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Review On Salmonellosis, Economic And Public Health Importance

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Abstract: Salmonellosis is an infectious disease of humans and animals caused by organisms of the two species of Salmonella (Salmonella enterica, and S. bongori). Although primarily intestinal bacteria, salmonellae are widespread in the environment and commonly found in farm effluents, human sewage and in any material subject to faecal contamination. Salmonella organisms are aetiological agents of diarrhoeal and systemic infections in humans, 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 or secondary contamination of fruits and vegetables that have been fertilised or irrigated by faecal wastes. Salmonella passes through M-cells overlying Peyer's patches or through the epithelial lining of the lower part of small intestine or proximal colon to arrive in the sub epithelial location which is also transported to extra intestinal sites such as the liver, spleen and mesenteric lymph nodes. Bovine salmonellosis is caused by S. typhimurium and dublin. The disease in cattle is characterized by septicemia, acute or chronic entritis or abortion. Salmonella entrica sub species entrica develop a resistance to multi antibiotics in which results in increasing failure of treatment and severity of infection. Basic hygiene practices and the implementation of scientific based management strategies can efficiently mitigate the risks associated with animal contacts. However, the general public is frequently unaware of the specific disease risks involved and high-risk behaviors are common. The disease can be also controlled by vaccination of cattle.

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1. INTRODUCTION

1.1 Back ground

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) (Rao, 2004). Salmonella causes gastroenteritis and typhoid fever and is one of the major foodborne pathogens of significant public health concern) (Fluit, 2005). Salmonellosis is a disease caused by many serotypes of Salmonella and characterized clinically by one or more of the three major syndromes; septicemia, acute and chronic enteritis (Davison and S, 2005).

Salmonellae are common in cattle. They are often concern due to disease of cattle and the potential to infect human that come in contact with cattle or consume dairy product or bovine meat product. Meat processing and packaging at the whole sale or retail level contribute to higher levels of contamination in minced beef product compared to beef carcass. The presences of even small number of Salmonella in carcass meat and edible offal may lead to heavy contamination of minced meat. When meat is cut in to pieces more microorganisms are added and increased surface area of exposed tissue from the contaminated equipment. Raw meat particularly, minced meat has a very high total count of microorganisms of which Salmonella are likely to present large number (Ejeta *et al*., 2004).

Cattle Salmonelosis usually manifest clinically as a syndrome of septicemia, acute or chronic enteritis and abortion (Kemal, 2014). There are few serotypes that are associated with cattle and of this Salmonella enterica serotype Dublin (S. dublin) and Salmonella enterica subspecies enterica serotype Typhimurium (S. typhimurium) is the most common (McEvoy *et al*., 2003). The presence of S. typhimurium in cattle and the cross contamination of beef carcass tissue is one of the most common cause of Salmonella infection in developed countries (Kemal, 2014). In addition to causing infection many Salmonella isolates particularly S. typhimurium definitive type (DT) 104 have developed resistance to multiple antibiotics (Piddock 2002). The resistance organism may act as donor of resistant determinant to another facultative pathogen of the human commensal flora of intestinal tract which may later be associated with disease and, in turn, supply the resistances gene to other pathogen (Kemal, 2014). The economic loss associated in human salmonellosis is due to investigation, treatment and prevention of illness (Wray and Wray, 2000).

1.2. Objectives of the seminar

Therefore, the objectives of this review papers are:

- To overview the epidemiology of salmonellosis
- To highlight salmonellosis's potential zoonotic effects.

2. LITERATURE REVIEW

2.1 Classification

The current nomenclature of the genus Salmonella adopted worldwide through different publications is the one used by CDC is based on the recommendations from the WHO collaborating centre and it adequately addresses the concern and requirements of clinical and public health microbiologists(Deb M, Kapoor L (2005).

Scientifically Salmonella classification is described under:

Domain: Bacteria
Phylum: Protobacteria
Class: Gamma Protobacteria
Order: Enterobacteriales
Family: Enterobacteriaceae
Genus: Salmonella, and
Species: Salmonella enterica and Salmonella bongori (Hafez, H.M. 2005).

2.2 Etiology and Characteristics

Etiology and Characteristics Salmonellae are small, Gram-negative, non-spore forming; facultative anaerobic, rod-shaped, motile bacteria that belong to the family Enterobacteriaceae (Jay, 2000; Patterson and Isaacson, 2003).The cells are typically 0.7-1.5 µm by 2-5 µm. They grow at 7-48oC with an optimum growth at 37oC (mesophile) and at pH 4.05-9.5 with an optimal growth at pH 6.5-7.5 (neutrophile). Salmonella grows optimally at a water activity of 0.995 and are chemo-organotrophs. They have both fermentative and oxidative metabolism. The primary route for metabolism of carbohydrates is the Embden-Meyerhof pathway (glycolysis). They ferment glucose to formate (with the production of gas) and to ethanol, acetate, or lactate (Craig DE. and James MS, 2006).

Strains of genus Salmonella are the group of 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. typhi and S. dublin) (Johnson et al., 2007). Salmonella multiply optimally at a temperature of

35oC to 37oC, pH about 6.5-7.5. They are also able to multiply in the environment with low level or no oxygen (Kemal, 2014). The bacteria are sensitive to heat and will not survive a temperature above 70oC; so it is sensitive to pasteurization, but resist to drying even for years. Especially in dried feces, dust and other dry materials such as feed and certain food (Radostitis *et al*., 2007). The most common serovars of Salmonella that infect livestock and syndrome they induce are shown in the Table 1.

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Table 1: The most common serovars of Salmonella that infect livestock and syndrome

Table 1: The most common serovars of Sal 1

Species	Serovars	Common syndrome
Cattle	*S. dublin and S. typhimurium*	Septicimia, acute and chronic enteritis and abortion
Sheep	*S. typhimurium*	Septicemia, typhocolitis and abortion
Pig	*S. choleraesuis, S. typhimurium, S.typhisuis*	Septicemia
Horses	*S.typhimurium*	Septicemia, acute colititus and abortion
Chicken	*S. pullorum, S. gallinarum*	Septicemia, acute and chronic enteritis
Human	*S. enteritidis, S. typhi, S. paratyphi*	Gastroenteritis, bacteremia

Source: (Kemal, 2014).

2.3 Epidemiology

The epidemiology of Salmonella is complex which often makes control of disease difficult. Epidemiological pattern of prevalence of infection and incidences of disease differ greatly between geographical area depending on climate, population density, land use farming practice, food harvesting and processing technologies and consumer habits. In addition, the biology of serovar differs so widely that Salmonella infection or Salmonella contamination are inevitably complex (Radostitis *et al*, 2007).

2.3.1 Geographical distribution

S. entritidis is the most prevalent species followed by S. typhimurium which are a worldwide distribution. Change in the relative frequency of serotypes can be observed over a short period of time. Some times within one or two years only limited number of serotypes is isolated from man or animals in a single region or country and the predominance of one or other can vary over a time. Some serotypes like S. entritidis and S. typhimurium are found worldwide in contrast to S. weltevreden which seems to be confined to Asia (Kemal, 2014). Sibhat *et al*. (2011) found the serovars Newport, Anatum and East bourne to be the most prevalent in Ethiopia.

2.3.2 Occurrence

The rate of infection in domestic animal has been estimated from 1-3%. In 1980, 16274 strains of 183 serotypes of Salmonella were isolated in USA from samples of meat obtained from slaughter house. In other examination of animals positive culture was obtained from 4.59% of 141, 827 bovine fecal samples. Epidemiological surveillance of animals including bird is of the most important since source of large majority of non-typhoidal salmonellosis cases are of food animal origin. There is scarce of data from developing countries in this regard ((Kemal, 2014).

Salmonellae have a wide variety of domestic and wild animal hosts (Acha and Szyfres, 2001). All members of the genus are considered to be potentially pathogenic, although serovars may differ widely in their host range and the pathogenic syndromes that they produce (Table 1).

Some serovars appear to show a degree of host adaptation and primarily infect one animal species. They also tend to cause more severe illness than the other serovars. For epidemiological purposes, the Salmonellae can be placed in to three groups (Jay, 2000): Those that infect humans only: These include *S. Typhi, S. Paratyphoid A* and *S. Paratyphi C*. This group includes the agents of typhoid and the paratyphoid fevers, which are the most severe of all diseases caused by *Salmonellae*. The host adapted serovars (some of which are human pathogens and may be contracted from foods): included are *S. Gallinarum* (poultry), *S. Dublin* (cattle), *S. Abortusovis* (sheep) and *S. Choleraesuis* (swine). Unadapted serovars (no host preference). These are pathogenic for humans and other animals, and they include most foodborne serova (Wray and Davies, 2003).

Table 2: Host-specific Salmonella serovars and the diseases, disease symptoms and pathological effects

Serovar	**Host**	**Disease, symptoms, pathological lesions**
S. Typhi	Humans	Typhoid fever,
S. Paratyphi A, B, C	Cattle and calves	paratyphoid fever
S. Dublin	Pigs	Cattle: diarrhea, fever necrotic enteritis Calves:
S. Choleraesuis	Chickens, turkeys	diarrhea, fever, enteritis Septicaemia, pneumonia,
S. Pullorum	Chickens, Turkeys	hepatitis Pullorum disease
S. Gallinarum	Horses	Fowl typhoid
S. Abortusequi	Sheep	Abortion
S. Abortusovis		Abortion

Source: (Poppe, 2002)

Worldwide there are 16 million annual cases of typhoid fever, 1.3 billion cases of gastroenteritis and 3 million deaths due to Salmonella. In the US annually there are 2-4 million cases with a death rate of 500-1,000 and an economic loss of about 3 billion dollars. A recent CDC report indicates that the incidence of S. typhimurium decreased significantly (42% decline) from 1996–1998 to 2005; however, the incidence of other serotypes are on the rise such as *S. enteritidis* and *S. heidelberg,* each of which increased by 25% and *S. enterica serovar* Javiana increased by 82% (Arun and Bhunia ,2008).

2.3.3 Morbidity and mortality

In a case control study of S. typhimurium DT 104 infection in cattle in Great Britain, Evans and Davies (Radostitis OM., 2007) reported an overall case fatality rate of 44%. In the herd with outbreak of S. typhimurium DT 104 the case fatality rate was 51.2% in calves, 37.4% in adult cattle and 26.2% in fattening cattle (Davies R., 1996). In dairy sucker and mixed herd the case fatality rate was found 44% where in calf rearing unit and dealer herd was found 50%-100% (Kemal, 2014). However modern antibiotic therapy may have reduced this rate. In an outbreak of S. Dublin in calf rearing unit 29 (13.5%) of 214 calves died (Arun and Bhunia, 2008). Mortality was significantly higher in group reared calves (19.25%) than in calves in single pens (9.2%). Mortality and morbidity is usually highest in calves under 12 week of age. In all species case fatality rate often reach 100% if treatment is not provided (Radostitis OM., 2007).

2.2 Source of infection and Transmission

Most Salmonella infection in farm animals are likely to acquire from animals of the same species, especially in the case of the host adapted serovars. In adult cattle there are important differences in the behavior of *S. dublin* and *S. typhimurium.* Those animals which recover from *S. dublin* infection may become persistent excreters, shedding up to 106 organisms per gram of feaces daily. Other herd may harbor infection and excrete the organisms only when stressed particularly at parturition. Aerosol transmission has long been suggested as a means by which Salmonella may be transmitted and experimental infection of calves by aerosol has been reported recently. In addition pasture contamination results when flooding occurs and there are many reports of clinical case in adult cattle arising from grazing recently flooded pasture (Kemal, 2014).

Human salmonellosis is generally foodborne and is contracted through consumption of contaminated food of animal origin such as meat, milk, poultry and eggs. Dairy products including cheese and ice cream were also implicated in the outbreak. However, fruits and vegetables such as lettuce, tomatoes, cilantro, alfalfa-sprouts and almonds have also been implicated in recent out-break (Kemal, 2014).

Acute gastroenteritis is usually acquired from consumption of food which may be directly or indirectly contaminated with Salmonella. A wide variety of animal species have been shown to be capable of harboring the organisms and in the developed world turkey, chicken, swine and cattle are found to be infected carriers in the studies conducted in the abattoirs. These carriers may readily shed Salmonella during transportation to the abattoir and contaminate abattoir workers or equipment during slaughter. The progressive trend forwards mass processing and distribution of food products has been an important factor in the increase incidences of Salmonella foodborne diseases. Person to person spread has been demonstrated on many occasions and may take place in young children and group living under poor socioeconomic condition where effective sanitation is lacking. Person to person spread also may occur in hospitals, nursing homes, mental institution in which large number of outbreak has occurred. Amplification of infection in these institutions may occur from contaminated food or asymptomatic carrier's babies being at special risk (Barrow *et al*., 2010).

Direct or indirect contact with animals colonized with Salmonella is another source of infection, including contact during visits to petting zoos and farms (Friedman *et al*., 1998). Fecal oral route and vehicle born infection may result from ingestion of food or water that have been contaminated with human or animal feaces or from direct exposure to animals or their waste. A lower infectious dose of organism is usually required in the elderly, the immunocompromised, antibiotic users and those with achlorhydria or regular use of antacid and related medication. The commonly recognized vehicle of transmission includes inadequate cooked or raw meat, unpasteurized milk or milk product, contaminated and inadequately treated drinking water (Kemal, 2014). Contamination of milk may occur by a variety of route. Animal may occasionally, excrete the organisms in milk during the febrile stage of the disease or more likely infected feaces, from either a clinically infected cow or healthy carrier may contaminate the milk during the milking process. Milk also may be contaminated from use of polluted water from dirty equipment or from dairy workers. Indirect contamination also has been described when cattle have become contaminated with Salmonella. Contamination of food also may occur directly from Salmonella infected food handlers or indirectly from sewage polluted water (Jones, 2005).

2.3 Economic importance

Salmonellosis is a significant cause of economic loss in farm animals because of the cost of clinical disease, which include death, diagnosis and treatment of clinical cases, diagnostic laboratory cost, the cost of cleaning and disinfection and cost of control and prevention. In addition when the disease is diagnosed in the herd, it can create a considerable apprehension in the producer because of difficulty on identifying infected animals. An estimation of economic impact of an outbreak of S. Dublin infection in calf rearing unit indicate that the cost of disease represented a substantial proportion of gross margin of rearing calves (Radostitis OM, *et al*.,2007). Estimated annual costs for salmonellosis have ranged from billions of dollars in United States to hundreds to millions of dollars in Canada and millions of pounds in United Kingdom. Analysis of five Salmonella outbreak due to manufactured food in North America gave direct cost with range from $36,400-$62 million, there have been few studies in to the cost and benefit of preventing Salmonella infection, but it has been suggested that for every £1 spent on investigation and curtailment of the outbreak there is a saving of £5 (Peters AR.,1985).

2.4 Pathogenesis

Salmonella spp. are facultative intracellular pathogens. Salmonella can invade different cell types, including epithelial cells, M-cells, macrophages, and dendritic cells. As a facultative anaerobic organism, Salmonella uses oxygen to make ATP in an aerobic environment (i.e, when oxygen is available). However, in an anaerobic environment (when oxygen is not available), Salmonella produces ATP by fermentation; by substituting one or more of four less efficient electron acceptors than oxygen at the end of the electron transport chain: sulfate, nitrate, sulfur, or fumarate. The ability of Salmonella strains to persist in the host cell is crucial for pathogenesis, as strains lacking this ability are non-virulent (Bakowski MA *et al*., 2008).

Following the engulfment of Salmonella into the host cell, the bacterium is encased in a membrane compartment called a vacuole, which is composed of the host cell membrane. Under normal circumstances, the presence of a bacterial foreign body would activate the host cell's immune response, resulting in the fusion of the lysosomes and the secretion of digesting enzymes to degrade the intracellular bacteria. However, Salmonella uses the type III secretion system to inject other effector proteins into the vacuole, causing the alteration of the compartment structure. The remodeled vacuole blocks the fusion of the lysosomes, and this permits the intracellular survival and replication of the bacteria within the host cells. The capability of the bacteria to survive within macrophages allows them to be carried in the reticuloendothelial system (RES) (Monack DM *et al*., 2004).

Salmonella pathogenicity islands (SPIs), gene clusters located at the large chromosomal deoxyribonucleic acid (DNA) region and encoding for the structures involved in the invasion process, are where the remarkable genetics underlying this brilliant strategy can be found(Grassl GA.,2008). The epithelial cells lining the intestinal wall are typically penetrated by the bacteria when they enter the digestive tract through contaminated water or food. SPIs encode type III secretion systems, multi-channel proteins that allow Salmonella to inject its effectors across the intestinal epithelial cell membrane into the cytoplasm. The bacterial effectors then activate the signal transduction pathway and trigger the reconstruction of the actin cytoskeleton of the host cell, resulting in the outward extension or ruffle of the epithelial cell membrane to engulf the bacteria. The morphology of the membrane ruffle resembles the process of phagocytosis (Takaya A., 2003).

2.4.1 Entrance Molecular Mechanism

The mechanisms of infection differ between typhoidal and nontyphoidal serotypes due to their different targets in the body and the different symptoms that they cause. Both groups must enter by crossing the barrier created by the intestinal cell wall, but once they have passed this barrier, they use different strategies to cause infection.[29] (Li D et al.,2013).

2.4.2 Switch to virulence

While traveling to their target tissue in the gastrointestinal tract, Salmonella is exposed to stomach acid, to the detergent-like activity of bile in the intestine, to decreasing oxygen supply, the competing normal gut flora, and finally to antimicrobial peptides present on the surface of the cells lining the intestinal wall. Salmonella can detect all of these types of stress, respond to them by forming virulence factors, and as a result, control when they transition from their normal growth in the intestine into virulence.[30] (Ivan R, and Barrow PA, 2005).

2.4.3 Mechanism of entry

Non-typhoidal serotypes preferentially enter M-cells on the intestinal wall by bacterial-mediated endocytosis, a process associated with intestinal inflammation and diarrhea. They are also able to disrupt tight junctions between the cells of the intestinal wall, impairing the cells' ability to stop the flow of ions, water, and immune cells into and out of the intestine. The combination of the inflammation caused by bacterial-mediated endocytosis and the disruption of tight junctions is thought to contribute significantly to the induction of diarrhea (Haraga *A et al*., 2008).

Salmonellae are also able to breach the intestinal barrier via phagocytosis and trafficking by CD18-positive immune cells, which may be a mechanical key to typhoidal Salmonella infection. This is thought to be a more-stealthy way of passing the intestinal barrier, and may, therefore, contribute to the fact that lower numbers of typhoidal Salmonella are required for infection than non-typhoidal Salmonella. Much of the success of Salmonella in causing the infection is attributed to two types III secretion systems (T3SS), which are expressed at different times during the infection. The T3SS-1 enables the injection of bacterial effectors into the host cytosol. These T3SS-1 effectors stimulate the formation of membrane ruffles, allowing the uptake of Salmonella by non-phagocytic cells. Salmonella further resides within a membrane-bound compartment called the Salmonella-containing vacuole (SCV). The acidification of the SCV leads to the expression of the T3SS-2. Salmonella must secrete T3SS-2 effectors to effectively survive in the host cytosol and cause systemic illness. In addition, both T3SS are involved in the colonization of the intestine, the induction of intestinal inflammatory responses and diarrhea. These systems contain many genes which must work cooperatively to achieve infection (Kerr MC, *et al*.,2010).

2.4.4 Host adoption

S. enterica, through some of its serotypes such as Typhimurium and Enteritidis, shows signs of the ability to infect several different mammalian host species, while other serotypes such as Typhi seem to be restricted to only a few hosts (Johnson R *et al*.,2018).

Some of the ways that Salmonella serotypes have adapted to their hosts include loss of genetic material and mutation. In more complex mammalian species, immune systems, which include pathogen-specific immune responses, target serovars of Salmonella through the binding of antibodies to structures such as flagella. Through the loss of the genetic material that codes for a flagellum to form, Salmonella can evade a host's immune system(Den Bakker HC *et al*., 2011).

By directly base pairing with the messenger ribonucleic acids (mRNAs) of the flip gene that encodes flagellin and encouraging degradation, the mgt leader RNA from the bacteria's virulence gene (mgtCBR operon) reduces the amount of flagellin produced during infection. Pathogenic serovars of S. enterica were found to have certain adhesins in common that have developed out of convergent evolution. This means that, as these strains of Salmonella have been exposed to similar conditions such as immune systems, similar structures have evolved separately to negate these similar, more advanced defenses in hosts. Still, many questions remain about the way that Salmonella has evolved into so many different types, but Salmonella may have evolved through several phases. Salmonella most likely evolved through horizontal gene transfer, the formation of new serovars due to additional pathogenicity islands, and an approximation of its ancestry. So, Salmonella could have evolved into its many different serotypes through gaining genetic information from different pathogenic bacteria. The presence of several pathogenicity islands in the genomes of different serotypes has lent credence to this theory(Choi E *et al*.,2017).

Salmonella Newport has signs of adaptation to a plant colonization lifestyle, which may play a role in its disproportionate association with a foodborne-illness linked to produce. A variety of functions selected for Newport persistence in tomatoes have been reported to be similar to those selected for Typhimurium from the animal hosts. The papA gene, which is specific to the Newport strain and has homologs in the genomes of other Enterobacteriaceae that can colonize plant and animal hosts, contributes to the strain's fitness in tomatoes(De Moraes MH *et al*.,2018).

2.4.5 Resistance to oxidative burst

A hallmark of Salmonella pathogenesis is the ability of the bacterium to survive and proliferate within phagocytes.[37] Phagocytes produce DNA-damaging agents such as nitric oxide and oxygen radicals as a defense against pathogens. Thus, Salmonella spp. must face attacks by molecules that challenge genome integrity. Mutants of S. enterica lacking RecA or RecBC protein function are highly sensitive to oxidative compounds synthesized by macrophages, implying that successful systemic infection by S. enterica requires RecA- and RecBC-mediated recombinational repair of DNA damage(Quinn PJ *et al*.,2011).

2.5 Clinical Sign of Salmonellosis

Adult cattle generally contract either acute or subacute enteric salmonellosis and pregnant animal may abort during the early stage of acute enteric disease. Severely affected animals show fever, depression, in appetence and drop in milk yield. These sign are followed by diarrhea which is fowl smelling, the faces being mucoid and usually containing a clot of blood and shred of necrotic intestinal mucosa. Sign of colonic congestion of mucus membrane and dehydration may be evident. The acute disease last for about a week. S. dublin in particular but also other serovars may cause abortion in cows at any stage of pregnancy. Abortion may either precede the onset of dysentery or follow it within two or four weeks. Alternatively abortion may occur in cows that show no sign of illness, septicemia and/or placentitis being the case of death of fetus. Retention of the placenta occurs in approximately 70% of cases that abort but subsequent fertility is not usually affected (FDA/CFSAN, 2008).

In calves clinical disease is most common 2-6 week of age. Clinical sign vary but typically the enteric form of diseases predominate which is characterized by pyrexia, dullness and anorexia, followed by diarrhea that may contain fibrin and mucus. The feaces may become blood stained and "stringy" due to the presences of necrotic intestinal mucosa. Calves rapidly become weak and dehydrated unless treated. Infected calves usually die 5-7 days after the onset of disease. At this stage the organisms has become systemic as a result of reduced innate immunity and may be isolated from variety of tissue including blood. Calves that recover from infection do not typically remain carrier. Salmonellosis is very variable and in some animals particularly in very young animals rapid multiplication occur both in intestine and systemically associated with poor absorption of specific immunoglobulin G from colostrums or with calves receiving in sufficient or no colostrums (L. Plym *et al*., 2006).

In human the effect and clinical sign depends on the incubation period and the number of bacteria ingested,and varies from 5-72 hours to be manifested. Affected individual's experience sudden nausea, vomiting and watery fowl smelling diarrhea which is in most case last only a few hours. If the colon is affected, the stool may also contain blood and or mucus. Fever up to 39°C is not uncommon. Convalescences within 1-2 days but the illness may last for 5-7 days (Krauss *et al*., 2003).

More severe symptom may occur in people who are at high risk like those extreme age groups (the young because their immune system are immature and the elderly because the immune system are declining), person with decreased gastric acidity (because gastric acid is the first line of defense for the ingested Salmonella), person with altered gastric intestinal bacteria (including those taking broad spectrum antibiotics, purgatives or who have had bowl surgery) and person taking opiate drug in which the bowl movement is decreased. In these highest risk groups of people Salmonella may invade beyond the gastrointestinal tract (GIT) to cause severe systematic illness (Kemal, 2014).

Gastroenteritis caused by Salmonella is usually a self-limiting illness and fatality is uncommon. Biopsy and endoscopic examination have demonstrated the colon to be a major site of infection. The change in the colon ranges from edema of lamina propria with a focal or diffuse inflammatory infiltrate to a more intensive inflammation with disruption of the surface epithelium and multi-focal micro abscesses. In more severe cases, vascular congestion, infiltration of the lamina proporia with polymorphonuclear leucocytes and abscess formation has been recorded (L. Plym *et al*., 2006).

2.6 Post mortem findings

There may be no gross lesion in animals that have died peracutely but extensive submucosal and subserosal petechial heamorrhage are usually evident (Radostitis, *et al*., 2007). In adult cattle, a typical case reveals acute muco/necrotic enteritis, especially of the ileum and large intestine. The wall is thickened and covered with yellow-grey necrotic material overlying a red, granular surface. The mesenteric lymph nodes and spleen may be enlarged. In calves, the small intestine typically shows a diffuse mucoid or mucohaemorrhagic enteritis and the mesenteric lymph nodes are oedematous, congested and greatly enlarged (Barrow *et al*., 2010).

2.7 Public Health Importance

Salmonellosis is an important global public health problem causing substantial morbidity and thus also has a significant economic impact. Although most infections cause mild to moderate self-limited disease, serious infections leading to deaths do occur (de Jong and Ekdahl, 2006). In spite of the improvement in hygiene, food processing, education of food handlers and information to the consumers, foodborne diseases still dominate as the most important public health problem in most countries (Domínguez *et al*., 2002).

Salmonellosis incidence is defined as the identification of Salmonella from animals or group of animal's product or surrounding which can be specifically related to identifiable animals or from animals feed. On the human side, a registered medical practitioner in the US required under the Public Health (Control of Disease) act to notify the local authority, if the patient is suffering from or suspected of having foodborne disease (Kemal *et al*., 2014).

Studies provide increasing evidence of adverse human health consequences due to the occurrence of resistant microorganisms. Use of antimicrobial agents in human and animal affects the intestinal tract placing those concerned at increased risk of certain infection. This is defined as the proportion of Salmonella that would not have occurred if the Salmonella were not resistant. In addition antimicrobial agent used in animal can result in increased transmission of resistant microorganisms between animal and therefore would results in case of transmission of such microorganisms to human through food. Increased frequency of treatment failure and increase severity of infection may be manifested by prolonged duration of illness. Salmonella dublin is largely but not entirely specific to cattle with average 10 human case reported in each year in Ireland. Apart from its pathogenicity two other characteristics of S. dublin make it particularly important for Ireland from a public health viewpoints. First, it is very prevalent on Irish farms and secondly in evolutionary terms, it is only one step away from S. enteritidis, a common Salmonella serotype in poultry and the main case of clinical salmonellosis in humans. In genetic terms, difference between the serovars S. dublin and S. enteritidis are no greater than those found within each serotypes. This indicates that, S. dublin and S. enteritidis share a common ancestor. One branch evolved in to a poultry adapted serotype capable of causing disease in human, the other in to host specific cattle pathogen. If S. dublin has been confirmed in breeding herd there is a significant risk of persistent infection in carrier cows for as long as animal which were present at the time of the outbreak remain in the herd(Jones *et al*., 2007).

2.8 Animal Risk Factors

The size of the challenge dose and the animal's immunological status, which in turn depends on colostrum intake in neonates, prior infection, and stressor exposure, particularly in older animals, determine the animal's response to infection with a Salmonella spp (Radostitis OM *et al*.,2007).

2.8.1 Environmental and Management Risk Factors

Intensification of husbandry in all species is recognized as a factor contributing significantly to an increase in the new infection rate. Any significant change in management of the herd or a group of animals can precipitate the onset of clinical salmonellosis if the infection preexists in those animals. Temperature and wetness are most important, as Salmonellas are susceptible to drying and sunlight (Degneh E *et al*.,2017).

2.8.2 Pathogen Risk Factors

Salmonella are facultative intracellular organisms that can withstand the bactericidal effects of antibodies while living in the phagolysosome of macrophages. Salmonellas are more tolerant of different environmental factors than other members of their family. They multiply at temperatures between 8 °C and 45 °C, at water activities above 0.94, and in a potential of hydrogen (PH) range of 4-8. They are also able to multiply in an environment with a low-level of or no oxygen(Eguale T *et al*.,2016).

2.8.3 Human source

Environmental and personal hygiene is one of the knowledge and practice restrictions of humans from beef/dairy farms and abattoir food processing plants.

On the other hand, food getting contaminated depends largely on the health status of the food handlers (Degneh E *et al*., 2017).

In both developed and developing nations, including Ethiopia, foodborne diseases are a public health concern. Contamination can happen at any stage of the food supply chain, including during production, processing, distribution, and preparation. In dairy farms and industries that process food, high standards of employee hygiene must be upheld (Eguale T *et al*.,2016).

2.8.4 Other sources

International trade and its introduction through international travel, as well as the trade in food, livestock and animal feed, all present challenges; Water source: Salmonellae can be found in contaminated water; inanimate objects. A further ambiguity in the environment surrounding food processing is the rise in antimicrobial resistance to Salmonella in recent years due to the widespread use of antimicrobial drugs in the human and veterinary sectors (Chaudhry R *et al*.,2003).

2.9 Diagnosis of Salmonellosis

The clinical sign and finding at postmortem examination are not unique to salmonellosis although a tentative diagnosis may be made. They should confirm either in diseased animal or at necropsy by isolation of organisms in their feces and determination of viable counts. Fecal samples rather than swabs should be taken and these should obviously be obtained before administration of antibiotics. It may be also possible to isolate organism from oral secretion and by blood culture although these are less reliable than feces culture and must be taken with care to avoid contamination. Animal that died of salmonellosis usually have large number of Salmonella distributed throughout their tissue and sample of spleen, liver, hepatic, mediastinal and bronchial lymph nodes may yield count in excretion of 106 organisms/gram. Similar concentration may be present in the wall and content of the ileum, cecum, colon and associated lymph nodes. Sample should be taken from internal organs in order to distinguish animal that have died of enteritis without septicemia (Jones *et al*., 2007).

2.10 Bacteriological Culture Methods

The traditional Salmonella culture method involves pre-enrichment, selective enrichment, isolation of pure culture, biochemical screening and serological confirmation, which requires 5-7 days to complete. The USDA and FDA recommended method involves a 6-24 h pre enrichment step in a nonselective broth such as lactose broth, tryptic soy broth, nutrient broth, skim milk, or buffered peptone water with a recommended incubation temperature of 37°C. The selective enrichment step requires additional 24 hours incubation in RappaportVassiliadis (RVS) broth, selenite cystine (SC) broth, or Muller Kauffmann tetrathionate broth. The inoculation temperature of 41.5°C ± 1°C for RV broth and 37°C ± 1°C for SC and MKTT broth is used. Bacterial cells are isolated from selective agar plates such as Hektoen enteric agar (HEA), Xylose Lysine Deoxy-cholate (XLD). Biochemical testing is done using Triple sugar iron agar, urease test, indole test, MR test, VP test, Simmon citrate test (IMVIC test) and Gram staining, which requires an additional 16- 24 hours of incubation for growth (Hans *et al*., 2006).

***2.10.1 Detection of antibodies by enzyme immunoassay (EIA*)**

The detection of antibodies to Salmonella by EIA offers a sensitive and cost-effective method for mass screening of animal herds for indications of a past/present Salmonella infection. The limitation of the method is that the immune response of the individual animal is not elicited before 1-2 weeks after infection takes place. A number of commercial kits are available for testing poultry, cattle and pigs. An obvious advantage of this method is that it can be automated and no incubation is required to increase the numbers of bacterial cells (Zamora and Hartung, 2002).

The EIA is a well-established technique for assaying antigens. Antibodies labeled with an enzyme are bound to Salmonella antigens, and the level of antigen present is determined by enzymatic conversion of a substrate, usually resulting in a color change which can be read visually or by a spectrophotometer. The EIAs rely on the standard cultural procedures for pre-enrichment and selective enrichment to provide enough Salmonella cells for detection. EIA technology that enables detection at an earlier stage of resuscitation and/or culture can provide even more rapid results. Serological test, such as ELISA, serum agglutination and complement fixation can be used for the retrospective diagnosis of salmonellosis or the detection of carriers (Kemal, 2014).

2.10.2 Nucleic acid-based assays

Real-time quantitative polymerase chain reaction using PCR (Q-PCR), reverse transcriptase PCR (RT-PCR), and Nucleic acid sequence-based amplification (NASBA) have been used for detection of Salmonella from various food samples. NASBA method has been used for detection of viable Salmonella cells and it has been demonstrated to be more sensitive than RT-PCR, and moreover, it requires fewer amplification cycles than the conventional PCR methods (Arun and Bhunia, 2008).

2.11 Treatment of Salmonellosis

Although Salmonellae are usually sensitive in vitro to many antibiotics, their use for treatment of uncomplicated gastroenteritis until recently has been generally contraindicated by their lack of favorable effect on the course of the disease and by prolongation of Salmonella shedding. Following the introduction of fluoroquinolones a number of clinicians have advocated their use for treatment of only on enteric fever but also of Salmonella gastroenteritis because of their efficacy in reducing the duration of illness and of Salmonella shedding. In case of patient with bacteremia and other complication antimicrobials are used. Likewise the treatment of enteric fever necessitates the use of antimicrobial drugs with chloramphinicol, ampicillin, amoxicillin, trimethoprim, sulfamethoxazole and newer fluoroquinoazoles being drug of choice against sensitive Salmonella. Proper management of fluid and electrolyte balance is impotant in all patients with Salmonella gastroenteritis but is crucial in young children and elder individuals (Jones *et al*., 2007).

In animal treatment supportive treatment with intravenous fluid is necessary for patients that have anorexia, depression, significant dehydration. Individual patient may be treated aggressively following acid base and electrolyte assessment. Oral fluid and electrolyte may be somewhat helpful and much cheaper than IV fluid for cattle demand to be mildly or moderately dehydrated. The effectiveness of oral fluid may be somewhat compromised by malabsorption and maldigestion in salmonellosis patient but still should be considered useful. Cattle that are willing to drink can have specific electrolyte (NaCl, KCl) added to drinking water to help correcting electrolyte (Kemal, 2014). The implementation of broad prophylactic strategies that are efficacious for all Salmonellae may be required in order to overcome the diversity of Salmonella serovars present on farms, and the potential for different serovars to possess different virulence factors (Mohler VL. *et al*. 2009).

Early treatment is essential for septicemic salmonellosis but there is controversy regarding the use of antimicrobial agent for intestinal salmonellosis. Oral antibiotic may alter the intestinal micro flora and interfere with competitive antagonism and prolong shading of the organism. There is also a concern that antibiotic resistance strain of Salmonella selected by oral antibiotic may subsequently infect human. Antibiotic such as ampicillin or cephalosporin lead to lyses of bacteria with release of endotoxin. NSAID may be used to reduce the effect of endotoxemia (Davison, 2005).

2.12. Differential diagnosis

The differential diagnosis of *Salmonella enterocolitis* in humans include viral gastroenteritis and bacterial enteric infections including those caused by *Shigella, Enterotoxigenic E-coli, Campylobacter species, Vibrio species and Yersinia enterocoliticia*. The disorder must also be differentiated from toxin-mediated foodborne illness including those caused by Staphylococcus aureus, Bacillus cereus and Clostridium perfringens. Compared to the patient with toxin mediated disorder person with salmonellosis usually have less prominent vomiting and are the more likely have prolonged diarrhea and fever. The shorter incubation period of toxin mediated foodborne illness can be important to distinguish them from salmonellosis. A recent history of ingestion of raw milk, undercooked meat and contact with farm animals 48 hours before the onset of illness suggests the diagnosis of salmonellosis(Krauss HM e tal., 2003).

2.13 Control and prevention

Prevention and control in animals

Condition that contribute to an increasing incidence of epidemic salmonellosis include large herd size, more intensive and crowded husbandry and the trend of free-stall barn with loose housing, which contribute to the feacal contamination of the entire premise.

When salmonellosis has been confirmed in a herd, the following control measure should be considered;

- Isolate obviously affected animals to one group if possible, treat severely affected animals,
- Affected animals institute- measure to minimize public health concern like (no raw milk should be consumed) physically clean the environment and disinfect the premise following resolution of the outbreak or crises period.

- A mastitis survey should be conducted that include bulk tank surveillance. Prevention is best accompanied by maintaining a cross herd and culturing new feed additives and components before using the entire ration (Arun and Bhunia , 2008).

Vaccination of calves at 1-3 weeks of age with a modified aromatic dependant, S. dublin bacteria have detectable anti-lipoplisaccharide immunoglobins after immunization. Safe live oral vaccine against S. typhimurium and S. dublin has been constructed and shown to control protection against experimental infection with virulent wide type strain of the organisms. A virulent S. choleraesuis vaccine is efficacies experimentally against salmonellosis due to *S. dublin* in calves to protect young calves. The best program is to vaccinate the cow during pregnancy which will give passive protection to calves for 6 weeks (Radostitis *et al*., 2007).

Generally it is agreed that supportive therapy and good nursing are important. These include oral or parentral re-hydration, correction of electrolyte balance and stabilization of acid base equilibrium (Danielle, 2006). Both live and attenuated vaccines produced from rough strain in bacteria commercially. There is some evidence that inactivated bacterins can induce a lower level of protection (Danielle, 2006). The Veterinarian research institute produced vaccine against bovine salmonellosis in activated bacteria prepared from isolate of *S. dublin, S. typhomurium* and S. bovis morbificans and a live attenuated vaccine containing a virulent rough mutant of *S. dublin* (Kemal, 2014).

Prevention and control in human

There is no vaccine to prevent salmonellosis in human whereas, vaccine against *Salmonella typhi* has been developed, especially in children, but is only 60% effective. A person given this vaccine would still have a strong chance of developing salmonellosis. It is not expected that there will be a single vaccine that is effective against all the different forms of Salmonella soon. Ongoing research is investigating what can be done to produce a useful human vaccine for Salmonella (Danielle, 2006).

People should not eat raw or uncooked meat, they should not drink raw milk or unpasteurized dairy product, cross contamination of food should be avoided. Uncooked meat should be kept separate from cooked food ready to eat. Hands, cutting boards or knifes and other utensils should be washed thoroughly after handling uncooked food. Hands should be washed before handling any food and in between handling different food items. People should have to wash their hands after contact with animal's feces (Arun and Bhunia , 2008)

Pasteurization of milk and treating municipals water supply for reducing risk of Salmonella infection, improvement in farm animal hygiene in slaughter process in food harvesting and in packaging operation have helped to prevent salmonellosis (Hans *et al*., 2006). A periodic surveillance of the level of Salmonella contamination in different food product and environment is necessary to control spread of the pathogen. Reducing Salmonella prevalence requires comprehensive control strategy in animal and animal foodstuff with restriction in the infected flock until they have been cleaned from infection. In addition mandatory testing before slaughter should be conducted like the one implemented in Sweden (Boqvist and Vågsholm, 2005). Ensuring safe food production requires knowledge on the nature and origin of animal, animal feed, the health status of animals at the farm, the use of veterinary medicinal data regarding ante mortem and postmortem findings and the risk association with post harvests production strategies (Kemal , 2014).

3. CONCLUSION 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. Having animals and raw products it is not possible to be free from zoonotic agent; however the occurrences can be minimized by applying high standard of hygiene in all steps of the food production. Infected animals can present with a great variety of clinical symptoms, and risk factors for transmission to humans clearly differ by animal species, age groups, animal purpose and geographic region. In addition, strains of Salmonella resistant to multiple antibiotics have been isolated from dairy cow during salmonellosis outbreak on dairy operation. The same strains have also been isolated from ill people. A high degree of interaction between medical and veterinarian surveillance is needed. Finally, implementing basic and applied research to the agent that cause foodborne salmonellosis will be a crucial point for new approaches to prevent and control the disease.

Depending on the above facts the following points are recommended:

- Strict hygiene of the slaughter house and lairage
- People should not drink unpasteurized milk or milk products and should not eat raw meat Education of food handlers
- Vaccination of cattle
- Maintenance of cold chains

- Sanitary examination of the product
- Collaboration between government agencies, professional organizations and special interest groups.

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