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REVIEW ARTICLE

Epidemiology and Public Health Importance of Bovine Salmonellosis

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Abstract

Bovine salmonellosis caused by *Salmonella enterica* subsp. enterica serovar Dublin (S. Dublin) is a significant public health and economic concern globally. It leads to severe health issues in cattle, including enteritis, septicaemia, and abortion, with high mortality rates, especially in newborn calves. The disease not only impacts the well-being of the animals but also results in substantial economic losses through treatment costs, reduced milk production, and potential outbreaks. The transmission of S. Dublin is primarily through contaminated food, water, and environmental exposure, with the faecal route being the most significant mode of spread. The pathogenesis of *S.* Dublin involves complex interactions between the bacteria and the host immune system, with the bacteria capable of persisting in the herd as carriers, further complicating control measures. Effective control strategies are critical to minimizing its spread, and understanding the epidemiology, clinical signs, and diagnostic methods is key. This review demonstrates the public health importance, clinical manifestations, economic importance and diagnostic techniques of bovine salmonellosis.

Keywords: Bovine, Epidemiology, Food, Public health, Salmonellosis, S. Dublin

INTRODUCTION

Salmonellosis is a serious public health concern which affects multiple animal species and humans [1,2]. It is a foodborne bacterial infection that is caused by *Salmonella enterica* subsp. *enterica* serovar Dublin *(S.* Dublin) in bovines [3,4]. *S.* Dublin is a Gram-negative, non-spore-forming, oxidase-negative, motile and rod-shaped bacteria that belongs to family *Enterobacteriaceae* [5,6]. The survivability of *S.* Dublin depends on the environmental conditions, temperature, pH and other microflora [7,8]. It can survive for years in dried faecal matter and for months in different organic matters such as soil, cattle manure, and slurry [9,10]. However, *S.* Dublin does not resist antibiotics, sunlight, and disinfectants [11,12]. Multidrug-resistant strains can be isolated from dairy and beef sources [13,14]. The bacteria have the ability to reproduce in moist and warm conditions outside the host cell [15,16]. Salmonellosis cause severe health problems in bovines, which include 2 major syndromes: enteritis (inflammation of small intestine) and septicaemia (blood poisoning) [17,18]. However, other clinical signs include pyrexia, dysentery, and abortions in pregnant animals [19,20]. The severity of clinical signs of Salmonellosis depends on the age of the animal, infection dose, immune response, and physiological state of the host [1,17,21]. In newborn calves, septicaemia with enteritis is most commonly seen [18,22]. However, pneumonia and neurological signs may also occur [23,24]. In case of young ones or animals with age more than one-week, acute enteritis mostly occurs without systemic involvement [25,26]. The infection starts with pyrexia (40.5-41.5°C [105-107°F]) followed by dysentery and sometimes with tenesmus [27,28]. Mortality rates in both newborn calves and young ones may increase to 100%, depending on the virulence and infection load [29,30]. Milk production may drop in lactating animals [13,31]. Salmonellosis is a serious concern for economic losses and public health that needs critical attention [32-34]. However, different alternative therapeutics, mainly plant-based compounds, are under study to control multiple diseases [35,36]. To minimize the salmonellosis around the globe, we must understand the pathogenesis and epidemiology as drug resistance is increasing dramatically [37-39].

S. Dublin most commonly causes infection after direct transmission through contaminated food, water, and environment [40,41]. However, the severity of the disease depends upon the infectious dose of the pathogen [15,42]. *Salmonella* bacteria colonize the gut of the host, followed by invasion in columnar enterocytes through the lymphatic system [43-45]. *Salmonella* can also enter the macrophages, which is a critical barrier [46,47]. The bacteria replicate in the macrophages, and during the replication they can easily enter the blood, lymph, lungs, liver, spleen, tonsils and lymph nodes [48,49]. *S.* Dublin can become the latent carrier, which leads to the persistence of the infection in the herd [50-52]. However, *S.* Dublin has been found in the internal organs of the animals while they show no signs of the infection [53-55]. Different stages of the *S.* Dublin infection have been reported, including per-acute, acute, chronic, passive carrier, active carrier and latent carrier stage [56-58]. The infected animal may or may not shed the bacteria in these different stages [59]. However, the *S.* Dublin may shed through urine, saliva, milk, faeces and vaginal discharge [60,61]. The duration and amount of bacterial excretion vary greatly among infected animals [62,63]. This is because the faecal material of the animal contains the highest number of bacteria, and they are produced in the large quantities [64,65]. So, the faecal route of the transmission is the most important route to cause the infection [66,67]. Humoral and cellular components of the immune system work together to fight pathogenic bacteria [68,69]. The first line of defence against the *S.* Dublin consists of neutrophils, polymorphonuclear leukocytes, macrophages, natural killer cells and their secreted cytokines [70,71]. This non-specific immune system activates the adaptive immune response [72,73]. IgG and IgM titres begin to increase, and IgG attains maximum titre between 6-11 weeks after the inoculation [74,75]. However, *S.* Dublin is host adopted to cattle, but there is a lack of agreement on the mechanism of the host adoption [76].

To prevent the *S.* Dublin infection, the mechanism of host adoption is not much important [77,78]. However, this feasibility of the host interaction with *S.* Dublin initiates the effective control programs without involving the other livestock sectors [4,79]. These effective control programs aid in preventing bovine salmonellosis and other important foodborne and public health important diseases from spreading [80,81]. This review emphasises the pathogenesis, public health importance and epidemiology of *S.* Dublin to adopt better preventive measures and control strategies. We will briefly discuss the economic importance, clinical signs, diagnosis, pathogenesis and public health aspect of bovine salmonellosis of *S.* Dublin.

Economic Importance of Bovine Salmonellosis

The high cost of treating clinical salmonellosis in farm animals leads to significant economic losses [82,83]. This includes the cost of diagnosis, treatments, cleaning and disinfectants, laboratory tests, cost of prevention and control, and death of the infected animal [84,85]. However, other related economic losses include a drop in the milk production in the lactating animals, poor growth and pregnancy loss in some severe cases of salmonellosis [86]. If one animal is diagnosed positive in a large herd of the animals, it would be difficult to diagnose all animals if they are infected with *S.* Dublin or not [87 88]. This will increase the cost of diagnostic tools and prevention strategies. The annual estimated loss due to bovine salmonellosis in the United States is billions of dollars, millions of pounds in United Kingdom and $160 million in Canada [89]. However, in North America, economic loss due to 5 outbreaks was $36.400-$62 million [90]. It is strictly suggested that every £1 spent on the investigation and control strategies can save £5 [91,92].

Clinical Manifestation of Bovine Salmonellosis

S. Dublin is usually endemic in bovine herds and bovines are the most important carrier of *Salmonella* infection [90,93]. They can carry *S.* Dublin for a longer period or sometimes it may be for a lifetime [94,95]. In calves, signs and symptoms of clinical ailment are present at the age of 2-6 weeks [96]. Signs and symptoms may vary with the infectious dose of the pathogen [97]. However, enteric form of salmonellosis is present in young calves which is characterized by dullness, pyrexia, and anorexia that is followed by severe diarrhoea [98]. Blood can also be present in the faecal material and faeces may become stringy because of the presence of necrotic mucosa of intestine [99]. While in adult animals, subacute or acute salmonellosis mostly occurs with abortion in the pregnant animals during the early stage of acute enteric disease [100]. Animals with severe infection show signs of pyrexia, depression and anorexia [101]. However, other important clinical manifestations include drop in the milk production, fowl smelling diarrhoea, bloody and mucoid faeces, with shreds of necrotic mucosa of intestine, dehydration, and congestion of mucous membrane [102]. Another most common clinical manifestation of bovine salmonellosis is retained placenta, which occurs in approximately 70% of the cases [103]. The acute phase of the bovine salmonellosis may only last for 1 week. However, the postmortem findings may vary [104,105].

The animal died in per-acute stage of the infection may have no gross lesions in the postmortem findings [106]. But extensive petechial haemorrhages are usually present in subserosal and submucosal layer [107]. In young calves, the mesenteric lymph nodes are enlarged in size, congested and oedematous [108]. The small intestine shows muco-haemorrhagic or diffused mucoid enteritis [109]. Necrotic enteritis, particularly affecting the ileum and large intestine, occurs in adults [110]. Spleen and mesenteric lymph nodes are enlarged and swollen [111]. However, the wall of the intestine becomes thickened and covered grey-yellow necrotic material overlying granular, red surface [108].

Infectious Stages and Pathogenesis of S. Dublin

There are multiple infection stages of *S.* Dublin that include per-acute, acute, chronic, passive carrier, active carrier and latent carrier [112,113]. In per-acute stage of the infection, animals die within a very short period of time usually in 1-2 days [114]. Death of animals occurs even before they start to shed the bacteria [115]. While the acute phase may remain from 1 to 2 weeks to 5-9 weeks [116]. In this stage, animals shed bacteria in a large amount continuously or intermittently through faeces, urine, milk and vaginal discharge [101]. The amount of the bacteria in the acute stage of the infection varies from 1 to 10^8 CFU/g [51]. The chronic infection may remain for months, and the infected animal may or may not shed bacteria [117]. However, other carrier stages may remain from weeks to years and infected ones may or may not shed bacteria [118]. When the animals shed bacteria in the carrier stage, it may be in a continuous pattern or intermittent [119,120]. The amount of the bacteria may be low (10^1-10^4 CFU/g faeces), moderate (10^4-10^5 CFU/g faeces) and high (>10^5 CFU/g faeces). These amounts depend on the infection dose and pathogenesis of *S.* Dublin [121].

S. Dublin most commonly enters by ingestion of contaminated feed or water in cattle [122]. After entering the body of host, it directly goes to the rumen or stomach where it faces harsh conditions [123]. *S.* Dublin adopt to survive against the gastric acid and normal flora of the stomach/rumen [124]. After successfully adopting the conditions, the bacteria enter the epithelium of the intestine for colonization purpose [125]. Intestinal motility and mucus work as defence of the host in the intestine and *S.* Dublin have fimbriae lipopolysaccharide to overcome the host defence [126]. Host secretes neutrophils and macrophages when the bacteria evade the host defences [127]. *S.* Dublin have the ability to secrete the effector proteins by TTSS-1 & 2 (Type III secretion system) that combat the macrophages and neutrophils [25]. When the bacteria overcome the host defence system, the bacteria spread systemically, and enteritis has been induced in the host [128,129]. In response to systemic salmonellosis, pyrexia has been developed [130]. Detailed pathogenesis is explained in *Fig. 1*.

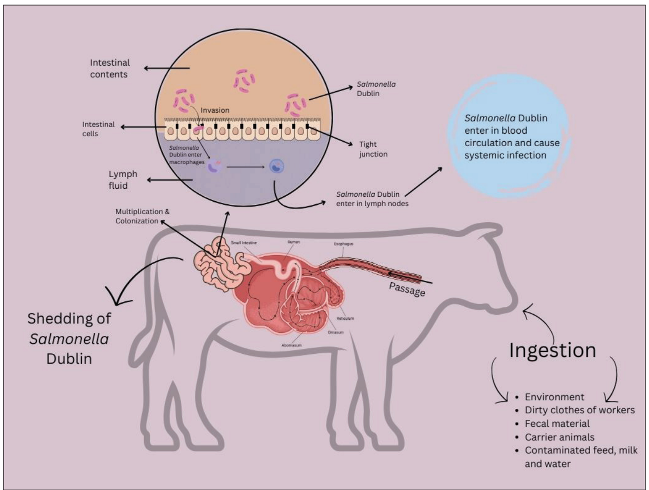

Fig 1. Pathogenesis of *Salmonella* Dublin in bovines

Public Health Importance of Bovine Salmonellosis

Salmonellosis is an important public health concern around the globe that causes a large amount of mortality and morbidity [131]. Although most of the cases are self-limiting and moderate, the serious cases may lead to death [132]. Over 3 million deaths of the humans are because of the salmonellosis annually [133,134]. In US, 500-1000 deaths occur out of 2-4 million cases annually [135]. Regardless of the hygiene, education and food processing, salmonellosis still remains an important public health concern that needs attention [136]. *S.* Dublin cause infection in average 10 humans per year in Ireland [137]. In Ireland, bovine salmonellosis is considered as the most important public health disease as it is a major threat to the livestock of the Ireland and because of the genetic evolutions of *S.* Dublin [138]. It is believed to have evolved recently due to the consistency in its multi-locus enzyme genotype and fliC flagellin DNA sequence analysis [139]. *S.* Dublin is considered being one step away from *S. enteritidis* (a common *Salmonella* serotype in humans and poultry) [140,141]. However, the genetic distinction between these two serovars is insignificant [18]. If *S.* Dublin have been diagnosed in the herd of cattle, there is a significant risk of persistent infection in the carrier cows for as long as the cow remains in the herd [52,142]. To diagnose the bovine salmonellosis in the herd, there are multiple options which are given in detail as follows.

Diagnosis

Diagnosis of the disease in the herd of the animal is the most important key to prevent the economic loss and maintaining health of the animals [143,144]. Pathological, postmortem findings and clinical signs are not adequate for diagnosing salmonellosis [145]. For definitive diagnosis, there are multiple techniques including cultivation of bacteria, clinical examinations and counting the antibodies against *S.* Dublin [146]. Detection of bacteria in fluids, body organs, faeces, and environmental samples can be done by conventional culture methods of bacteria [147]. The main advantage of detecting bacteria is tracing infection in large groups of animals during the investigation of an outbreak. This method has a disadvantage of low sensitivity [148]. The new techniques for the detection of the bacteria are based on the genetic material, i.e., Polymerase chain reaction (PCR) techniques [149,150]. The PCR techniques are considered being the more sensitive techniques, but subsequent typing is not always possible [151,152]. The detailed diagnostic techniques are given as follows:

Culture Techniques

Culturing techniques are stepwise procedure in order to isolate the live bacteria in the sample [153]. The steps to isolate the bacteria in the sample include pre-enrichment, selective enrichment, plating and confirmation [154]. For positive results, bacteria must have the ability to grow in the enrichment steps [155]. This method should be able to detect the minimum CFU in the sample; up to 1 CFU [156]. However, this may not be always true in every case. For faecal samples of *S.* Dublin, the specificity is assumed to be 100% while the sensitivity in faecal samples is less than ideal [157]. For more accurate sensitivity test, faecal cultures should be used repeatedly to detect the active carriers [158].

PCR Techniques

PCR-based techniques are considered being more precise and accurate to detect the bacteria in the sample material [159,160]. These techniques are based on the detection of the genetic material of the bacteria (*S.* Dublin) [141]. However, there are 2 basic principles of PCR technique: real-time PCR and the traditional PCR [161,162]. The traditional PCR technique only gives qualitative results (whether the bacteria is present or not) while in real-time PCR, the exact amount of the DNA copied after every cycle is counted by the computer [149,163]. The performance of the test depends on the proper functioning of probes, internal control systems, and primers [164]. However, the PCR tests do not provide the information of the serotype of the *Salmonella* [165]. To detect the serotype *S.* Dublin in the tested sample, a follow-up culture test must be conducted on the positive samples [166]. Multiple studies show that the specificity and sensitivity of the PCR tests is not accurate [167,168]. In a case of naturally infected animals with *S.* Dublin, the sensitivity results of rt-PCR found poorer than compared to the conventional culture method [169].

Antibodies Detection

Antibodies detection has been proven very effective in checking the previous or current infection [170,171]. Enzyme-linked immunosorbent assays (ELISA) can be used to detect the O-antigens from *S.* Dublin in milk and blood samples [172]. This measures the humoral immune response that specifies the infection (previous or early) [173]. IgG antibody titre increases up to measurable amount in the animals after one too few weeks of the infection [174]. This method of diagnosis has multiple benefits of low cost and sampling feasibility. ELISA is used widely for the surveillance purpose, evaluation of control strategies and supporting decision [175]. In Denmark, bulk milk is collected regularly or alternative days for milk testing [176]. The samples have been tested for the surveillance of *S.* Dublin, Infectious Bovine Rhinotracheitis (IBR) and Bovine Viral Diarrhoea virus (BVDv) [177]. This routine testing helps in effective control strategies. Serum ELISA can also be performed to check the antibodies titre as its sensitivity is close to the individual milk ELISA testing [178]. However, other genomic and molecular methods are available for the differentiation of *S.* Dublin strain [179]. The details of these methods are beyond the scope of this review.

Conclusion

Bovine salmonellosis caused by *Salmonella enterica* subsp. enterica serovar Dublin (*S.* Dublin) is a significant public health and economic concern globally. It leads to severe health issues in cattle, including enteritis, septicaemia, and abortion, with high mortality rates, especially in newborn calves. The disease not only impacts the well-being of the animals but also results in substantial economic losses through treatment costs, reduced milk production, and potential outbreaks. The transmission of *S.* Dublin is primarily through contaminated food, water, and environmental exposure, with the faecal route being the most significant mode of spread. The pathogenesis of *S.* Dublin involves complex interactions between the bacteria and the host immune system, with the bacteria capable of persisting in the herd as carriers, further complicating control measures. Effective control strategies are critical to minimizing its spread, and understanding the epidemiology, clinical signs, and diagnostic methods is key. Current diagnostic tools, such as culture techniques, PCR, and antibody detection methods, while valuable, have limitations and require further refinement to enhance sensitivity and specificity. From a public health perspective, S. Dublin represents a major risk, especially due to its potential to evolve and cross-infect humans. As such, continued vigilance and research into prevention, control strategies, and early detection are essential for mitigating the public health risk posed by bovine salmonellosis. The development of more efficient surveillance systems and control measures will be vital in preventing the spread of this zoonotic pathogen, ensuring the health of both livestock and humans.

Declarations

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