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Global impact of salmonellosis on health and economy

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Abstract
Salmonella is 1 of 4 key global causes of diarrhoeal diseases. Salmonellosis is caused by various *Salmonella* serovars. It is one of the most common and widely distributed foodborne diseases. It constitutes a major public health burden and represents a significant cost in many countries. Millions of human cases of salmonellosis are reported worldwide every year resulting into thousands of deaths. This disease has become an important public health problem throughout the world which also contributes to negative economic impacts due to the cost of surveillance investigation, treatment and prevention of illness. Average fatality rate in *Salmonella* infections has been reported to be 5.3%, but certain serotypes can cause a fatality rate up to 21%. Higher case fatality rate has been observed among infants less than 12 months old and HIV patients. Multidrug resistant *Salmonella* Typhimurium definitive phage type (DT) 104 strains are responsible for a high number of infections in human beings and are primarily zoonotic in origin. CDC estimates *Salmonella* causes about 1.2 million illnesses, 23,000 hospitalizations, and 450 deaths in the United States every year. The costs of food-borne *Salmonella* alone are estimated to reach up to € 2.8 billion annually in EU countries altogether. Salmonellosis can be prevented and controlled by treatment of patients with antibiotics in severe cases, adequate heat treatment of milk and meat and their products including eggs, hygienic measures and *Salmonella* testing on poultry farms and removal of infected poultry.

Keywords: *Salmonella*, health, economy, susceptibility, transmission, management

Introduction
Various types of foods particularly those of animal origin have been identified as common vehicles for transmission of *Salmonella* to humans and spreading them to processing and kitchen environment. Raw and inadequately cooked meat, eggs, milk and especially poultry are the most commonly implicated vehicle for *Salmonella* infection.
In recent years, problems related to human salmonellosis have increased significantly, both in terms of incidence and severity. While some countries have managed to reverse the increasing trend of human salmonellosis, but the new problems identified are the matters of great concern. Since the beginning of the 1990s, strains of *Salmonella*, which are resistant to a range of antimicrobial agents, including first-choice agents for the treatment of humans, have emerged and are threatening to become a serious public health problem. This resistance results from the use of antimicrobial agents both in humans and animal husbandry. Multi-drug resistance to "critically important antimicrobials" is compounding the problems (FAO/OIE/WHO, 2003) [10]. Salmonellosis is an emerging zoonotic disease. It has been reported from time to time in different parts of India. Several data are available regarding prevalence of *Salmonella* in various animal species including human beings. In India, more than 235 serovars has been reported (Singh, 2005) [14] and this number is on constant increase.
The emergence of MDR *Salmonella* strains with resistance to fluoroquinolones and third-generation cephalosporins is a serious development which has limited the possibilities of effective treatment of human infections. Resistance to the fluoroquinolones often emerges as a result of mutations in the bacterial genome (DNA), resistance to other antimicrobials often spread by transfer of DNA between bacterial strains. In some cases multidrug-resistance is transferred through plasmid. Plasmids in *Salmonella* control medically important properties including virulence factors and resistance to heavy metals, phages or utilization of alternative carbon sources. There is another group of plasmids of usually high molecular weight which

play important role in the development of antibiotic resistance (Rychlik *et al*., 2006) [13].

Drug-resistant *Salmonella* emerges in response to irrational anti-microbial usage in food animals. Selective pressure from the use of antimicrobials is a major driving force behind the emergence of resistance, but other factors also need to be taken into consideration. A recent example is the global spread of a multidrug-resistant *S.* Typhimurium phage type DT104 in animals and humans. While the spread of DT104 may have been facilitated by the use of antimicrobials, international and national trade of infected animals is thought to play a major role in international spread.

Factors Contributing to Emergence of Salmonellosis

The dynamics of *Salmonella* infections is quite variable and affected by changes in human demographics and lifestyles, changes in human behaviour, changes in industry and technology, changes in travel and commerce, the shift towards global economy, microbial adaptation, breakdown in the public health infrastructure and the lack of knowledge on food safety and handling practices among consumers (Hall, 1997) [11].

Host Susceptibility

The population of highly susceptible persons is expanding worldwide because of ageing, malnutrition, HIV infections and other underlying medical conditions. *Salmonella* Typhimurium and other *Salmonella* serovars can cause a more invasive infection in immunocompromized patients which can be life threatening. Age is an important factor in susceptibility to food-borne infections because those at the extremes of age have either not developed or have partially lost protection from infection. Particularly for the elderly, foodborne infections are likely to invade their blood stream and lead to severe illness with high mortality rates.

People with a weakened immune system also become infected with foodborne pathogens at lower doses which may not produce an adverse reaction in healthier persons. Seriously ill persons and suffering from cancer or AIDS are more likely to succumb to infections with *Salmonella* and other foodborne pathogens. In developing countries, reduced immunity due to poor nutritional status render people particularly infants and children, more susceptible to foodborne infections. Children are at the highest risk for *Salmonella* infection. Children under the age of 5 have higher rates of *Salmonella* infection than any other age group (CDC, 2014) [7]. Young children, older adults, and people with weakened immune systems are the most likely to have severe infections (CDC, 2012) [6].

Transmission

Salmonella lives in the intestinal tract of humans and animals, including birds. *Salmonella* is usually transmitted to humans by eating foods contaminated with animal faeces. Salmonellae are widely distributed in nature and they survive well in a variety of foods. Poultry, eggs and dairy products are the most common vehicles of salmonellosis. In recent years, fresh produce like fruits and vegetables have gained concern as vehicles of transmission where contamination can occur at multiple steps along the food chain. Poultry products are frequent vehicles in the transmission of *Salmonella*, dominating other foods of animal origin as potential source of infection (Bryan and Doyle, 1995) [3]. *Salmonella* Enteritidis silently infects the ovaries of apparently healthy hens and contaminates the eggs before the shells are formed which may cause infection in the consumers if eaten raw or undercooked.

Pork is the second most important source of *Salmonella* organisms in some countries and many outbreaks of salmonellosis reported in the last decade have been traced to the consumption of pork (Molbak *et al*., 1999) [12]. Beef and dairy products have been identified as important vehicles in the outbreaks of salmonellosis (Bean *et al*., 1990) [1]. In addition, risks to humans in contact with streams contaminated with *Salmonella* from dairy herd have been reported.

Health Impact of Salmonellosis

There are various serovars of *Salmonella* spp. which can cause disease in the animals and humans. Currently, there are more than 2, 579 recorded serovars of *Salmonella* (WHO, 2007) [18] and of these, the most common non-typhoidal serovar isolated from human is *S.* Typhimurium followed by *S.* Enteritidis, whereas, the most common serovar of non-human origin is *S.* Typhimurium followed by *S.* Newport (CDC, 2006) [5]. Among all the serovars of *Salmonella enterica*, *Salmonella* Typhimurium is most commonly associated with enteric infections in man and animals. This serovar has diverse host range, which includes humans, cattle, pigs, sheep, horses, rodents and birds. Typically, *Salmonella* Enteritidis, *Salmonella* Typhimurium and *Salmonella* Heidelberg are the three most frequent serotypes recovered from humans each year (Boyen *et al*., 2008) [2].

Salmonella Typhimurium and *Salmonella* Enteritidis are not only involved in severe outbreaks of avian salmonellosis and causing significant economic losses to the poultry industry**,** but also pose a serious public health hazard, as poultry are known to be the major transmitters of non-host adapted salmonellosis in humans. Human gastroenteritis caused by *Salmonella enterica* infection represents one of the most important foodborne zoonoses worldwide. Multidrug resistant *Salmonella* Typhimurium definitive phage type (DT) 104 strains are responsible for a high number of infections in human beings and are primarily zoonotic in origin.

The incubation period varies from 6 to 72 hours. The disease is characterized by sudden onset of nausea, vomiting, foul-smelling diarrhea and fever. The stool may contain mucous and blood. Complications may lead to systemic infections and cause arthritis, osteomyelitis, pyelonephritis, peritonitis, cholecystitis, meningitis and endocarditis. Average fatality rate in *Salmonella* infections has been reported to be 5.3%, but certain serotypes can cause a fatality rate up to 21%. Higher case fatality rate has been observed among infants less than 12 months old and HIV patients. A small number of people with *Salmonella* develop pain in their joints. This is called reactive arthritis. Reactive arthritis can last for months or years and can lead to chronic arthritis, which can be difficult to treat. People with reactive arthritis can also develop irritation of the eyes and painful urination (Carter and Hudson, 2009) [4].

Antimicrobial resistance is a global public health concern and *Salmonella* is one of the microorganisms in which some resistant serotypes have emerged, affecting the food chain (WHO, 2018) [16]. Resistance to combination of several classes of antimicrobial agents has led to the emergence of multidrug-resistant strains that may pass from food animals to humans. Resistance to two or more classes of drugs (MDR phenotype) is becoming increasingly widespread in *Salmonella* species. Multidrug-resistant (MDR) strains of *Salmonella* are now encountered frequently and the rates of multidrug-resistance have increased considerably in recent years. There are three most common MDR organisms

(MDROs) such as Methicillin-Resistant *Staphylococcus aureus* (MRSA), Vancomycin Resistant enterococci (VRE) and Extended Spectrum Beta-Lactamase producing Enterobacteria (ESBLs).

Economic Impact of Salmonellosis

Salmonellosis constitutes a major public health burden and represents a significant cost to society in many countries. Very few countries report data on the economic cost of *Salmonella*; data related to the cost of foodborne disease are generally not available from developing countries (WHO, 2005) [17]. The burden of foodborne diseases is substantial: every year almost 1 in 10 people fall ill and 33 million of healthy life years are lost. CDC estimates *Salmonella* causes about 1.2 million illnesses, 23,000 hospitalizations, and 450 deaths in the United States every year. Food is the source for about 1 million of these illnesses (CDC, 2018) [8].

According to David Byrne, EU Commissioner for Health and Consumer Protection, the costs of food-borne *Salmonella* alone are estimated to reach up to € 2.8 billion annually in EU countries altogether (European Commission, 2003) [9]. In Denmark, the annual estimated cost of food-borne salmonellosis is US$ 15.5 million in 2001, representing approximately 0.009% of the country GDP. A *Salmonella* control programme has been conducted for several years in the country, and the annual cost of this control programme is estimated around US$ 14.1 million (WHO, 2005) [17]. In the Netherlands, annual social costs caused by human salmonellosis are estimated between 32 and 90 million Euro (Van Pelt and Valkenburgh, 2001) [15].

Management of Salmonellosis

1. **Treatment of Cases:** Most cases of salmonellosis are mild; however, sometimes it can be life-threatening. The severity of the disease depends on host factors and the serotype of *Salmonella* (WHO, 2018) [16]. The illness usually lasts 4-7 days, and most people recover without treatment. However, in the very young and the elderly, and in cases when the bacteria enter the bloodstream, antibiotic therapy may be needed.

   Routine antimicrobial therapy is not recommended for mild or moderate cases in healthy individuals. This is because antimicrobials may not completely eliminate the bacteria and may select for resistant strains, which subsequently can lead to the drug becoming ineffective. However, health risk groups such as infants, the elderly, and immunocompromized patients may need to receive antimicrobial therapy. Antimicrobials are also administered if the infection spreads from the intestine to other body parts. Because of the global increase of antimicrobial resistance, treatment guidelines should be reviewed on a regular basis taking into account the resistance pattern of the bacteria based on the local surveillance system (WHO, 2018) [16].

   Generally antibiotic treatment is not required in case of acute *Salmonella* gastroenteritis. Antibiotic therapy is indicated in severe cases, infants, small children and immuno-deficient patients. Ciprofloxacin is now the drug of choice, and can be used @ 500 mg orally, twice a day for 10 days. Amoxycillin @ 0.5-1.0 g orally, four times a day for one week can be used as an alternative antibiotic for the treatment of salmonellosis. Treatment in severe cases also requires electrolyte replacement (to provide electrolytes, such as sodium, potassium and chloride ions, lost through vomiting and diarrhoea) and rehydration.
2. **Heat Treatment of Food:** Basic food hygiene practices, such as "cook thoroughly", are recommended as a preventive measure against salmonellosis. Poultry meat, eggs, pork etc. should be thoroughly cooked before their consumption.
3. **Hygienic Measures:** Purification and protection of drinking water supply, improvement of basic sanitation and promotion of food hygiene are important measures to prevent the transmission of disease. Patients and carriers should not be allowed to work in any food processing and food serving establishments.
4. **Other Measures:** Poultry are important reservoir of *Salmonella*; therefore, *Salmonella* testing should be carried out in poultry breeding farms. Control of rodents and prevention of wild birds from mingling with poultry on farms are also important measures to prevent the spread of the disease.

International Action against Salmonellosis

WHO is working towards the strengthening of food safety systems in an increasingly globalized world. WHO is strengthening the capacities of national and regional laboratories in the surveillance of foodborne pathogens, such as *Campylobacter* and *Salmonella*. WHO has developed the Global Foodborne Infections Network (GFN) for promoting the integrated surveillance of antimicrobial resistance of pathogens in the food chain, collecting samples from humans, food and animals and analyzing data across the sectors. WHO Advisory Group on Integrated Surveillance of Antimicrobial Resistance (AGISAR) is working on foodborne diseases. WHO, jointly with FAO, is assisting Member States by coordinating international efforts for early detection and response to foodborne disease outbreaks through the network of national authorities in Member States. The International Food Safety Authorities Network (INFOSAN) is a global network of national food safety authorities, managed jointly by FAO and WHO with the secretariat in WHO. WHO provides scientific assessments as basis for international food standards, guidelines and recommendations developed by the FAO/WHO Codex Alimentarius Commission to prevent foodborne diseases.

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