CODEN [USA]: IAJPBB ISSN : 2349-7750

INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES
SJIF Impact Factor: 7.187

Avalable online at: http://www.iajps.com *A Review Article*

SHIGELLOSIS (BACILLARY DYSENTERY): A REVIEW

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Article Received: January 2021 **Accepted:** January 2021 **Published:** February 2021

Abstract:

Shigellosis is an acute infection of the intestine caused by bacteria in the genus Shigella. There are 4 species of Shigella: S. dysenteriae, S. flexneri, S. boydii, and S. sonnei (also referred to as group A, B, C, and D, respectively). Several distinct serotypes are recognized within the first 3 species. The accurate estimate of morbidity and mortality is lacking in case of shigellosis. This review is focused upon the epidemiology, disease burden and therapeutic approaches and developments of shigellosis.

Key Words: Shigella, diarrhea, Enterobacteriaceae, shigellosis

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Please cite this article in press Savitha Mol. G. M et al, ***Shigellosis (Bacillary Dysentery): A Review****., Indo Am. J. P. Sci, 2021; 08(02).*

INTRODUCTION

Shigellosis is a bacterial infection that affects the digestive system. Shigellosis is caused by a group of bacteria called *Shigella*. The *Shigella* bacterium is spread through contaminated water and food or through contact with contaminated feces. The bacteria release toxins that irritate the intestines. The primary symptom of shigellosis is diarrhea. Shigella species, members of the family Enterobacteriaceae, are responsible for causing acute gastroenteritis which is one of the most common causes of morbidity and mortality in children in developing countries [1].

Shigellosis Transmission

The main approach of transmission is by feco-oral mode and as low as 10–100 FCU can cause an infection. Such low infective doses enable *Shigella* for causing the large outbreak. The high incidences of *Shigella* in the developing countries are mainly imputed to the absence of immaculate water, poor cleanness, malnutrition, and contact of the close persons. The outbreak has been related to person-to-person transmission in crowded or unhygienic environments such as asylums and prisons. The eco-factors such as temperature and rainfall may clarify to affect the transmission [2]. The expression of the virulence gene is activated when the bacterium is ranged from 30 to 37°C, in the medium of pH 7.433, and mild osmotic stress. The infections of *Shigella* may be occurred in the year, but peak prevalence in summer months has been reported [3].

Routes of transmission/reservoirs and meteorological factors

The primary mode of transmission is by faeco oral route and as low as 10-100 bacteria can cause infection. Such a low infective dose enables *Shigella* to cause large outbreaks. The high incidence of *Shigella* in the developing world is generally attributed to lack of clean water, poor hygiene, malnutrition and close personal contact. Outbreaks have been associated with person-to-person transmission in crowded or unhygienic environments like prisons and asylums. Environmental factors such as rainfall and temperature have been shown to affect the transmission. The expression of virulence genes is activated when bacteria are shifted from 30 to 37°C, in medium of moderate osmotic stress and *p*H 7.4[4]. *Shigella* infections can occur round the year, but peak prevalence in summer months has been reported. In most communities the incidence is highest in hot and dry weather, possibly because the scarcity of water in such conditions limits hand-washing and other hygiene measures that reduce person-to-person transfer of the bacteria. From Bay of Bengal islands, shigellosis is reported to occur mainly during rainy seasons, while low numbers of cases are recorded in winters. Less commonly known route of transmission is through contaminated food and water or fomites. The ready-to-eat foods and beverages prepared by street-vendors can also be a source of shigellosis [5].

Microbiology:

Shigella is a Gram-negative, non-motile bacillus belonging to the Enterobacteriaceae family. There are four species of Shigellae: S. dysenteriae, S. flexneri, S. boydii and S. sonnei (designated as serogroups A, B, C and D respectively). The first three species include several 19 serotypes. Acquired immunity to Shigella is serotype-specific. While S. boydii and S. sonnei usually cause a relatively mild illness (watery or bloody diarrhoea only), S. flexneri and S. dysenteriae are chiefly responsible for endemic and epidemic shigellosis (respectively) in developing countries, with high transmission rates and significant case fatality rates [6].

Epidemiology & Pathogenesis

On a global scale, of the estimated 165 million Shigella diarrhoeal episodes estimated to occur each year, 99% occur in developing countries, mainly in children. 5 In 1999, a systematic review reported Shigella to be responsible for 1.1 million deaths per year, 61% of which in children less than 5 years of age, based on prevalence in diarrhoea cases and limited data on case-fatality rates amongst hospitalised children. In 2013, these estimates were revised using a similar modelling strategy, but with updated mortality risk data, suggesting between 28,000 and 48,000 deaths annually amongst children under 5 years due to Shigellosis [7]. In 2016, a quantitative molecular analysis from the Global Enteric Multicentre Study (GEMS) identified an increased burden of Shigellosis and reported it as the leading pathogen among the top six attributable pathogens causing childhood diarrhoea [8].

Cellular Pathogenesis of Shigellosis

Shigella is transmitted by the fecal-oral route and enter the human body via the ingestion of contaminated food or water. The bacteria are highly infectious, since as few as 10 to 100 microorganisms are sufficient to cause disease. This low infectious dose can at least partially be attributed to the presence of effective acid resistance systems, which enable *S. flexneri* to survive the acidic environment in the stomach [9]. Furthermore, it was shown that *Shigella* spp. are able to downregulate the expression of antimicrobial peptides, which are important antibacterial effectors constantly released from the mucosal surfaces of the intestinal tract. After passage through the stomach and small intestine, the bacteria reach the large intestine, where they establish an infection.

Most of the current knowledge on mechanisms underlying *Shigella* pathogenesis is derived from studies of *S. flexneri*. Infection with the invasive pathogen *S. flexneri* is a multistep process. To gain access to the intestinal mucosa, *S. flexneri* crosses the intestinal epithelium, which evolved as a physical and functional barrier to protect the body against the invasion of commensal and pathogenic bacteria [10]. In the initial phase of infection, *S. flexneri* apparently does not invade the epithelial barrier from the apical side but instead triggers its uptake into microfold cells (M cells) and is transcytosed across the epithelial layer. M cells are specialized epithelial cells (EC), which continuously sample particles from the gut lumen and deliver them to the underlying mucosal lymphoid tissue, where immune responses can be initiated. The use of M cells as an entry port is consistent with the in vitro observation that *S. flexneri* barely interacts with the apical surface of polarized EC and enters these cells preferentially through the basolateral pole [11].

Treatment for Shigellosis

Combating dehydration is the main goal of treatment for most cases of shigellosis. It is important to drink plenty of fluids, especially electrolyte solutions, many of which are available over the counter. It is usually not advisable to take any type of medication to relieve your diarrhea, as this will keep the bacteria in your system longer and may make the infection worse.

Moderate or severe infections may require medical treatment. Treatment will usually include antibiotics to eliminate the bacteria from your digestive tract. Your doctor may test your stool to confirm that *Shigella* is the source of the infection. Confirmation of *Shigella* helps your doctor to choose the right medication to fight shigellosis. Drug options include powerful antibiotic medications, such as:

azithromycin

ciprofloxacin

sulfamethoxazole/trimethoprim

Hospitalization for shigellosis is rare. However, in some severe situations, hospitalization is required. If you have extreme nausea and vomiting, you may need intravenous fluids and medication [12].

Prevention and Control

The most effective measure to decrease transmission of shigellosis is proper washing of hands, especially after defaecation. Community health education must emphasize upon good personal hygiene, adequate disposal of faeces, as well as the imminent threat of MDR pathogens. The widespread practice of misuse of antibiotics in viral diarrhea should be discouraged by means of education as well as legislation [13]. Better awareness about general measures such as washing, peeling and cooking of all fruits and vegetables, avoidance of food preparation by personnel who change diapers in daycare centres, proper handling and refrigeration of food, encouraging prolonged breastfeeding in infants, and appropriate case reporting to health authorities may be helpful to prevent further transmission85. Though public health measures to reduce exposure and transmission are highly effective, the establishment of such infrastructure in developing countries is resource intensive and thus remains challenging [14].

Vaccines

There is a strong need for an effective, safe and cheap vaccine against shigellosis. The high disease burden of shigellosis in developing countries, children <5 yr of age as the main victims, difficulty in achieving adequate sanitation and personal hygiene in these regions and scarce therapeutic alternatives for emerging MDR *Shigella* point towards vaccination as a hope for effective and sustainable strategy against shigellosis[15]. Shigellosis is targeted by WHO as one of those enteric infections for which new vaccines are most needed, the target populations being travellers from developed countries and military service personnel, as well as children living in endemic areas
[16].

Although the need for a *Shigella* vaccine is urgent, not much progress has been done due to the antigenic complexity, lack of inter-species cross-protective epitopes, and gaps in understanding of the protective immune response. Several different types of vaccines against *Shigella* have been experimentally tested in animal models and in volunteer trials12. Various live attenuated vaccines such as CVD103, CVD104, CVD107, CVD108, SC602 and WRSS1 have been developed in the past12, however, most were serotype specific with no cross-protectivity [17]. These vaccines progressed into phase 1/2 trials but none could go beyond 12. (Ipa, B, C) subunit vaccine approach has been used for Invaplex (*Shigella* invasion complex) containing invasion plasmid antigens B and C, and lipopolysaccharide (LPS), which was found to induce protective immunity in experimental animals. Similarly, outer membrane proteins are being developed as attractive vaccine options[18]. However, apart from a live, non-invasive *S. flexneri* 2a-*S. sonnei* bivalent vaccine used in China, there are currently no licensed vaccines available100. The current vaccine candidates are either not sufficiently attenuated or not properly immunogenic. Thus, the goal for an effective, safe and successful multivalent vaccine targeting prevalent species and serotypes is yet to be achieved [19].

Key Investigations for Public Health Response

• Stool culture is recommended for symptomatic contacts of a case (e.g., household, child care facility contacts).

• Investigation of food, water and milk supplies for source of infection. Collection of implicated food/water samples for testing (usually performed by Public Health Inspectors).

• Investigation of sewage and/or garbage facilities.

• Travel history, especially when travel has occurred to areas with poor sanitation.

• History of sexual practices placing individuals at higher risk of infection (e.g., oral-anal contact) [20].

Re-Infection by the Shigella Bacteria

Shigella is a group of several different bacteria. Once you have been infected with one type of Shigella, you are not likely to be infected by the same bacteria again. However, you may become infected by a different bacterium from the same family [21].

You can prevent shigellosis by practicing good personal hygiene. Wash your hands before and after you use the bathroom or change a diaper. Discard dirty diapers in a closed bag or trashcan to prevent the spread of the bacteria. Use soap and warm water every time you wash your hands. Wipe down changing tables and kitchen counters with antibacterial wipes before and after use. Avoid close personal contact with someone who is infected with Shigella until at least 2 days after the diarrhea has ended.People who have shigellosis should not prepare food for others until they feel better and stop having diarrhea. Your doctor may test your stool again after your symptoms end to be sure Shigella is no longer present [22].

Funeral Precautions

Funerals for patients who die of shigellosis can contribute to the spread of the disease within the community, especially among persons who have direct contact with the corpse. Corpses must be disinfected with a 2% chlorine solution. Fill the mouth and anus with cotton wool soaked in the chlorine solution. Bandage the head to keep the mouth shut. Persons preparing the corpse must wear gloves, apron and mask. Corpse-carriers must wear gloves. Before and during the funeral ceremony, physical contact between the family and the corpse should be avoided. If this is not possible, make sure family members wash their hands with soap after touching the corpse. Make clean water and soap available for the ceremony [23]. The number of persons attending the funeral gathering should be reduced to the minimum acceptable. If a funeral feast is organized, the preparation and distribution of food should be avoided. However, if food must be provided, persons who prepare or handle it should not touch the corpse at any time. Meticulous hand-washing with soap and clean water is essential before food is prepared and handled. A designated health worker present at the funeral gathering should provide advice on hygienic practices [24].

CONCLUSION:

More than 100 years after this disease discovery, *Shigella* spp. still pose a worldwide major health problem due to the devastating diarrhea that the bacteria may cause. Research performed over the last 25 years has tremendously contributed to our understanding of shigellosis on molecular, cellular, and organismic levels. Thus, we gained profound insight into the evolution of *Shigella* spp. originating from harmless enterobacterial relatives, the structure and function of the major virulence factors, including a T3SS and cognate effector proteins, as well as the interactions of *S. flexneri* with various host cells. Shigella spp. are amazing enteric pathogen with dual mode of pathogenesis (both invasiveness and toxigenesis) and have very low infectious dose. They have arrays of virulence factors that enable them from escaping and down regulation of the immune system. In addition, they possess effectors protein acting as invasins and enterotoxins. The resistance to the empiric therapeutic options may push an alarm to seek about new choices.

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