ORIGINAL RESEARCH PAPER

Veterinary Science

KEY WORDS: Salmonella, Pathogenesis, Enteric Fever, Foodborne

SALMONELLOSIS: A REVIEW

Sujata S. Bhave Senior Research Fellow, Department of Veterinary Public Health, Bombay Veterinary College, Parel, Mumbai – 400012.

ABSTRACT

Salmonella is 1 of the 4 important worldwide causes of diarrhoeal diseases. Mostly *Salmonella* causes mild cases; however, sometimes it results in life-threatening illness. Host factors and serotype of *Salmonella* decide the severity of disease. Till now, almost more than 2500 *Salmonella* serotypes have been known and more than half of them belong to *Salmonella enterica* subsp. *enterica*, which accounts for the majority of Salmonella infections in humans. Prophylactic measures have been suggested to reduce the incidence and eliminate the spread of salmonellosis. While basic food hygiene practices, such as "cook thoroughly" and water sanitation are the foremost preventive measures, immunization is also effective against the illness. This review gives an overview of *Salmonella* infection, pathogenesis, clinical manifestations and prevention of *Salmonella*.

INTRODUCTION

Globally, *Salmonella* infection is considered as a major public health concern due to its contribution to the economic burden of underdeveloped as well as industrialized nations by the finances associated with surveillance, prevention and treatment of disease (Crump *et al*., 2004). The burden of foodborne diseases is significant: almost 1 in 10 people fall ill and 33 million of healthy life years are lost every year. Diarrhoeal diseases are the most common illnesses resulting from unsafe food, 550 million people falling ill each year, including 220 million children under the age of 5 years (WHO, 2018). The most widespread manifestation of Salmonella infection all over the world is gastroenteritis which is followed by bacteraemia and enteric fever (Majowicz *et al*., 2010). Morphologically, *Salmonella* is a rod shaped Gram-negative facultative anaerobic bacteria which belong to the family Enterobacteriaceae (Barlow & Hall, 2002). Approximately, 2600 serotypes of genus Salmonella have been identified with the use of the standard Kauffman-White scheme (Allerberger *et al.*, 2003). Salmonella is the most commonly isolated food-borne pathogen and is principally found in poultry, eggs and dairy products (Silva *et al*., 2011). Fresh fruits and vegetables are the other sources of food involved in the transmission of *Salmonella.* One of the main sources of carcass and organ contamination with Salmonella is the slaughtering process of food animals at abattoirs (Gillespie *et al*., 2005).

CLASSIFICATION AND NOMENCLATURE

In 1855, Theobald Smith discovered and isolated the *Salmonella* for the first time from the pig intestine infected with classical swine fever. The name of the bacterial strain was given after Dr. Daniel Salmon, an American pathologist who worked with Smith. At present, the nomenclatural system of *Salmonella* is recommended by the World Health Organization (WHO) Collaborating Centre and it is used by the Centres for Disease Control and Prevention (CDC) (Popoff *et al*., 2003). As per this system, the genus *Salmonella* is classified into two species namely, *Salmonella* enterica (type species) and *Salmonella* bongori, depending on the differences in their 16S RNA sequence analysis. The type species, *S. enterica*, could be again devided into six subspecies based on their genomic relatedness and biochemical characteristics (Reeves et al., 1989) which are denoted with roman numeralsI, *S. enterica* subsp. enterica; II, *S. enterica* subsp. *salamae*; IIIa, *S. enterica* subsp. arizonae; IIIb, *S. enterica* subsp. diarizonae; IV, *S. enterica* subsp. houtenae; and VI, *S. enterica* subsp. indica. Amongst all the subspecies of *Salmonella*, *S. enteric* subsp. enterica (I) is chiefly isolated from mammals and around 99% of Salmonella infections in warm-blooded animals and humans are cause due to *S. enteric* subsp. enterica (I). On the contrary, the rest five five *Salmonella* subspecies and *S. bongori* are predominantly found in the environment and also in cold-blooded animals however, they are rarely isolated from humans (Brenner *et al.*, 2000).

Other than the classification given by WHO based on phylogeny, Kauffman and White developed a method to categorize Salmonella depending upon the three major antigenic determinants: somatic (O), capsular (K) and flagellar (H) (Brenner *et al*., 2000). The heat-stable somatic O antigen is the oligosaccharide constituent of lipopolysaccharide situated at the external bacterial membrane. The heat-labile H antigens are seen in the bacterial flagella which are involved in the activation of host immune responses. The K antigens are heat-sensitive polysaccharides placed at the bacterial capsular surface that are the least common antigens found in the serotypes of Salmonella.

PATHOGENESIS

Based on the serotype involved and the health status of human host, the severity of *Salmonella* infections in humans varies. Children under 5 years of age, old age people and patients with immunosuppressant disease are more susceptible to *Salmonella* infection than healthy ones. More or less all strains of *Salmonella* are pathogenic since they all have the capacity to invade, replicate and survive in human host cells, subsequently resulting in the potentially fatal disease (Eng *et al.*, 2015).

The capability of Salmonella strains to persist in the host cell is crucial for causing pathogenesis because strains deficient in this ability are non-virulent (Bakowski *et al*., 2008). After the *Salmonella* is engulfed into the vacuole of the host cell, it makes use of its type III secretion system to insert other effector proteins into vacuole, resulting in the change of the vacuole structure. This allows the intracellular existence and replication of the Salmonella within the host cells. The potential of the bacteria to exist in the macrophages permits them to be carried in the reticuloendothelial system (RES) (Monack *et al*., 2004).

CLINICAL MANIFESTATIONS

Salmonella strains could be divided into typhoid *Salmonella* and non-typhoid Salmonella (NTS) based on the clinical patterns of human salmonellosis. The four clinical manifestations in humans are enteric fever, gastroenteritis, bacteraemia and other related extraintestinal complications, and a long term carrier state (Sheorey & Darby, 2008).

ENTERIC FEVER

The causal agent of typhoid fever is *Salmonella* Typhi while aetiological agent of paratyphoid fever is S. Paratyphi A, B and C. However, the clinical symptoms caused by paratyphoid fever and typhoid fever are indistinguishable from each other and thus the term 'enteric fever' is collectively used paratyphoid as well as typhoid fever. Furthermore, S. Typhi and S. Paratyphi both are termed as typhoid *Salmonella* (Connor & Schwartz 2005). The only reservoir for the two strains of typhoid *Salmonella* is humans. The transmission of the organism occurs via the ingestion of food or water contaminated with the faeces of infected person. After incubation period of one week or more, the prodromal symptoms including headache, abdominal pain and diarrhea or constipation are seen which are followed by the onset of fever (Bhan *et al*., 2005). Children commonly suffer from diarrhoea, on the contrary patients with immunosuppressing disease have more chances of developing constipation (Thielman & Guerrant 2004). A characteristic pattern of enteric fever is observed during the illness with an initial low grade fever which gradually progresses into

high-grade fever in the second week. In addition to fever, bradycardia, hepatomegaly, splenomegaly, myalgia and rose spots on chest and abdomen may be developed on infected patient (Kuvandik *et al*., 2009).

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GASTROENTERITIS

Strains of *Salmonella* other than S. Typhi and S. Paratyphi are called as Non Typhoidal Salmonella (NTS) and are mainly isolated from animal reservoirs. Infections caused by NTS are characterized by gastroenteritis or 'stomach flu' which is an inflammatory condition of the gastrointestinal tract. The gastroenteritis is caused with other symptoms such as non-bloody diarrhea, nausea, vomiting, headache, abdominal cramps and myalgias. Hepatomegaly and splenomegaly are less likely to be observed in patients with NTS (Hohmann 2001). NTS infections have a lesser incubation period of 6-12 h as compared to typhoid infections. Moreover symptoms of infections caused by NTS are usually self-limiting and last only for 10 days or less (Crump *et al*., 2008). Cholecystitis, pancreatitis and appendicitis are some of the gastrointestinal complications of NTS infections. The most susceptible population to NTS infections includes Infants, young children, elderly people and immunocompramized patients (Scallan *et al*., 2011).

Bacteraemia And Other Extraintestinal Complications

Bacteraemia caused by *Salmonella* is a condition in which the bacteria enter the bloodstream following invasion in the intestine. Though most of the serotypes of *Salmonella* can cause Bacteraemia, the two invasive strains S. Dublin and S. Cholearaesuis are most commonly associated with the bacteraemia manifestations (Woods *et al*., 2008). High fever is distinctive feature of bacteraemia similar to enteric fever, but unlike the enteric fever, rose spot formation is not observed in bacteraemia. In severe illness, the immune response activated by bacteraemia can result in septic shock which leads to high mortality rate. The symptoms of bacteraemia are frequently observed in NTS infections than in typhoid *Salmonella* infections.

Prevention

The foremost route of transmission of enteric fever is the contaminated food or water. In the history it is found that the USA and Western Europe were endemic for enteric fever, but the incidence of *Salmonella* infection declined considerably with proper sanitation of food and water, pasteurization of milk and milk products (Eng *et al*., 2015). Currently, prophylactic measures for reducing the incidence of enteric fever include access to safe water and food, proper sanitation and usage of typhoid vaccines.

The main aim for eliminating the possible modes of transmission of both typhoid *Salmonella* and NTS is to provide the safe and potable water for consumption (Eng *et al*., 2015). By this important measure, incidence of *Salmonella* infection have been successfully reduced in industrialized countries such as in the USA and Europe, however the same results have not been observed in developing and underdeveloped countries (Clasen *et al*., 2007). Other that water, *Salmonella* spp. can be isolated from various types of foods, mostly poultry, eggs and dairy products. The bacterial contamination in food can be eradicated by proper handling and cooking of food. Food irradiation is strongly supported in many countries owing to its efficiency in decreasing the risk of food contamination.

Immunization is an effective prophylactic measure against enteric fever. At present, the two types of vaccine approved for the prevention of enteric fever are the inactive parenteral and oral live attenuated vaccine. But, these licensed vaccines are only limited to infants and infections caused by S. Paratyphi and NTS are not prevented by these vaccines (Lin *et al*., 2001).

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