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A REVIEW ON TYPHOID INFECTIOUS BACTERIAL DISEASE

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ABSTRACT

Typhoid fever is most current in the Asian part of the world especially in the developing countries of Asia like Pakistan and India, caused by a gram-negative bacterium Salmonella enterica serval Typhi. It's an orally transmitted transmissible complaint caused by consuming defiled food and impure water. The incubation period of the complaint is 7 to 14 days. Symptoms include high fever, rash, weakness, abdominal pain constipation, headache, and poor appetite. Antibiotic resistance is a major problem to treat it effectively Salmonella typhi is serologically positive for lipopolysaccharide antigens O9 and O12, protein flagellar antigen Hd, and polysaccharide capsular antigen Vi.S. typhi Vi-positive strains are more contagious and malign than Vi-negative strains. The fever is also accompanied by chills, headache, malaise, anorexia, nausea, vague abdominal discomfort, dry cough and myalgia. These are followed by carpeted lingo, tender tummy, hepatomegaly, and splenomegaly. Azithromycin (10mg/ kg) given formerly daily for seven days has proven effective in the treatment of typhoidfever in some grown-ups and children. A cure of 1g per day for five days was also set up to be more effective in utmost grown-ups. Of the third generation cephalosporins, oral Cefixime (15- 20 mg per kg per day, for grown-ups, 100-200 mg doubly daily) has been extensively used. Intravenous third generation cephalosporins (ceftriaxone, cefotaxime) are effective. Aztreonam and imipenem are implicit third line medicines.

KEYWORDS: Typhoidal Salmonella, Antibiotic, Pathogen.

INTRODUCTION

200 times agone, one of the major causes of morbidity and mortality in the western world was typhoid fever or for that matter enteric fever.[1] Because of advancements in sanitation and overall health situations, the conditions have greatly bettered now and the deadly complaint of

yester times is veritably scarce now in the USA and the Europe. still, typhoid fever is still a deadly complaint in developing countries, particularly in India.[2] Typhoidal Salmonella transmit dominatingly via water or food defiled with the feces of mortal.[3] The hazard of complaint is high in underdeveloped nations where typhoidal Salmonella is aboriginal and there's poor hygiene and sanitation andnon-availability of safe food and water.[4]

Enteric fever in high- pay nations is generally attained abroad and is related with movement to homes of endemicity, in malignancy of the fact that bunches might be related with food preparers who are interminable liaisons of Salmonella serovar Typhi.[5]

An ongoing report on worldwide weight of typhoid fever blazoned 27 million conditions and,000 to,000 passing every time because of typhoid fever.[6] The International Vaccine Institute reported11.9 million typhoid fever affections and,000 expirations in low- and center pay nations in 2010.[7] These issues bear the aggregate exertion of governments, the pharmaceutical business, social insurance suppliers and shoppers. A typhoid inoculation program in schoolchildren alongside the academy grounded association of Td (typhoid and diphtheria) or, with the coming of new conjugate antibody VI immunization, as a element of the extended program of vaccination, ought to be considered. Other imperative preventative measures incorporate upgrades in sanitation, availability of clean drinking water, advancement of safe food taking care of practices, and general good instruction.[8]

Epidemiology

As indicated by the worldwide gauge, every year around 27 million new instances of typhoid happen with mortality in around 200,000. The most noteworthy dismalness and mortality are noted in South Central and Southeast Asia.[9]

In total, taking all these standardized studies, typhoid epidemiology data were abstracted from 47 countries across the entire global regions. Data were also obtained from population-based and prospective vaccine studies for 13 countries. The remaining incidence data were collected by typhoid fever surveillance systems in the several developed regions where regular and systematic national-level surveillance was in vogue. Paratyphoid fever incidence data were available for only 9 countries of which the USA, despite having an advanced and regular surveillance system, did not have even a single case of paratyphoid fever during the entire period of their study. The incidence of typhoid was high (>100 cases per 100,000 population per year) in Asia (excepting Japan) and Southern Africa. It is medium (10-100 cases per

100,000 population per year) in North Africa, Latin America, Caribbean islands and Oceania. The incidence of typhoid fever was estimated to be low in Europe, North America, Australia and New Zealand (<10 cases per 100,000 population per year).previous typhoid fever incidence rates (IR) reported in Egypt during various vaccine trials varied from 209/100,000 in 1972-73 to 48/100,000 personin 1978-81.[10] In one of the investigation led in matta, swat predominance of enteric fever was discovered 13.5%.[11] A Serological Diagnosis of Salmonella Typhi in District Hospital Quarter of Charsadda was performed and indicated 22% of prevelance.[12] Typhoid is found to be a seasonal disease; in the monsoon itself there is occurrence of 45% of the total annual reported cases. In South Asia the disease occurrence is highest during July to October because of heavy rainfall during that period.[13]

Aetiology

The complaint typhoid fever is an orally transmitted contagious complaint caused by the bacteria Salmonella Typhi. It's generally caused by consuming impurified water and defiled food. AsS. typhi bacteria can survive in water for days, impurity of face water similar as sewage, fresh water and ground water acts as major aetiological agent of typhoid. Defaecation in open places is another notable cause of typhoid transmission. Amidst food, cut fruits kept uncovered for some time are an important cause of impurity in utmost developing countries. Papaya has a neutral pH and its cut face can support the growth of colorful microorganisms. It was observed by Hosoglu et al in a Turkish study that eating cut papaya, lettuce salad and some traditional raw foods in Turkey (e.g. cig kofte) was an important causative factor.[14]

Bacteriology

Salmonella enteric serovar typhi(S. typhi) is a facultative intracellular pathogen that causes typhoid fever in people. Salmonellae are individualities from the family Enterobacteriaceae. The organism isnon-capsulated, nonsporulating, tanned, Gram-negative anaerobic bacilli and external fleece antigens. The bacterium is serologically positive for lipopolysaccharide antigens O9 and O12, protein flagellar antigen Hd, and polysaccharide capsular antigen.[15,16]

Pathogenesis

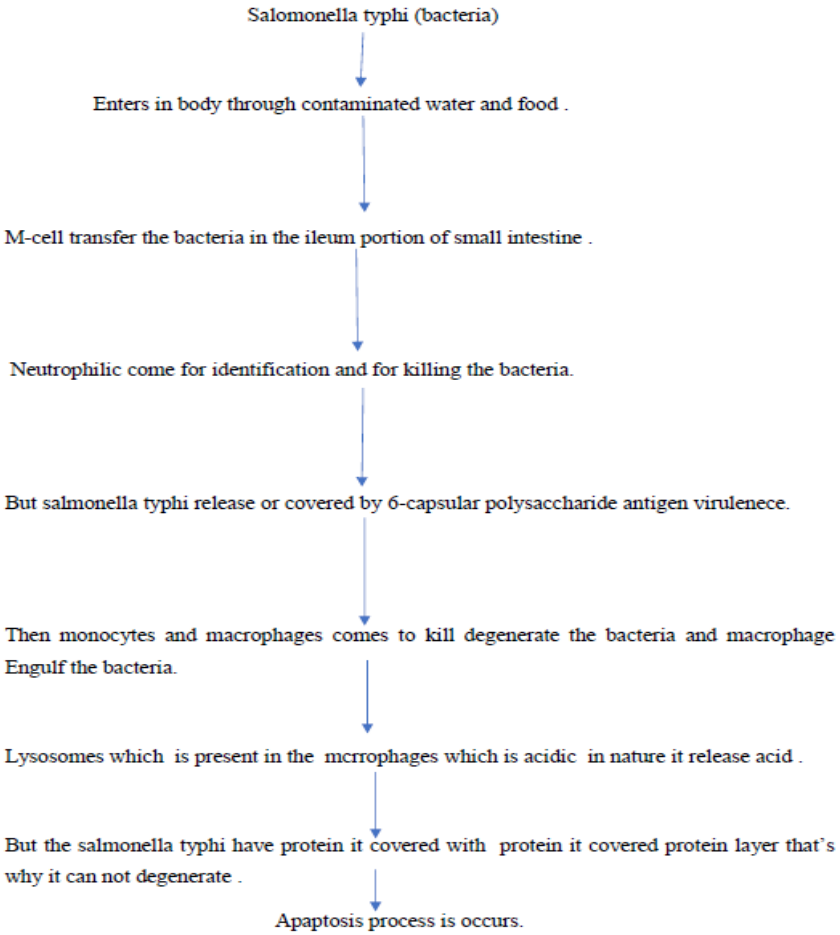
Between 1000 and 1 million organisms are required to create the disease typhoid in a human being, which therefore is said tobe the infectious dose of S. enterica serotype typhi. Obviously, S. typhi Vi-positive strains are more infectious and more virulentthan Vi-negative strains of S. enterica serotype typhi. High gastric acidity is one important barrier against invasion of S. typhiand a low gastric pH is therefore an important defence mechanism. Aging, gastrectomy,

proton-pump inhibitors or antacidsleads to achlorhydria and facilitates typhoidinfection.[17,18]

In the small intestine, the bacteria first adhere to mucosal cells and then invade the mucosa following which they rapidly penetrate the mucosal epithelium via either microfold cells or enterocytes and arrive in the lamina propria, where they rapidlyelicit an influx of macrophage that ingest the bacilli but do not generally kill them. Some bacilli remain within the macrophage of the small intestinal lymphoid tissue and some microorganisms translocate to the intestinal lymphoid follicles and thedraining mesenteric lymph nodes and by which they enter the thoracic duct and the generalcirculation.[19,20] 7 to 14 days is usually the incubation period of typhoid. After that there is an interaction between host immunologic mediator and bacterial factors leading ultimately to the necrosis of Peyer's patches.[19,21,22]

Interestingly, in Africa the disease is often due to nontyphoidal salmonellae such as Typhimurium. In contrast to the Asian situation; however, the two are clinically indistinguishable.[23]

Flow Chart of Thypoid (Pathogenesis)



The World Health Organization (WHO) assess for yearly worldwide rate of typhoid fever, around 21 million cases, is likely a disparage in view of poor diagnostics.[24] A few choices exist for diagnosing enteric fever: clinical signs and side effects; serological markers; bacterial culture; antigen discovery; and DNA intensification. None is totally acceptable. The clinical conclusion of typhoid fever is troublesome in light of the fact that the indications of the ailment are differing and there are numerous reasons for delayed fever in typhoid endemic areas.[7]

Abdominal

Gastrointestinal perforation, gastrointestinal haemorrhage, Hepatitis, Cholecystitis (usually subclinical).

Routine blood tests

Fifteen to 25% patients show leucopoenia and neutropenia. Leucocytosis found in intestinal perforation and secondary infection.[25] In younger children, leucocytosis is common association and may reach 20,000-25,000/mm3.

Liver function tests

These may be deranged. Although significant hepatic dysfunction is rare, some studies and case reports showed there was hepatic derangement simulating acute viral hepatitis and also present as hepatic abscess.[26,27]

Blood culture

This is the standard diagnostic method; it is positive in 60 to 80 per cent of patients with typhoid. Culture of the bone marrow is more sensitive, around 80 to 95 per cent patients, evenin patients taking antibiotic for several days, regardless of the duration of illness. Blood cultureis less sensitive than bone marrow because there is lower number of organism in blood than bone marrow. The sensitivity of blood culture is higher in the first week of illness, increases with the volume of blood cultured (10- 15ml should be taken from school-children and adults, 2- 4ml are required from toddlers and preschool children). Toddlers have higher level of bacteraemia than adult.

Other cultures

Cultures have also been made from the buffy coat of blood, streptokinase treated blood clot, intestinal secretion (with the use of duodenal string capsule), and skin snips of rose spots. The sensitivity of stool culture depends on the amount of faeces cultured, and the positivity rate

increased with the duration of illness. Stool cultures are positive in 30 per cent of patients with acute typhoid fever.[28,29]

Felix-Widal test

The classic Widal test is more than 100 years old.[26] It detects agglutinating antibodies to the O and H antigens of S. enterica serotype typhi. The levels are measured by using doubling dilutions of sera in large test tube.[29] Although easy to perform, this test has moderate sensitivity and specificity.[26] Its reported sensitivity is 70 to 80 per cent with specificity 80 to 95 per cent. It can be negative in up to 30% of culture proven typhoid fever, because of blunted antibody response by prior use of antibiotic. Moreover, patients with typhoid may show no detectable antibody response or have no demonstrable rise in antibody titre. Unfortunately, S. enterica serotype typhi shares these antigens with other salmonella serotypes and shares these cross-reacting epitopes with other Enterobacteriaceae. This can lead to false positive results. If paired serums are available a fourfold rise in the antibody titre between convalescent and acute sera is diagnostic.[28,29]

Considering the low cost of Widal test, it is likely to be the test of choice in many developing countries. This is acceptable, as long as the results of the test are interpreted with care, on the background of prior historyof typhoid, and in accordance to appropriate local cut-off values for the determination of positivity.[29]

New diagnostic tools

Tubex test detect IgM antibodies, Typhidot detect IgM and IgG antibodies against 50 kD antigen of S. typhi.[30] Tubex has not been evaluated extensively but in preliminary studies, this test performed better than Widal test in both sensitivity and specificity. Although culture remains gold standard, Typhidot-M is superior to culture method in sensitivity (93%) and has high negative predictive value. In some studies, it has shown that for total Ig estimation ELISA has superior sensitivity when compared to other tests.[31]

Recently DNA probes and polymerase-chain-reaction (PCR) have been developed to detect S. enterica serotype typhi directly in the blood.[28,26] Urine antigen detection has 65-95% sensitivity. PCR has still not been used in clinica practice.

Cardiovascular

Asymptomatic electrocardiographic changes, Myocarditis, Shock.

Neuropsychiatric

Encephalopathy, delirium, psychotic states, cranial or peripheral neuritis, Guillain- barre syndrome, meningitis, impairment of coordination.

Respiratory

Bronchitis Pneumonia (Salmonella enterica serotype typhi, Streptococcus pneumoniae).

Hematologic

Anaemia, Disseminated intravascular coagulation (usually subclinical), thrombocytopenia, haemolytic uremic syndrome.

Others

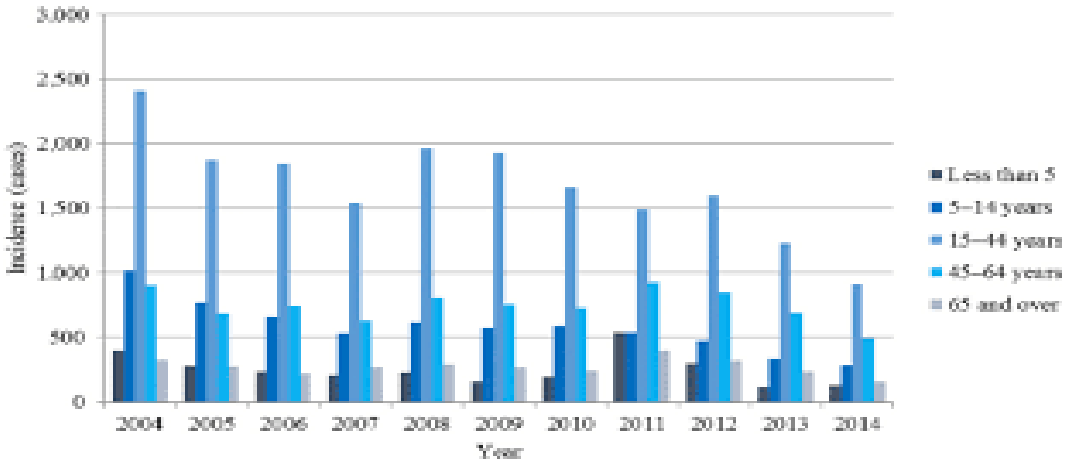
Focal abscess, pharyngitis, miscarriage, relapse, chronic carrier, influenza, dengue, leptospirosis, infectious mononucleosis, brucellosis, rickettsial diseases etc. should be considered.[26,28]

Treatment

Typhoid fever is a noteworthy good solicitude in the creating World. Most lately in last two decades there's development and spread of multidrug inhibition against customary antityphoid medicines(chloramphenicol, cotrimoxazole, and ampicillin) among the typhoid salmonellae, particularly in South and Southeast Asia, including Pakistan.[32] The rise of drug safe typhoid has been another stressing enhancement. After sporadic flare- ups of chloramphenicol safe typhoid in the vicinity of 1970 and 1985, multitudinous strains of S typhi created plasmid intermediated multidrug protection from the three essential antimicrobials employed (ampicillin, chloramphenicol, andCo-trimoxazole)[33] Prompt institution of applicable antibiotics following early opinion is essential for optimal operation. Knowledge of the antibiotic vulnerability is pivotal in determining which medicine to use. further than 90 of cases can be managed at home with oral antibiotic and regular follow- up. still, cases with severe illness, patient vomiting, severe diarrhoea, and abdominal distension, bear hospitalisation and parenteral antibiotic treatment. Chloramphenicol was the medicine of choice for several decades after its preface in 1948. still, the emergence of plasmid intermediated resistance and development of serious side effect like bone gist aplasia had pushed this medicine away. Trimethoprimsulfamethoxazole and ampicillin were employed to fight chloramphenicol resistance in 1970, but it was also discarded because of development of plasmid intermediated resistance. In 1992, emergence of multidrug resistance enteric

fever(resistant to chloramphenicol, ampicillin and trimethoprim- sulfamethoxazole) was explosivelyaddressed in Bangladesh; around36.58 cases were reported in a large study In the 1980s, ceftriaxone and ciprofloxacin came the medicine of choice. Although Fluoroquinolones attain excellent towel penetration, rapid-fire remedial response and veritably low rate of post treatment carriage, strains of bacteria have surfaced in Asia that show resistance to them in theonce decade. Resistance to the fluoroquinolone may be total or partial. The nalidixicacid- resistant strain has reduced vulnerability to fluoroquinolone medicine compared to nalidixic- acidsensitive strain. Although isolates are nalidixic acid resistant but these can be susceptible to fluoroquinolones in slice perceptivity testing. Slice perceptivity testing is defined as a ciprofloxacin MIC of0.12- 1 mg/ L, and isn't always detected by testing of nalidixic acid resistance. The available fluoroquinolones(ofloxacin, ciprofloxacin, perfloxacin) are largely active and original in efficacity. For nalidixic- acid-resistant infections, a minimum of sevendays of treatment at the maximum permitted lozenge is necessary and 10- 14 days are generallyneeded.

Culture Perceptivity data of Department of Microbiology of BSMMU showed8.6 sensitive to nalidixic acid, whereas ciprofloxacin is still 67 sensitive. Indeed a many days before it was allowed that gatifloxacin is better than aged fluoroquinolones. The bacteria demanded binary point mutations (in the DNA- gyrase and Topoisomerase- 4 genes) to come resistant to gatifloxacin. utmost studies in aboriginal countries have linked gyrA mutation inS. enterica as a medium of resistance. Because there's no reported pattern of perceptivity to gatifloxacin in India or Bangladesh or utmost of the western countries for that matter and of its recent reports of some venom it has been withdrawn and no longer used for any systemic illness. Azithromycin in a cure of 500 mg(10mg/ kg) given formerly daily for seven days has proven effective in the treatment of typhoid fever in some grown-ups and children. A cure of 1g per day for five days was also set up to be more effective in utmost grown-ups. Of the third generation cephalosporins, oral Cefixime(15- 20 mg per kg per day, for grown-ups, 100- 200 mg doubly daily) has been extensively used in children in a variety of geographical settings and set up to be satisfactory. still, in some trials Cefixime showed advanced rates of failure and relapse than fluoroquinolones. But antibiotic perceptivity pattern in BSMMU showed advanced perceptivity around78.8. Intravenous third generation cephalosporins(ceftriaxone, cefixime, cefotaxime) are effective with low relapse(3 to 6) and fecal carriage(< 3) rates. Ceftriaxone is effective at a cure of 2- 4gm diurnal in single or two disunited boluses.[33,34]



Typhoid fever cases by age group from 2004-2014. The dark blue bars show the proportion of typhoid fever cases in children younger than 5 years. The navy blue bars represent the number of typhoid fever cases in children aged 5-14 years. The pale blue bars indicate the cases of typhoid fever in individuals aged 15-44 years. The sky blue bars show typhoid fever cases in adults aged 45-64 years. The gray-blue bars represent typhoid fever cases in those aged 65 years and older.[35]

CONCLUSION

Indeed moment, enteric fever is a global public health problem, particularly in developing countries. Studies show the number of civic cases of typhoid is around 800- 900/ time. Widal test, though cheap and available should be interpreted with caution. We should be apprehensive about the advanced prevalence of typhoid fever in India and other developing countries. Massive juggernauts should be initiated to make people understand the preventative measures, part of vaccines, significance of visiting croaker and the suchlike. Croakers should be conscious about the gradationally developing antibiotic resistance and the arising safe and effective newer antibacterial agents. The ultimate includes newer fluoroquinolones and macrolides in large boluses, and incipiently third generation cephalosporines both in oral and injectable forms. Over and over, the profession should look forward to newer restorative and preventative measures.

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