Typhoid fever in Indonesia

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Introduction

Typhoid fever or enteric fever is one of the most common infectious diseases in developing countries. Approximately, there are 216,000 deaths and 21 million cases of typhoid a year. It manifests as a systemic disease, characterized by fever and abdominal pain.1 The disease is most common among children, especially in Asia and Africa.2 Transmission occurs mostly by the fecal oral mechanism. Both environmental sanitation and food hygiene contribute to the distribution of the disease. Thus, developing countries are suitable location for the spreading of the infection.

Figure 1. Global Distribution of Typhoid Fever1

Salmonella enterica serotype Typhi and S. Paratyphi A are the etiologic agents for typhoid fever. The bacteria are members to the family Enterobacteriaceae. Antigens associated with this pathogen are lipopolysaccharide antigen O, flagellar antigen H, and polysaccharide capsular antigen Vi.3 These antigens are related to either pathogenicity-virulence of bacterium, response of the
host immune system, serologic diagnosis and also an interesting research area for the vaccine development. *Salmonella* Typhi uses human as the main reservoir in the nature. Typhoid chronic carriers carry the colonies of *Salmonella* Typhi in their gall bladders. Their ability to survive in the food chain is due to its capability to respond effectively to the environmental changes. Multidrug-resistant *S.* Typhi exists in many areas of Asia, although some are still susceptible to all first-line antibiotics. Transfers of multidrug-resistant plasmid occur from the MDR strains to the naive strains.

Indonesia is an endemic country for typhoid fever. Based on the World Health Organization data more than 100/100.000 people are affected every year. In 2007, the national prevalence of typhoid fever was 1.6%. It was based on Basic Health Research data from the National Institute of Health Research and Development. Twelve provinces have the prevalence number higher than the national prevalence number. The prevalence was found the highest in school-age (5-14 years) children.\(^5\)

**Pathogenesis of typhoid fever**

![Figure 2. Dissemination of *Salmonella* Typhi During Systemic Infection](image)

Cited from de Jong HK, Parry CM, vdPoll T, Wiersinga WJ\(^2\)
The organism enters the human body mostly via the oral route, especially contaminated food and drink. It requires $10^3$-$10^8$ *Salmonella* to produce clinical or subclinical infection in human. Host factors determine the progression of the infection. Gastric acid acidity, normal intestinal microbial flora, and local intestinal immunity (S IgA) are the determinant host factors. Incubation period ranges from 7 to 14 days. The Microfold (M) cells are the specialized epithelial cells overlying the Peyer’s patches that become the internalization site of the bacterium. After penetration, the invading *Salmonella* translocate to the intestinal lymphoid tissues and phagocytized by the macrophage. Salmonella organisms are able to survive and multiply in the macrophages; following the lymphatic draining to mesenteric lymph nodes and some pass to the reticuloendothelial tissues include liver and spleen. Host response involves the pattern recognition receptors (PRRs) such as Toll-like receptors (TLRs) and NOD-like receptors (NLR) of innate immunity to recognize the pathogen and initiate the immune response and bridging the innate and adaptive immunity. Pro-inflammatory cytokines Interleukin (IL)-6, IL-1β, tumor necrosis factor (TNF)-α, and interferon (IFN)-γ are produced by the macrophages after immune system activation. IFN-γ is required to eradicate the infection. During the bacteremia, the bacteria are widely disseminated in the host body. Secondary infection occurs after bacteremia phase. It can occur at liver, spleen, bone marrow, gallbladder and Peyer’s patches. Gallbladder becomes the reservoir for the chronic infection cases. *Salmonella* forms biofilm on gallstone that is likely to be the cause of chronic carriage and shedding of it.6

The clinical manifestation and severity of the disease are varying from patients. Most patients develop fever and malaise during the bacteremia. Flu-like illness, a dull-frontal headache, anorexia, nausea, poorly localized abdominal discomfort, myalgia, diarrhea and constipation also can develop. Case definitions are based on the laboratory evidence of the presence of *Salmonella*. Confirmed case is a patient with fever (38 degree Celsius and above) that has lasted for at least three days, with a laboratory-confirmed positive culture (blood, bone marrow, bowel fluid) of S. Typhi. Probable case is a patient with fever with a positive serodiagnosis or antigen detection test but without S. Typhi isolation. Notable complications of
typhoid fever include gastrointestinal perforation, chronic infection state, peritonitis, septicemia, hepatitis, pancreatitis, and typhoid encephalopathy.

Antimicrobial therapy with fluoroquinolone and chloramphenicol are the drug of choice for the susceptible case, while the multidrug resistant case requires azithromycin or cefixime. There is available vaccination for typhoid fever. The two variants are Ty21a (a live attenuated oral vaccine) that gives protective efficacy 42-53% after 2.5 years (study in Indonesia) and parenteral Vi-capsular vaccine that gives protection 72% after 17 months (study in Nepal).³

**Determinants of typhoid fever**

There are multiple risk factors associated with the typhoid fever. Several studies were carried out in Southeast Asia to describe the risk factors of this disease. This disease is associated with waterborne infection, foodborne infection, and other risk factors that are mostly related to hygiene and sanitation.⁷

Waterborne infection mostly correlated with drinking non-boiled water.⁸ Non-boiled water stores include non-boiled spring water, tap water, ice cubes from a street vendor and other sources than municipal water network.⁹,¹⁰ These water resources are considered to be contaminated and have the high coliform index.

Foodborne infections are more associated by eating food and ice cream from street food stall or mobile food vendor and also contaminated fruit and vegetables.¹⁰,¹¹ Typhoid Mary case can be used to explain it. Street-food vendors who probably are chronic typhoid carriers have the higher risk to spread the infection to the costumers. There is also lack of adequate surveillance from Food-Monitoring Department regarding this issue.

Other risk factors, like unemployed¹⁰, low economic level¹³, living in the crowded area, poor kitchen hygiene, poor garbage handling⁹, poor water sewage management¹⁰, poor hand washing hygiene¹⁰, being a single student living away from family¹⁴, recent contact with typhoid fever patients/chronic carriers¹³, and taking antimicrobial in the 2 weeks preceding the onset of symptoms.¹¹ Being unemployed with low economic status makes people live in the area with less hygiene condition. Overcrowding area makes the disease transmission much easier, considering the close contact among people.
Health System in Indonesia

Problems of health systems in Indonesia in the context of the burden of typhoid fever includes leadership, financing, health workforce, medical products-vaccine and technology, and service delivery. Leadership represented with Ministry of Health had released a decree to the clinical and public health management for typhoid fever.\textsuperscript{15} But the problem is the application still varying among regions, and sometimes the decree works just as a recommendation rather than obligation. It is required further analysis regarding this issue. Health care financing is in the progress for the national health coverage by 2019.\textsuperscript{16} Previously, the insurance system only worked for civil servants, military and police members, and small number of poor people covered by people’s health insurance/regional people’s health insurance. In the current situation the government applies the national health coverage with national insurance system, which is shared among people throughout the country with minimum payment of US$2.5 per capita. Health workforce is another problem faced by Indonesia. The ratio of general practitioner and population is 37.2 per 100,000 populations (2013), which almost exceeded the ideal requirement 40 per 100,000 populations. But the problem is with the unequal distribution of GPs throughout the country. The general physicians are concentrated in Java Island, Bali, North Sumatera Province and South Sulawesi Province.\textsuperscript{17} Medical products; vaccines and technology problems include availability of blood culture lab as the gold standard diagnostic test for typhoid, and also government-covered typhoid vaccine. Several clinical and public health researches on typhoid have been done, but the results implementation still related to the suggestive efforts. Service delivery problems are being faced in rural areas, mainly due to lack of medical doctors and proper diagnostic lab, thus most of cases are diagnosed by non-MD health workers using syndromic approach/clinical manifestations based diagnosis.\textsuperscript{18,19}
Global Initiatives

There were several global initiatives related to typhoid fever and water-borne diseases in Indonesia. Coalition Against Typhoid is a coalition with the members from UN agencies, Bill-Melinda Gates Foundation, US CDC, and many others that had conducted the typhoid vaccine efficacy in several developing countries including Indonesia.\(^ {19, 20}\) The research purposed to determine the importance of typhoid vaccination in endemic countries. And the result was vaccination effective for school-age children for preventive action. USAids, and Ausaids helped to provide access to clean and safe drinking water. The funding was distributed to several regions in the country with unsafe drinking-water access.\(^ {21}\)

Primary Health Care in Indonesia

Typhoid fever primary health care approach was based on the community health center (community clinic) in each district. The promotive and preventive actions including recommendation cooking food, washing and, and using safe drinking water or boil the water before consuming it, also street food surveillance and education for chronic typhoid carrier. Community involvement including promoting people to defecate in latrines, trash and sewage management. Curative action is done in community health center. Management of patient with suspected typhoid fever started from history taking, physical examination, laboratory-workup (serologic mostly) and in hospital it is possible to do blood culture. Empiric antibiotic therapy can be done in community health centers while Antibiotic Sensitivity Test in hospitals.\(^ {18}\)

References