observation &Referral Unit, Dhaka Shishu (Children) Hospital, Dhaka, Bangladesh*
Corresponding Author:Dr. NurunNahar

Abstract:
Introduction*: Typhoid fever, caused by Salmonella enteric serovarTyphi, is a global public health concern due to increasing antimicrobial resistance (AMR). Characterization of* S. *Typhi genomes for AMR and the evolution of different lineages, especially in countries where typhoid fever is endemic such as Bangladesh, will help public health professionals to better design and implement appropriate preventive measures. Enteric fever is a life threatening febrile illness caused by SalmonellaTyphi and Paratyphi found highly prevalent in developing countries like Bangladesh. The government and non-government organization is working together for minimizing the burden of disease through active surveillance, ongoing collection of data, analysis and interpretation of data.*
Objective*: The aim of the current study was to estimate the prevalence in different sentinel sites using data of laboratory confirming diagnosis, identification of high risk population, risk factors for acquiring the disease, and antimicrobial susceptibility of S.Typhi and S. ParatyphiA.*
Methods*: During the study period May, 2014 to December, 2015 specimens were collected from ten different hospital facilities divided into seven divisions. The TPTest and blood culture methods were used for understanding the disease burden as well as serotyping of enteric fever. Total 2036 and 2068 specimens were tested by TPTest and blood culture respectively. During the two years of surveillance two peak seasons have been observed. The first peak was observed in month of August and second peak was November-December of 2014 and 2015.*
Results*: A total of 530 (26.03%) specimens were positive by the TPTest; whereas 59 (2.85%) cases were positive by blood culture. Among blood culture positive specimens 46 (78%) cases were S. Typhi and 13 (22%) were S. Paratyphi A. The highest number of enteric fever positive cases was found in Dhaka (TPTest 57.17%; blood culture 59.32%) division followed by Barisal and Chittagong. Males (36 cases was culture positive) were more positive than females (10 cases was culture positive).*
Conclusion*: A higher number of the febrile patients had taken antibiotics (33.6%) before enrolment rationalized the lower incidence rate of blood culture. Among the isolated S.Typhi and S. Paratyphi A strains, 100% had shown reduced susceptibility to ciprofloxacin. This study demonstrates that enteric fever is highly prevalent in Bangladesh. The findings of the study also impart the importance of proper vaccination program with an effective and immunogenic vaccine.*
Key Words:*TP Test, Blood Culture, Microbial Resistance*.

Date of Submission: 05-04-2019 Date of acceptance: 20-04-2019

I. Introductions

Typhoid fever is a life-threatening infectious disease caused by *Salmonella enteric* serovarTyphi. *S.* Typhi colonizes only humans, is transmitted through the fecal-oral route, and is endemic in tropical countries, especially in Africa and South and Southeast Asia. Worldwide, approximately 17 million people are infected every year by this pathogen. In 2010, data has shown the incidence rate of typhoid and paratyphoid fever was 3.9/1000 persons per year. Lack of safe drinking water and food, unhygienic sanitation is the considerable reason of the enteric fever to become endemic in some region. Although the incidence of enteric fever is quite high but the actual data on the diagnosis of febrile patient and epidemiology is not sufficient.S. typhi is one of

the most resistant organisms with multi-drug resistant phenotype. Outbreaks of typhoid fever caused by multidrug-resistant strains pose therapeutic challenges for physicians. While resistance to single antibiotic occurs, development of multi-drug resistance by this bacterium has complicated the health problem.Travelers from different countries has mostly affected by enteric fever. A large typhoid fever outbreak in Pakistan has resulted in 5,372 XDR Typhi cases reported during 2016–2018, and five travel-related cases in the United States travelers.

Pathophysiology: All pathogenic *Salmonella* species, when present in the gut are engulfed by phagocytic cells, which then pass them through the mucosa and present them to the macrophages in the lamina propria. Nontyphoidal salmonellae are phagocytized throughout the distal ileum and colon. With toll-like receptor (TLR)–5 and TLR-4/MD2/CD-14 complex, macrophages recognize pathogen-associated molecular patterns (PAMPs) such as flagella and lipopolysaccharides. Macrophages and intestinal epithelial cells then attract T cells and neutrophils with interleukin 8 (IL-8), causing inflammation and suppressing the infection.,The presence of a specific gene called pathogenicity islands (**PIs**) has distinguished the virulence factor of pathogenic bacteria from non- pathogenic species. In case of Enteric fever, the virulent factor clustered in certain area of *Salmonella* pathogenicity island (SPI), till today 15 SPI have been discovered whereas two of them are SPI-1 and SPI-2 .The invasion and intracellular proliferation has been controlled by genes in SPI-1, the intracellular pathogenesis is controlled by genes in SPI-2.T3SS (Type 3 Secretion System) is a complex protein crucial for the invasion of virulent factor into the host cell. The structure of T3SS form a base interact the target cell and a needle like structure form the conduit within the cytoplasm of pathogen and the cell membrane of target cell. The combination of SPI-1 and T3SS allows the require protein to be transferred from the bacterial cytoplasm to the host cell

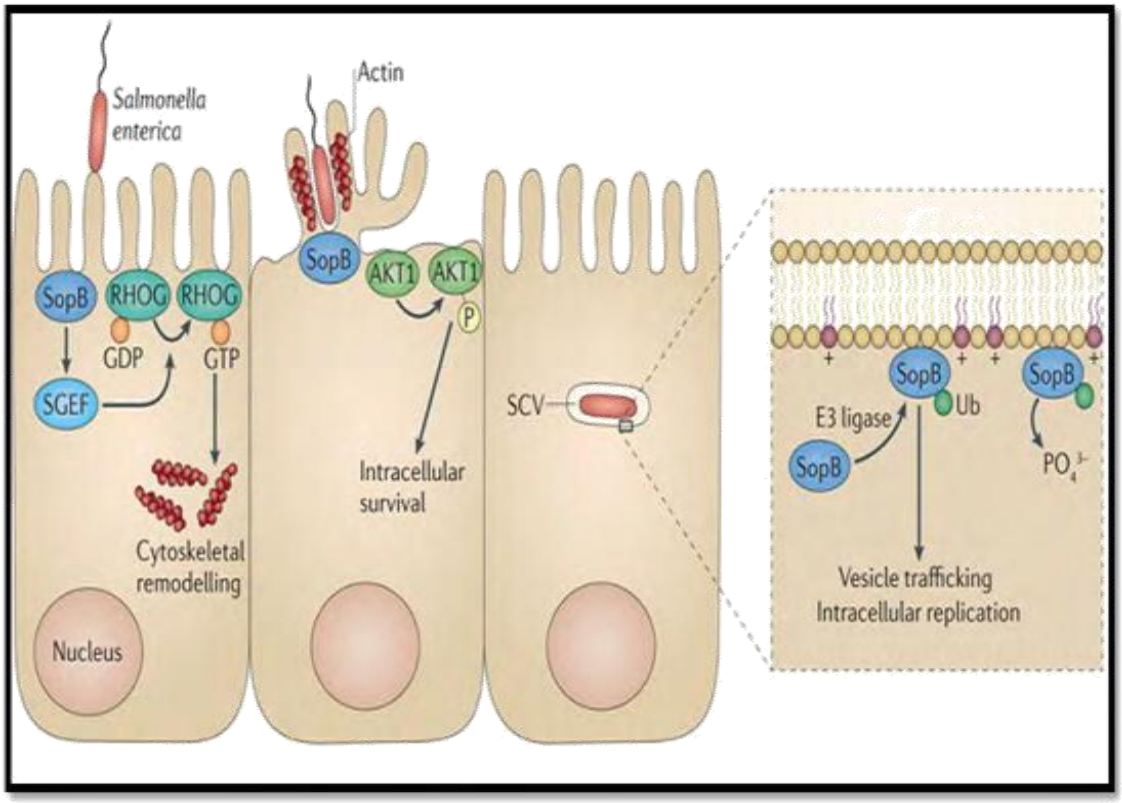

Figure 1: Schematic representation of the Salmonella pathogenicity. http://www.nature.com.

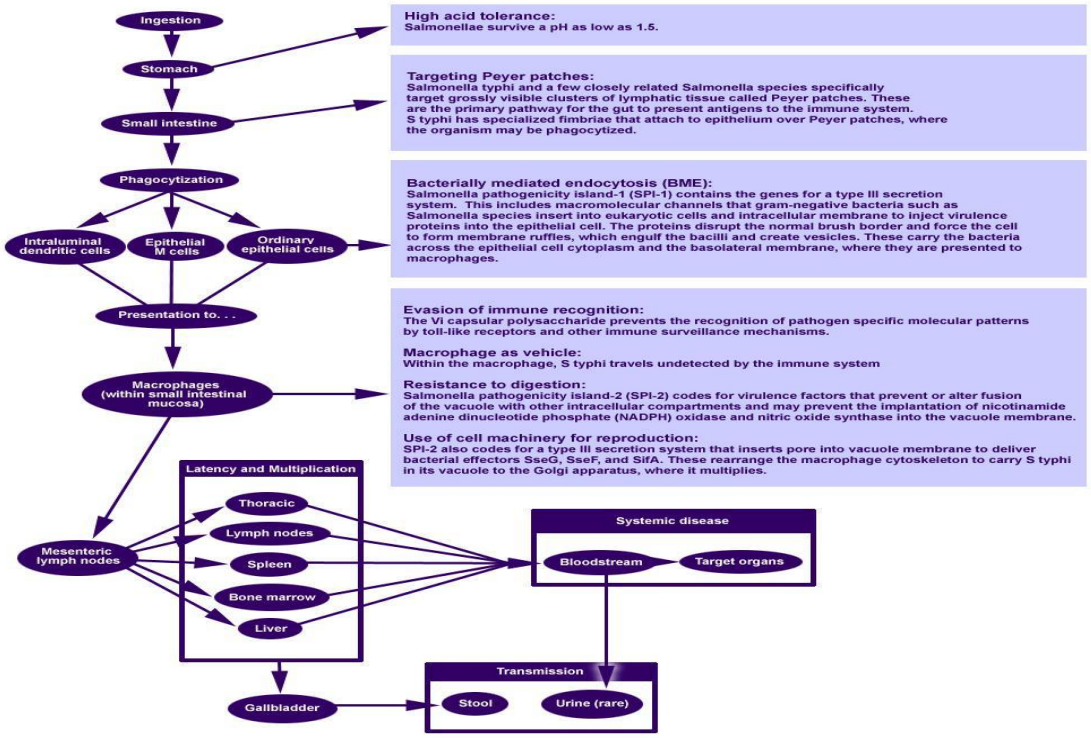

Figure 2: Life Cycle of Salmonella Typhi . (https://emedicine.medscape.com/article/231135-overview#a5)

*almonella*Pathogenicity Island (SPI1) function is required for the initial stages ofsalmonellosis, i.e. the entry of *Salmonella* into non- phagocytic cells by triggering invasion and the penetration of the gastrointestinal epithelium. Furthermore, SPI1 function is required for the onset of diarrheal symptoms during localized gastrointestinal infections

Epidemiology: Enteric fever in Bangladesh is very common while the country is suffering from the unsafe drinking water and food, inadequate sanitation, unhealthy street food and poor hand wash practice during eating. In 2013, a study conducted in Bangladesh has shown that S.Typhi is the most frequent pathogen causing the invasive bacterial disease. Total number of isolated pathogen was 143, where 93 cases (65%) was *S.*Typhi and 15 cases (10%) was *S.*Paratyphi A.a review of Dhaka shishu (children) hospital Dhaka hospital's records of typhoid patients admitted from January 2010 to December 2012 showed that typhoid fever is prevalent throughout the year in Dhaka. Young children and young adults are the common sufferers of this illness, while older patients with typhoid fever are rare among the admitted patients in Dhaka shishu (children) hospital Dhaka hospital. Vaccination of children at a young age might prevent them from getting this illness.

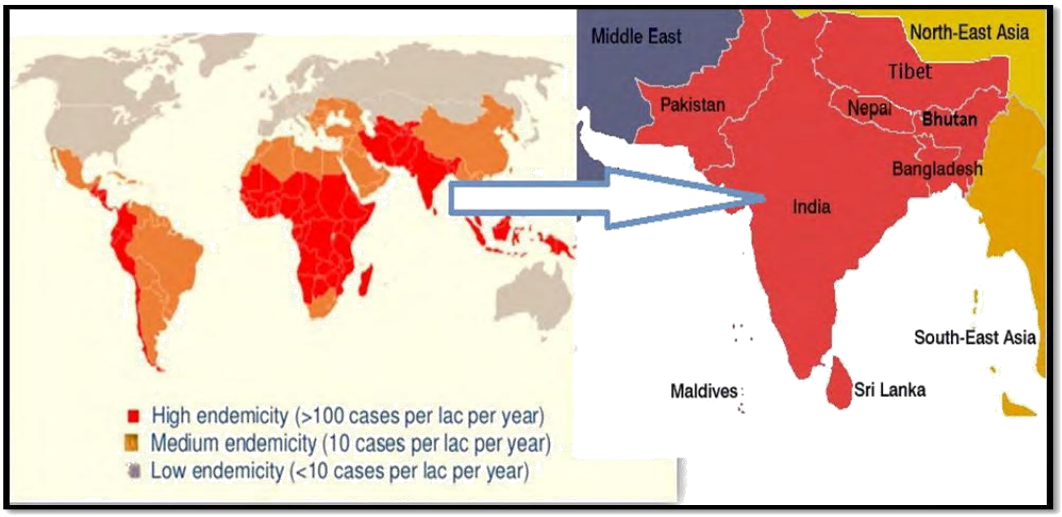

Figure 3: Global Scenario of Enteric fever.

Enteric fever is a life threatening febrile illness, making it a globally concerned topic. In 2000, the estimated number of illness due to typhoid fever was 21.7 million, resulting in 217,000 deaths. About 5.4 million illness is estimated as paratyphoid fever. A report shows that about 80% of people traveling from the USA to India, Philippines, Pakistan, El Salvador and Haiti are affected by typhoid fever. The most risk zone has been found while traveling to the Indian subcontinent, and the number of people increased from 23.4 to 81.2 per 100 000. In South Asian region, the enteric fever incidence has been encountered in the province Punjab in India. The total number of patients was 340 where *S.*Typhi and Paratyphi A was 334 and 6 respectively. Again the surveillance study was conducted over the densely populated area of Kolkata and it showed the lower number of paratyphoid fever in Kolkata compared to typhoid fever although the patients were older. Whereas a significant number of blood culture positive S. Typhi and *S*. Paratyphi A has been isolated in two urban settlement of Karachi in Pakistan respectively 67% and 36% out of 4027 blood sample collected from people.The risk of travel to the Indian subcontinent (estimated rate >100 cases per million travelers), or Southeast Asia and Africa (estimated 5 to 14 cases per million travelers) is significantly higher (*Mermin et al.*, 1998; CDC, 2013).

II. Objective

This study is designed for the understanding of different risk factor, isolation and identification of pathogen by the collection of blood sample .The objective of the study was to estimate the prevalence of enteric fever caused by *S.*Typhi and Paratyphi among the individual who came to seek treatment from the study site across Bangladesh. The Principal objectives of the present study were as follows:

a) Diagnosis of Typhoid and Paratyphoid fever through blood culture and TPTest method by using the blood sample of infected patient.
b) The possible outbreak of enteric fever in the urban and rural area as well as the Management of risk factor which is responsible for the disease outbreak.
c) Identification of the high risk population and the respective endemic area for the typhoid and paratyphoid fever and comparison of high risk population between the seven divisions of Bangladesh.

III. Methods and Materials

Study Methods: It's a surveillance Study.

Study Sample: A total of 2113 specimens were collected from febrile patients attending ten different study sites in Bangladesh from May 2014 to December 2015. Blood culture and TPTest was done in 2068 and 2036 specimens respectively. The specimens were analyzed using microbiological, biochemical and immunological techniques for the isolation of *Salmonella*Typhi and Paratyphi A, B, C types. For each specimen the blood culture and TPTest method was used for the laboratory confirmation of enteric fever.

Place of the Study and duration: The study was held in the Mucosal Immunology and Vaccinology laboratory at the Dhaka Shishu (Children) Hospital in Dhaka, Bangladesh from May 2014 to December 2015. Blood specimen is collected from ten sentinel site across the seven division of Bangladesh. The study site has been organized in such a way that overall incidence rate of enteric fever in Bangladesh would estimate. The demographic, socioeconomic, clinical data has been collected from every patient and required volume of blood sample is collected for identify the risk factor, prevalence area, and the development of the prevention as well as the control measurement against typhoid and paratyphoid fever.

Sample Collection: The blood sample was collected from 2113 patient, attending the hospitals. The inclusion criteria set for the patient was sustained fever more than three consecutive days and the temperature above 38˚C / 100.40F. During the sample collection, one portion of blood is taken into blood culture bottle and rest of the blood is taken into heparinized tube. The patient id is written in the culture bottle and the heparinized tube for the identification. Then the sample has been sent to Dhaka Shishu (Children) Hospital laboratory.

Study Design: About 8 mL and 5 mL venous blood was collected from the adult age ≥18 years and child age 0-17 years respectively. The collected blood specimen was used to diagnose typhoid and paratyphoid fever using blood culture and TPTest (Typhoid and Paratyphoid Test) technique.[12]

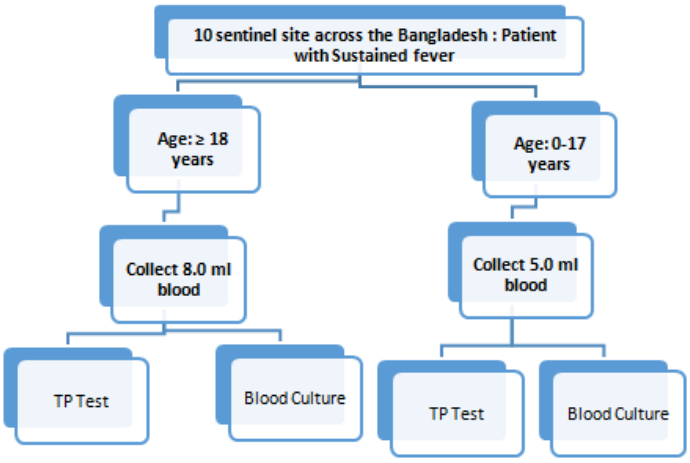

Figure 4: Overview of the Study Design

Laboratory Based Method Used in the Study

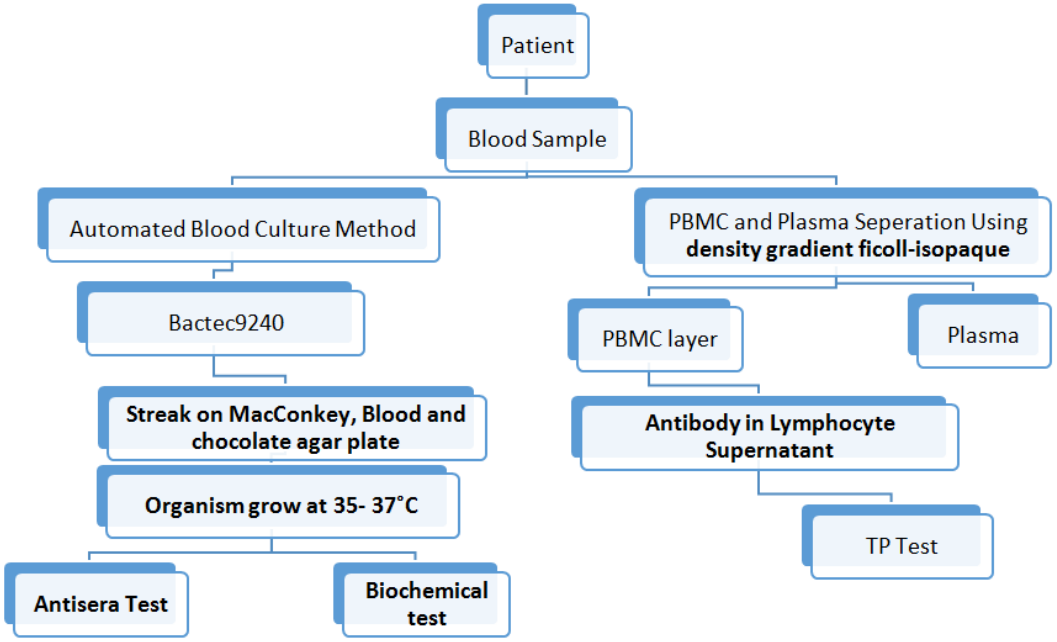

Figure 5: The flow chart of the laboratory procedure

Diagnostic procedure: In this study, Different diagnostic procedure applied for identification of the pathogenesis and others characteristics of the Salmonella species. For BloodCulture, The blood specimen collected in yellow cap culture bottle and the procedure is performed by Bechtel 9240 automated system. Biochemical Test specially Triple Sugar Iron (TSI) Agar Medium, Motility Urea Indole (MIU) Medium, Citrate Agar, Serological detection of *Salmonella* and serovers, Anti-sera test has been performed for the identification of different server of *Salmonella* containing different antigenic properties .Typhoid and Paratyphoid Test (TPTest), The available diagnostic tests for the detection of typhoid and paratyphoid fever is not well-recognized. For the current study, Test was used because of the highest specificity and sensitivity as well as the required volume of blood to be tested is feasible for the study. Detectable increase of antigen-specific antibody secreting lymphocytes in the peripheral circulation and this response can be measured in lymphocyte secretions by the TPTest as a diagnostic tool.

Ethical Consideration: This surveillance study was approved by the Research Review Committee (RRC) and the Ethical Review Committee (ERC) of Dhaka Shishu (Children) Hospital. The written consent was taken from the participants during the enrollment in the study. In case of children, the consent was taken from rom the legal guardian. The purpose, risk and benefits was written and explained to the participants. The whole study was supported by IEDCR (Institute of Epidemiology, Disease Control and Research), A Government organization collaborate with Mucosal Immunology and Vaccinology Laboratory, Dhaka Shishu (Children)

Hospital. The major concern of this collaboration was systemic and ongoing collection of data and the confirmation through laboratory analysis of clinical sample for the proper utilization of resources and advancement of public health sector of Bangladesh.

IV. Results

A total of 2113 specimens were collected from febrile patients attending ten different study sites in Bangladesh from May 2014 to December 2015. The degree of diarrhea, vomiting and clinical severity of the patients were assessed by physician. The median age of patients was 18 years. The Average duration of fever was 7 days. The temperature of the patients during admission was a bit higher (102 °F) while the patients were interviewed (101°F) (Table 2). Blood culture and TPTest was done in 2068 and 2036 specimens respectively. Among them 46 were positive for the *S*. Typhi and 13 for *S*. Paratyphi A. Overall 2.85% culture positive specimens were confirmed as enteric fever. (Figure 8). The incidence rate of enteric fever in Dhaka was 59.32% (n=33) out of total culture positive sample. The other region comprised 40.68% (n=11) of total organism. Among other divisions, Chittagong was covered by two study sites (250 bedded district sadar hospital,Cox's Bazar and BITID, Chittagong) and the prevalence was found higher 13.56% (n=8) . Khulna, Barisal, Rajshahi, Sylhet, Rangpur was less prevalent for enteric fever 10.16% (n=6), 6.77% (n=4), 5.08% (n=3), 23.39% (n=2), 1.69% (n=1) respectively.

Figure 6, 7&9 Showed thatincidence rate in Dhaka 57.17% (n=303) and found it to be the most prevalent when compared to the other 6 divisions**.** Medium level of prevalent area was found in Barisal 12.06% (n=64) and Chittagong 10.75% (n=57). The prevalence was comparatively lower in Sylhet 7.92% (42), Rangpur 4.72% (n=25), Khulna 4.34% (n=23) and Rajshahi 3.02% (n=16).

All the Study blood samples of the suspected febrile patients were tested. From 59 culture positive isolates, *Salmonella*Typhi was 46 (78%) and Paratyphi A was 13 (22%). From Biochemical test, findings showed higher incidence rate of typhoid fever in Dhaka 63%. The medium level of typhoid fever incidence rate was observed in Khulna 13.04% and Chittagong 10.86%, Barisal 4.34%, Sylhet 4.34%, Rangpur 2.17% and Rajshahi 2.17% in descending orders.The number of *S*.Paratyphi A was also significantly higher in Dhaka 46% (n=6), followed by Chittagong 23.08% (n=3), Barisal 15.38% (n=2), Rajshahi 15.38% (n=2).There were no *S*.Paratyphi A found in Sylhet, Rangpur, Khulna. Isolated suspected colonies from blood agar plates were also analyzed for other organisms. The number of other organism isolates were 83 and *Pseudomonas spp* and *E.coli*were significantly from May 2014 to December 2015.

During study period, all of the respective information has been collected and compared with different months in a year. For the TPTest method, we have observed two peak seasons. The first peak was observed in the months August 2014 and 2015, the number of positive cases was 34 and 44 patients respectively. The second peak season was observed in November and December of the study period where the number of detected cases was 40, 40 in 2014 as well as 28, 27 in 2015 respectively. The occurrence of enteric fever was low in May (2), 2014 and gradually increased till August, the next two months showed low incidence which gradually rises to highest incidence month. From 2015 onwards, the incidence of enteric fever was quite similar from January to April 2015, 41, 30, 27, 31 respectively, the lower occurrence of enteric fever took place in May (23), June (23), July (8). The incidence of typhoid and paratyphoid fever were analyzed separately. Typhoid fever incidence rate was significantly higher than paratyphoid fever (figure 3.7). Study revealed that the highly significant number of patients was suffering from headache (80%). Abdominal pain was a symptomatic problem for enteric fever (56.1%).The number of patients suffering from constipation and vomiting were quite high (38% and 38.7%). Rash was found to be a rare symptom for enteric fever. Another very important finding about enteric fever was that 33.6% patients were enrolled for current study took antibiotics before admission. During the study period three age categories was obtained for disease estimation in Bangladesh. Among 537 patients infected by enteric fever, 278 were adults (age ≥18), the second prevalent enteric patient age category was 176 (6-17 years). Enteric fever was highly prevalent among adults. In the blood culture method, *S*. Typhi was isolated mostly from younger child 6-17 years (22) and *S*. Paratyphi A was also isolated mostly from age ≥6 (12 out of 13). The prevalent of enteric fever was little bit higher for TPTest positive. Contaminated water was the major reason for any outbreak (outbreak) that took place prior to the occurrence. So the current study was focused on the drinking water source of participants. But the results showed a significantly higher number of patients were using tube well water (1558; 73.7%). Only 0.1% (n=2) people were using pond water. The use of tap water was second most common after tube well 511 (24.2%).(56.6%) males are mostly affected than females (43.4%). Male patients were three times more culture positive than females (Table 4).

Study Sample was also analyzed for the identification of antibiotic resistance pattern of isolated organism. The most significant results were 100% resistant to Nalidixic acid and 100% patients reduced susceptibility to ciprofloxacin. The resistance to Azithromycin (21%), Clotrimazole (21%), and Chloramphenicol (21%) was also significant.

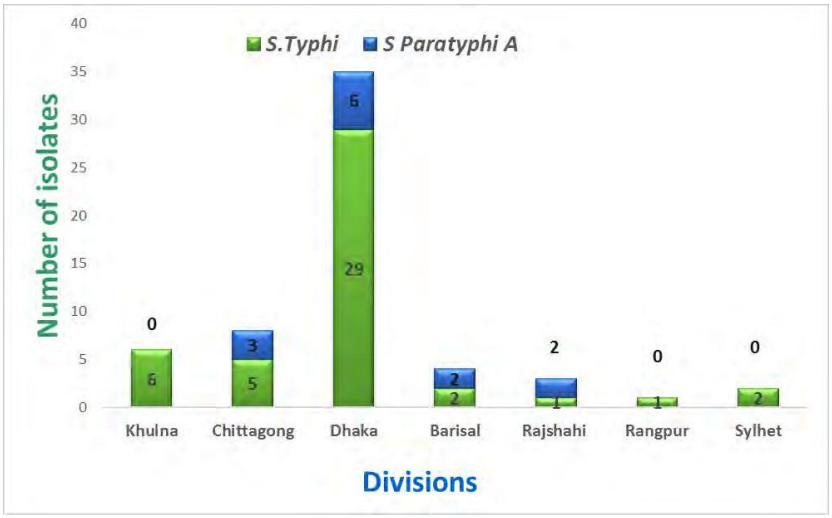

Figure 6: TP test respondents percentage by Seven Divisions

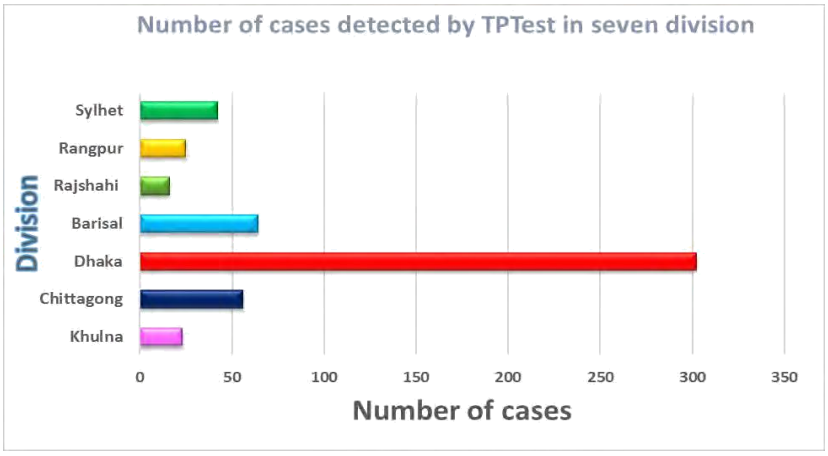

Figure 7: Frequency of enteric fever detected by TPTest method in seven divisions of Bangladesh.

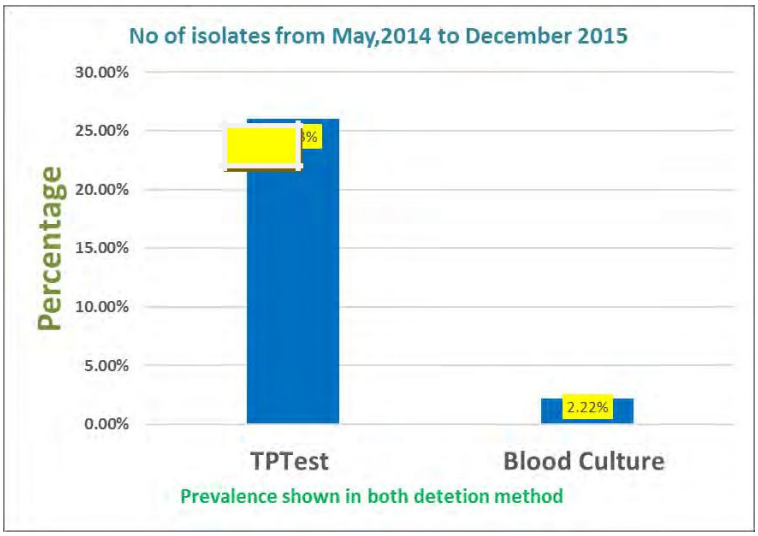

Figure 8: Overall prevalence of enteric fever (TPTest and blood culture) in Bangladesh from May 2014 to December 2015

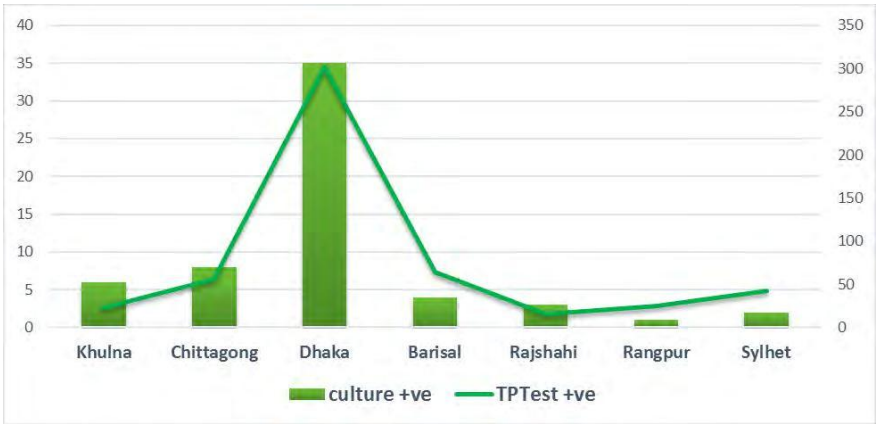

Figure 9: Cases of Enteric fever patients detected by TPTest and blood culture method

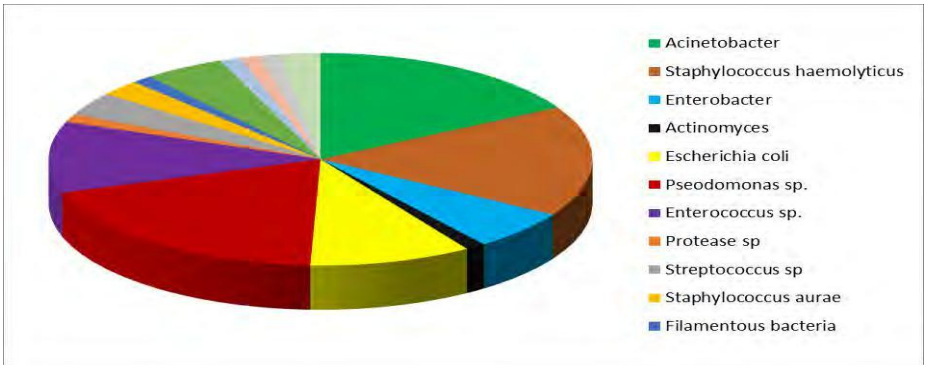

Figure 10: Isolation of other organism from blood

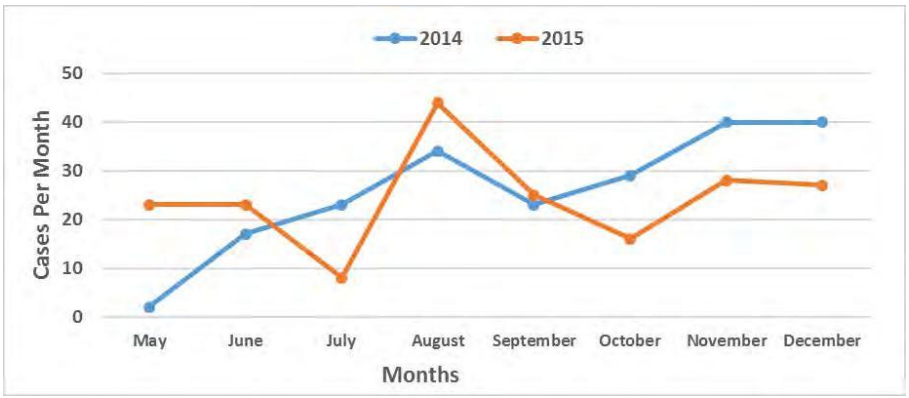

Figure 11: Seasonality of Enteric Fever

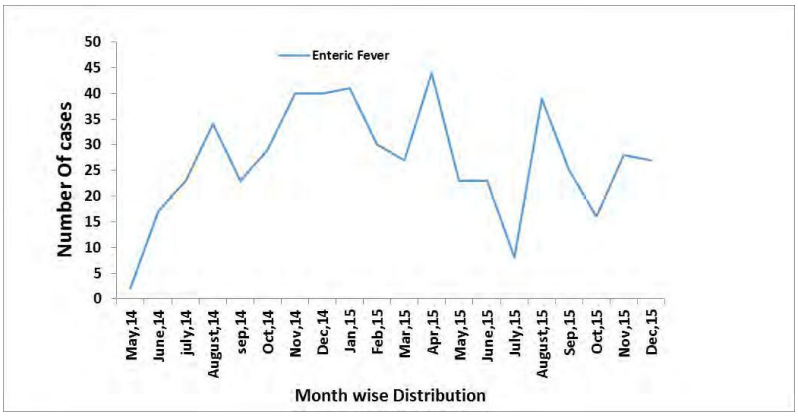

Figure 12: Numberof TPTestpositive infection cases between May 2014 toDecember 2015

Table 1: Important clinical features of the enteric fever patients (Total number of patients n =2113)

Clinical features	Frequency (%)
Headache	**1694 (80%)**
Abdominal pain	**1185 (56.1%)**
Constipation	**803 (38%)**
Diarrhea	**467 (22.1%)**
Vomiting	**818 (38.7%)**
Rash	**147 (7%)**
Use of antibiotics before admission	**711 (33.6%)**

Table 2: Baseline demographic data of the enteric fever patients (Total number of patients n=2113)

Features	Median	Percentile (25^{th} ,75^{th})
Median age in year (SD)	20 years	
Temperature During	101˚F (38.33˚C)	100.40 ˚F (38 ˚C),102
interview		˚F (38.88 ˚C)
Temperature During	102 ˚F (38.89 ˚C)	101.00 ˚F (38.33˚C),
admission/Visit		103 ˚F(39.44˚C)
Duration of fever in days	7 days	6, 10
Duration of taking	3.57 days	Not available

Table 3: Age Wise TP Test and Blood Culture by Respondents (Total number of patients n=2113)

Feature	TPTest positive	Blood culture positive	
		*S.*Typhi	*S.*Paratyphi A
0-5 years	76 (14.3%)	8	1
6-17 years	176 (33.2%)	22	6
≥18 years	278 (52.5%)	16	6
No. of males (%)	300 (56.6%)	36(78.3%)	9(69.2%)
No. of females (%)	230(43.4%)	10(21.7%)	4(30.8%)

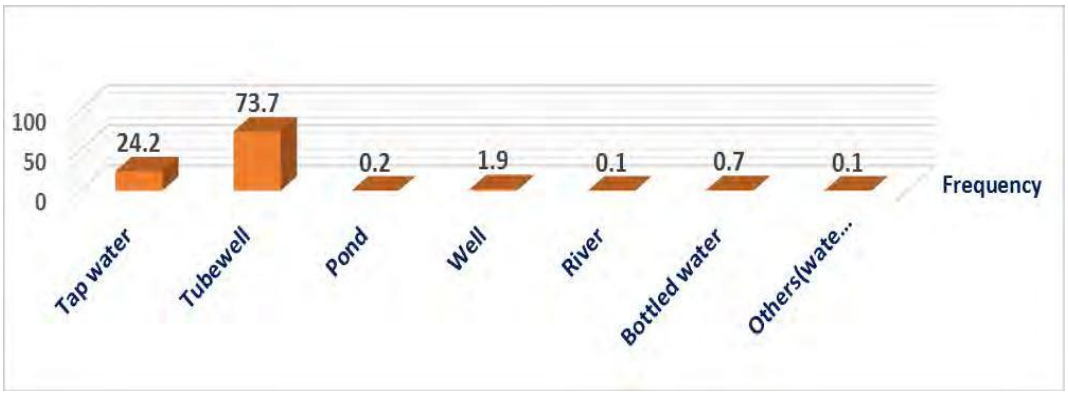

Figure 13: Source of water distribution among the participants of study

Table 4: Antimicrobial Resistance (Total number of patients n=2113)

Antibiotics	Number (%)
Resistance to Ampicillin	**10(21)**
Resistance to Azithromycin	**10(21)**
Resistance to Nalidixic acid	**46(100)**
Reduce susceptibility to Ciprofloxacin	**46(100)**
Resistance to Clotrimazole	**10(21)**
Resistance to Cloramphenicol	**10(21)**
Resistance to Ceftriaxone	**0**

Table 5: Antibiotic susceptibility pattern of isolatedParatyphoid A strains (n=13)

Antibiotics	Frequency (%)
Resistance to Ampicillin	**0**
Resistance to Azithromycin	**7(54)**
Resistance to Nalidixic acid	**11(85)**
Reduced susceptibility to Ciprofloxacin	**13(100)**
Resistance to Clotrimazole	**1(8)**
Resistance to Cloramphenicol	**0**
Resistance to Ceftriaxone	**0**

V. Discussion

Total 2036 specimens were analyzed by the TPTest method and the study detected 530 positive patients. Besides, from 2068 total specimens 59 patients were positive in blood culture method. Overall about 26% prevalence was found using TPTest technique and 2.85% by the blood culture method. The sensitivity of TPTest was 100% and specificity was 78-97% whereas the sensitivity and specificity of blood culture was 40-60%. Moreover 33.6% people took antibiotics before seeking treatment from study hospitals and the duration of taking antibiotics was 3-4 days. These findings might have affected the blood culture detection of enteric fever found in similar studies conducted in Dhaka where the intake of antibiotics was found to reduce the number of blood culture positive cases.In the TPTest method, it was found that enteric fever was highly prevalent in Dhaka (57%) followed by Barisal (12.06%) and Chittagong (10.75%). A study was carried out in 2005 where it was found that people living in urban slum of Dhaka was highly susceptible for typhoid and paratyphoid fever. In the Dhaka division, the highest incidence rate was observed in UttaraAdhunik medical college hospital (67%) which might have resulted from contaminated municipal supply water and street-vended foods, which have been previously reported as risk factors of typhoid fever [6] [8]. On the other hand, the least prevalent area was found in Rajshahi (AdhunikSadar hospital Naogaon). The specimen received from that site was only 3% TPTest positive. These results give an indication for selection of areas for future vaccination program.

Similar prevalence rate was observed by the blood culture method. Dhaka was the most prevalent zone for typhoid (63%) and paratyphoid (46%) fever. This finding also showed that people in Bangladesh are more susceptible to typhoid fever rather than paratyphoid fever. TPTest and blood culture method showed similar patterns of enteric fever positive cases in similar zones of Bangladesh. A total number of 59 *Salmonella* species were identified by serological analysis during this study period. Of these 46 were positive for *S*. Typhi and 13 were positive for *S*. Paratyphi A. One of the previous studies had shown three peak seasons for typhoid fever which were April, August and December. But the current study has shown two peak seasons which are August and November-December. A decreased number of febrile patients were detected in April in this study. Seasonality of febrile illness in the study period indicates that there is a higher chance of getting infected by the pathogens in winter and late rainy season in the study areas. The spreading of the pathogen may occur by the overflow of river and pond water during rainy season. Other environmental factors such as lower levels of surface water during winter and summer seasons also may enhance the transmission of the organism by the fecal oral route. This observation will be helpful for the understanding of seasonal variation of enteric fever. Thus improving infrastructure of banks and increasing the density of river may result in minimizing the hospitalization rate in different times of a year.Another previous study had shown that children of 0-5 years of age were more prone to enteric fever. But the current study revealed that younger children and adolescent (6 - 17 years) and adults (age ≥18 years) are infected more. This updated data of the prevalent age of typhoid and paratyphoid fever suggests that we should give consideration about vaccination or necessary preventive measures among people of all ages to reduce the disease burden. The prevalence of enteric fever was much higher in males (78.3%) compared to females (21.7%).Almost all febrile patients were suffering from headache (80%). Constipation (38.0 %) and vomiting (39%) were also very common among the hospitalized patients. About 56% patients had abdominal pain. Significant rise of temperature was observed in almost all patients. In 2011, use of supply water without boiling was found significant for enteric fever prevalence. The present study revealed that 73% of participants were using tube well as a source of drinking water which is much higher than the previous report. This findings probably attributes to the fact that the majority of the participants in this study were from the rural areas. The sources of drinking water of the patients with typhoid and paratyphoid could not be ascertained and it might be sources other than tap and tube well water.The isolated organisms were tested for susceptibility to various antibiotics. *S.*Typhi and paratyphi A showed 100% resistance to nalidixic acid and reduced susceptibility to ciprofloxacin. In a previous study, similar results were reported. As a result we found that multi drug resistance strains are emerging and causing disease severity.

VI. Limitation of the Study

The limitation of the study was that a number of samples could not be analyzed due to the inadequate quality of the specimen. Overall this study resulted in giving an updated result of prevalence of enteric fever and the antibiotic resistance pattern in Bangladesh; it will help to estimate the disease burden of febrile diseases caused by *S*. Typhi and *S*. Paratyphi A. This will also help in characterization of the enteric pathogens and thus lead to planning for vaccine intervention. The designing and proper choice of vaccine for the people particularly for Bangladesh and other enteric fever endemic countries to minimize the prevalence of disease.

VII. Conclusion

During the study period, the prevalence of enteric fever was positive. In percentage, 26% of the total number of patients was enteric fever positive by the TPTest detection method. In the blood culture method, 2.85 % of the patients were enteric fever positive where 2.22% was infected with *Salmonella*Typhi and *Salmonella*Paratyphi A was 0.62%. But there were no *S*. Paratyphi B and *S*. Paratyphi C isolated.The major findings was both detection method revealed Dhaka 57% was the most prevalent division for enteric fever in Bangladesh. The blood culture method showed relatively high prevalence of enteric fever in Khulna 10.16%. Chittagong division remained similarly highly prevalent in both TPTest and blood culture detection method. *Salmonella*Typhi was 46 (78%) and Paratyphi A was 13 (22%). Specific antiserum was used to detect the agglutination with specific Vi-polysaccharide then the colonies were found positive. Biochemical test was also performed and isolates the specific pathogen responsible for sustained fever. The current study was focused on the drinking water source of participants. But the results showed a significantly higher number of patients were using tube well water (1558; 73.7%). Only 0.1% (n=2) people were using pond water. The use of tap water was second most common after tube well 511 (24.2%).The spreading of the pathogen may occur by the overflow of river and pond water during rainy season. Other environmental factors such as lower levels of surface water during winter and summer seasons also may enhance the transmission of the organism by the fecal oral route. The most significant results were 100% resistant to Nalidixic acid and 100% patients reduced susceptibility to ciprofloxacin. The resistance to Azithromycin (21%), Clotrimazole (21%), and Chloramphenicol (21%) was also significant.

Conflict of interest: The Author has no conflict of interest of the study.

Acknowledgement: We acknowledged the IEDCR, Seven district administration of the Hospital authority, and related personnel who was engaged in the surveillance.

Reference

[1]. Salmonella entericaSerovarTyphi in Bangladesh: Exploration of Genomic Diversity and Antimicrobial ResistanceArif M. Tanmoy, Emilie Westeel, Katrien De Bruyne, Johan Goris, Alain Rajoharison, Mohammad S. I. Sajib, Alex van Belkum, Samir K. Saha, Florence Komurian-Pradel, Hubert P. Endtz
[2]. Crump JA, Luby SP, MintzED. 2004. The global burden of typhoid fever. Bull World Health Organ 82:346–353.
[3]. Taibur Rahman *1, I.H., Sajib Chakraborty2, A Rapid Glimpse on Typhoid Fever: An
[4]. Updated Mini Review. Journal of life medicine, 2013. 1(3): p. 71-82.
[5]. Date, K.A., et al.,Typhoid Fever surveillance and vaccine use-South-East Asia and Western Pacific regions, 2009â€“2013. MMWR.Morbidity and mortality weeklyreport. 63: p. 855-60.
[6]. Keith PK, John RK. Hidden epidemic of macrolide resistant Pneumococci.Emerging Infectious Diseases. 2005;
[7]. 11 (6): 802 – 807. 11. Rathish KC, Chandrashekar MR, NageshaCN.An outbreak of multidrug resistant typhoid fever in Bangalore. Indian J. Pediatr. 1995; 62: 445-448.
[8]. Mourad AS, Metwally M, Nour El Deen A, Threlfall EJ, Rowe B, Mapes T, Hedstrom R, et al. Multiple drug-resistant Salmonella typhi. Clinical Infectious Diseases. 1993; 17: 135-136
[9]. Emergence of Extensively Drug-Resistant Salmonella Typhi Infections among Travelers to or From Pakistan — United States, 2016–2018. Kevin Chatham-Stephens, MD; FelicitaMedalla, MD; Michael Hughes, MPH; Grace D. Appiah, MD; Rachael D. Aubert, PhD; Hayat Caidi, PhD; Kristina M. Angelo, DO; Allison T. Walker, PhD; Noël Hatley, MPH; Sofia Masani, MSN; June Nash; John Belko, MD; Edward T. Ryan, MD; Eric Mintz, MD; Cindy R. Friedman, MD
[10]. Raffatellu M, Chessa D, Wilson RP, Tükel C, Akçelik M, Bäumler AJ. Capsule-mediated immune evasion: a new hypothesis explaining aspects of typhoid fever pathogenesis. Infect Immun. 2006 Jan. 74(1):19-27. [Medline].
[11]. Parry CM, Hien TT, Dougan G, et al. Typhoid fever. N Engl J Med. 2002 Nov 28. 347(22):1770-82. [Medline].
[12]. Kaur, J. and S.K. Jain, Role of antigens and virulence factors of Salmonella entericaserovarTyphi in its pathogenesis. Microbiol Res. 167(4): p. 199-210.
[13]. https://emedicine.medscape.com/article/231135-overview#a5
[14]. Hospital Surveillance Progress Report. 2013.
[15]. Dhaka Shishu (Children) Hospital 2012-Review
[16]. Crump, J.A. and E.D. Mintz, Global trends in typhoid and paratyphoid Fever. Clin Infect Dis. 50(2): p. 241-6.
[17]. Connor, B.A. and E. Schwartz, Typhoid and paratyphoid fever in travellers. Lancet Infect Dis, 2005. 5(10): p. 623-8.
[18]. Kanungo, S., S. Dutta, and D. Sur, Epidemiology of typhoid and paratyphoid fever inIndia. J Infect DevCtries, 2008. 2(6): p. 454-60.
[19]. Khan, M.I., et al., Enhanced disease surveillance through private health care sectorcooperation in Karachi, Pakistan: experience from a vaccine trial. Bull World HealthOrgan, 2006. 84(1): p. 72-7.
[20]. Mermin et al., 1998; CDC, 2013
[21]. Hardy, D.J., B.B. Hulbert, and P.C. Migneault, Time to detection of positive BacT/Alertblood cultures and lack of need for routine subculture of 5- to 7-day negative cultures. JClinMicrobiol, 1992. 30(10): p. 2743-5.
[22]. Schwabe, L.D., et al., Evaluation of BACTEC 9240 blood culture system by using high-volume aerobic resin media. J ClinMicrobiol, 1995. 33(9): p. 2451-3.
[23]. Taibur Rahman *1, I.H., Sajib Chakraborty2, A Rapid Glimpse on Typhoid Fever: An
[24]. Updated Mini Review. Journal of life medicine, 2013. 1(3): p. 71-82.