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Review Paper

Innovative Pharmaceutical Interventions Against Typhoid Fever: A Comprehensive Review

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ABSTRACT

Typhoid fever, a major public health concern, is growing rapidly in developing regions with poor sanitation. This fever, caused by Salmonella enterica serotype Typhi, is proving to be fatal due to late diagnosis and resistant strains. Traditional antibiotics like azithromycin, ampicillin, and fluoroquinolones are proving to be ineffective against the multidrug-resistant strains. Recent development of innovative pharmaceutical interventions, which includes novel drug delivery systems, nanotechnology-based therapeutics, and next-generation conjugate vaccines, has shown great promise in enhancing treatment efficacy and preventing infections

INTRODUCTION

Typhoid fever, often known as enteric fever, was a leading cause of morbidity and mortality in the western world 200 years ago [1]. According to WHO, typhoid fever is a systemic infection caused by the bacterium Salmonella enterica serotype Typhi. It is transmitted by ingestion of contaminated food or water and is characterized by prolonged fever, abdominal pain, weakness, and other systemic symptoms [2]. Direct contact between people or the consumption of tainted food or water can both spread typhoid. Typhoid symptoms are similar to those of several other infectious diseases that are prevalent in the tropical region, including leptospirosis, dengue fever, and malaria. With over 16 million cases recorded annually, typhoid fever continues to be a serious public health concern in many parts of the world. Typhoid fever is a contagious illness that can spread throughout the world [3]. Salmonella enterica serotype Typhi (Salmonella Typhi) is the causative agent of the deadly bacterial infection known as typhoid fever. It is most prevalent in places with inadequate sanitation and is mainly transmitted by tainted food and water [4]. In the tropics and subtropics, where the majority of fevers are infectious in nature, fever is the most

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frequent reason for consultation. In its early stages, typhoid fever typically manifests as fever and headache without any localizing symptoms or diarrhea. However, the clinical appearance of malaria is similar to that of many other viral and parasitic illnesses (Cheesbrough 1985). The Widal test is the most often used method for diagnosing typhoid fever in many African nations, including Cameroon, due to its ease of use, low cost, and low equipment and training requirements [5]. Even 137 years after German scientist Gaffky isolated the bacterium that causes typhoid disease, the mystery still surrounds it. Salmonella typhi and Salmonella paratyphoid (serotypes A, B, and C) are the causative agents of typhoid and paratyphoid, or simply enteric fever. The most prevalent is type A. In Europe, type B is prevalent. Only in Eastern Asia is Type C found. In many impoverished nations with inadequate sanitary facilities and safe drinking water, typhoid is endemic. About 4 million people have S. paratyphoid, and 12 million people have S. typhi. Typhoid fever causes more than 15,000 deaths worldwide each year. 1, 2 The highest incidence of enteric fever was observed in children aged 2 to 4 years, with an annual incidence of 377 (178–801) and 105 (74–148) cases, respectively, per 100,000 people in India. Since illness distribution varies by geography and there are insufficient blood culture facilities in semiurban and rural areas, it is challenging to determine the true disease burden in India [6]. Patients who experience one or more problems must be admitted to the critical care unit (ICU). In the second week and beyond, problems are frequently observed when early diagnosis and treatment are not received. 5. Management has been challenging in India due to the emergence of ciprofloxacin resistance and the rising trend of ceftriaxone's and azithromycin's minimum inhibitory concentration (MIC), the current medication of choice [7].

Needs for Innovative Pharmaceutical Approaches:

The increasing need for safer, more effective, and more economical treatments has put the pharmaceutical industry at a pivotal juncture. Traditional drug discovery and development techniques are no longer adequate as global health issues change, including the rise in chronic conditions, antibiotic resistance, and emerging diseases. To improve treatment outcomes, speed up drug development, and increase access to therapies for patients around the world, innovative pharmaceutical approaches are desperately needed [22]. The growing complexity of diseases is one of the main forces behind pharmaceutical innovation. Conventional "one-size-fits-all" medications are unable to address the complex biological mechanisms underlying conditions like cancer, Alzheimer's disease, diabetes, and autoimmune disorders. A revolutionary strategy is personalized medicine, which is fuelled by developments in proteomics, genomics, and bioinformatics. Pharmaceutical companies can improve efficacy and reduce side effects by customizing treatments based on a patient's genetic and molecular profile [27]. By decreasing ineffective treatments, this move towards precision medicine is not only improving patient outcomes but also making the most use of healthcare resources [28].

Objectives:

The goal of pharmaceutical treatments for typhoid fever is to stop and cure infections brought on by Salmonella enterica serovar Typhi.

Antibiotics like azithromycin, ceftriaxone, and fluoroquinolones are used in current strategies, though resistance is becoming a bigger issue.

In order to overcome multidrug resistance, innovative approaches concentrate on creating new antimicrobials, optimizing dosage schedules, and employing combination therapies.

Conjugate vaccines provide children with long-term immunity and effectiveness, making vaccinations a crucial preventive strategy. To improve treatment results and successfully manage the worldwide typhoid fever burden, ongoing research into pathogen genomics, resistance mechanisms, and novel drug targets is crucial.

Pathogenesis

Typhoid, which is known as the infectious dosage of S. enterica serotype typhi, is a disease that requires between 1000 and 1 million organisms to infect a human [1]. S. Typhi is unique among enteric pathogens in that it only infects humans, is ingested, passes through the intestinal epithelium without initially causing harm or diarrhoea, and grows intracellularly in phagocytes found in the liver, spleen, and bone marrow. However, this is typically not the main symptom, although a small percentage of patients—7–27% [3–10]—expel the organisms in their faeces. Due to underlying gall bladder stones, 1–4% of patients—mostly females—become chronic asymptomatic faecal carriers after recovering from clinical disease [6]. Numerous factors, such as the infectious species, pathogenicity, host immunity, and infectious dosage, influence the pathophysiology of typhoid fever.

Rho GTPases are activated within the host cell by the transferred proteins. Colonization by Salmonella can happen even at lower levels. Foods and beverages help bacteria enter the small intestine by acting as buffers against stomach acid [7].

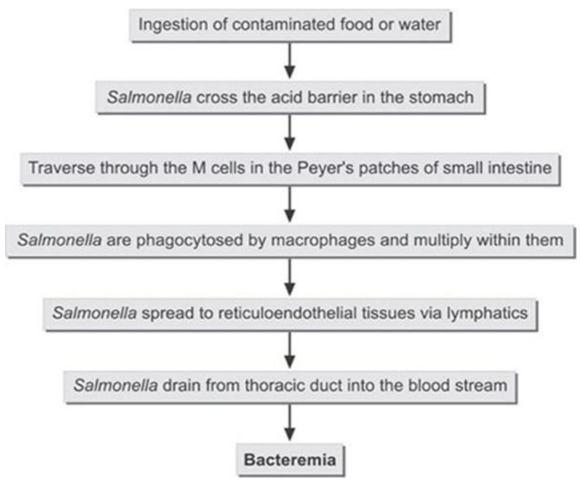

Fig.1 pathogenesis of typhoid fever [21].

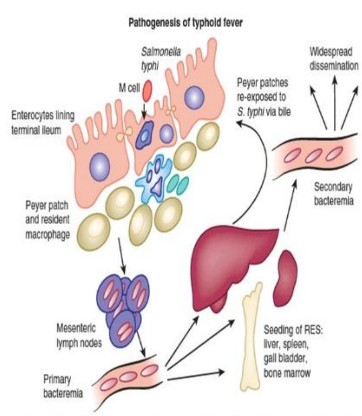

Fig. 225.5 Pathogenesis of typhoid fever. RES, Reticuloendothelial system. (Adapted from Richens J: Typhoid fever. In Cohen J, Opal SM, editors: Infectious diseases, ed 2, London, 2004, Mosby, pp 1561–1566.)

Clinical features and Diagnosis

Chills and a rising (step-ladder) fever are possible during the first week of sickness. Additionally, relative bradycardia, also known as pulse-temperature dissociation, could be observed. During the second week, abdominal pain is typical, and "rose spots" could appear. After that, hepatosplenomegaly could be found.[8]. Ileocecal lymphatic hyperplasia may cause an intestinal perforation later in the third week, which could result in secondary sepsis and peritonitis.

Males are more likely to have perforations. They are admitted to the intensive care unit [9].

After an acute infection, a patient should be identified with a chronic carrier condition and treated appropriately if they continue to excrete the germs in their urine or stool for more than a year [5]. A common early sign is diarrhoea or constipation, which is characterized by loose,

watery stools. A common dermatological sign of typhoid fever is rose spots, which are tiny, flat, pink lesions on the abdomen [10]. Hepatomegaly and splenomegaly are also prevalent and frequently found during physical examinations. [11] Typhoid fever is a highly contagious illness that needs to be diagnosed and treated well in order to enhance patient outcomes and lower morbidity and death. Usually, laboratory testing, patient history, and clinical presentation are used to make the diagnosis [12]. Depending on when the culture is performed, blood cultures have a sensitivity of 40% to 80%, making them the gold standard for confirming typhoid fever. When blood cultures come back negative, stool and urine cultures might be performed as supplementary testing. bloodstream serotype Typhi, but they have poor sensitivity and specificity, especially in endemic regions where there may be cross-reactivity with other infections [13]. According to a retrospective study conducted at AIIMS in New Delhi, 87.9% of S. typhi infections were responsive to chloramphenicol. whereas S. Paratyphoid A infections were susceptible to 94.2%, 90.1%, and 74.5% of amoxicillin (75.5%) and cotrimoxazole (87.3%), respectively. For S. typhi, the susceptibilities to ciprofloxacin and levofloxacin were 71.3%, 70.8%, and 0.9%, while for S. Paratyphoid A, they were 58.1%, 57.4%, and 57.1%. For S. typhi with azithromycin, the MIC50 and MIC90 were 8 and 12 µg/mL, respectively, and the susceptibility was 98.9% [14].

Management

A common dermatological sign of typhoid fever is rose spots, which are tiny, flat, pink lesions on the abdomen [10]. Hepatomegaly and splenomegaly are also prevalent and frequently found during physical examinations [11]. Typhoid fever is a highly contagious illness that needs to be diagnosed and treated well in order to enhance patient outcomes and lower morbidity and death. Usually, laboratory testing, patient history, and clinical presentation are used to make the diagnosis [12]. Depending on when the culture is performed, blood cultures have a sensitivity of 40% to 80%, making them the gold standard for confirming typhoid fever. When blood cultures come back negative, stool and urine cultures might be performed as supplementary testing. bloodstream serotype Typhi, but they have poor sensitivity and specificity, especially in endemic regions where there may be cross-reactivity with other infections [13]. According to a retrospective study conducted at AIIMS in New Delhi, 87.9% of S. typhi infections were responsive to chloramphenicol. whereas S. paratyphoid A infections were susceptible to 94.2%, 90.1%, and 74.5% of amoxicillin (75.5%) and cotrimoxazole (87.3%), respectively. For S. typhi, the susceptibilities to ciprofloxacin and levofloxacin were 71.3%, 70.8%, and 0.9%, while for S. paratyphoid A, they were 58.1%, 57.4%, and 57.1%. For S. typhi with azithromycin, the MIC50 and MIC90 were 8 and 12 µg/mL, respectively, and the susceptibility was 98.9% [14].

General management

When treating typhoid fever, supportive treatments such as oral or intravenous hydration, antipyretic medication, proper diet, and blood transfusions when necessary are crucial. With oral antibiotics, dependable treatment, and careful monitoring for side effects or medication failure, over 90% of patients can be treated at home. However, hospitalization and intravenous antibiotic therapy may be necessary for patients who have severe diarrhoea, prolonged vomiting, and abdominal distension [13].

Antimicrobial therapy

When choosing which first-line antibiotics to employ in underdeveloped nations, effectiveness, cost, and availability are crucial factors to consider. Compared to the previous first-line medications, ampicillin, amoxicillin, trimethoprim-sulfamethoxazole, and chloramphenicol, they are more quickly and consistently effective and are well tolerated. The fluoroquinolones have superior tissue penetration, kill S. typhi in monocytes and macrophages when it is in its intracellular stationary stage, and produce larger quantities of active medication in the gallbladder than other medications. Thiamphenicol or chloramphenicol is still often administered in underdeveloped nations to treat typhoid fever. For 14 days, the ideal dosage is 75 mg/kg per day, split into four doses. Adults typically take 500 mg four times a day. The succinate salt has a somewhat higher bioavailability when taken orally as opposed to intramuscularly or intravenously. Adults can take 160 mg of trimethoprim-sulfamethoxazole + 800 mg of SMZ twice a day for 14 days, either orally or intravenously [14].

Management of Severe Typhoid Fever

Fluoroquinolones are administered for at least 10 days in cases of severe typhoid (Table 1). Typhoid fever patients should be continuously watched for the emergence of complications, whether they are inpatients or outpatients. Morbidity and death can be avoided or decreased with prompt intervention15.

Emerging Challenges in Typhoid Management

Even though S. Typhi is becoming less common, it is still difficult to isolate the virus from blood cultures [11]. After receiving antimicrobials in the community, patients suspected of having typhoid fever are referred to a tertiary care facility for blood cultures. The most often used and accessible over-the-counter combinations in India are those based on ofloxacin, such as ofloxacin plus cefixime or ofloxacin plus azithromycin. The center for Disease Dynamics, Economics & Policy reports that between 2000 and 2014, the standard units/1000 population of cephalosporin use rose from 1887 to 7269. Similarly, between 2000 and 2014, the number of standard units/1000 people using macrolides increased from 1166 to 1862. Fluoroquinolone use, on the other hand, varied between 2000 and 2014, ranging from roughly 2608 to 2661 standard units/1000 population [12]. This suggests that cephalosporins, fluoroquinolones, and macrolides are widely used in Indian medicine. A false-negative blood culture is therefore likely to occur in patients who have taken a cephalosporin-based combination (cefixime + ofloxacin) [23].

Innovative Pharmaceutical Intervention

Modern vaccine technologies combined with novel drug delivery systems (NDDS) have transformed global healthcare outcomes, patient compliance, and therapeutic efficacy. In addition to developing new compounds, pharmaceutical innovation now concentrates on the safe, efficient, and accurate delivery of these molecules.

1.Novel drug delivery system

Nano technology based system:

Lipid nanoparticles (LNPs) are widely used in mRNA vaccines to deliver and protect nucleic acids, such as in COVID-19 mRNA vaccines.

Polymeric nanoparticles: Provide targeted delivery to particular tissues or cells with controlled release.

Micelles and dendrimers: Improve solubility and lessen systemic toxicity for hydrophobic medications.

Smart drug delivery system:

Drugs are released by stimuli-responsive systems in reaction to changes in temperature, pH, enzymes, or redox conditions.

Targeted delivery: Site-specific action is guaranteed by ligand-receptor systems, such as antibody-drug conjugates.

Enhance local retention for ocular or mucosal delivery with bioadhesive and mucoadhesive carriers.

Long acting and control release system:

Implants and injectables for long-term treatments, such as depots made of PLGA.

Microneedle arrays and transdermal patches for non-invasive prolonged release.

1.Advances in vaccine Development

mRNA and DNA Vaccine:

Offer scalability and quick design.

self-adjusting qualities through the activation of the innate immune system.

For instance, COVID-19 and emerging pathogens' mRNA-LNP platforms.

Viral vector vaccine:

To create strong immunity, use non-replicating or attenuated vectors (such as adenovirus-based).

Both preventative and therapeutic uses are possible (e.g., cancer vaccines).

Nano vaccine Adjuvant Innovation:

Vaccines based on nanoparticles enhance the stability and presentation of antigen.

New adjuvants (such as saponin-based TLR agonists) improve the duration and specificity of immune responses.

Oral, Nasal and Transdermal vaccine:

Strive for methods based on mucosal immunity and free of needles.

Mucoadhesive nanoparticles and microneedle patches are being researched for increased compliance and uptake [24].

Existing Marketed formulation of Typhoid drugs [16]

Drug	Formulation(marketed)	Examples of brand name	Typical route
Azithromycin	Tablets(250mg,500mg) Suspension(250mg/5ml) IV Infusion (500 mg, vial)	Zithromax, Azithral, Azee	Oral, IV
Ciprofloxacin	Tablets(250mg,500mg,750mg) IV infusion(100-400mg) \100ml	Ciprobid, Ciproxin, Ciprobay	Oral, IV
Levofloxacin	Tablets(250mg,500mg,750mg) IV infusion(500mg/100ml)	Levaquin, Tavanic	Oral, IV
Ofloxacin	Tablets(200mg,400mg) IV infusion(200mg/100ml)	Zanocin, Oflox, Floxin	Oral, IV
Ceftriaxone	Injection (500mg,1g,2gvials for IV/IM)	Rocepin, Monocef, Cefaxone	IM, IV

Cefotaxime	Injection(500mg,1g,2gvials)	Claforam, Taxim	IM, IV
Cefixime	Tablets(200mg,400mg) Suspension(50mg/5ml,100mg/5ml)	Suprax, Taxim-o, Zifi	Oral
Chloramphenicol (rarely used now)	Capsules(250mg,500mg) Suspension, Injection	Chloro mycetin	IM, IV Oral
Amoxicillin (resistant in Many regions)	Tablets(250mg,500mg,875mg) Suspension(125-100mg/5ml)	Amoxil, Moxatag	Oral
Trimethoprim-Sulfamethoxazole	Tablets(80/400mg,160/800mg) Suspension(40/100mg/5ml)	Bactrim, Septra	Oral, IV

Novel approaches of Typhoid drugs [17]

Novel approach	**Description**	**Mechanism**	**Status**	**Progress year**
Anti- virulence therapy	Target salmonella's virulence factors	Disrupt Type III Secretion system(T3S S) To prevent infection	Preclinic al studies	Initial key studies began about 2015-2017 ongoing research as 2023 focuses on T3SS inhibitors
Bacteriopha ge therapy	use of virus that inject and kill S. Typhoid	Lytic phases Target salmonella directly	Trials	Demonstrat ed success in2018-2022 with increasing in post 2022
Quorum sensing inhibitors	Blocks bacterial communicati on Pathways that regulate pathogenicity	Inhibits quorum Sensing molecules	Research stage	Studies appeared b/w 2016-2021 research remain experimenta l
Nanoparticle s-Based drug delivery	Uses nanoparticles To deliver Drugs more Efficiently and Bypass resistance	Enhance delivery of Existing or new Drugs to infect ed cells	preclinic al	Gained momentum from 2019-2024 with multiple studies showing improved therapeutic outcomes

Role of Nano Technology in Typhoid Control

In many parts of the world, typhoid fever is still a major health concern. Salmonella enterica serovar Typhi (S. Typhi) is the primary cause of typhoid fever. Strains of S. enterica from serovars A, B, and C are also somewhat responsible. This is a highly adapted, human-specific pathogen that is more common in developing nations with high rates of overcrowding and inadequate sanitation.

The most accurate estimates available worldwide indicate that typhoid fever causes at least 16 million new cases and 6,000,000 fatalities annually. Depending on their age, sex, and course of treatment, 1–5% of patients who have an acute typhoid infection have been found to develop into chronic carriers of the infection. Moreover, gallbladder cancer has also been linked to this chronic carrier state.

Clinically diagnosing typhoid fever is challenging because its symptoms are varied and resemble those of other common feverish illnesses like malaria and mild dengue fever.

The preferred technique for laboratory diagnosis is still the isolation of serotype Typhi from blood. S. typhi is typically detected using traditional techniques such as polymerase chain reaction (PCR) slide agglutination and the Widal test and culturing. These techniques are difficult and time-consuming to use, despite the fact that they can yield extremely sensitive results for both qualitative and quantitative analysis.

Given the aforementioned shortcomings, it is necessary to suggest efforts to create a S. typhi determination method with improved sensitivity and selectivity as well as a shorter analysis time. These days, surface plasmon resonance enzyme immunoassay and electrochemical immunoassay are substitute techniques for biological molecular analysis. Due to its inherent simplicity, high sensitivity, low cost of equipment, and miniaturisation, immunoassay has garnered a lot of interest for the detection of S. 110 typhi.

As nanotechnology has advanced, different nanoparticles and nano-quantum dots have been employed as labels to increase the electrochemical immunoassay technique's sensitivity.

For the determination of immunoglobin G (IgG), a model of electrochemical immunoassay with low detection limits ranging from 1.0 ng/mL to 0.25 pg/mL, copper, silver, and gold-enhanced colloidal gold have recently been reported. The remarkable signal amplification brought about by the catalytic precipitation of metals onto the gold nanoparticles is combined with the high sensitivity of stripping metal analysis in the metal-enhanced colloidal gold electrochemical stripping metal immuno assay [25].

Prevention Strategies

Vaccination Programs in east Africa

Kenya

Through collaborations with Gavi and the WHO, Kenya has carried out several typhoid fever immunisation campaigns. As part of a massive pilot effort in Nairobi in 2019, Kenya launched the typhoid conjugate vaccine (TCV) with the goal of immunising children ages six months to fifteen. High coverage and a decrease in the incidence of typhoid were attained by the program, which included Public health education initiatives stressing the value of vaccination in conjunction with better hygienic practices have been implemented in Kenya in tandem with its immunisation efforts. The incorporation of typhoid vaccine into already-existing health facilities, such as maternal and paediatric health clinics, is one of Kenya's program's main advantages.

Uganda

Uganda has a long history of using vaccination campaigns to fight typhoid disease, especially in reaction to significant outbreaks in urban areas. Following a significant epidemic in 2018, Uganda launched a large vaccination program employing TCVs in Kampala, the country's capital, vaccinating approximately 600,000 people.

Rwanda

Strong government leadership and efficient data utilisation to guide public health initiatives define Rwanda's typhoid immunisation strategy. In 2020, Rwanda included TCVs in its national vaccination program, focussing on children and teenagers in high-burden regions. Rwanda has one of the greatest vaccination coverage rates in East Africa, demonstrating the program's great success.

Rwanda's strong governmental commitment, well-developed healthcare system, and use of mobile health (mHealth) technology to monitor vaccine coverage and delivery are all factors in the country's success. Campaigns for public awareness have also been very important in encouraging adoption of vaccines [18].

Comparative Evaluation of Vaccine Distribution and Coverage for Typhoid

Rwanda has the highest vaccination rate thanks to effective health facilities and a strong governmental commitment.

Although coverage issues still exist in rural areas, Kenya and Uganda have made notable progress in metropolitan areas.

Ethiopia and Tanzania have launched immunisation initiatives, although they encounter logistical challenges, particularly in remote regions.

Burundi's persistent political and economic instability makes it difficult to maintain regular vaccination coverage [19].

Government and International Support

International collaborations, especially those with Gavi, the Vaccine Alliance, and the WHO, are advantageous to all nations. Though government commitment varies, Rwanda and Kenya have shown the most leadership in establishing and expanding immunisation programs. Long-term sustainability is an issue because nations like Ethiopia and Burundi mainly depend on foreign help to maintain their programs.

Integration with Other Public Health Initiatives

Typhoid vaccination has been effectively included into regular immunisation regimens and larger public health initiatives in Rwanda and Kenya.

WASH programs and vaccination have been coupled in Tanzania and Uganda, albeit program performance varies by region [20].

Future Respective and Research Directions

Improved Diagnostics

Current challenges: Inability to differentiate typhoid from other feverish diseases (e.g., dengue, malaria).

reliance on blood culture, which has a low sensitivity (about 40–60%) and is slow and expensive.

Future directions:

Molecular diagnostics: The creation of PCR or isothermal amplification tests that are quick, accurate, and field deployable.

Finding biomarkers: Determining metabolite signatures or host gene expression for typhoid-specific diagnosis.

Point-of-care tests (POCT) are inexpensive, portable diagnostic kits that can be used in environments with limited resources.

Anti-microbial Resistance (AMR) Surveillance

Current challenges:

increasing strains of Salmonella Typhi that are extensively drug-resistant (XDR) and multidrug-resistant (MDR), particularly in South Asia and Africa.

FUTURE DIRECTIONS:

Genomic surveillance: Whole-genome sequencing (WGS) is used to track the evolution and global spread of AMR.

Novel antimicrobials: The creation of fresh treatment alternatives or combination treatments aimed at resistant strains.

Phage therapy and antimicrobial peptides: Investigating peptide-based and bacteriophage-based antibiotic substitutes.
Vaccine development and Implementation

Current challenges:
inadequate vaccination coverage in regions where the disease is endemic.
Uncertainty regarding cross-protection and immunity duration against S. Parat.

Future Directions:
Conjugate vaccines of the next generation: greater coverage, enduring protection, and infant suitability.
Combination vaccinations include multivalent enteric fever or typhoid-paratyphoid vaccines.
Public health and Policy Research

Future Directions:
Combining interventions for safe water, sanitation, and immunisation is known as an integrated control strategy.
Strengthening health systems: Improving the ability to diagnose, report, and treat.
Community engagement: Social science and behavioural research to increase vaccination and hygiene practice acceptance.
Digital and Data-Driven Approaches
AI and machine learning: For predicting outbreaks, analysing AMR trends, and improving the design of interventions.
mHealth tools: Public education and disease reporting via mobile devices in endemic regions [26].

CONCLUSION

Typhoid fever remains a serious global health issue, particularly in low- and middle-income countries with inadequate sanitary and medical facilities. Despite decades of advancements in medicine, Salmonella enterica serotype Typhi is still a persistent disease due to the emergence of extensively drug-resistant (XDR) and multidrug-resistant (MDR) strains. This resistance crisis emphasises the pressing need for innovative pharmaceutical strategies that go beyond conventional antibiotic treatments. I recently created a microsphere for azithromycin and other nanotechnology applications to stop the growing typhoid burdens in public health. In a similar vein, new vaccine technologies, like those based on DNA, mRNA, and viral vectors, represent a new frontier in long-term prevention, especially for children residing in endemic areas. All countries benefit from international partnerships, particularly those with the WHO, the Vaccine Alliance, and Gavi.
Rwanda and Kenya have demonstrated the greatest leadership in establishing and growing immunisation programs, despite differences in government commitment. Because countries like Ethiopia and Burundi primarily rely on foreign assistance to sustain their programs, long-term sustainability is a concern. AI and machine learning: To better design interventions, analyse AMR trends, and forecast outbreaks.
mHealth resources: In endemic areas, mobile devices are used for disease reporting and public education. insufficient immunisation rates in areas where the illness is prevalent.
Cross-protection and immunity duration against S. Parat are unknown. All things considered, a comprehensive strategy that incorporates cutting-edge medications, sophisticated diagnostics, and successful immunisation techniques is necessary for long-term typhoid control. Reducing the worldwide burden of typhoid fever and protecting public health from future threats from antibiotic resistance require ongoing research, international collaboration, and policy strengthening.

REFERENCES

1. Paul Uttam Kumar, Bandyopadhyay Typhoid fever: A review. Internal Journal of Advances in Medicines, 2017 April, page no: 300-306.
2. Zein Umar Management of Severe Typhoid fever. The 1st International Conference on Tropical Medicine and Infectious Diseases, 2017 November, page no: 01-05.
3. House Deborah, Bishop Anne et al. Typhoid fever: pathogenesis and disease. Current Opinion in Infectious diseases, 2001 November, page no: 573-578.
4. Nsutebu Fru Emmanuel, Martins peter et al. Prevalence of Typhoid fever Febrile patients with symptoms clinically compatible with typhoid fever in Cameroon. Tropical Medicine and International Health, vol: 8 no 6, 2003 June, page no: 575-578.
5. Ray Banaber, Raha Abhijeet Typhoid in Enteric fever Intensive care unit. Indian Journal Critical Care Medicine, 2021;2025 May, page no: S145-149.
6. T. Butler Treatment of typhoid fever 21st Century: promises and shortcomings. Clin Microbial Infect, 25 April 2011, page no: 959-963.
7. Gouda Zainab Ali Enteric fever (typhoid and para typhoid fever). 6 April 2024, page no: 56-62.

1. 8.Mandil Ahmed, Rashidian Arash Enhancing capacity and use of digital health in the Eastern Mediterranean Region: An urgent priority for action. Eastern Mediterranean Health Journal, vol: 27 no 11 2021 November, page no: 1020-3397.
2. 9. S. Irakoze Mukamana Pathogenesis and Manifestations of Typhoid fever. ROJBAS Publications, 2025, page no: 60-63.
3. 10. Mahmoud Ashraf, Oluyemisi Adekunbi Recent advances in the diagnosis and management of typhoid fever in Africa: A review International Journal Health Plan management, 7 November 2022, page no: 317-329.
4. 11. Susanto Tirta Darmawan, Glenis Gabrielle Diagnostic Test and Management of Typhoid fever with family approach: A case report. KESANS International Journal of health and Science, 30 August 2024, page no: 542-551.
5. 12. Aarif Sam, Kartika Dewi et al. Management of Typhoid fever in children: A Literature Review. Nursing Genius Journal Original Research, vol: 2 no 2 30 April 2025, page no: 70-82.
6. 13. Singh P. Thipendra, Igulu. T Kingsley et al. An Intelligent Approach Coast- effective Management of Typhoid fever in Children. ICSC, 16 May 2025, page no: 265-271.
7. 14. Singh P. Thinpendra, Igulu. T Kingsley et al. AN Intelligent Approach Coast- effective Management of Typhoid fever in Children. ICSC, 16 May 2025, page no: 265-271.
8. 15. Amos Rai Jimba Studies on Indigenous Knowledge in the Management of Typhoid fever and Wound Infections using Calotropis Procera leaf extracts against selected microorganism. University of Abuja, 29 February 2024, page no: 1-13.
9. 16. S. Gurunath Dhadde, et al. A Review on Microspheres Types, Method of preparation and Characterization and Application. Asian journal of pharmacy and Technology, vol: 11 2021 June, 01- 07.
10. 17. Yadav Vishal et al. A Review on Microspheres: Preparation, Characterization and Application. Asian journal of pharmaceutical Research and Development, 15 December 2022, page no: 128-133.
11. 18. K. Emmanuel Mugisha Comparative study of Vaccination programs against Typhoid fever in East Africa. Eurasian Experiment journal of Scientific and Applied

Research, vol: 06 2024 December, page no: 33-37.

12. 19. Kim Chaelin et al. Association of water, sanitation, hygiene with typhoid fever in case-control studies: a systemic review and meta-analysis. BMC Infectious diseases, 29 August 2023, page no: 12-17.
13. 20. Carey E. Megan et al. Typhoid fever Control in 21st Century: Where are we now. Current opinion in infectious disease, 2022 August, page no: 425-430.
14. 21. M.D Good pasture. W Ernest Concerning the Pathogenesis of Typhoid fever. American journal of pathology vol: XIII, 14 December 1936, page no: 175-185.
15. 22. Mather G Richard et al. Redefining Typhoid diagnosis: What would an improved test need to look like. BMJ Global Health, 5 October 2019, page no: 01-09.
16. 23. Veeraraghavan Balaji et al. Typhoid fever: Issues in Laboratory detection Treatment options and Concern in management in developing countries. Future Science OA, 26 June 2018, page no: 1322- 1336.
17. 24. Ugwu, O.P.C, Alum, E.U and Uhama, K.C role in phytochemical Rich food mitigating Diarrhea among diabetic patients. Research invention journal of Scientific and experimental Sciences, 2024, page no: 45-55.
18. 25. Mitra Rahul Nanotechnology and the Diagnosis of typhoid fever. Digest journal of Nanomaterials and Biostructure, vol 4 2009 March, page no: 109- 111.
19. 26. Martin B Laura et al. Vaccines against invasive Salmonella disease. Human Vaccines and Immunotherapeutics, vol 10 issue 6, 7 May 2014, page no: 1479-1495.
20. 27. Sapkota Jyotsna et al. Diagnostic for typhoid fever: Current prospectives and future outlooks for product development and Access. Infectious diseases society of America, 11 October 2025, page no: S17-S20.
21. 28. So D Anthony et al. Technology innovation for infectious diseases in developing world. Infectious diseases of poverty, 2012, page no: 03-09.
22. 29. Adinugraha et al. KERASIONALAN PENGUNNAN ANTIBIOTIC DI PUSKESMAS. Journal of pharmaceutical care Anwar Medika, 2022, page no: 82-87.
23. 30. Sur D, Ochiai RL, Bhattacharya SK, Ganguly NK, Ali M, Manna B, et al. A cluster-randomized effectiveness trial of Vi typhoid vaccine in India. N Engl J Med. 2009; 361:335-44.
24. 31. Upadhyay R, Nadkar RM, Muruganathan A et al. 2015, API Recommendations for the Management of Typ, Journal of The Association of Physicians of India,Vol. 63, November 2015.
25. 32. Kingsley RA, Baumler AJ. Host adaptation and the emergence of infectious
26. disease: the Salmonella paradigm. Mol Microbiol 2000; 36:1006–1014.
27. 33. Cheesbrough M (1985) Medical Laboratory Manual for Tropical Countries, 1st edn. Butterworth, Cambridge, pp. 257–261.
28. 34. Bhandari J, Thada PK, DeVos E. Typhoid fever [Updated 2020 Nov 23]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2021.
29. 35. Threlfall EJ, Ward LR, Skinner JA, Smith HR, Lacey S. Ciprofloxacinresistant Salmonella typhi and treatment failure. Lancet 1999; 353: 1590 1591.
30. 36. B. M. Stuart and R. L. Pullen, “Typhoid,” Arch. Intern. Med., vol. 78, pp. 629–661, 1946.
31. 37. Al-Mandhari A; Marmot M; Ghaffar A; Hajjeh R; Allen J; Khan W; et al. COVID-19 pandemic: a unique opportunity to ‘build back
32. fairer’ and reduce health inequities in the Eastern Mediterranean Region. East Mediterr Health J. 2021;27(3):217-219 https://doi.

33. org/10.26719/2021.27.3.217.
34. 38. Zhang, S. H., et al. (2021). Current Understanding of Typhoid Fever: From Pathogen to Vaccine. Frontiers in Immunology, 12,740086.
35. 39. Bhutta ZA, Gaffey MF, Crump JA, et al. Typhoid fever: way forward. Am J Trop Med Hyg. 2018;99(3_suppl):89-96.
36. 40. Van Camp, Roscoe O., & Shorman, Mahmoud. (2023). Typhoid vaccine. In StatPearls [Internet]. StatPearls Publishing.
37. 41. Andas, A. M., Harahap, D., Purnamasari, A., & Prima, A. (2022). Effectiveness of cognitive behaviour therapy (CBT) to improve the sleep quality of the elderly in hospital. International Journal of Health Sciences, 1669–1678.
38. 42. G. I. Webb, “Multiboosting: A technique for combining boosting and wagging,” Machine learning, vol. 40, pp. 159–196, 2000.
39. 43. K. T. Igulu and N. R. Saturday, “An overview of artificial intelligence and blockchain technology in telehealth systems,” 2024.
40. 44. Springfield, E.P. and Weitz, F. (2006). The Scientific merit of carpobrotus mellei. Base on antimicrobial activity and chemical profiling. African Journal of Biotechnology, 5: 1289-1293.
41. 45. Manoj Kumar Das, Microsphere a Drug Delivery System–A Review, International Journal of Current Pharmaceutical Research, 2019 11(4), Page 34-41.
42. 46. Olaro, C., & Opio, A. (2021). Addressing vaccine hesitancy in Uganda: Lessons from the typhoid vaccination campaign. Journal of Public Health in Africa, 12(s1), 43–45.
43. 47. John J, Van Aart CJC, Grassly NC. The burden of typhoid and paratyphoid in India: systematic review and meta-analysis. PLoS Negl.
44. Trop. Dis. 10(4), e0004616 (2016).
45. 48. Ling CL, Roberts T, Soeng S, et al. Impact of delays to incubation and storage temperature on blood culture results: a multi-centre study. BMC Infect Dis 2021; 21: 173.
46. 49. Im J, Islam MT, Ahmmed F, Kim DR, Islam Khan A, Zaman K, et al. Can existing improvements of water, sanitation, and hygiene (WASH) in urban slums reduce the burden of typhoid fever in these settings? Clin Infect Dis. 2021;72(11):e720–6.
47. 50. Kartik, V., & Haile, G. M. (2023). Overcoming barriers to typhoid vaccination in rural East Africa: The role of public-private partnerships. Global Health Research and Policy, 8, 11.

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