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Typhoid fever in children: A Review

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Abstract

Typhoid fever was a chronic systemic infection caused by *Salmonella enteric*, serovar typhoid, gram-negative bacteria. Low sanitation and public health standards are serious public health issues in underdeveloped countries in the tropics and subtropics. Multidrug resistant (MDR) typhoid fever has a varied diagnostic pattern and a higher rate of harmful impacts than regular typhoid fever (20%). The epidemiology, pathophysiology, clinical features, diagnosis, and current treatment trends for typhoid fever in children are discussed in this review article. Infections, relapsing, and typhoid fever were covered.

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Introduction

Typhoid was a chronic, infectious, and potentially fatal fever-related illness caused by *Salmonella* enteric serovars, Typhi, Paratyphi A, B, C were all typhoid Salmonella, though some are classified as non-typhoid Salmonella. Typhoid strains were human host-confined life forms that cause typhoid and paratyphoid fever, also known as enteric fever, Salmonella serovar Paratyphi A has been found to be involved in the emergence of enteric fever in some countries in Asia (Crump *et al*., 2004; Eng *et al*., 2015). Typhoidal Salmonella spreads primarily through contaminated water or food with human feces (Antilln *et al*., 2017). The risk of disease was highest in poor economies where typhoidal Salmonella was endemic, there was poor hygiene and sanitation, and there was a lack of safe food and water (Gunn *et al*., 2014). Enteric fever in high-paying nations was generally acquired abroad and is related to travel to endemic areas, despite the fact that clusters may be related to sustenance preparers who were chronically infected with Salmonella serovar Typhi (Zaki *et al*., 2011).

In the last two decades, salmonella typhoid has developed and spread multidrug resistance to common anti-typhoid drugs (chloramphenicol, co-trimoxazole and ampicillin), particularly in South and Southeast Asia, including Pakistan (Mara *et al*., 2010). MDRTF episodes necessitate the use of expensive and often inaccessible medications in order to be successfully treated. This adds to the weight of the medical services sector in developing countries. In this manner, emphasis should be placed on sickness avoidance, which can incorporate both short and long-term measures that must be strictly adhered to. Here and now, measures incorporate inoculation of the high-hazard populace in endemic zones and balanced and reasonable anti-microbial recommendations by wellbeing experts (Ochiai *et al*., 2008). These issues necessarily involve a collective approach from governments, the pharmaceutical industry, social insurance providers, and consumers. A typhoid immunization program in schools, in addition to the school-based organization of Td (typhoid and diphtheria), or, with the introduction of new conjugate antibody immunization, as part of the overall vaccination program, should be considered; other imperative preventive measures incorporate upgrades in sanitation, accessibility of clean drinking water, advancement of safe sustenance taking care of practices, and general wellbeing instruction (Park., 1999).

Epidemiology

Typhoid fever was a tropical infectious disease, with 80 % appearing in countries in Asia (Park *et al*., 1999, Kliegman *et al*., 2008). It was a water-borne, food-borne disease spread by eating infected food or beverages (Rahman *et al*., 2007, WHO, 2003, Long, *et al*., 2003). The mode of transmission, clinical presentation, and consequences differ significantly between developing countries (Park, 1999, Davidson's, 2010). The most common were school children. The symptomatology of children and MDR patients varies widely (Rahman *et al*., 2007, Davidson's, 2010, Khan *et al*., 2007, Chinh *et al*., 2000). Many countries, like Pakistan, Indonesia, Bangladesh, India, Vietnam, China, Malaysia and Tajikistan, are endemic for MDR typhoid (Park, 1999, Mirza *et al*., 1993, Gupta, 1999). Where S. Typhi infection was usually associated with migrant workers from the endemic zone, but epidemics can occur; sporadic infection occurs in Europe and North America, most widely in immigrants having returned home for holidays (Saha *et al*., 2006, Lianou *et al*., 2017, Moudgil *et al*., 1985).

Pathophysiology

Immunogenicity, virulence, pathogenicity, and infection have all been identified as factors influencing the pathogenesis of typhoid fever, and Salmonella was the cause of typhoid fever in patients with weakened or compromised immunity; it was acid-sensitive bacteria, which commonly dies in the stomach (Kohbata *et al*., 1986). Even with low amounts of antacids and antihistamines, Salmonella colonization occurs in people with achlorhydria, food and beverages also act as buffers against gastric acid, permitting organisms to access the gastrointestinal tract more easily (van de *et al.*, 2005). Toxins, a polysaccharide capsule, a lipo-saccharide O antigen and the Flagella H antigen determine the pathogenicity of Salmonella. Even with the same number of microorganisms, strains positive for the antigen had a twice-as-high attack rate as negative bacteria. The presence of the antigen in S. Typhi, but not in non-typhoidal *Salmonella,* was one of the primary distinctions between the two strains. The fundamental function of the antigen was to act as an anti-phagocytic agent, keeping macrophages from attacking the O antigen and therefore protecting it from the anti-body; the Flagella H antigen allows bacteria to move around and adhere to the mucosa of the gut wall, Bacteria attached to M cells were absorbed and ejected into the luminal space by bacteria created by the type III secretion system, which was capable of transporting bacterial proteins into enterocytes and M cells (specialized epithelial cells in the gut mucosa or lymphoid tissue that act as antigen-presenting cells), During this process, M cells were destroyed, showing the basal lamina.

It facilitates the disease invasion by allowing easy access to pathogens, worsening the situation (Raffatellu *et al.*, 2008). Patients with an abnormal cystic fibrosis trans-membrane conductance regulator (CFTR) protein were resistant to typhoid because the (CFTR) was thought to be important in Salmonella uptake (Sultana *et al.*, 2016).

Sign and Symptoms

When Salmonella was ingested, serovar Typhi or Paratyphi A, an asymptomatic period lasts for 7 to 14 days; during this period, the predominant symptom was fever. Fever and rashes were two main symptoms. Typhoid fever is particularly high, gradually increasing over several days to 39 or 40°C; the rash, which does not affect every patient, consists of rose-colored spots, particularly on the neck and abdomen (Ayub *et al.*, 2015). Other symptoms can include malaise, headache, abdominal pain, abdominal distension, and other constitutional symptoms. Constipation is an earlier symptom, though many patients experience diarrhea at some point. Raised temperature, relative bradycardia, leukocytosis, hepatomegaly, abdominal tenderness, and meningism were all physical findings. Intestinal hemorrhage, urinary retention, intestinal perforation, thrombophlebitis, pneumonia, myocarditis, cholecystitis, osteomyelitis, nephritis, myocarditis, and meningitis were all serious complications (Ayub *et al.*, 2015, Morinigo *et al.*, 1993).

The diagnosis

The World Health Organization (WHO) assessed the worldwide yearly rate of typhoid fever, around 21 million cases, is likely a slander in view of poor diagnostics (Mathai *et al.*, 1995). There were a few options for diagnosing enteric fever: Serological markers, bacterial culture; antigen discovery; and DNA intensification are all examples of clinical signs and side effects; none was totally acceptable. The clinical conclusion of typhoid fever was troublesome in light of the fact that the indications of the ailment differ and there were numerous reasons for delayed fever in typhoid endemic areas (Parry *et al.*, 2010).

Blood culture inefficiency in developing economies was caused by the incorrect use of anti-infective agents. Because of the higher bacterial content in bone marrow, which is unaffected by antitoxins, bone marrow transplantation requires more contact than blood culture (Bhutta , 2006). Stool culture was an important aid in disease detection because it can be confirmed when blood cultures are negative, and it was thought necessary to monitor *S. typhi* transfusion after clinical repair survey, which was a risk factor for case groups (Zhou *et al.*, 2010). S. Typhi is currently isolated from faecal utilization using advanced media containing selenite. This is since there are so many competing microorganisms, especially Escherichia coli (Ali *et al.*, 2009). Some many destinations have been refined, but they have been rarely used as examples: Although the culture of the upper gastrointestinal tract with a duodenal string is important, children withstand it ineffectively. *S. Typhi* could be developed from rose spots, but climbed spots were regularly hard to see and may just be available in 4% of cases. *S. Typhi* could likewise be developed from pee but might be related to urinary tract disease as opposed to typhoid fever (Haque *et al.*, 2001).

Molecular diagnosis

To overcome the constraints of social and serologic tests, a sub-atomic technique for typhoid fever diagnostics has been developed. Several researchers have looked at using polymerase chain reaction (PCR) to distinguish certain DNA sequences of organisms introduced into clinical samples. Tested PCR as a typhoid fever diagnostic method for the first time in 1993, they found that it effectively increased the flagellin quality of *S. typhi* in all cases of culture-confirmed typhoid fever and in none of the solid controls (Butt *et al.*, 2003, Coulter , 2003). Correct analysis of typhoid fever remains an unclear region due to the lack of accessibility of adequate symptomatic apparatuses, particularly those that are field-based. As a result, researchers in developing countries should focus their efforts on the development of more current and straightforward indicators (Hay *et al.*, 2001, Cotran *et al.*, 1994).

Clinical features

Fever and malaise accompany the onset of bacteremia. (Parry *et al.*, 2008). In children, the conventional three steps of illness, like prodromal, toxic, and defervescence, are shorter (Zulfiqar *et al.*, 1991). Patients are commonly introduced to the hospital with influenza, nausea, malaise, fever, anorexia, a headache, poorly localized stomach discomfort, a dry cough, and myalgia through the end of the first week (Topley , 1986). The fever is low-grade at first, but it gradually climbs, and by the second week, it is frequently high (390-400C) and persistent (Johnson *et al.*, 1994).

In addition to the fever, gastrointestinal symptoms such as vomiting, abdominal pain, and loose stools were frequent in children with typhoid fever. Children under the age of five may experience convulsions (Colon *et al.*, 1975). Patients may appear with pneumonia or meningitis symptoms (Parry *et al.*, 2002). They may occasionally show open neuropsychiatric symptoms that resemble Alzheimer's catatonic, which was more common in Africa and India (Colledge *et al.*, 2010). Patients were agitated, confused, or obtunded, but comas or stupor were rare.. In Indonesia and Papua New Guinea, these neuropsychiatric manifestations vary from 10 to 40% of hospitalized typhoid patients but are fewer than 2% in Vietnam and Pakistan (Crump *et al.*, 2010). On examination, youngsters do not have relative bradycardia, but a paradoxical link between high temperature and low pulse rate can be seen (Sinha *et al.*, 1999). In less than half of instances, there are a few rose spots, and some have been observed in 5-30 % of the cases. They commonly appear on the abdomen and chest, although they can also appear on the back, limbs, and legs. Hepato-splenomegaly, a coated tongue, and a painful abdomen are all common symptoms (Gupta *et al.*, 2005).

The most common physical sign in children with typhoid fever was hepato-splenomegaly, followed by abdominal pain. Another study of children with typhoid fever found hepatomegaly in 85.3 percent of patients and splenomegaly in 27.5 percent (Crump *et al.*, 2010). According to certain Bangladesh research, the palpable liver was found in 58 % of cases, palpable spleen in 33 % of cases, and hepato-splenomegaly was seen in 44.1 % of cases; in Bangladesh research, abdominal distension and a coated tongue are common results (Gupta *et al.*, 2005).

Prevention

Typhoid fever epidemics have been reduced using a combination of vaccination and improved water sources. There are several vaccines available to prevent typhoid fever. The VI conjugate vaccine, on the other hand, has been shown to have a protective efficacy of greater than 90% for children aged 2 to 5 years in Viet Nam for at least 27 months after vaccination (Crump *et al.*, 2004). As a result, mass vaccination in endemic areas, travelers, and antimicrobial-resistant places is recommended, as well as public education, improved sanitation, and planned water, and improved personal hygiene. To combat the burden of drug resistance, medical practitioners in our nation should be aware of the abuse and misuse of fleuro-quinolones and the cephalosporin family of medications in the treatment of typhoid fever (Levinson, 2008).

Anti-microbial resistance

The majority of antibiotic resistance is caused by an organism's genetic changes, such as chromosomal mutations, plasmid acquisition, or transposons. Resistance by plasmid is more common in multidrug-resistant typhoid, but coma or stupor is uncommon (Winstaniey *et al.*, 2001). T. Woodward was the first to successfully treat typhoid fever with chloramphenicol in 1948. Resistance to chloramphenicol was first discovered in *S. typhi* strains in 1970, followed by ampicillin and co-trimoxazole resistance. MDR *S. typhi* appeared only infrequently. The first outbreak of multidrug resistance was observed in Malaysia in 1984 (Woodward *et al.*, 1984). MDR *S. typhi* has since expanded throughout Southeast Asia and China, becoming endemic. In most cases, resistance to chloramphenicol and ampicillin can be transferred to plasmids alone or as a group (Kidgell *et al.*, 2002, Morshed *et al.*, 1986). Plasmids are extrachromosomal supercoiled DNA loops that are thought to have originated from bacteriophages (Datta *et al.*, 1981, Sharma *et al.*, 1979).

They can transfer plasmids from one host bacterium to another when their size exceeds 40 kbp. There are two types of plasmids identified in *S. typhi*. First, as a pH CM2 cryptic plasmid capable of carrying the gene encoding DNA metabolism, replication, and virulence mechanisms found in Asia rather than Africa. Second, make a self-transferable plasmid with a size of 140-180 kbp (Connerton *et al.*, 2000). These large plasmids can then be transferred to and from enteric gram-negative bacteria such as *E. coli*, *Klebsiella pneumonia*, and *Salmonella enterica*, especially when antibiotics are used. In several parts of Asia, chromosomally acquired quinolone resistance in *S. typhi* has been discovered (Wain *et al.*, 2001). Which could be the result of the widespread indiscriminate use of these drugs.

Conclusion

Salmonella typhi is a human pathogen that has a host specificity. SPIs contribute to its pathogenicity. SPI-1 is required for the bacteria's penetration into epithelial cells, while SPI-2 is required for the bacteria's survival and multiplication in the host cells. Salmonella has been around for a long time, and there has been researched conducted in an attempt to combat its infections. However, the process has been fraught with difficulties. Multidrug resistance in microorganisms and vaccine failure to establish a long-term protective effect are two of these problems. Other issues include the developing world's inability to finance treatment and preventive measures due to a lack of resources. Salmonella has recently emerged as a vaccine vector that can contain antigens from other disease-causing organisms, allowing for dual protective therapy. However, more research is needed to determine whether these new methods of treatment can be used as a preventative measure against infectious diseases.

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