Shigellosis; A Clinical Perspective

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ABSTRACT

The complexities of Shigellosis and a highly transmissible gastrointestinal illness brought on by pathogenic Shigella spp., are examined in this book chapter. This disease is extremely important worldwide, especially in nations of low economy and poor sanitation conditions. Shigellosis is a serious risk to a wide range of age groups, and it is more severe in susceptible groups. The chapter explores medical intervention, personal cleanliness, and sanitation habits as preventive measures, highlighting the critical role that oral dehydration therapy plays in managing dehydration and lowering mortality. A critical analysis of public health interventions such as handwashing and cleanliness is prompted by the growing problem of antibiotic resistance in severe instances. The ongoing efforts to create vaccines are emphasised, and it is acknowledged that further study is necessary to improve our knowledge of Shigella species and shigellosis.

Keywords: Shigellosis, Shigella spp., Gastrointestinal, Preventive measures, Vaccines

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1. INTRODUCTION

Shigellosis, commonly known as bacillary dysentery, is a gastrointestinal disorder caused by pathogenic Shigella spp. Shigellosis is a widespread public health concern that affects millions of people globally, particularly in regions where clean water, sanitation, and medical treatment are scarce (Rehman et al. 2011; Moxley 2022). This extremely infectious disease develops on poor hygiene, making it difficult to manage and prevent its propagation. It can affect people of all ages, but small children, the elderly, and those with compromised immune systems are more vulnerable (Sharif et al. 2018). Shigella are relatively resistant to stomach acid and only a small number of bacteria is capable of causing infection (Bavishi and Dupont 2011). After ingestion, bacteria replicate in the small intestine and moving to the large intestine, where it releases Shigella enterotoxin and serotoxin type 1, resulting in watery or bloody faeces (Navaneethan and Giannella 2008). Clinical signs typically develop 12 hours to 3 days following consumption of the organism, with a 3-day mean incubation time. High fever, vomiting, and cramping pain in the stomach are common symptoms, followed by bloody mucous diarrhea. The condition normally resolves itself after 5 to 7 days of the onset of symptoms (Niyogi 2005). However, the condition may lead to problems and even death in susceptible individuals (Aslam and Okafor 2018). The goal of this chapter is to provide an overview over shigellosis in depth, explore its numerous clinical perspectives, and emphasize its worldwide significance.

2. ETIOLOGICAL AGENTS

The main etiological agents of shigellosis are

- Shigella (S.) dysenteriae (12 serotypes) Serotype A
- Shigella (S.) flexneri (6 serotypes) Serotype B
- Shigella (S.) boydii (23 serotypes) Serotype C
- Shigella (S.) sonnei (a serotype)

The S. flexneri and S. dysenteriae result in bloody diarrhea, whereas S. sonnei causes moderate illness that may be limited to lung abscesses (Niyogi 2005; Yang et al. 2005).

3. SHIGELLA DISCOVERY: A HISTORY

Kiyoshi Shiga isolated and found the first Shigella species, S. dysenteriae type 1, in 1896. Shiga worked as a research associate at the Institute of Infectious Diseases, directed by Kitasato. Shiga was first assigned to the Department of Tuberculosis and Diphtheria, but in late 1897 Kitasto switched his focus to the microbiological investigation of a Skiri (dysentery) epidemic (Yang et al. 2007; Lampel et al. 2018). The Japanese word "skiri" means "red diarrhea" and is derived from the Chinese character "skiri". Epidemics of dysentery were common in Japan in the last decade of the 19th century, affecting thousands of people and developing a significant number of fatalities (Niyogi 2005; Shaw-Taylor 2020). The 1897 sekiri outbreak killed almost 91,000 people, with a death rate of more than 20%. At the Institute of Infectious Diseases, Shiga examined 36 dysentery cases. He isolated a bacillus from bowel that fermented dextrose, was negative in the indole reaction, and did not produce acid from mannitol. When fed to dogs, the organism's subculture induced diarrhea (Trofa et al. 1999; Lampel et al. 2018). However, a simple agglutination procedure was the key to his incredible discovery. Shiga found that when exposed to the serum of convalescent dysentery patients, the organism usually aggregated. He gratefully acknowledged Dr. Kitasato's help in his publication of his findings (Bartholomew 1998; Lampel et al. 2018). Shiga continued to characterize the microbe, which was first known as Bacillus dysenterie. He specifically discussed the organism's generation of harmful substances. Shiga toxin, one of these components, has recently been assessed in historical perspective. In the period right after Shiga's discovery of the dysentery bacillus, similar microbes were reported by other researchers

over the next 40 years. Three more species of related microbes were identified and taxonomically grouped into the genus Shigella. These species were named Shigella dysenteriae, Shigella flexneri, Shigella boydii, and Shigella sonnei in honor of their discoverer Shiga, Flexner, Boyd, and Sonei (Niyogi 2005). Shigella was named for the first time according to the 1930 edition of Bergey's Manual of Determinative Bacteriology (Trofa et al. 1999; Lampel et al. 2018).

4. CHARACTERISTICS OF SHIGELLA

The genus Shigella belongs to Enterobacteriaceae family. They are small, non-enveloped, non-motile, gram-negative and facultative anaerobic bacteria (Ashkenazi 2004; Bintsis 2017). In DNA hybridization tests, Escherichia coli and Shigella spp. could not be differentiated at the polynucleotide level; nevertheless, the latter species' virulence phenotype was distinct (Khot and Fisher 2013). Enteroinvasive Escherichia coli (EIEC), which has a similar biochemistry to Shigella, can also cause diarrhea and/or dysentery (Ud-Din and Wahid 2014; Belotserkovsky and Sansonetti 2018). Shigella is also serologically linked to several EIECs. EIEC serotype 124, for example, binds S. dysenteriae type 3 in antisera (Belotserkovsky and Sansonetti 2018). Shigella are classified into four distinct groups based on biochemical and serological differences: S. dysenteriae (serogroup A, with 13 serotypes); S. flexneri (serogroup B, with 15 serotypes including subtypes); S. boydii (serogroup C, with 18 serotypes); and S. sonnei (serogroup D, with a single serotype) (Niyogi 2005; Nataro et al. 2011). It is based on the O-antigen component of the lipopolysaccharide that makes up the cell wall's outermost membrane. Serogroups A, B, and C are physiologically quite similar, although S. sonnei may be differentiated from other serogroups by D-galactosidase and ornithine decarboxylase biochemical responses (Hale and Keusch 1996; Niyogi 2005; 2013). The major cause of epidemic dysentery is thought to be S. dysenteriae serotype 1, commonly known as Shiga bacillus (Opintan and Newman 2007). Shigella plaque outbreaks have expanded around the world during the last 40 years (Jun et al. 2016; Lampel et al. 2018).

5. Epidemiology

Shigellosis is a serious health issue globally even after more than 100 years it was first identified. This is especially true in developing nations with poor hygiene and contaminated water supplies (Girma 2015; Mama and Alemu 2016). Humans are the sole natural host of Shigellathis bacterium (Lampel 2013). Shigellosis is most common in children aged 1 to 4 years, however outbreaks of S. dysenteriae type 1 affect people of all ages (Niyogi 2005; Passwell et al. 2010). Shigella typically causes a recurrent looping process of increased nutritional issues, repeated infections, and stunted growth in underprivileged children (Giannattasio et al. 2016). Children in daycares, migrant workers, travelers to underdeveloped nations, prisoners, and homosexual men are the most often infected in the United States and Europe (Hargro and Ferrante 2009; Taneja and Mewara 2016).

The most common mode of transmission is faeco-oral contact. Shigella is very virulent despite having a low infectivity inoculum (almost 10 bacteria) (Sansonetti et al. 1982). People with diarrhea are the primary source of transmission. More infrequently, transmission is associated with contaminated water and food or wastes; yet, the organism's survival in the environment is frequently challenging (Bryan 1977; Kotloff et al. 2018). Flies, notably the common housefly, can act as vectors for the transmission of shigellosis in specific circumstances, where human faeces are not well handled (Levine and Levine 1991; Issa 2019). Shigellosis affects everyone; however, some people are more vulnerable than others. Shigella has been linked to 5 to 15% of cases of diarrhea and 30 to 50% of cases of dysentery (Das et al. 2012; Pons et al. 2013; Taneja and Mewara 2016). Epidemic Shigellosis is the most common form of Shigella infection in underdeveloped countries, but the majority of Shigella infections are endemic (Bennish and Ahmed 2020). In developing countries, endemic Shigellosis accounts for around 10% of all diarrheal cases in children under the age of

five, and it is responsible for up to 75% of diarrheal deaths (Podewils et al. 2004; O'Ryan et al. 2005). S. flexneri is a frequent pathogen in underdeveloped nations, accounting for around 10% of all incidents of diarrhea in children under the age of five (Alam and Ashraf 2003; Reither et al. 2007). Shigella type 1 causes epidemiological and endemic disorders, whereas rare outbreaks of S. sonnei, transmitted by raw food or polluted water, account for more than 75% of cases in developed countries per year (Girard et al. 2006). S. sonnei-caused illnesses are generally less severe (Ashkenazi 2004). S. boydii, a fourth species discovered in India, is now rarely found outside the Indian subcontinent. Surprisingly, although being isolated three times more frequently than S. flexneri in the United States, the latter is most common in homosexual males (Niyogi 2005; Aggarwal et al. 2016).

The HIV epidemic is linked to the spread of shigellosis in many parts of the world. HIV-associated immunodeficiency causes more severe clinical symptoms of Shigella infection, such as chronic or recurrent intestinal illness and bacteremia (Logan et al. 2016). Several reports indicate that wild-type Shigella infection conferring protective immunity. Long-term exposure to high-risk situations reduces disease incidence. The finding that this immunity is serotype-specific (e.g., against the organism's LPS-O antigen) is closely related to vaccine development. Shigella N-somatic antigen antibody responses emerge early after infection and follow the typical course of anti-LPS antibodies, with IgM responses peaking within a few weeks and decreasing after one to two years (Bonilla 2000).

6. STATUS OF SHIGELLOSIS IN PAKISTAN

Shigellosis epidemics have previously occurred in Pakistan, especially in regions with low hygienic conditions and insufficient access to clean water. The disease is frequently linked to unhygienic surroundings, tainted food, and lack of hygiene habits. Shigellosis is particularly dangerous for young children, especially those under the age of five. In order to prevent and control shigellosis, the Pakistani government has worked with international health organizations to upgrade the nation's sanitation system, encourage good hygiene habits, and increase public knowledge of the condition. These initiatives include giving people access to clean water, encouraging handwashing, and putting public health measures in place to stop the disease from spreading. It is recommended to contact reputable organizations like the Ministry of Health or the World Health Organization (WHO) to receive the most recent details on the state of shigellosis in Pakistan. They can provide access to the most recent data, epidemic updates, and preventative and treatment advice (Ahmed et al. 2003; Von Seidlein et al. 2006; Khan et al. 2009; Nisa et al. 2020).

7. PATHOGENESIS OF SHIGELLA AND VIRULENCE FACTORS

Shigella infections are usually restricted to the mucosa of the intestine. It's ability to penetrate and colonies the intestinal epithelium is a critical factor in the sickness (Alamdary et al. 2018). Shigellosis pathophysiology is complex, involving antecedent enterotoxic and/or potentially cytotoxic diarrhea, cytokine-mediated colitis, and colonic epithelial necrosis (Gascón 2006; Thompson 2019). Shigella invasion of the colonic epithelium and lamina propria causes the underlying physiological damage that initiates this inflammatory cascade (Phalipon and Sansonetti 2007). Colitis and mucosal ulcers result in bloody mucous stools and/or febrile diarrhea. The illness process is aided by the host's acute inflammatory response to Shigella infection and subsequent generation of cytokines. In recent years, much has been discovered about the complicated virulence mechanisms used by bacterium to enter epithelial cells and disseminate to neighboring cells (Philpott et al. 2000). Cell invasion and infection dissemination are complex processes that demonstrate various genetic involvement. The process can be split into at least four stages:

(1) Cell invasion;
(2) Intracellular proliferation;
(3) Intracellular and intercellular proliferation; and
(4) Host cell death (Guichon et al. 2001; Parsot 2005).
The organism can infiltrate the intestinal epithelium and M-cells, which are lymphoid follicles that line the mucosal specialized epithelial cells. Several phases are involved in the infection process, including micropinocytosis, escape into the cytoplasm, and subsequent spread and invasion of neighboring cells. A 'virulence plasmid' encodes the IpaJ protein, which facilitates micropinocytosis. Viral genes of Shigella are part of a complicated regulatory cascade that is still being investigated. Shigella penetrates epithelial cells through reorganizing the cytoskeleton, starting with a type III secretion system that appears to be GTPase-controlled. Other investigations discovered many plasmids and chromosomal locations. Interactions with membrane lipoproteins, Shigella nitric oxide-independent clearance, and interferon-dependence of drug resistance are all essential factors in Shigella virulence and invasiveness (Guichon et al. 2001; Parsot 2005; Burnaevskiy et al. 2013; Mattock and Blocker 2017).

8. TOXIN

Flexner discovered that parenteral injection of deceased Shigella cultures into mice resulted in death, only two years after Shigella completely defined as type 1 Shigella, and concluded that the disease was caused by "a toxic substance and not the infection itself" (Lampel et al. 2018). Conradi discovered three years later that a culture autolysis of S. dysenteriae type 1 produced diarrhea, paralysis, and mortality in young rabbits 48 to 72 hours after intravenous injection (Niyogi 2013; Lampel et al. 2018). As a result of these discoveries, the active substance is known as Shiga neurotoxin or simply Shiga toxin. Todd soon observed that injecting S. flexneri filtrate induced diarrhea but not paralysis, indicating that S. dysenteriae type 1 produces particular neurotoxins, which was later validated with the finding of the gene (Niyogi 2013; Lampel et al. 2018). These early researchers clearly observed a combination action of the endotoxin lipopolysaccharide (LPS) and the toxin Shiga protein. Shigella strains produce three types of enterotoxins: (a) Shigella enterotoxin 1 (SHET1), which is found in all S. flexneri strains. Shigella enterotoxin 2 (SHET2) was discovered on a big plasmid linked to Shigella virulence. SHET2 is found in many (but not all) Shigella and entero-invasive Escherichia coli (EIEC) serotypes. When evaluated in rabbit ileal loops, the soluble toxins SHET1 and SHET2 demonstrated considerable enterotoxic action in vitro. In addition, genetic engineering can be employed to attenuate novel vaccination candidates against Shigella and phage-transmitted Shiga toxins generated by S. dysenteriae (Noriega et al. 1995; Vargas et al. 1999; Gray et al. 2015; Kotloff et al. 2018).
Shiga toxins are neurotoxic, cytotoxic, and enterotoxic. They are encoded by chromosomal genes and have two domain structures, 1-A and 5-B, which are identical to Shiga-like toxins seen in an enterohemorrhagic E. coli infection (O'Loughlin and Robins-Browne 2001; CR et al. 2020).

9. EFFECT ON THE INTESTINE

Shiga toxins attach to receptors in the small intestine, blocking electrolytes, glucose, and amino acids from being absorbed into the intestinal lumen (Field 2003).

10. CYTOTOXICITY

The Shiga toxin B subunit binds to host cell glycolipids in the colon, and the A1 domain is internalized via receptor-mediated endocytosis, resulting in irreversible inactivation of the 60S ribosomal subunit, inhibiting protein synthesis, and cell death (Lee et al. 2016).

11. NEUROTOXICITY

Fever and stomach cramping are symptoms of neurotoxicity. Shiga toxin is not required for S. dysenteriae type 1 pathogenicity in primates, but it does add to the severity of clinical symptoms, especially bloody diarrhea/dysentery. Shigella infection normally has numerous stages, and the manifestations vary based on the infecting species, the host's age, the existence of risk factors, and the host's unique immunological status. In S. dysenteriae, the incubation period is 1-4 days but can last up to 8 days. Shigellosis, often known as acute bacterial dysentery, is an invasive infection of the human colon that causes symptoms ranging from brief diarrhea to inflammatory bowel disease (O'Loughlin and Robins-Browne 2001; Stearns-Kurosawa et al. 2010).

12. SIGNS AND SYMPTOMS

Clinical symptoms often manifest itself within 24 to 48 hours of ingestion of infectious dose, and is accompanied by systemic symptoms such as fever, tiredness, malaise, and anorexia. Watery diarrhea is often the only clinical sign of a moderate infection and usually precedes dysentery (Niyogi 2005). Dysentery can manifest itself over hours or days and is frequently accompanied by tiny volumes of bloody bowl, mucous, stomach pains, and tenesmus. The distal colon is primarily impacted in most individuals with dysentery, and the resulting inflammatory colitis is evidenced by loose and frequent stools due to ileal fluid leakage. Patients with severe dysentery can produce more than 20 dysentery stools each day (Lampel 2013). The daily loss of 200 to 300 ml of serum protein through the stool is another sign of dysentery. Serum protein loss depletes nitrogen stores and exacerbate starvation and retardation. Immune factor depletion also increases the risk of associated infectious illnesses and leads to mass mortality (Niyogi 2005; 2013). It is frequently observed in cases of shigellosis that anorexia may persist even as the patient is recovering, potentially leading to a decline in their nutritional well-being.. Shigellosis is rarely linked with severe dehydration and substantial fluid loss (Niyogi 2005; Lampel et al. 2018).

A variety of strange occurrences are also possible. Seizures are the most prevalent, usually occurring during a febrile condition with no associated encephalopathy. Microangiopathic hemolytic anemia may worsen Shiga toxin-produced infection and appear as uremic syndrome. Most cases of shigellosis in otherwise healthy people are self-limiting and recover without complications within 5 to 7 days. Acute life-threatening consequences in malnourished newborns and young children are especially common in underdeveloped nations (Lampel 2013; Lampel et al. 2018). Metabolic abnormalities i.e., dehydration, hyponatremia, and hypoglycemia, intestinal consequences i.e., toxic megacolon, rectal prolapse, and intestinal perforation, and, in rare cases, sepsis are other symptoms. Shigella bacteria have also been found in HIV patients and other immunocompromised individuals (Lampel 2013; Niyogi 2013). The most prevalent chronic symptoms are persistent diarrhea and malnutrition which is a rare post-infectious condition that primarily affects adults following infection. S. flexneri serotypes induce reactive inflammatory arthritis alone or as part of the Reiter's syndrome group comprising arthritis, conjunctivitis, and urethritis. A realistic approach to reduce shigellosis mortality must continue to emphasize prevention and early antimicrobial therapy over treating developed problems (Niyogi 2005; Lampel 2013; Niyogi 2013; Lampel et al. 2018).

13. CLINICAL DIAGNOSIS

Patients with watery diarrhea and fever should be evaluated for Shigellosis. Clinically, the diarrheal stage of illness is indistinguishable from other bacterial, viral, and protozoal infections. Shigella diarrhea can cause nausea and vomiting, however these symptoms can also be caused by atypical Salmonella spp. and enterotoxigenic E. coli infections. Shigellosis has been identified by bloody and mucous stool; however, the

differential diagnosis should include EIEC, Salmonella enteritidis, Yersinia enterocolitica, Campylobacter spp., and Entamoeba histolytica. Although blood is common in amebic faeces, it is usually dark brown rather than the vivid red as seen with Shigella infection. Shigellosis is characterized by diffuse erythema with small ulcers on the mucosal surface on sigmoidoscopy, whereas amebiasis is characterized by distinct ulcers without systemic inflammation (Hale and Keusch 1996; Niyogi 2005; Keusch 2009; Lampel 2013; Niyogi 2013; Lampel et al. 2018).

14. DIAGNOSIS IN LABORATORY

Although clinical indications of shigellosis can raise suspicion, the diagnosis is dependent on the isolation and identification of Shigella in the stool. Shigella can only live for a short time outside the human body; therefore, stool samples should be processed within a few hours of collection. Faecal samples should be collected early in the disease, when there are usually a high number of pathogens in the faeces, preferably before beginning antibiotic treatment (Niyogi 2005). Positive cultures are typically obtained from blood-stained mucus plugs in fresh stool specimens collected during the disease's acute phase. Rectal swabs can also be utilized for Shigella culture if the specimen will be processed swiftly or if the swab can be stored and transported in Cary-Blair transport medium. Shigella samples can also be transported on buffered glycerol medium (BGS). Although BGS remains basic (as seen by a continuous pink color after feces addition), it is thought to be superior to Carey-Blair medium (Lampel 2013).

In microbiology laboratories, Shigella is commonly isolated by primary passage cultures in differential/selective media with aerobic incubation to prevent the growth of normal anaerobic flora. MacConkey Agar, Hektoen Enteric, Salmonella-Shigella Agar, Xylose Lysine Deoxycholate, and Deoxycholate Citrate media are all common principal isolation medium. S. dysenteriae type 1 and S. sonnei do not grow well on Salmonella-Shigella Agar. These media contain bile salts, which hinder the growth of other gram-negative bacteria, as well as a pH indicator, which distinguishes lactose-fermenting bacteria (coliforms) from non-lactose-fermenting bacteria like Shigella. After a brief growth period, liquid enrichment medium can be seeded with faeces samples and cultivated on selective/differential agar media. After incubating the first batch of isolation medium overnight at 37 °C, the colorless, non-lactose-fermenting colonies can be inoculated with trisaccharide agar (TSI). Shigella generates a base-poor end and an acidic end in this media, and there are no air bubbles in the agar. This reaction indicated a possible identify, which was validated by slide agglutination tests using commercially available antisera against serogroup and serotype. Some normal gut flora E. coli biotypes are remarkably similar to Shigella. The capacity of these E. coli bacteria to decarboxylate lysine distinguishes them from Shigella. However, some coliform bacteria cause invasive intestinal disease because they carry virulent Shigella-like plasmids, and these pathogens are frequently discovered through extensive serological testing for EIEC serotypes (Lampel 2013; Lampel et al. 2018).

Shigella detection techniques that are sensitive and fast have been developed. Genetic probes or polymerase chain reaction (PCR) primers are used in these approaches. Virulence genes that have been specifically targeted, such as the plasmid locus (ipl) or the locus encoding the antigenic virulence factor IpaH, play a critical role in understanding and combating the pathogenic mechanisms of the associated microorganisms. Although more sensitive than traditional diagnostic methods, these procedures necessitate sophisticated facilities that may be too specialized for common clinical laboratory use (Theron et al. 2001; Niyogi 2005; Gómez-Duarte et al. 2009).

According to the National Committee for Clinical Laboratory Standards, all confirmed Shigella isolates should be evaluated for antibiotic susceptibility using the agar diffusion or Broth dilution procedure. To properly calculate the minimum inhibitory concentration (MIC), newer procedures such as the Epsilometer test (E-test) can be applied. Its biggest downside is its exorbitant price. A commercial PC-based geographic information system (GIS) was recently deployed in a S. sonnei infection outbreak in Fort Bragg, North

Carolina. GIS allows for the direct visualization of infectious disease transmission dynamics linked with community outbreaks (Wilson et al. 2006; Mirnejad et al. 2013).

15. PATIENT CARE

Rehydration therapy is an essential initial intervention that can be done to correct dehydration caused by any type of diarrhea and greatly reduce diarrheal fatalities. Oral dehydration therapy, developed by the World Health Organization, has proven to be effective and safe. It is a critical component of the life-saving treatment of acute watery and desiccant diarrhea, as well as a key component of worldwide diarrheal disease control program (Victora et al. 2000). Although severe dehydration is uncommon in shigellosis, it is usually self-limiting with proper fluid intake, and the choice to administer antibiotics is based on the severity of the ailment, the patient's age, and the possibility of further infection spread. Strong antimicrobials can considerably reduce shigellosis symptoms in 48 hours while minimizing the usual disease duration from 5-7 days to 3 days (Farthing et al. 2013). These additionally shorten the amount of time it takes to shed once symptoms disappear. Relapses of shigellosis can extend from 2 days to 10 days or more without antibiotic therapy, and the risk of serious complications or mortality is extensively raised, particularly in infections caused by S. dysenteriae type 1 or S. flexneri. Inadequate shigellosis treatment is a major cause of chronic diarrhea (Victora et al. 2000; Farthing et al. 2013).

If shigellosis is diagnosed, all patients with this kind should be treated with antibiotics, with the choice of drugs based on the antibiotic susceptibility pattern of the shigellosis strains prevalent in the region (Sack et al. 2001). If the patient improves after two days of treatment, a five-day course should be completed. If the patient's condition does not improve, the antibiotic should be changed. If the patient does not improve after a second antibiotic dose, the diagnosis should be reconsidered, and a stool microscopy, culture, and sensitivity tests should be conducted. However, due to widespread drug resistance difficulties, following WHO standards for shigellosis treatment can be problematic (Niyogi 2005; 2007; 2013).

A range of antimicrobial medicines are useful in the treatment of shigellosis. Options are restricted due to the emergence of resistance worldwide. Shigella resistance to sulfonamides, tetracyclines, ampicillin, and TMP-SMX is widespread, hence these medications are not indicated as first-line therapy. Quinolones were the medicine of choice for treating Shigella in the 1990s. All current quinolones show excellent in vitro action, and numerous trials show therapeutic efficacy. For known or suspected shigellosis, most authorities now prescribe oral quinolones (ciprofloxacin, levofloxacin, or norfloxacin). One or two doses are sufficient for mild to moderate dysentery, whereas a 3- to 5-day course of treatment is recommended for complex bacterial dysentery or confirmed S. dysenteriae type 1 infection. Although single doses of 800 mg norfloxacin and 1 g cypra-ofloxacin have been demonstrated to be beneficial against S. dysenteriae type 1 infections, but these are currently less effective. None of the newer fluoroquinolones are safe for youngsters or pregnant women to use. The use of fluoroquinolones in children is restricted due to the possibility of chondrotoxicity. However, there is mounting evidence that these are not dangerous. Although shorter treatment cycles have been explored, all previous research used a 5-day treatment plan. With quinolone resistance developing and concerns regarding its safety in youngsters, the search for alternative drugs begins. Although first and second generation cephalosporins are active in vitro, clinical trials have been unsatisfactory. Cefixime has been studied in the treatment of shigellosis in adults, with a success rate of just 53% (Spence 2004). Clinical trials in Israel, however, have demonstrated that cefixime and ceftriaxone have higher bacteriological and clinical cure rates and are safe for usage in children (Diniz-Santos et al. 2006).

Recently, it was discovered that azithromycin, a macrolide medication with good intracellular permeability and modest anti-Shigella action in vitro, is useful in the treatment of shigellosis. Non-absorbable antibacterial rifaximin is another option worth investigating further. In vitro antibiotic susceptibility and clinical efficacy did not have a perfect link. Although the antibiotics employed must be effective against pathogenic germs,

several medicines used in vitro are clinically useless. The use of inefficient antibiotics, that is, antibiotics to which the organism has developed resistance or that are clinically ineffective, can pose dangers. In addition to the drug's potential systemic side effects, it also disrupts the normal intestinal flora. Furthermore, changes in the frequency of serogroups in Shigella isolates, as well as changes in antimicrobial susceptibility patterns, make it challenging to discover effective medications to treat Shigellosis. As a result, the deployment of surveillance systems is critical for effective shigellosis treatment and control. Seizures, encephalopathy, and intestinal perforation are required to specialized therapy in addition to antibiotics and fluids (Niyogi 2005; 2007; 2013; Kotloff et al. 2018; Lampel et al. 2018).

16. ANTIBIOTIC'S RESISTANCE

The history of the genus Shigella indicates that it is subjected to acquire drug resistance. Shigella strains have been increasingly becoming resistant to the most widely used and affordable antimicrobial drugs over the past few decades, which has resulted in treatment failure and higher mortality rates (Lampel et al. 2018). Shigellosis, especially that brought on by S. dysenteriae type 1, is difficult to treat due to multidrug resistance. Sulfa medicines were quite effective in the 1940s, but by the 1950s, they were of little use. Tetracycline later proved to be very effective in the 1960s, followed by ampicillin and cotrimoxazole. From the late 1960s to the 1980s, there was an increase in resistance to these antibiotics. Ciprofloxacin and other fluoroquinolones, ceftriaxone, and azithromycin are antimicrobials that remain proven effective. Even within a single site spread across two different areas, antimicrobial resistance trends to vary from site to site. This might be a result of the emergence and distribution of clones that are resistant to antibiotics (Niyogi 2005; Lampel 2013; Chung et al. 2021).

17. CONTROL STRATEGIES

Ensuring an ample supply of clean water and practicing proper hygiene in managing feacal matter are crucial tactics in combating shigellosis, as is the case with various intestinal illnesses. At best, these public health measures are long-term approaches to prevent enteric illnesses in impoverished nations. Comprehensive media and personal awareness campaigns that feature the following components are among the most successful approaches for reducing mortality and morbidity;

1. Encourage handwashing after faeces and educate all households on how to actively prevent faecal contamination of food and water;
2. Promote the practice of breastfeeding; and
3. Encourage the use of oral treatment to treat acute diarrhea (Ahmed et al. 2003; Niyogi 2005; Kotloff et al. 2018).

18. VACCINATION

Despite the fact that S. dysenteriae type 1 was found to be the source of epidemic dysentery in Japan in 1898, no vaccine is currently authorized and there is no agreement on the mechanisms behind host immunity to Shigella (Kotloff et al. 2018). The creation of a new generation of vaccine candidates has been made possible by developments in biotechnology and significant improvements in our knowledge of the molecular processes underlying Shigella pathogenicity. Current Shigella vaccine choices have been proven to be safe and immunological in animal models and are based on attenuated S. flexneri or S. sonnei strains, dead S. flexneri strains, or certain synthetic polysaccharides (Niyogi 2005). Polysaccharide conjugates that are specific for S. freundii and S. sonnei have been proven to be kid-safe and immunogenic. In clinical trials, several of these vaccinations have previously been tried and have demonstrated promise in avoiding

diarrhea. Shigella immunity is serotype-specific, therefore the effectiveness of a Shigella vaccination in a given situation depends partially on how the serotypes are presented in the vaccine (Mani et al. 2016). Therefore, it is essential to comprehend the serotype distribution of clinical isolates in order to create novel vaccines and determine if these are appropriate for use in projects related to public health. There is a critical need for type 1 and type 2a Shigella vaccine development. Shigellosis still has a serious impact on the world and is not sufficiently managed by current preventive and treatment strategies. Innovative approaches, such as creating vaccinations against the most prevalent serotypes, might be very advantageous (Niyogi 2005; 2013; Mani et al. 2016; Lampel et al. 2018).

19. FUTURE PERSPECTIVES

To learn more about the Shigella species much more research is required. There is still a gap between the real origin of Shigella spp. and many elements of its pathophysiology and virulence mechanisms that have been revealed by investigations. The migration path of Shigella spp. from underdeveloped to developed nations remains in need of attention and explanation. The finding of intricate underlying processes required investigation of the structural and molecular aspects of Shigella spp. In order to comprehend the rising burden and changing environment globally, it was necessary to conduct proper surveillance and monitoring of its epidemiology in connection to other closely related species. The obligation of healthcare professionals and scientists to seek out better solutions and devise methods for the benefit of mankind has increased more than ever in recent years as a result of technological innovation, new lab instruments, equipment, protocols, and the decreasing cost of sequencing.

20. CONCLUSION

Shigellosis or bacillary dysentery is a highly contagious gastrointestinal disease caused by pathogenic Shigella spp. It constitutes a global health problem, especially in areas with poor sanitation, limited access to clean water and medical care. Shigellosis affects all ages, but is more dangerous for vulnerable groups. Prevention includes proper sanitation, personal hygiene and medical care. Oral dehydration therapy is essential to control dehydration and reduce mortality. In severe cases, antibiotic resistance is a challenge. Public health measures such as hand washing and hygiene are important. Vaccine development is ongoing. Further research is needed to better understand Shigella spp. and shigellosis.

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