Strengthening strategies to tackle salmonellosis, antimicrobial resistance and sanitation crisis

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Salmonellosis is an infectious disease caused by the enteric pathogen *Salmonella*, which is the leading causative agent of acute gastroenteritis and enteric fever globally. The catastrophic implications of salmonellosis vary depending on the host immune factors and virulence of the strain, but it can be life-threatening for pregnant women, infants, young children and adults with weak immune systems. Globally the typhoidal *Salmonella* accounts for 21 million cases of infection and 161,000 deaths annually[1], whereas non-typhoidal *Salmonella* (NTS) accounts for 93.8 million cases of enteric infections, with around 155,000 diarrheal deaths each year[2]. Salmonellosis continues to undermine the health, food security and socio-economic development of the endemic nation.

The undeniable and alarming increase in antimicrobial resistance (AMR) in infectious disease pathogens and its long-lasting detrimental impinge have exacerbated the morbidity and mortality in both paediatric and adult populations. Based on hazard level, the Centers for Disease Control and Prevention (CDC), USA, has ranked antibiotic-resistant *Salmonella* as a 'serious threat' that requires continuous surveillance and response to mitigate further dissemination. According to CDC, annually 100,000 cases of infection have been attributed to drug-resistant NTS and 3800 cases to ciprofloxacin-resistant *Salmonella typhi*[3]. Among the low and middle-income countries, India is the largest consumer of antibiotics. The unchecked and rampant use of antibiotics in food animals and human beings has led to the worldwide adverse effects of certain antibiotics. The paucity of novel therapeutic options in the current treatment regime is a major hurdle in the management of *Salmonella.* It is difficult to eliminate this intracellular pathogen from the infected host due to its stealthy ways to evade the host immune system and profound capability of biofilm formation. Recently, it has been reported that *Salmonella* remains persistent post-antibiotic treatment, and its infection leads to colonization and considerable brain tissue damage in a mouse model[4]. The drug resistance in typhoidal *Salmonella* mostly arises due to a chromosomal mutation or acquisition of a plasmid or transposon[5]. *S. typhi* is adept at the exchange of multidrug resistance R-plasmid with *Escherichia coli* and other enteric bacteria, which together with the misuse of quinolones account for the steep increase in resistance to fluoroquinolones[6]. It has been well documented that the treatment failures of non-typhoidal salmonellosis are primarily due to *in vivo* acquirement of extended-spectrum β-lactamase or fluoroquinolone resistance genes and mcr-1-encoding plasmids[7].

Poultry and poultry products are considered to be the primary vehicle of AMR *Salmonella* in the food chain, but livestock, aquaculture, environment, several cultural and behavioural factors also play a crucial role in the transmission of *Salmonella*[8]. Several epidemiological studies have revealed a close association between salmonellosis and the consumption of eggs, beef, pork, milk, fresh produce, seafood and spices, validating its ubiquitous and hardy nature[9,10]. The burden of salmonellosis is striking in developing countries with inadequate access to clean drinking water as well as poor sanitation and sewage disposal systems when compared to developed countries. Various strategies for the containment and management of the pandemic challenge of AMR from farm to fork have been developed in India[11].

The other issue faced by most of the low- and middle-income countries is sanitation crisis. Today we live in a world where around 2.1 billion people do not have access to clean and safe drinking water at home, among which 840 million do not even have basic drinking-water facility. An estimated 2.3 billion people still do not have access to basic sanitation facilities and among them 892 million still practice open defecation[12]. Apart from infectious diseases, poor sanitation is also directly linked to the transmission of several neglected tropical diseases resulting in the death of 361,000 children under the age of five years every year[12]. In a report on the assessment of faecal sludge management, WaterAid[13] has concluded that 70% of India's surface water is polluted and contaminated. A major contributor to this contamination is domestic sewerage. Most of the sewage generated in India remains untreated and is directly discharged into waterbodies. Contaminated water plays a crucial role in the transmission of *Salmonella*. Recently, a study from India has highlighted the issue of preharvest contamination of tomato by *Salmonella*, wherein the pathogen gets a lateral root-mediated entry into the plant from the contaminated soil[14].

The prevailing scenario of sanitation crisis, overpopulation, improper sewage management and urban slum makes India a safe haven for *Salmonella* to thrive. Thus, in the light of the evidence, linking sanitation crisis with salmonellosis and anti-microbial resistance (AMR), has far-reaching devastating effect on public health, it is of immense importance to ensure reliable surveillance, effective interventions to control AMR *Salmonella* for socio-economic development. Safe sanitation is vital for good health; it saves lives and is a human right. Any rationale to curb salmonellosis needs to solve the sanitation crisis at first. To safeguard our future it is of colossal importance to make sanitation everybody's business, because there is no life without water and there is no substitute for water.

Initiatives to reduce salmonellosis and address the challenge of sanitation and hygiene in India

The key to curb salmonellosis lies in: (i) Vaccination: Vaccination is a promising strategy to prevent and eradicate infectious disease. (ii) Improvement in hygiene and living standards, strengthening of surveillance, rapid detection and response to outbreaks. (iii) Prudent use of antibiotics and the discovery of novel drugs and combinations that incapacitate *Salmonella* of its antimicrobial resistance mechanism and virulence factors. (iv) Holistic approach and interventions: The flagship SANIPATH study to take on typhoid is one of its kinds which have a holistic approach to assess and curtail salmonellosis. Sanipath aims to assess the risk posed by dominant faecal exposure pathways to public health, characterize the magnitude and variability of faecal contamination and transmission of *Salmonella* in the environment and neighbourhood due to the exposure pathways. This study also includes behavioural exposure surveys and estimates the frequency of exposure of residents to faecal contamination,

interview the key city official and resident regarding the city infrastructure, water, and waste management[15].

Antimicrobial resistance policies

In India, AMR took centre stage with the discovery of NDM-1 (New Delhi metallo-beta-lactamase-1) in 2010. Since then many policies have been initiated to tackle the challenge of AMR. For example, the Chennai Declaration in 2012 was the first ever joint meeting by medical societies in India addressing antibiotic resistance. The ethos of the meeting was to lay down a roadmap to tackle the challenge of AMR from the Indian perspective. In 2013, the Indian Council of Medical Research (ICMR), New Delhi initiated a surveillance network to monitor AMR pattern in pathogens of public health importance at hospitals and medical institutions across the country[16]. Another initiative of ICMR is Antimicrobial Stewardship Programmes, aimed to provide guidance to Indian hospitals to ensure careful and responsible use of antibiotics, improve patient care and safety, as well as reduce treatment failures and healthcare cost. Subsequently, in 2016, the National Centre for Disease Control, New Delhi laid down treatment guidelines for antimicrobial use in infectious disease. Then, the Redline campaign was introduced to create awareness among citizens regarding the judicial use of antibiotics. In another attempt to curb antibiotic resistance, the National Action Plan for containment of Antimicrobial Resistance and Delhi Declaration was launched (2017–21), which assigned tasks to various government agencies to rationalize antibiotic use and scale-up antimicrobial surveillance and control strategies[16]. Further, to ensure safety of food products, the Food Safety and Standard Authority of India has notified the Food Safety and Standards Amendment Regulation, 2018, specifying the tolerance limit for antibiotic residue in processed meat, meat products, poultry, fish, seafood and milk.

Initiatives by the Government

Nation-wide campaigns like Swachh Bharat Abhiyan, Kayakalp, Swach Swasth Sarvatra scheme for improvement of hygiene, sanitation and infection control practices in Central government institutes and public health facilities, village-based initiatives to synergize health, water and sanitation (VISHWAS), National Mission for Clean Ganga, and the Atal Mission for Rejuvenation and Urban Transformation (AMRUT) which was launched to transform urban living conditions and address the issue of wastewater and faecal sludge management are some of the initiatives by the Government of India. The Mahatma Gandhi International Sanitation Convention which brought international sanitation ministers and other global leaders of wash, sanitation and hygiene (WASH) under one umbrella, has propelled India towards the path of cleanliness.

Under the cleanliness mission school children are the crusaders of cleanliness to make their surroundings cleaner and greener. Students are sensitized towards hand-washing, personal hygiene, waste disposal and reducing trash. These young minds carry the idea to their family, neighbourhood and foster the value of 'swachhta hi seva' in the community.

Future directions

Strengthen surveillance and early warning systems to detect the outbreak of infectious diseases.

A more multipronged, interdisciplinary approach to understand the impact of climate change and temperature on the distribution of infectious diseases and genetic mutation.

Inclusion of effective typhoid vaccine in national immunization programmes.

More assessment and interventions like SANIPATH at district and state levels.

Develop nanocarriers to deliver antimicrobials to the target site and potentiate their killing effect against intracellular drug-resistant pathogens.

Identify the critical knowledge gaps in our understanding of AMR and the underlying driving factors.

Better schemes and funding for collaboration between the scientific community and pharmaceutical companies and policymakers for the development of novel drugs.

Set up clear roadmaps, and a strict legal and regulatory framework to address AMR and ensure its compliance at all levels.

Set stringent guidelines and standard limits for antibiotic discharge in pharmaceutical industry effluents.

Integrate sanitation and faecal sludge management infrastructure in all the urbanization plans.

Upgrade technology for collection, transportation, treatment of wastewater and disinfection and safe disposal of faecal sludge.

Inclusion of sanitation and hygiene in the curriculum right from primary education, so that these values get imprinted in the psyche of the younger generation.

Engage mass media to raise awareness and sensitize people about sanitation and AMR and its public health linkage.

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