Antibiotic Resistance in *Salmonella* Species, a Serious Public Health Problem: A Review

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**Abstract:** Salmonellosis is an infectious disease of humans and animals caused by organisms of the two species of *Salmonella* (*S.*enterica and *S.*bongori). The occurrence of *Salmonella* is a global challenge in the public health and food production sectors. *Salmonella* organisms are etiological agents of diarrheal and systemic infections in humans and animals, most commonly as secondary contaminants of food originating from animals and the environment, usually as a consequence of subclinical infection in food animals leading to contamination of meat, eggs and milk. Antibiotics resistance may manifest through multiple mechanisms among these intrinsic and extrinsic resistance factors more common and also plasmid mediated resistance, chromosome mediated-resistance and reduced membrane permeability can contribute a lot. Antibiotics are important drugs used in the treatment of bacterial infections in both humans and animals. Unconstrained use of antimicrobial drugs in the face of continuing infectious disease transmission is fundamental to the emergence of bacterial pathogens resistant to antimicrobial drugs thereby posing a serious threat to public health. Antibiotics resistant *Salmonella* are increasing due to the use of antibiotics agents in food animals at sub-therapeutic level or prophylactic doses which may promote on-farm selection of antimicrobial resistant strains and markedly increase the human health risks associated with consumption of contaminated animal products. The veterinary professionals should address this problem at every level, including the veterinary curriculum, individual-animal medicine, herd health practice and advocacy of sound public policy. Continuous studies should be initiated to monitor the link between the *Salmonella* species and their resistance pattern between food animals and human.

**Key words:** Antibiotics • Food Borne • Resistance • *Salmonella* Species

**INTRODUCTION**

*Salmonella* is one of the members of Entrobacteriaceae family. The genus *Salmonella* was named after Daniel E. Salmon who first reported the isolation of *Salmonella* from a pig in 1885 and named the organism *Bacterium choleraesuis* currently known as *Salmonella enterica* serovar choleraesuis [1]. According to the latest nomenclature, which reflects recent advances in taxonomy [2] formerly, the genus *Salmonella* consists of only two major species: *S.*enterica and *S.*bongori. However, currently the third putative species *S.*subterranea, has also been proposed following the isolation of a single unusual environmental strain [3] but more recent unpublished data suggest that this organism does not actually belong in the genus *Salmonella* [2].

The Kauffman-White classification shows that majority of the *Salmonella* involved in human disease belong to groups A, B, C2, D and E. The serovars of the other subspecies are more likely to be found in poikilothermic (Cold-blooded) animals and in the environment, but are occasionally associated with human disease. Some serovars of sub species *arizonae* and sub species *diarizonae* have been associated with disease in turkeys and sheep and others may be carried by free-living or captive reptiles and amphibians [4].

Although, *Salmonellae* are primarily intestinal bacteria, they are present in the environment and may commonly be found in farm effluents, human sewage and in any material subject to fecal contamination. Salmonellosis has been recognized in all countries, but appears to be most prevalent in areas of intensive animal
husbandry especially; in poultry and pig farms are more common. The disease can affect all species of domestic animals; young and pregnant animals are the most susceptible. As feed contamination may occasionally be caused by Salmonella serovars of relevance to public health, feedstuffs should be investigated for the presence of Salmonella [5].

The development of antibiotics resistance is the main undesirable side effect of antimicrobial use in both humans and animals and results from the continuous positive selection of resistant bacteria clones, whether these are pathogenic, commensal or even environmental bacteria. This will modify the population structure of microbial communities, leading to accelerated evolutionary trends with unpredictable consequences for human health. The use of antimicrobials can differ in humans and food producing animals, in terms of both the methods of administration and the quantities administered; there are important variations between and within food-producing animal species, as well as between countries [6].

The use of antibiotics can differ in humans and food producing animals, in terms of both the methods of administration and the quantities administered; there are important variations between and within food-producing animal species, as well as between countries. Bacterial resistance to antibiotics occurring in food-producing animals can spread to people not only via food-borne routes, but also by routes such as water or environmental contamination, as well as through direct animal contact. The commensal bacterial flora can also form a reservoir of resistance genes which may transfer between bacterial species, including transference to organisms capable of causing disease in both humans and animals [6]. Since the 1990, some strains of Salmonella became resistant to a range of antibiotics. The resistance is caused by the use of antibiotics in humans and animals husbandry. Nowadays, multidrug resistance (MDR) has become a critically important issue in public health [7].

Recently amonophasic variant of S. typhimurium (DT193) with resistance to ampicillin, streptomycin, sulphonamides and tetracycline has emerged in pigs and caused outbreaks of salmonellosis in humans in several countries worldwide and there are several other emergent monophasic strains with varying resistance patterns that have been recognized in various animal species and humans in many countries in recent years [8]. Many S. typhimurium isolates recovered in the extra intestinal organ in 2007, were found to have a resistance profile typical of that conferred by the presence of the SGI-1; 63% resistant to ampicillin, 64% to sulphonamides, 71% to tetracycline, 61% to streptomycin and 42% to chloramphenicol were recorded.

Resistance levels were generally higher in isolates from pigs and turkeys than from broilers, laying hens, breeding hens and cattle. Among the Salmonella spp. isolates from meat, the highest levels of resistance to ciprofloxacin and nalidixic acid were noted in broilers and turkeys. Microbiological resistance to the third-generation cephalosporins (Cefotaxime) in Salmonella species from meat was either not discerned or detected at low levels, with the notable exception of the isolates from broiler and turkey meat tested, where high or very high resistance to cefotaxime was observed [9].

Resistance to tetracyclines, ampicillin and sulphonamides in Salmonella spp. typically ranged from moderate to extremely high in meat. Generally, the highest levels of resistance to tetracyclines, ampicillin and sulphonamides were found among isolates of S. infantis from broiler meat and S. typhimurium, including the monophasic variants from pig meat, resulting in extremely high levels of multi-resistance in greater than 70.0% of isolates which poses public health risk [9]. Therefore, the objective of this review is to over review antibiotic resistance in Salmonella species and its public health risks.

**General over View of Salmonella Species:** Salmonella strains are serologically classified using Kauffmann White scheme and at the present the genus contains more than 2500 serotypes [10]. However, a report from the Centre for Infectious Disease Research and Policy (CIDRAP) classifies members of the Salmonella species into more than 2541 serotypes (Serovars) according to their somatic lipopolysaccharide (O), flagellar (H) antigens and at times capsular (VI) antigen and most strains show diphasic variation of the flagellar antigens. However, this number is constantly being increased.

**Evolution and Population Structure:** It is speculated that the genera of Escherichia coli and Salmonella diverged from a common ancestor about the time of the emergence of mammals and emerge as mammalian and avian pathogens through the acquisition of pathogenicity islands and of a virulence plasmid, through variation in lipopolysaccharide antigens, through development of
mechanism for flagellar antigen phase shifting and in other ways. Some writers estimated Salmonella diverged from the genus Escherichia 120–160 million years ago [11]. [12] Found that the close DNA relatedness among Salmonella serotypes is evidence for their clonal origin and based on the degree of sequence divergence, it can be estimated that a common ancestor of the genus existed about 25 to 40 million years ago in 1892.

[13] Described the causative agent of murine typhoid, then known as Bacillus typhi, that caused an epidemic typhoid fever-like disease in mice. Recently, Salmonella typhi was identified in ancient skeletal material, thereby incriminating typhoid fever for the plague that devastated Athens in 430–426 B.C. It is hypothesized that accumulation of single mutations, insertions or deletions with the genome of modern-time Salmonella typhi appears to have generated many pseudogenes, suggesting its recent evolutionary origin [14]. There are also regular changes to serovar classifications as new evidence on genetic relatedness becomes available, e.g. S. pullorum is now classified as S. gallinarum biovar pullorum and S. thomassville is designated as an antigenic variant of S. orion [2].

Most of our current understanding of the population structure of S. enterica relies on a series of seminal publications from Selander’s group in the 1990s. These publications showed that some serovars consisted of monophyletic groups the so called clonal groupings but many other serovars confounded isolates from multiple lineages and were therefore polyphyletic [15].

More recent studies have indicated that genetic diversity within S. enterica reflects considerable homologous recombination in addition to mutation [16]. As a result, the sequence diversity of S. enterica resembles a starburst radial expansion and lacks phylogenetic evolutionary development information [17]. Individual monophyletic lineages, some of which equate to a serovar, are arranged at the tips of the starburst and their evolutionary histories are only beginning to be elucidated [18].

**Classification and Characteristics:** The current nomenclature of the genus Salmonella adopted worldwide through different publications is the one used by CDC based on the recommendations from the WHO collaborating centre and it adequately addresses the concern and requirements of clinical and public health microbiologists Table 1) [19]. Scientifically Salmonella classification is described underdomain: bacteria, phylum: protobacteria, class: Gamma Protobacteria, order: Enterobacteriales, family: Enterobacteriaceae, genus: Salmonella and species: Salmonella enterica and Salmonella bongori [20]. The species Salmonella enterica being divided into six subspecies (I–VI) on the basis of biochemical characteristics (biotype), differences observed in multilocus enzyme electrophoresis (MLEE), phylogenetic analysis using 16S rRNA or other sequences, or analyses using other molecular techniques such as Amplified-fragment length polymorphism (AFLP) [21] as follow indicated in Table 1.

For the serovars of S. bongori, the symbol V was retained to avoid confusion with the serovar names of S. enterica sub specie Enteric [4]. Members of Salmonella enterica sub species I account for 99% of all human infections [21].

Strains of genus Salmonella obey the definition of the family Enterobacteriaceae, they are straight rod usually motile with peritrichous flagella except S. pullorum and S. gallinarum, facultative anaerobe, ferment glucose usually with production of gas (Except S. typhium and S. dublin), but failed to ferment lactose, sucrose, salicin and urea, reduce nitrate to nitrite and most are phototropic [22]. The cell wall of Salmonella compounds the structure of lipids, polysaccharides, protein and lipoproteins. The lipopolysaccharide portion of the cell wall and lipid A is endotoxin. Endotoxin is responsible for the biological effects. The common center monosaccharaides and polysaccharides of endotoxin are also called somatic O antigens. Salmonella has about 60 of O antigens that are nominated by numbers. Furthermore; there are some flagella (H) antigens that they are recognized by numbers and letters [2] and capsular antigen called Vi which occurs in only three Salmonella serovars namely; S. typhi, S. paratyphi C and S. dublin. The O factors determine the serogroup and the H factors define the serotype of a Salmonella strain [23].

Salmonella multiply optimally at a temperature of 35 to 37°C, pH about 6.5-7.5 and water activity between 0.94-0.84. Salmonella grows readily on blood agar, MacConkey agar, Bismuth Sulfate agar or deoxycholate agar. They are chemo-organotrophic organisms, obtaining their energy from oxidation and reduction reactions using organic sources. Most Salmonella species produce H2S, which can readily be detected by growing them on media containing ferrous sulfate such as triple sugar iron (TSI) where Salmonella is able to produce H2S from thiosulphate. The bacteria are sensitive to heat and will not survive a temperature above 70°C so it is sensitive to pasteurization, but resist to drying even for yearse specially in dried feces, dust and other dry materials such as feed and certain food [24].
Table 1: Current nomenclature of Salmonella serovars

<table>
<thead>
<tr>
<th>Original Subgenera</th>
<th>Current Nomenclature</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subspecies I</td>
<td>Subspecies enterica</td>
</tr>
<tr>
<td>Subspecies II</td>
<td>Subspecies salamae</td>
</tr>
<tr>
<td>Subspecies IIIa</td>
<td>Subspecies arizonae</td>
</tr>
<tr>
<td>Subspecies IIIb</td>
<td>Subspecies diarizonae</td>
</tr>
<tr>
<td>Subspecies IV</td>
<td>Subspecies houtenae</td>
</tr>
<tr>
<td>Subspecies VI</td>
<td>Subspecies indica</td>
</tr>
</tbody>
</table>

Source: [2].

Table 2: Currently recognized number of Salmonella serovars

<table>
<thead>
<tr>
<th>Salmonella species and subspecies</th>
<th>No. of serovars within subspecies</th>
<th>Usual habitat</th>
</tr>
</thead>
<tbody>
<tr>
<td>Salmonella enteric group</td>
<td>2557</td>
<td>Warm blooded animal</td>
</tr>
<tr>
<td>S. enteri sub spps. Enteric</td>
<td>1531</td>
<td>Cold blooded animals and environment</td>
</tr>
<tr>
<td>S. Salamae sub spps. Salamae</td>
<td>505</td>
<td>Cold blooded animals and environment</td>
</tr>
<tr>
<td>S. Arizonae sub spps. Arizonae</td>
<td>99</td>
<td>Cold blooded animals and environment</td>
</tr>
<tr>
<td>S. Diarizonae sub spps. Diarizonae</td>
<td>336</td>
<td>Cold blooded animals and environment</td>
</tr>
<tr>
<td>S. Houtenae sub spps. Houtenae</td>
<td>73</td>
<td>Cold blooded animals and environment</td>
</tr>
<tr>
<td>S. Indica sub spps. Indica</td>
<td>13</td>
<td>Cold blooded animals and environment</td>
</tr>
<tr>
<td>Salmonella bongori group</td>
<td>22</td>
<td>Cold blooded animals and environment</td>
</tr>
</tbody>
</table>

Source: [2].

Table 3: The most common serovars of Salmonella that infect livestock and syndromes induced

<table>
<thead>
<tr>
<th>Species affected</th>
<th>Serovars</th>
<th>Common syndromes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cattle</td>
<td>S. dublin and S. typhimurium</td>
<td>Septicemia, acute and chronicenteritis and abortion</td>
</tr>
<tr>
<td>Sheep</td>
<td>S. typhimurium</td>
<td>Septicemia, typhocolitis and abortion</td>
</tr>
<tr>
<td>Pig</td>
<td>S. choleraesuis S. typhimurium, S.typhisuis</td>
<td>Septicemia</td>
</tr>
<tr>
<td>Horses</td>
<td>S.typhimurium</td>
<td>Septicemia, acute colitis and abortion</td>
</tr>
<tr>
<td>Chicken</td>
<td>S. pullorum, S. gallinarum</td>
<td>Septicemia, acute and chronicenteritis</td>
</tr>
<tr>
<td>Human</td>
<td>S. enteritidis, S. typhi, S.paratyphi</td>
<td>Gastroenteritis, bacteremia</td>
</tr>
</tbody>
</table>

Source: [26]

The usual habitat of different Salmonella species and subspecies is the intestines of both cold and warm blooded animals. The bacteria can also be found throughout the natural environment. Environmental sources of the organism include water, soil, insects, factory surfaces, kitchen surfaces, animal feces, raw meats, raw poultry and raw sea foods. Even though Salmonella cannot multiply outside the host digestive tract, the bacteria can live for number of weeks in water and some years in soil if there are favorable conditions such as temperature, pH and humidity [2]. Recently, Diagnostic Services of Monitoba (DSM) suggested the number of Salmonella serotypes that causes disease in human and animals are now approaching 3000 and new serotypes are identified continuously [25] as summarized in Table 3.

**Antibiotics Resistance in Salmonella Serovars**

**Global Trends in Resistance Pattern:** Antibiotics resistance is one of the biggest challenges facing global public health. Although antimicrobial drugs have saved many lives and eased the suffering of many millions, poverty, ignorance, poor sanitation, hunger and malnutrition, inadequate access to drugs, poor and inadequate health care systems, civil conflicts and bad governance [27]misdiagnosis, counterfeit drugs and lack of education in developing countries have tremendously limited the benefits of these drugs in controlling infectious diseases worldwide [28]. Recent studies of almost 400 different bacteria have demonstrated about 20,000 possible resistance genes (R genes) [29].

**Classification of Resistance:** Antibiotics are important drugs used in the treatment of bacterial infections in both humans and animals. Emerging antibiotic resistance among certain bacteria is now frequently observed, thereby posing a serious threat to public health. Once these micro-organisms become resistant to one or more antibiotics, they do not respond to therapy. Resistance to most traditional, regulatory-approved, or naturally-occurring food antimicrobial agents is difficult to characterize because of the lack of a precise definition for such resistance [30].
From a functional perspective, resistance correlates with failure of a given antimicrobial treatment; whereas from a laboratory perspective, resistance is denoted through a Minimal Inhibitory Concentration (MIC) which is the lowest concentration of an antimicrobial drug, expressed in \( \mu g/ml \) or mg/L, which under defined invitro conditions within a defined period of time inhibits growth of the microbial inoculums value that exceeds a threshold value, which may or may not be associated with a clinical outcome [31].

A microorganism is resistant if it exhibits significantly reduced susceptibility when compared with that of the original isolate or a group of sensitive strains. Resistance means temporary or permanent ability of a microorganism and its progeny to remain viable and/or multiply under conditions that would destroy or inhibit other members of the strain[30]. Resistance can result from mutations in housekeeping structural or regulatory genes, or alternatively, horizontal acquisition of foreign genetic information. In some cases, resistance may manifest through multiple mechanisms [31].

**Innate (Intrinsic) Resistance:** Innate (Intrinsic) resistance is inherent to all specimens of the species. In such cases, in general, the gene that encodes the intrinsic resistance is chromosomal. Innate resistance is related to the general physiology or anatomy of a microorganism and stems from pre-existing mechanisms or properties. More specifically, Gramnegative bacteria are innately resistant to penicillin G by virtue of their double membrane structure, which prevents the antibiotic from accessing the cell wall target. Innate resistance is not considered an important clinical problem because antibiotics were never intended for use against intrinsically resistant bacteria. There are certain circumstances in which antimicrobial agents do not adversely affect bacteria that are generally susceptible to the particular agent. Exposure conditions, such as the environmental conditions (Temperature, pH and food composition) of the antimicrobial application, or interaction of the antimicrobial with components of the suspension medium or food product can influence the efficacy of the antimicrobial agent [29].

**Acquired (Extrinsic) Resistance:** Acquired (Extrinsic) resistance results from genetic changes that occur through mutation of the antimicrobial’s target site within the bacterium or acquisition of genetic material encoding resistance via plasmid or transposons, genetic element that physically moves from one genetic position within the chromosome or plasmid in which it resides to another, containing integron sequences. Acquired resistance, the most common type of antibiotic resistance, has been well studied for antibiotics, but has not been well studied for food antimicrobial agents and sanitizers. Acquisition of genes for \( \alpha \)-lactamase (An enzyme capable of breaking down and inactivating \( \alpha \)-lactam antibiotics penicillins and cephalosporins) and mutation of one of the subunits of DNA gyrase, the target of fluoroquinolones, are examples of this type of resistance [32].

**Adaptation:** Adaptation may be demonstrated by exposing a microorganism to a stepwise increase in concentration of the substance. This type of resistance, however, is often unstable; the microorganism may revert back to the sensitive phenotype when grown in an antimicrobial-free medium, termed as back-mutation. In the absence of selection pressure, the mutations associated with resistance may actually reduce fitness of the bacterial strain compared to the wild type, parental strain. Stabilizing, secondary, compensatory mutations are sometimes needed to maintain resistance and reduce fitness cost associated with the original resistance mutation [33].

**Mechanisms for Emergence and Dissemination of Antibiotics Resistance:** Bacteria can evade the actions of antibiotics using diverse mechanisms. The origin of antibiotic resistance extends much further back in evolutionary terms and reflects the attack and counterattack of complex microbial flora in order to establish ecological niches and survive [34]. Early treatment failures with antibiotics did not represent a significant clinical problem because other classes of agents, with different cellular targets were available. The major problem in the clinic today is the emergence of multiple-drug resistance, resistance to several types of antimicrobial agent [35]. The origin of antibiotic resistance genes are unclear; however, studies using clinical isolates collected before the introduction of antibiotics demonstrated susceptibility although, conjugative plasmids were present [34].

**Plasmid mediated resistance:** Are often codes for enzymes that destroy or modify drugs; for examples, the hydrolysis of penicillin or the acetylation of chloramphenicol and aminoglycoside drugs. Plasmid associated genes have been implicated in resistance to aminoglycosides, chloramphenicol, penicillins, cephalosporins, erythromycin, tetracycline, sulphonamides and others [36].

The mechanism of drug resistance usually mediated by acquisition of R plasmids involves: initially inactivation of the drug which is a common cause of resistance that destroys or inactivates antimicrobial agents. The bacterial pathogens resist attack by inactivating drugs through chemical modification. One enzyme of this type is β-lactamase. Several β-lactamase exist in various bacteria. The best known example is the hydrolysis of the β-lactam ring of Penicillin by the enzyme penicillinase. They are capable of breaking the β-lactam ring of penicillin and some cephalosporins. The initial strains of antibiotic-resistant S. typhi carried chloramphenicol acetyltransferase type I, which encodes an enzyme that inactivates chloramphenicol via acetylation [37]. Chloramphenicol contains two hydroxyl groups that can be acetylated in a reaction catalyzed by the enzyme chloramphenicol acetyltransferase with acetyl CoA as the donor.

**Reduced Membrane Permeability:** Reduced membrane permeability simply by preventing entrance of the drug. The alteration in membrane permeability occurs when new genetic information changes the nature of proteins in the membrane. Such alterations change a membrane transport system pores in the membrane, so an antimicrobial agent can no longer cross the membrane. In S. typhi, resistance to tetracycline, quinolones and some aminoglycosides have occurred by this mechanism. A decrease in permeability can also lead to sulfonamide resistance [36].

**Modification of Target Resistance Site:** Modification of target site resistance arises when the target enzyme or cellular structure of the pathogen is modified so that it is no longer susceptible to the drug. This mechanism is found in S. typhi and other sulfonamide-resistant bacteria. These organisms have developed an enzyme that has a very high affinity for p-aminobenzoic acid (PABA) and a very low affinity for sulfonamide. Consequently, even in the presence of sulfonamides, the enzymes work well enough to allow the bacterium to function [38].

**Rapid Extrusion or Effluxpumps:** Rapid extrusion or efflux of the antibiotics a resistance mechanism works by pumping the drug out of the cell after it has entered. Some pathogens have plasma membrane translocases, often called efflux pumps, that expels drugs. Because they are relatively nonspecific and can pump many different drugs including quinolones, these transport proteins often are called multidrugresistance (MDR) pumps. Many are drugproton antiporters, proton enter the cell as the drug leaves [38]. Resistance to sulfonamides is mediated by a plasmid encoded transport system that actively exports the drug out of the cell [34]. Many genes, such as plasmid mediated β-lactamases, tetracycline-resistance genes and aminoglycoside-modifying enzymes, are organized on transposons.

**Chromosome Mediated-Resistance:** Chromosome mediated-resistance has been attributed to a mutation in the gene that codes for either the target of the drug or the transport system in the membrane that controls the uptake of the drug [34]. The frequency of spontaneous mutations usually ranges from $10^{-2}$ to $10^{-4}$ which is much lower than the frequency of acquisition of resistance plasmids. The chromosomal-mediated drug resistance phenomenon against fluoroquinolones has been reported recently as a result of selective pressure on the bacterial population due to their uncontrolled use. This has been attributed to a single point mutation in the quinolone resistance determining region (QRDR) of the topoisomerase gene gyrA, which encodes DNA gyrase [37]. Resistance to trimethoprim is due primarily to mutations in the chromosomal gene that encodes dihydrofolatereductase, the enzyme that reduces dihydrofolate to tetrahydrofolate. Also, resistance to sulfonamides has been found to be mediated by a chromosomal mutation in the gene coding for the target enzyme dihydropteroatesynthetase, which reduces the binding affinity of the drug [34].

The Role of Veterinarian in Controlling the Emergence and Dissemination of Drug Resistant: A number of different components of the veterinary curriculum relate directly to the emergence and dissemination of antimicrobial resistant pathogens. These include veterinary public health and zoonotic infections, antimicrobial pharmacology, epidemiology and population medicine, the ecology of infectious diseases and hospital infection control [39].

Antibiotics resistance is just one example of important current problems and challenges that will continue to challenge the veterinary education establishment to train veterinarians capable of playing a role in modern society broader than that of individual animal curative medicine. Antimicrobial resistance and antimicrobial use practices present many ethical dilemmas, at various levels including individual animal medicine, herd health practice and the message of the profession at the level of public policy and law [40].
At the level of the individual animal, it faces exactly the same challenge as medical doctors prescribing a cutting edge drug may slightly increase the probability of a favorable outcome for any individual case, while adding to the risk of treatment failure for future cases and it is unfortunately very easy to choose the immediate benefit over the future risk [41]. At the level of production animal agriculture, herd health veterinarians must balance sound principles like that of the World Health Organization. The routine prophylactic use of antimicrobials should never be a substitute for good animal health management with market structures and economic forces that dictate the opposite [42]. For many of these issues, the profession is challenged with balancing the interests of public health and sound public policy with the interests of clients, commodity groups, drug companies and others. In veterinary sciences, veterinary professionals studies on the frequency and distribution of antimicrobial resistant Salmonella and other food borne bacterial pathogens are usually undertaken: to monitor and improve management systems, to ensure the production of foods free of antimicrobials and drug-resistant pathogens, to decrease threats to the health of the consumer and to promote the international trade of food and food products.

**Multiple Antimicrobial Resistant Salmonella Serotypes in Ethiopia:** In developing country like Ethiopia a limited number of investigation have been studied the presence of antimicrobial resistance of Salmonelae serovars in food animals [43, 44]. The situation of antibiotic resistance is more complex and difficult, because Salmonella and other major zoonotic bacterial pathogens are not routinely cultured and their resistance to commonly employed antimicrobials both in public health and veterinary practices is rarely determined.

The connection between S. concord and Ethiopia has been made by the investigation of babies in Europe and America who were adopted from Ethiopia [45]. There has been no report in the international literature about the actual source of S.concord in Ethiopia. Isolates are usually resistant to ampicillin, aztreonam, cefazolin, cefepime, cefpodoxime, cefazidime, ceftiofur, cefuroxime, cephalothin, chloramphenicol, streptomycin, sulfamethoxazole, trimethoprim and ceftriaxone [46]. Furthermore, an increase in the resistance of Salmonella to commonly used antimicrobials has also been noted in both public health and veterinary sectors in Ethiopia. Even the studies conducted in Gondar, Jimma and Addis Ababa show that serogroup B isolates were the most common and for some hospital based studies, S. typhi was predominant. According to [47] more than 80% of the Salmonella isolates from an abattoir in Ethiopia exhibited resistance to at least one type of antimicrobial tested where at least 50% of the isolates exhibited resistance to two or more antimicrobials tested.

**Antibiotic use in Food Producing Animals:** Antibiotics are used in food producing animals to treat or prevent illnesses for example during the weaning period of young animals. They may also be used for long periods at low levels to promote growth, increase feed efficiency, or compensate for unsanitary growing conditions on concentrated animal feeding operations [48]. Increased feed efficiency means animals require less feed per pound of weight gain, which translates to lower costs for producers. Many animal producers believe the use of antibiotics for growth promotion also prevents disease.

In the industrial model of animal husbandry, large numbers of pigs, chickens, or cattle are raised in confined areas. In the pork and chicken industries, large-scale concentrated housing systems reduce costs for labor, feed and housing. However, the increased stress of crowding and unsanitary conditions makes animals more susceptible to the spread of infectious diseases. Many producers commonly administer an antibiotic to an entire flock or herd via feed or water, but that gives them less control over the dosage consumed by individual animals. The non-therapeutic use when animals are treated in the absence of bacterial disease or exposure to disease use of antibiotics, sometimes administered throughout an animal’s life, is among the practices of greatest concern for the development of antibiotic resistance [49].

**Public Health Perspective of Salmonella Serovars**

**Global Overview:** In spite of the improvement in hygiene, food processing, education of food handlers and information to the consumers, food borne diseases like salmonellosis is still dominate as the most important public health problem in most countries [50]. Many foods, particularly those of animal origin, have been identified as vehicles for transmission of these pathogens to human beings and spreading them to the processing and kitchen environment [51]. In developed countries food is recognized as the most frequently implicated vehicle of transmission and causes heavy financial burden on health care systems [52]. In many countries incidence of human Salmonella infection has increased drastically over the years. S. enteritidis and S. typhimurium were reported to be the two most frequent serotypes of Salmonella in the world [53].
Status in Developing Countries: According to [54] available information suggests that there have been increases in the occurrence of resistance in *Salmonella* in developing countries. The increase of antimicrobial resistance in developing countries is possibly caused by drug abuse and availability of drugs without prescription. Meanwhile, in developed countries the situation of MDR *Salmonella* is linked to the consequences on the use of antimicrobial drugs in food producing animals. However, other scholars argue that the emergence of MDR strains in developed countries have been introduced by the returning travelers [55].

The major epidemiological development in salmonellosis is the emergence of multiple antibiotic resistant *Salmonella*, particularly in the developing countries. With the increasing population in the developing world, there is an increasing demand for meat and meat products which will force the present resource driven system of livestock production to a demand driven system which will increase the disease transmission risks [56]. There is also a multifactorial risk of food borne hazards in the developing countries due to poor sanitation and inadequate access to potable water.

Health and Economic Impact: Food-borne pathogens cause important economic and health problems in the world. In recent years, *Salmonella* has been one of the most common causes of food borne disease [57]. *Salmonella* species are leading causes of acute gastroenteritis in several countries and *salmonella* serovar resistance remains an important public health problem worldwide, particularly in the developing countries [58].

The transmission of resistance of *salmonella* strains to human beings often occurs through food, especially food products with an animal origin in which acquire resistance before such as meat, milk, egg, animal foods and sometimes vegetables in the food chain [59]. In developing countries, estimation of *Salmonella* serovar resistance is difficult because there has not been sufficient surveillance [60]. Therefore, globally, many studies have been performed reporting that the prevalence and kind of *Salmonella* serotypes are different based on geographical regions [61].

Antibiotic use in animal production systems has long been suspected to be a cause of the emergence and dissemination of antimicrobial resistant *Salmonella*. This practice promotes the development of drug resistant bacteria that can spread to humans. Thus food borne diseases, when associated with resistant bacteria, are harder to treat, resulting in longer hospitalization, higher mortality and morbidity, decreased productivity and increased costs. Likewise, antibiotic resistance is like a fluid and constantly evolving challenge. Further transfer of antibiotic resistant bacteria to humans via food chain has been reported [62].

CONCLUSIONS AND RECOMMENDATIONS

*Salmonella* is a leading cause of foodborne disease in human and consumption of both meat and milk has been implicated in salmonellosis outbreaks of people. Many foods, particularly those of animal origin, have been identified as vehicles for transmission of these pathogens to human beings. Antibiotic resistance is one of the biggest challenges facing global public health. The transmission of resistance of *Salmonella* strains to human beings often occurs through food, especially food products with an animal origin which acquire resistance before such as meat, milk, egg, animal foods and sometimes vegetables in the food chain. Resistance to most traditional, regulatory-approved, or naturally-occurring food antibiotics agents is difficult to characterize because of the lack of a precise definition for such resistance. Many isolates are usually resistant to ampicillin, aztreonam, cefazolin, cefepime, cefpodoxime, cefazidime, ceftiofur, cefuroxime, cephalothin, chloramphenicol, streptomycin, sulfamethoxazole, trimethoprim and ceftriaxone. In conclusion, antibiotic use in animal production systems has long been suspected to be a cause of the emergence and dissemination of antimicrobial resistant *Salmonella*, this practice promotes the development of drug-resistant bacteria that can spread to humans. Moreover, antibiotic resistance in developing countries is possibly caused by drug abuse and availability of drugs without prescription.

Based on the above facts the following recommendations are forwarded:

- Veterinary professionals should address this problem at every level, including the veterinary curriculum, individual animal medicine, herd health practice and advocacy of sound public policy regarding drug use.
- People should not drink unpasteurized milk or milk products and not to eat improperly cooked meat so that avoid infection by antibiotic resistance *Salmonella* strains
- Create awareness among animal producers not to use antibiotics as additives and growth promoters in food producing animals.
• New legislations about drug use or public awareness campaigns should be implemented to avoid drug abuse and availability of drugs without prescription in developing countries.

• Continuous studies should be initiated to monitor the link between the Salmonella serovars and their resistance pattern between food animals and human.

REFERENCES


42. WHO, 19970. Multi-drug resistant Salmonella typhimurium. Fact Sheet No., 139.


