Enteric fever: A review
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Introduction
Typhoid fever remains an underestimated important health problem in the developing countries. It is a distinctive acute systemic febrile infection of the mononuclear phagocytes. It may be caused by several serovars (S. typhi, S. paratyphi A, S. paratyphi B and occasionally S. typhimurium); many clinicians prefer the term enteric fever. Actually in 1869, given the anatomic site of infection, the term enteric fever was proposed as an alternative designation to distinguish typhoid fever from typhus.

Epidemiology
• A global health problem
• 13 to 17 million cases worldwide
• 200,000 deaths occur worldwide per year
• Children <1 year of age are most susceptible
• Endemic in most developing regions, especially the Indian subcontinent, South and Central America, and Asia

Clinical course
• The incubation period ranges from 3 to 21 days.
• The most prominent symptom is prolonged continued or remittent fever (38.8°C to 40.5°C, or 101.80F to 104.9F).
• Prodrome of nonspecific symptoms
  - Chills
  - Weakness
  - Headache
  - Sore throat
  - Anorexia
  - Dizziness
  - Cough
  - Muscle pains
• Gastrointestinal symptoms are quite variable
  - Abdominal pain
  - Diarrhoea or Constipation
• Epistaxis
In general, the symptoms associated with S. typhi are more severe than those associated with S. paratyphi.

Early physical findings of enteric fever include
• Relative bradycardia.
• Rash (‘rose spots’):
  - A faint, salmon-colored, blanching, maculopapular rash
  - Located primarily on the trunk and chest
  - Evident in ~ 30% of patients at the end of the first week and
  - Resolves after 2 to 5 days without leaving a trace
  - Difficult to detect in dark-skinned patients
• Hepatosplenomegaly
Toxic patients manifest neuropsychiatric symptoms described as a “muttering delirium” or “coma vigil” with picking at bedclothes or imaginary objects.

Sequelae
• Without therapy, the illness may last for 3 to 4 weeks and death rates range between 12% and 30%.

Complications
• Complications are most common in untreated adults and include
  - Intestinal perforation and/or
  - Gastrointestinal hemorrhage
• Other complications include
  - Pancreatitis
  - Hepatic and splenic abscesses
  - Endocarditis
  - Pericarditis
  - Orchitis
  - Hepatitis
  - Meningitis
  - Nephritis
  - Myocarditis
  - Pneumonia
  - Arthritis
  - Osteomyelitis
  - Parotitis

Despite prompt antibiotic treatment, relapse rates remain at 10% in immunocompetent hosts. Asymptomatic chronic carriers (1 to 5%) shed S. typhi in either urine or stool may continue for >1 year. The incidence of chronic carriage is higher among women and among persons with biliary abnormalities (e.g., gallstones, carcinoma of the gallbladder) and gastrointestinal malignancies.

Laboratory investigations
No specific laboratory test is diagnostic for enteric fever.
• Blood examination

- Leukopenia and neutropenia (15 to 25%)
- Normal WBC count despite high fever in the majority of cases
- Leukocytosis can develop in typhoid fever (especially in children) during the first 10 days of the illness, or later. The diagnostic “gold standard” is culture for S. typhi or S. paratyphi. The yield of blood cultures is quite variable: It can be as high as 90% during the first week of infection and decrease to 50% by the third week
• Bone marrow cultures remain highly (90%) sensitive despite >5 days of antibiotic therapy
• Stool cultures
  - Negative (60 to 70%) during the first week,
  - Can become positive during the third week of infection in untreated patients.
• Serologic tests
  - Classic Widal test for “febrile agglutinins”
  - However, given high rates of false-positivity and false-negativity, these tests are not clinically useful.

Treatment
General supportive management
- Bed rest
- Nutrition and hydration
- Antipyretics, if necessary

Specific
• Ciprofloxacin 500mg to 750 mg tablet 12 hourly for 14 days Other antibiotics can be used:
  - Cotrimoxazole
  - Amoxicillin
  - Chioramphenicol
  - Ofloxacin
  - Pefloxacin
  - Ceftriaxone
  - Cefotaxime
  - Azithromycin
• Pyrexia can persist for 5 days after starting antibiotic
• Even with effective antibiotic there is danger of
  - Complications
  - Recrudescence and
Discussion
With improvement in environmental sanitation in the United States, the incidence of S. typhi infection has dropped to a low level. From 1930 to 1950, the typhoid incidence initially around 22 per 100,000 diminished by 90%. Known global hotspots for typhoid fever include Peru, Alexandria (Egypt), Jakarta (Indonesia), India, Pakistan and Nepal. In recent years, multidrug-resistant strains of Salmonella typhi have emerged in tropical countries. Typhoid fever is also endemic in our country. Although the sanitation has improved a lot in our country, typhoid fever is still a major public health problem. But exact incidence or prevalence of enteric fever in Bangladesh is not known. Multidrug-resistant S. typhi is becoming more prevalent in many endemic countries. Patients infected with resistant strains present with more severe illness, look “toxic” and have a higher incidence of disseminated intravascular coagulation and hepatomegaly and a threefold higher mortality rate. Moreover, it is related to the longer duration of disease and to prior ineffective oral antibiotic therapy. Studies on multidrug-resistant enteric fever have been carried out in Dhaka, Khulna and Rajshahi that revealed that commonly used drugs were poorly sensitive to Salmonella sp. The prevalence of resistance to multiple first-line oral drugs has been rising among strains of Salmonella in developing countries especially in the Indian subcontinent and Southeast Asia, due to the acquisition of plasmids encoding inactivation β-lactamases and chloramphenicol acetyl transferases. Chloramphenicol-resistant Salmonella typhi was first reported in 1972. Alam et al., Ahasan et al. and Ekram et al. reported outbreak of multidrug-resistant enteric fever in different parts of Bangladesh few years back in separate studies. Where multidrug-resistance is a problem a 4-fluoroquinolone or ceftriaxone should be used initially to adults over 17 years of age and ceftriaxone is the best choice for children. However, evaluation of the safety of ciprofloxacin in the dose of 15 to 25 mg/kg for 9 to 16 days in series of children who were between 8 months and 13 years of age did not reveal any cartilage damage on nuclear magnetic resonance scans. This safety profile with cost effectiveness of ciprofloxacin is important as most of our poor people cannot afford 3rd generation cephalosporins. Because of increasing resistance worldwide to conventional anti-typhoid drugs, and in view of the efficacy of the quinolones, these drugs have become the first choice of treatment for these important enteric infections.

Conclusion
Enteric fever is a global health problem; risk is highest among persons living in poverty in the developing world like Bangladesh. Increasing resistance to available antimicrobial agents, including fluoroquinolones may foretell dramatic increases in case-fatality rates. Epidemics and high endemic disease rates have occurred in the Central Asian Republics, the Indian subcontinent, and across Asia and the Pacific Islands. Growing evidence of previously unrecognized disease in children aged <5 years is a newer problem. However, the role of new and effective vaccines as control measures for epidemics and as tools for elimination remains to be explored.

References