ANTIMICROBIAL RESISTANCE IN SALMONELLA ENTERICA SEROVAR TYPHI: UNDERSTANDING THE MECHANISMS AND PATHOGENICITY OF INFECTION” A COMPREHENSIVE REVIEW

ANWAR A*, AYAZ N, AHMAD S, HAFSA, NAZ F, NADIR K

Institute of Microbiology, University of Agriculture Faisalabad, Pakistan
*Corresponding author's email address: ahmedanwaruf@gmail.com

(Received, 17th October 2023, Revised 08th December 2023, Published 18th January 2024)

Abstract: Typhoid Fever is a contagious disease caused by Salmonella enterica serovar typhi. It is also the cause of bloodstream infections in most of the developing countries. The pathogen can escape from the host's immune response, a feature linked with the capsular structure of bacteria, which contributes to its virulence and is a crucial factor in the dissemination of infection. Salmonella enterica serovars are classified as typhoidal and nontyphoidal salmonella. In this review, we will discuss the ecumenical occurrence of immune strains of Salmonella enterica. We cover the mechanism of antimicrobial resistance in Salmonella, including plasmid-mediated resistance. Antibiotic resistance can occur through various mechanisms, such as deactivation of antibacterial medications, changes in therapeutic targets, and acquisition of foreign DNA coding for resistance determinants through horizontal gene transfer. Additionally, bacteria can employ different efflux pumps to resist antibiotics. These are some of the common ways in which antibiotic resistance is developed. We will explore the factors contributing to its virulence, such as the improper use of antibiotics, gene transfers, recurrent infections, and reduced host immunity. Proper hygiene practices and accurate treatment are necessary to combat typhoid disease, which can be better understood by studying its pathogenesis and diagnosis. The widal test and Typhidot test are essential for the diagnosis of salmonella. Vaccines are available against typhoid. We can overcome disease development through vaccination by choosing safe delivery methods and control strategies.

Keywords: Typhoid Fever, Contagious disease, Bloodstream infections, Immune response, Capsular structure, Virulence

Introduction

Human typhoid is caused by the Gram-negative bacteria Salmonella enterica serovar Typhi, or simply S. Typhi (Khan and Shamim, 2022). In several developing countries, it is the primary source of bloodstream infections acquired in the community (Deen et al., 2012). Because of its virulence and ability to evade phagocytosis in the host's body, the bacterium is coated in a capsule that aids infection. These intracellular pathogens can evade the host's immune system and withstand it, effectively increasing their virulence and spreading the infection. Using the Kauffmann and White classification scheme, about 1600 serovars of Salmonella bacterium have been categorized and placed into the sub-species of enterica. Typhoidal Salmonella is the collective term for the Salmonella enterica serovars Typhi, Paratyphi A, B, and C; the other serovars are categorized as nontyphoidal Salmonella (NTS). The general term "enteric fever" refers to both typhoid and paratyphoid fever, which are caused by human host-restricted typhoidal Salmonella strains. NTS strains can infect a limited number of non-human animal species or be host-specific and infect or colonize a wide variety of vertebrate animals (Feasey et al., 2012).

Its transferal method is primarily indirect and is typically vehicle-borne through putrescent water and food reservoirs. Even though S. Typhi may endure in the environment for longer, it does not proliferate in areas with access to food and water (Li and Microbiology, 2022). Two patterns of S. Typhi transmission are recognized. "short-cycle transmission" describes the bacterium's shedding into the surrounding environment or close quarters, contaminating food and water supplies (Gauld et al., 2022b). This process is typically associated with food handlers and facilitated by inadequate hygiene and sanitation practices. Isolating S. Typhi from the environment makes it harder to track down long-cycle transmission pathways (Gauld et al., 2022a; Nair et al., 2019). The pathogen entry site is the mouth, where it might enter by consuming infected food or drink. Following infection, the incubation time shortens, and the illness risk rises directly to the dosage consumed (Karkey et al., 2013). Typhoid fever is thought to be primarily caused by S. Typhi, which is often attained by the consumption of deleterious water or food, and it is frequently seen as a condition linked to travel (Masueet-Aumatell et al., 2021; Parry et al., 2002). The primary reported cause of pediatric septicemia in nations like Pakistan is the causative infection. Furthermore, Salmonella species are known to be significant foodborne pathogens worldwide, with less than 50,000 cases documented in Europe alone and over 80 million cases reported in 2020. Dairy products, meat, eggs, and live poultry are known to provide a significant risk. Furthermore, in low and middle-revenue nations, the risk of disease is linked to a variety of factors, primarily inadequate hygiene and a lack of water that is safe to drink, as well as environmental hazards and lifestyle choices; in high-income countries, on the other hand, the leading risk factor is associated with fundamental contamination of sources of fruits, vegetables, and meat (Authority et al., 2019; Carstens et al., 2019; Rudd et al., 2020).
Despite several improvements in medical science and healthcare practices, more individuals are at risk of acquiring typhoid, which may be a significant cause of mortality in severe or complex cases. The mortality risk from typhoid fever was between 10% and 30% before antimicrobial medication therapy, but it is currently less than 1%. The current danger to the efficient treatment of S. Typhi is the development of immune strains that can resist antimicrobial therapy (Saha et al., 2019). Historically, trimethoprim-sulfamethoxazole, ampicillin, and chloramphenicol have been the first-line treatment drugs for typhoid fever. In the late 1970s and early 1980s, strains of S. Typhi that were resistant to three of these antibodies were first discovered to be multidrug-resistant (MDR) strains (Klemm et al., 2018b).

Early in the 1990s, ciprofloxacin (CIP) resistance started to appear. Over 90 percent of clinical isolates from endemic areas now exhibit decreased ciprofloxacin susceptibility. Due to these developments, azithromycin and ceftriaxone (CRO) are two examples of other antimicrobial medicines that are now the first-line and experimental therapies (Choudhary et al., 2013). Sadly, instances of resistance to these drugs have recently been reported. Furthermore, a recent study from Pakistan reported the first widespread epidemic of a highly drug-resistant (XDR is known as MDR in addition to resistance to ceftriaxone and ciprofloxacin) S. Typhi clone (Tamnoy et al., 2018).

The European Food Safety Authority (EFSA) 2018/2019 antimicrobial resistance data indicates that over 25% of human cases of multidrug-resistant Salmonella spp. were found to be prevalent. Even though the disease mortality rate is lower in affluent nations, typhoid fever still claims more than 200,000 lives each year globally. The management of healthcare's budget and resources, which are crucial for public health control, depends on this information. Furthermore, due to frequent transmission of the disease, it is crucial to have the necessary information and understanding of its present trend (Crump et al., 2004).

2. Diagnosis of Typhoid Fever:

Isolating S. Typhi from blood is the most accurate approach to determining typhoid fever infection. While bone marrow bacterial culture has more sensitivity, it is also more invasive, challenging to obtain, and impractical for routine use. Despite their limited sensitivity, blood cultures are still regarded as the gold standard for diagnosis (Wijedoru et al., 2017). Furthermore, because culturing takes not less than 48 hours to provide results, its optimal application is hindered in assets-constrained countries where typhoid fever is expected due to a lack of medical facilities and suitably qualified laboratory personnel (Ajoba et al., 2018).

A serological method called the Widal test finds agglutinating antibodies against the H and O antigens. Owing to its affordability and ease of use, it is extensively utilized; nevertheless, its sensitivity is poor and heavily dependent on the operator, with significant regional variations in values (Andualem et al., 2014; Olsen et al., 2004). Additionally, to correctly interpret the results of the Widal test, sera from two visits must be collected (spaced 10–14 days apart)(Parry et al., 2002). Since there is no set titer threshold to identify the disease, each nation must also decide on an appropriate antibody titer to diagnose typhoid. This is because a typical, healthy population living in a zone where typhoid fever is endemic and has a background level of antibodies. The Widal test is inadequate for antibiotic resistance because it does not show the results about susceptibility (Klemm et al., 2018a; Pathi et al., 2017).

Many commercially accessible typhoid fast antibody tests can produce outcomes in as little as two minutes, enabling patients who test positive to get antibiotic treatment immediately. Pre-dotted antigen strips are used in one qualitative test called Typhidot® to check for the presence or absence of immunoglobulin (Ig)M and (Ig)G antibodies to an exterior membrane protein (Klemm et al., 2018a). Anti-O:9 antibody titers are determined using a semi-quantitative colorimetric assay (IDL TUBEX® TF) that examines color responses visually and subjectively. However, this kind of testing can perform poorly in performance comparison studies that use blood culture as the comparator (Keddy et al., 2011). According to a current meta-analysis, TUBEX has an average sensitivity of 78 percent (95% confidence interval [CI] 71–85) for true positives and a specificity of 87% (95% CI 82–91) for true negatives. The average sensitivity and specificity of all typhoid variations analyzed were 84% (95% CI 73–91) and 79% (95% CI 70–87), respectively. The sensitivity of typhoid fast antibody tests may be as little as 60.2% (95% CI 49.3–71.2) and 59.6% (95% CI 50.1–69.3), according to recent research on patients from Bangladesh. These findings highlight the challenges associated with typhoid laboratory diagnosis (Islam et al., 2016).

The gold standard for identifying chronic typhoid carriers does not yet exist. The conventional method for identifying typhoid transmission involves serially analyzing stool and through samples of urine (using the cultivation method). However, this approach has limited sensitivity and is logistically challenging. It can be challenging to diagnose S. Typhi infection in endemic locations because the signs and symptoms of typhoid fever are similar to those of other pyretic infections, such as malaria, dengue, or other arbovirus fever (Gunn et al., 2014).

Consequently, it presents a diagnostic problem when separating S. Typhi infections from other causes of fever in endemic locations. In most endemic areas, the only accessible procedures for identifying a feverish patient are the thick smear of blood for malaria or the Widal tube agglutination test for typhoid fever. (at least in Africa). Research has revealed that the Widal test performs poorly. In environments with few resources, frequent issues include inadequate healthcare infrastructure, poor monitoring and misdiagnosis brought on by insensitive procedures, and absence of diagnosis because tests are not requested. To accurately identify typhoid patients and chronic carriers, new sensitive, specific, scalable, and economical approaches are needed to limit the spread of infection and estimate the worldwide burden of S. typhi (Isma'il, 2000). Finding out the individual's travel history is essential for patients who have been to nations where typhoid is not widespread (Parry et al., 2002).

3. Pathogenesis of Typhoid Fever

The typhoid is a systemic disease with varying degrees of severity. Recently, a novel paradigm that permits the
examination of S. Typhi pathogenicity in a humanized model of severely combined immune deficient (SCID) non-obese diabetic (NOD) mice was described. Typhoid fever pathophysiology is now better understood, particularly about the molecular and cellular events that cause the clinical symptoms of the disease (Hornick et al., 1970). This is due to several significant discoveries, which are mentioned below:

The type III protein-secreting system of bacteria is one of them.

The virulence genes of Salmonella species encode five distinct Sips (Salmonella invading protein) A-E. These proteins can cause macrophages to undergo apoptosis.

The function of the Toll R2 and R4 receptors was first identified in Drosophila on the surfaces of macrophages. The gut lumen and internal organs function as immune defense lines, and macrophages use lipopolysaccharide-binding protein (LBP) and CD14 with Toll family receptors to carry out cell signaling.

The core function of endothelial cells (singular: Endothelium is the inflammatory diversion of blood arteries into bacterially infected tissues (Hornick et al., 1970).

Intestinal mucosal immune system (first-line of defense):
In volunteers, the contagious dosage of S. Typhi ranges from 1000 to 1 million organisms. Since the bacteria must pass through the gastric acid barrier to enter the small intestine, the low pH of the stomach serves as a crucial defense mechanism. Bacteria enter the small intestine through the Peyer's patches by passing through an intestinal transitional cell layer (CEI) and arriving at the M cells. Over Peyer's patches, specialized cubical dome epithelial cells are known as Micro fold cells, most likely developed from CEI and tiny mucosal surface pockets. The pathogenic bacteria are quickly internalized after coming into touch with M cells. Once they get to a set of cells that present antigens called antigen-presenting cells (APCs), they undergo the process of partial phagocytosis and neutralization. Infecting phagocytes are arranged into distinct foci surrounding normal tissue and develop into diseased lesions.

Membrane adherence molecules such as (Inter-Cellular Adhesion Molecule 1) ICAM1 and (Vascular Cell Adhesion Molecule 1) VCAM-1 are necessary for dynamic lesion formation. Additionally, the harmonized action of cytokines [interleukin IL-12, IL-18, IL-14, IL-15, tumor necrosis factor (TNF)-α and interferon (IFN)-γ] is also required. The bacteria proliferate and spread abnormally in the infected tissue when pathological lesions fail to develop. Some bacteria get past this barrier and land in the mature lymphoid follicles, also known as Peyer's patches. These are mostly made up of dendritic cells and mononuclear cells that function as T lymphocytes. DC exposes immune cells to bacterial antigens, which cause T and B lymphocytes to become activated (Kaur and Jain, 2012).
cell activation. In systemic salmonellosis, such as typhoid fever, Salmonella may selectively target host cells, such as macrophage and dendritic cells, which aid in the pathogen's dissemination via the blood streams and lymph to the tissues and the mesenteric lymph nodes (MLNs) beneath the skin. After that, the liver, spleen, and bone marrow get the transferred material. Bacteria may exist in the gall bladder, bone marrow, and MLNs for an infinite amount of time. Furthermore, there might be mucosal surface shedding in addition to recurrent mucosa reseeding via the medium lumen of the small intestine and the bile ducts. Interferon-(IFN-γ) is released by T cells, and it is responsible for controlling Salmonella intracellular proliferation and maintaining persistence. Interleukin (IL)-12 and the inflammatory cytokine tumor necrosis factor-α (TNF-α) can also manage persistent Salmonella. IL-12 can increase the production of IFN-γ. Dissemination from the lamina propria of the intestinal mucosa
T and B cells can leave lymphatic nodules and migrate to the spleen and liver thanks to the reticuloendothelial system. These organs' macrophage system mainly employs phagocytosis to eliminate the bacteria. Nevertheless, mononuclear phagocytic cells can support and harbor Salmonella. The level at which the bacteria are relinquished from their sequestered intracellular location and enter the circulation is ascertained by the number of bacteria, their pathogenicity, and the host’s immune system. The phase of the illness known as bacteremia is characterized by the dissemination of germs. The most common secondary infection sites include spleen, liver, gallbladder, and bone marrow infections, particularly Peyer's patches close to the end of the ileum. S. Typhi stimulates the Kupffer-Browicz cells in the liver (House et al., 2001).

4. Antimicrobial Resistance:
Antimicrobial resistance (AMR) is the capability of bacteria to survive and proliferate in the existence of antimicrobial medications (Holmes et al., 2016). AMR is a significant worldwide issue. Acquired resistance, or AMR, is the capacity of bacteria to withstand the adverse reactions of antimicrobial drugs that were once successful in treating illnesses brought on by such infections. Bacteria and other microorganisms grow resistant to some antibiotic treatments, making them insensitive (Murugaiyan et al., 2022).

Mechanism of Antimicrobial Resistance in S. Typhi
Antimicrobial resistance in Salmonella species, especially S. Typhi, may be mediated via chromosomal or plasmid DNA. The deactivation of antibacterial medications, alteration of the therapeutic targets, horizontal gene transfer acquisition of foreign DNA coding for resistance determinants from global cell adaptation mechanisms, and utilization of different efflux pumps are the usual ways in which resistance occurs. Gene transfer employing pathogenicity plasmids, phages, and mobile genetic elements can actively mediate extrinsic causes of resistance, or genes producing drug-degrading enzymes and pumping agents for efflux can be produced by point mutation (Carattoli, 2013; McEwen and Collignon, 2018; Munita and Arias, 2016).
incompatible (Inc) plasmids, categorized as IncH1, IncH2, and IncH3. A composited transposon made up of plasmids R27, pHCM1, and pAKU1 can carry resistance to multiple drugs in multi-drug resistant S. Typhi strains (Guiney and Fierer, 2011).

**Genes Associated with Antimicrobial Resistance in S. Typhi**

In Gram-negative bacteria, the primary source of antibacterial resistance is the extended-spectrum β-lactamases (ESBLs). Three main ESBL types—SHV, CTX-M, and TEM—found in Salmonella species provide resistance to both cephalosporin and penicillin. These enzymes typically break down antibacterial compounds by breaking the β-lactam ring (Al-Gallas et al., 2022). Selection pressure resulting from inappropriate use of broad-spectrum antibiotics and horizontal transfer of resistance-associated genes in other gram-negative bacteria species have been related to the presence of these genes in S. Typhi. The function of tetracycline-resistant genes (tetA, tetB, and tetG) is to encode resistance to tetracycline by stimulating the efflux pump, which reduces the drug concentration by removing it from the cell (Ahamed Riyaz et al., 2018). The pentapeptide proteins encoded by the genes giving resistance against quinolones such as (qnrA, qnrB, qnrC, and qnrS) provide DNA gyrase and other enzymes with bonding and protection. The acetyltransferase enzyme inactivates chloramphenicol, which is how the cat1 and cat2 genes influence resistance. Integrons are genetic components that uniquely identify mobile gene cassettes carrying genes resistant to many drugs. Antimicrobial resistance in S. Typhi is distributed equally when integrons (class 1 and 2) are present, with class 1 being more prevalent (Kim et al., 2021; Odoch et al., 2018).

**5. Factors contributing to Resistance Development:**

The following are some of the factors that lead to S. typhi resistance developing:

**Inappropriate use of antibiotics:**

S. typhi can become resistant to antibiotics due to overuse, abuse, or inappropriate usage of antibiotics. This involves giving antibiotics more often than required, administering them incorrectly, and not finishing the prescribed course of action (Rather et al., 2017).

**Horizontal gene transfer:**

This is a method by which S. typhi can pick up resistance genes. This happens when bacteria trade genetic material, including resistance genes. Within bacterial populations, this technique may aid in the spread of drug resistance (Arnold et al., 2022).

**Carriers and episodic infections:**

S. typhi can create chronic carriers, which keep bacteria in their feces for an extended period. These carriers can serve as reservoirs and aid in the spread of drug-resistant strains among individuals.

**Reduced host immunity:**

S. typhi infections may persist longer in those with impaired immunity, such as those suffering from HIV/AIDS or
malnutrition. Antibiotic resistance is more likely to develop during such an ongoing illness when there is prolonged exposure to drugs (Handel et al., 2009).

Self-medication

The act of taking medication against one's will or at the recommendation of an unqualified expert is known as self-medication. In addition, it involves patients actively participating in the prophylactic, diagnostic, and therapeutic facets of their condition in addition to decision-making. Lack of access to a medical facility with the necessary equipment and inability to pay a specialized doctor's consultation fee to get the proper medicines are the leading causes of self-medication. After a diagnosis, self-medication helps individuals feel more in control of maintaining their health by treating persistent and recurrent ailments (Hernandez-Juyol and Job-Quesada, 2002).

6 Vaccination against Salmonella typhi

FIRST-GENERATION TYPHOID VACCINES

Since the late 1800s, typhoid vaccinations in the form of whole-cell inactivated vaccines, inactivated by phenol and heat, have been available. Typhoid disease was far less common among American and British military once these vaccinations were extensively given to them. In the 1960s and 1970s, controlled field tests were conducted in Britain, the nation of Guyana, Tonga, Egypt, and the Union of Soviet Socialist Republics to examine the efficacy of these vaccinations. Research revealed that the immunizations had a 51.5–88% productive duration of protection against typhoid disease for up to seven years. Regrettably, because reactogenicity (illness, headache, and site of injection discomfort) is so common among vaccine recipients, these vaccines were removed from routine immunization programs (Levine et al., 1989).

SECOND-GENERATION TYPHOID VACCINES

Two typhoid fever vaccines, now recommended to replace the prior reactogenicity, a deactivated whole-cell vaccine, have been licensed and made available in several countries since the 1990s. It has been shown that the injectable polysaccharide vaccine (based on pure Typhi Vi antigen; ViPS vaccine) and the live attenuated oral Ty21a vaccine are both safe and efficacious in a range of situations (Goodkin and Hertsgaard, 1982).

Live Attenuated Vaccine

Typhoid vaccine Ty21a, which is live attenuated, was created by chemically mutating the Ty2 S. typhi strain. Large-scale efficacious studies conducted in Chile, Egypt, for example, and Indonesia revealed that the preventive efficiency of three dosages varied from 42 to 96% (Simanjuntak et al., 1991). The liquid formulation (preserved liquid reconstitution in buffer, for usage in individuals ≥ two years of age) and enteric-coated capsules (for usage in individuals ≥5 years of age) were developed and evaluated in clinical studies. Both vaccine types were tolerated well after three doses and offered protection for seven years (Simanjuntak et al., 1991). Currently, there is just one commercially available capsule formulation for usage in adults over the age of five.

Table: Comparative Analysis of Parenteral and Oral Vaccines: A Focus on Adverse Responses, Protection Rates, and Immunization Requirements

<table>
<thead>
<tr>
<th>Empty cell</th>
<th>Whole-cell vaccine</th>
<th>Vi vaccine</th>
<th>Ty21a vaccine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Administration route</td>
<td>Parenteral</td>
<td>Parenteral</td>
<td>Oral</td>
</tr>
<tr>
<td>Adverse overall responses</td>
<td>11-21%</td>
<td>3%</td>
<td>&lt;1%</td>
</tr>
<tr>
<td>Adverse local responses</td>
<td>11-50%</td>
<td>11-40%</td>
<td>NA</td>
</tr>
<tr>
<td>Rate of protection</td>
<td>70-80%</td>
<td>66-70%</td>
<td>65-80%</td>
</tr>
<tr>
<td>Protection Duration</td>
<td>Seven years</td>
<td>&gt;18-22 months</td>
<td>5-7 years</td>
</tr>
<tr>
<td>Booster shots and immunization</td>
<td>Three years</td>
<td>1-3 years</td>
<td>1-8 years</td>
</tr>
<tr>
<td>A medical expert is required for vaccinations.</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
</tr>
</tbody>
</table>

Capsular Polysaccharide Vaccine:

A subunit vaccine was created by the US National Institutes of Health (NIH) for S. typhi strain Ty2 using pure Vi capsular polysaccharide (Thiem et al., 2011). Sanofi Pasteur also created a comparable injectable version of the Vi-polysaccharide, which, after a single dosage, produced an anti-Vi antibody reaction in 85–95% of elderly individuals than 2. S. typhi vaccination effectiveness was 64–72% for 17–21 months and 55% for three years (Ivanoff et al., 1994). Numerous producers from both industrialized and developing nations have created vaccinations containing Vi-polysaccharides. They have been extensively employed in several contexts and regular vaccination campaigns. The WHO has prequalified only one Vi-polysaccharide vaccine (made by Sanofi Pasteur). As adverse effects of this vaccination, discomfort, redness, swelling at the place of injection site, plus fever are common. Rare reports of allergic reactions and skin rashes have been made after vaccination. Like other Vi-polysaccharide vaccines, this one is only authorized for use in people over two and does not produce immunogenicity in younger children. Because protective immunity wears out quickly, revaccination is recommended after every three years (Date et al., 2015b).

7. Strategies for typhoid vaccinations:

A vaccine delivery method and a disease control plan are necessary to implement typhoid vaccinations. Below, we've categorized each of these approaches:

**Techniques for preventing disease by vaccination:**

**Preemptive:** These measures include immunization against endemic diseases to control them without an epidemic or as a crisis or disaster reaction to stop an outbreak. The targeted audience might include age groups or high-risk geographic locations. To identify high-risk populations or regions, a preventive approach has to be informed by local typhoid epidemiology, which might be gathered through surveillance or specialized research (Date et al., 2015a; Sur et al., 2009).

**Reactive (outbreak response) vaccination:** This is provided in response to an ongoing typhoid outbreak. Targeted audiences might include age groups or high-risk geographic locations. Understanding the typhoid epidemiology during the epidemic is necessary for a reactive plan to identify the impacted groups or places (Date et al., 2015a).

**Vaccinations of food handlers:** Vaccinations of people who have demonstrated food handling ability. A person who works in the food business and handles food or items that could potentially come into contact with food is commonly referred to as a food handler. Because there is a lack of published data on food handler immunization to reduce typhoid occurrence during this research, we are not going into further depth about it here (Date et al., 2015a).

**Methods for administering vaccines**

**Community-based routine:** The routine provision of vaccinations using already-existing medical facilities, such as outreach programs, clinics, or health centers (Dewan and Welfare, 2013).

**Campaign in the community:** Vaccine administered as a follow-up vaccination multiple times or as part of a regular schedule (e.g., annual campaigns in high-danger zones before the monsoon season) (Dewan and Welfare, 2013; Hebdomadaire).

**School-based:** Immunizations are administered to children of school age through schools. This covers immunization of unenrolled children in schools but not of the general public utilizing schools as a place of attendance. For practical reasons, vaccinations are frequently administered in a campaign to all children who are eligible at one time (Yang et al., 2005)
8. Prevention and Control:
Calculating the illness load and the function of surveillance systems, Typhoid fever control involves advocating for personal cleanliness and implementing Water and Sanitation Hygiene (WASH) interventions once a robust monitoring system has been implemented to assess the disease load. Early detection and treatment also reduce the risk of illness transmission from patients to the general public. These procedures are lengthy and have significant financial costs, though. In this context, immunization could offer a chance for temporary control (Steele et al., 2016). Insufficient national surveillance in the afflicted nations sometimes makes typhoid management more difficult. Since the new immunization plans rely on data from surveillance networks to determine the disease burden and prioritize risk groups, these help provide essential input for focused disease preventive initiatives. While some worldwide programs have been implemented to monitor typhoid fever, there is still a significant need for improvement (Sur et al., 2018).

One of the most recent research efforts is the Surveillance of Enteric Fever in Asia Programme (SEAP), which was begun at the Sabin Vaccine Centre in the U.S. This is a hospital surveillance system for typhoid fever across India, Pakistan, Bangladesh, and Nepal and among other Asian countries. The retrospective research carried out in India has clarified the outcomes, patterns of antibiotic resistance, and presentation and dissemination of the disease. Better planning for future monitoring technology has led to this (Sur et al., 2018).

The Integrated Disease Surveillance Programme (IDSP) is a part of the public Healthcare Mission for every state. In 2004, Union Territories were established, and their primary goal was to develop and enhance a decentralized computerized laboratory-based disease surveillance system that could detect and appropriately respond to 22 diseases, including enteric fever (John et al., 2018).

Conclusion
Salmonella bacteria is the leading cause of typhoid fever. The most essential ways of its transmission are contaminated food and water. It is usually associated with food handlers due to inadequate hygiene and sanitation practices. Salmonella species, particularly S. Typhi, can develop resistance to antimicrobial drugs through chromosomal or plasmid DNA. Resistance can also occur due to gene transfer using pathogenicity plasmids, phages, mobile genetic elements, and phages. Overuse, abuse, or inappropriate use of antibiotics, horizontal gene transfer, carriers & episodic infections, and reduced host immunity contribute to the development of Salmonella typhi resistance. Infections are primarily found in developing countries. There is a dire need to implement preventive and monitoring actions. It is essential to select an appropriate delivery method and develop a disease control plan to prevent the transmission of infections like typhoid. Additionally, food handlers should be vaccinated using different methods.

Declarations

Data Availability statement
All data generated or analyzed during the study are included in the manuscript.

Ethics approval and consent to participate
Approved by the department concerned.

Consent for publication
Approved

Funding
Not applicable

Conflict of interest
The authors declared the absence of a conflict of interest.

Author Contribution

AHMED ANWAR (M. Phil Scholar)
Coordination of collaborative efforts.
Conception of Study, Development of Research, Review of manuscript, final approval of manuscript

NAWAL AYAZ (M. Phil Scholar)
Manuscript revisions, critical input.
Coordination of collaborative efforts.

SAMRAN AHMAD (M. Phil Scholar)
Manuscript revisions, critical input.
Coordination of collaborative efforts

HAFSA (M. Phil Scholar)
Manuscript revisions, critical input.
Coordination of collaborative efforts

FARAH NAZ (M. Phil Scholar)
Manuscript revisions, critical input.
Coordination of collaborative efforts

KASHMAL NADIR (M. Phil Scholar)
Manuscript revisions, critical input.
Coordination of collaborative efforts

References


Carattoli, A. J. i. o. m. m. (2013). Plasmids and the spread of resistance. 303, 298-304.


Thiem, V. D., Lin, F.-Y. C., Canh, D. G., Son, N. H., Anh, D. D., Mao, N. D., Chu, C., Hunt, S. W., Robbins, J. B., Schneerson, R. J. C., and Immunology, V. (2011). The Vi conjugate typhoid vaccine is safe, elicits protective levels of IgG anti-Vi, and is compatible with routine infant vaccines. 18, 730-735.


Open Access This article is licensed under a Creative Commons Attribution 4.0 International License, which permits use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if changes were made. The images or other third party material in this article are included in the article’s Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article’s Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit http://creativecommons.org/licenses/by/4.0/. © The Author(s) 2023