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Review on Necrotic Enteritis

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Abstract: Necrotic enteritis (NE) is an important enteric disease in poultry production that has re-emerged as a concern for poultry producers, due in part to banning, by many countries, of the use of antimicrobial growth promoters in feeds. Therefore, the aim of this paper is to give an overview on NE caused by *Clostridium perfringens*, which is a gram positive, anaerobic and spore forming bacterium that can be found in soil, litter, dust and at low levels in the intestine of healthy birds. *C. perfringens* type A and type C, in addition to producing toxins which can induce NE in poultry, produce enterotoxins at the moment of sporulation which can produce foodborne illness in humans. The disease can be transmitted by the fecal-oral route as well as through contaminated feed, water, housing structures and insects and through direct contact between infected and non-infected susceptible birds. The disease has a worldwide distribution in occurrence and of has main economic significance as a cause of high morbidity and mortality. NE develops when *C.perfringens* establishes and multiplies in the intestinal tract of chickens in the presence of multiple predisposing factors. Clinical signs include loss of appetite, droopy wings, huddling, ruffled feathers, depression in growth rate and diarrhea followed by an increase in mortality level. Diagnosis is based on clinical signs, gross and histopthological lesions, identification of the pathogenic agent and serological tests. Treatment is most commonly administered in the drinking water, with bacitracin, penicillin and lincomycin. The disease used to be prevent through prophylactic use of antibiotics however if antibiotics are not used in the feed, a strict hygiene management practice on farm and a careful selection of feed ingredients for diet formulation are all important in maintaining production efficiency.

Key words: Chickens · *Clostridium perfringens* · Re-Emergence

INTRODUCTION

Poultry sector is a fastest growing among the animal production activities. Offers an opportunity to feed the fastest growing human population and provide income resources for poor farmers [1]. Moreover, poultry in many parts of the modern world is considered as the chief source of not only cheaper protein of animal origin but also high quality human food. Important factors in continued growthof the poultry industry in many countries are the efficiency of poultry in convertingvegetable protein into animal protein, attractiveness and acceptability of poultry meat and egg to many people [2].

Enteric diseases are one of important disease concern to the poultry industry because of production losses, increased mortality, reduced welfare of birds and increased risk of contamination of poultry products for human consumption. One of the most clinically dramatic diseases amongst enteric bacterial diseases is NE.it has been perceived as a major global threat to the poultry industry, as it is the most common disease throughout all poultry growing areas of the world [3].

Necrotic enteritis is a worldwide disease caused by *Clostridium perfringens*, which is a ubiquitous anaerobic bacterium that is readily found in soil, dust, feces, feed, poultry litter and intestinal contents. The disease is of an increasing importance especially after restrictions on the preventive use of antimicrobial feed additives. However, conditions that result in damage to the intestinal mucosa as coccidiosis, mycotoxicosis, or others causing disturbance to the normal intestinal microflora, predispose birds to proliferation of clostridium infection [4].

The disease occurs almost exclusively in broilers, although layers are also affected with outbreaks reported in 3-6 month old chickens and turkey [3]. Free living birds

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Table 1: The most important *C. perfringens* toxins

Toxin	Gene location	Biological activity
Alpha toxin	Chromosome	Cytolytic, haemolytic, dermonecrotic, Lethal
Beta toxin	Plasmid	Cytolytic, dermonecrotic, lethal
Epsilon toxin	Plasmid	Oedema in various organs: liver, kidney and central nervous system
Iota toxin	Plasmid	Disruption of actin cytoskeleton and cell barrier integrity
Beta2 toxin	Plasmid	Cytolytic, lethal
Enterotoxin	Chromosome/ Plasmid	Cytotoxic, lethal, causes diarrhea by leakage of water and ions
Theta toxin	Chromosome	Lyses red blood cells and modulates the host inflammatory response

Source: Wise and Siragusa [15]

like quail and wild crows can also develop NE [5]. However NE is of major concern to the poultry industry due to the economic impact of the disease through lost productivity. The acute form of the disease leads to increasedmortality in the broiler flocks. This can account for 1% losses per day, for several consecutive days during the last weeks of the rearing period [6]. In the subclinical form, damage to the intestinal mucosa caused by *C. perfringens*leads to decreased digestion and absorption, reduced weight gain and increased feed conversion ratio [7]. The total global economic loss as a consequence of necrotic enteritis outbreaks in broiler farms is estimated to be over $2 billion annually [8].

Therefore, the objective of this seminar paper is to give an overview on Necrotic enteritis

Necrotic Enteritis

Etiology: Necrotic enteritis is caused by C. perfringens which is a gram-positive, rod-shaped anaerobe that forms oval sub terminal spores. It differs from most other clostridia in that the relatively large rods (0.6-2.4 x 1.3-9.0 μm) are encapsulated and non-motile. The colonies are smooth, round, glistening, surrounded by an inner zone of complete hemolysis caused by the theta-toxin and an outer zone of incomplete hemolysis caused by the alpha-toxin [9].

Clostridium perfringens is divided into 5 biotypes A, B, C, D and E based on the synthesis of four major lethal toxins: alpha, beta, epsilon and iota. Along with these four major toxins, enterotoxin (CPE) and beta2 (CPB2) toxins produced are considered as important toxins for enteric diseases. However, it is not clear whether CPE and CPB2 are involved in*C. perfringens* associated avian enteric diseases [10]. All 5 types produce toxins, typeA (α-toxin), type B (α, βand ε toxins), type C (α and β toxins), type D (α and ε toxins) and type E (α and ι toxins). As only *C. perfringens* types A and C are associated with NE, only α and net B toxins [11].

The infections in poultry are mostly caused by *C. perfringens* type A and to a lesser extent by type C. Because *C. perfringens* type A is highly prevalent in the intestines of healthy animals, controversy exists about its real pathogenic role [12, 13]. Additionally, it was shown that strains isolated from necrotic enteritis outbreaks did not produce more alpha toxin compared to isolates from the gut of clinically healthy broilers [14].

Epidemiology

Source of Infection and Transmission: Clostridium perfringens is a naturally occurring bacteriain the environment ofpoultry production facilities. It can be found in the dust, soil, feces, feed, poultry litter, egg shell fragments and fluff and in the intestinal tract of poultry. Feces of wild birds may also contain elevated numbers of C.perfringenswhich could further introduce the organism to poultry production facilities. When evaluating environmental samples on poultry farms, C. perfringens presence was detected on wall swabs (53%), fan swabs (46%), fly strips (43%), dirt outside the entrance (43%) and boot swabs (29%), indicating that the microorganism is ubiquitous throughout the environment [16].

*Clostridium perfringens*can be transmitted through fecal-oral route as well as through contaminated feed, water, housing structures and insects and through direct contact between infected and non-infected susceptible birds. During outbreaks of NE the major source of *C. perfringens* may be either contaminated feed or litter [17]. Sometimes feed components contaminated with bacteria may have also been a source of *C. perfringens* in NE outbreaks. There is a possibility that *C. perfringens*may be able to transmit vertically as bacteria have been found in the yolk sac of an embryonated egg [18]suggested that *C. perfringens* may be transmitted within the integrated broiler chicken operation. *C.perfringens* has also been reported to be transmitted mechanically and or biologically through house flies in poultry houses, resulting in the development of NE [3].

Predisposing factors:tocause the signs and symptoms of necrotic enteritis one or multiple predisposing factors may need to be present, such as

damage to the intestinal mucosa. Intestinaldamage, caused by coccidial pathogens, can result in the release of growth factors that may be utilized by C. perfringens in turn causing extensive proliferation in the lumen [15]. It has been documented that broiler chicks inoculated with sporulatedEimeria species coupled with the administration of *C. perfringens* contaminated feed had increased mortality when compared to contaminated feed alone [19]. Additionally, physical damage, possibly caused by littereating or fibrous material in the diet, may modify the mucosal lining [20].

Management-related factors such as feeding, water provision, temperature control and ventilation systems have been suggested to be precursors of NE [21]. Delayed initial feeding severely impairs the development of gut associated lymphoid tissue in the hind gut and slightly impedes the fore-gut during the first 35 days of life [22]. Nutritional stress can result from diets that lack balanced nutrients, predisposing birds to clostridial overgrowth and NE. For example, birds will consume more feed if the energy to- protein ratio of the diet is low, thereby exceeding their requirements for protein and causing an increase in the nitrogen content of the digest and manure [23]. It has been postulated that diet composition has a direct influence on the onset of necrotic enteritis in broilers. Diets rich in rye, wheat and barley in comparison to diets rich in corn, have high levels of indigestible, water-soluble non-starch polysaccharides. These diets are known to increase the viscosity of digesta, decreasing gut transit time and have been shown to lead to an increase of intestinal anaerobic bacteria [24].

Additionally, slower passage rates may increase the nutrient availability of *C. perfringens*. when broilers were fed corn-based *C. perfringens* contaminated feed for three consecutive days compared to broilers fed diets with high amounts of wheat, rye or barley, overall mortality ranged from 0-12% in the corn based diet compared to 26-35%in the wheat, rye or barley diets [20]. When birds were fed pellets instead of mash, there is an increase in digestibility and a decrease in the number of *C. perfringens* in the intestine. Diets high in protein, such as fishmeal, have been shown to increase numbers of ileal and cecal *C. perfringens*. Bone meal has also been associated with an increase in risk of NE [24].

Immunosuppressed chickens are more likely to develop NE, so that some researchers have used methods to induce immunosuppression. These methods mostly use Infectious bursal disease vaccine (IBD). It has resulted in a significant increase in NE lesions. This has been done by administering a usual dose of IBD vaccine with a medium pathogenicity (Intermediate class), or 10 times the dose of an IBD vaccine with relatively higher pathogenicity (intermediate plus). The lesion scores are higher when IBD vaccine is used, even with a normal dose of an intermediate class IBD vaccine [25].

Stressful conditions may decrease immunity and predispose to NE. Increasing stocking density, as a "Stressful" measure, combined with IBD vaccine, was used in an experimental model of NE, but was not evaluated independently of IBD. Welfare considerations preclude deliberately "stressing" chickens. As evident from this review, there are numerous other factors that can be used to induce disease reliably. Use of immunosuppression as part of the induction of NE is inappropriate if vaccines are being evaluated [26].

Geographical and Temporal Distribution: Epidemiological data on the incidence of NE are limited although a global survey found NE as a commonly occurring disease throughout the world [8]. Outbreaks of NE are sporadic, but have a high mortality with severe economic losses [27]. The disease has been reported from various countries, including United Kingdom [28] Canada [29] France [30]. The disease can occur more than once a year on any particular farm. Inthe UK the frequency of NE is at its highest in the winter months. Norway was similar to the UK with a peak incidence of NE during the winter and a lower incidence of NE during the warmer season. It is generally recognized that the disease is not seasonal, although discrepancies in occurrence between different latitudes that appear to contradict this are as yet unexplained [31].

Pathogenesisof NE is involves colonization of the site of disease, multiplication, acquisition of nutrients to allow further multiplication, evasion of host defenses, damage to the host and then transmission to the host. Although it can break down in to different elements, the process is likely essentially simultaneously. There may be an initial phase of displacement of other C. perfringens from the intestine or mucosal surfaces by bacteriocins [32].

The pathology associated with NE is a result of the alpha- and beta-toxins produced and released by *C. perfringens* within the mid-intestine. There continues to be debate over the specific events that initiate toxin production and the importance of relative numbers of clostridia within the intestine in healthy and diseased birds. Some studies have found *C. perfringens* to be the principal obligate anaerobic bacterium in the intestinal tract of healthy chickens, whereas others have reported it

only sporadically and in low numbers from the small intestine of normal chickens ranging in age from recently hatched to 5 months of age. It appears that the make-up of the intestinal population of *Clostridium perfringens* is determined by the health status of the bird. In flocks experiencing necrotic enteritis, isolates tend to be clonal within a flock with different diseased flocks having different clonal populations. Healthy flocks, on the other hand, have more diverse populations of *C. perfringens* isolates. Although the events that lead up to theproduction of toxin remain unclear, what is clear is the ability of the toxins to induce the lesions and clinical signs characteristic of NE [33].

Alpha-toxin is a phospholipase C. sphingomyelinase that hydrolyzes phospholipids and promotes mucous membrane disorganization which then stimulates the arachadonic acid cascade to induce the production of inflammatory mediators like leukotrienes, prostacyclin, platelet-agglutinating factor and thromboxane. These mediators lead to contraction of blood vessels, aggregation of platelets and myocardial dysfunction, leading to acute death. Beta-toxin induces hemorrhagic necrosis of the intestinal mucosa characteristic of the disease. Mucus secreted by intestinal epithelial cells onto their surface represents a major barrier to their colonization by bacteria. Mucus is rich in Oglycosylatedmucin glycoproteins and contains a diverse array of antimicrobial molecules designed to add a barrier to bacterial colonization of the intestinal Epithelia cells [32].

Clinical Signs and Lesions: Clinical signs:Sub-clinical Necrotic Enteritis (SNE) does not manifest any clinical signs and mostly under field conditions, only detected at the processing plant(s) by the rejection of carcasses [23].SNE is the disease may be suspected from a reduced weight gain and feed conversion efficiency in a broiler flock and high moisture content of the droppings or wet litter condition. SNE is more likely to cause these effects at 2-5 weeks of age but often without an increase in mortality [31].

Necrotic enteritis usually occurs in broiler chicks at 2-6 weeks of age and is characterized by a sudden onset of diarrhoea and mucosal necrosis [34]. Sick birds affected with NE are depressed, anorectic with ruffled feathers and huddle together. In the advanced stage of the disease the bird becomes lying in lateral recumbency as they are unable to stand, relatively immobileand very quickly die [35]. Mostly the course of the disease is short, with no clinical signs before the birds are just found dead. Acute symptoms of the disease are severe depression, decreased appetite and reluctance to move, ruffled feathers and diarrhoea. The period of illness is usually short (1-2 hrs) so, again, most of the birds are just found dead [20]. Birds that have died of NE have a foetid odor, are usually dehydrated with dark, dry pectoral musculature and pale kidneys [29]. The unopened intestinal wall is darker in colour than normal and distended due to the presence of large amounts of bile stained contents. In an affected flock the mortality rate can be anything from 1% to as high as 50% [16].

Gross lesions:Lesions of SNE are characterized by the development of necrotic lesion in the gut wall and liver [36]. They are usually present in one or more areas of the intestine. Mild lesion appear as small (In some cases barely visible o the necked eye) ulcers or light yellow spots on the surface of the mucosa, usually in the small intestine, in particular in the jejunum and ileum and less commonly, the caeca. More severe lesion may be seen on membrane covering the entire mucosa oflarge segment of the large intestine, in some cases even thecolo-rectum and the caecal tonsils [6]. In addition to small intestinal lesions C. perfringens is also associated with liver abnormalities;mostly enlargement. Sometimes severe congestion can be found in the liver [7].

Clinical NE is characterized by mucosal necrosis of large parts of the small intestine, covered with a yellow-brown or bile stained pseudo membrane [37]. Gross lesions are usually restricted to the small intestine, but lesions can also occur in other organs, such as the liver and kidney. Upon necropsy, the duodenum, jejunum and ileum are usually thin walled and filled with gas. Typically an intestinal wall is friable and easily torn. There is a marked distension of the intestine with the lumen usually filled with gas and dark brown fluid material. Ulcers can occur either singly or as aggregates in the mucosa of the intestine. In very severe cases, the intestinal mucosa is covered with a layer offibrino-necrotic material, or a diphtheritic membrane covering the mucosa in segments of variable length usually involving two thirds of the small intestine, the jejunum and ileum [23].

Histopathological changesMicroscopically lesions of NE from field cases consist of coagulation necrosis at the intestinal villous apices. A clear line of demarcation is visible between necrotic and viable cells. In some cases cellular degeneration may reach the sub-mucosa. From field cases, regeneration of the intestinal tract is characterized by a proliferation of epithelial cells, production of connective tissue network and decreased

numbers of goblet, columnar and epithelial cells. Overall regenerative changes leave the affected region with short, flat villi that have a reduced absorptive surface. An apparently visible psuedomembrane is made up of necrotic/ distorted villi, inflammatory cells and clumps of bacteria [38, 39].

Necrosis starts from the apical villous epithelium. Lesions typically develop from the tips of the villiandsmall demarcated areas of degeneration merged with areas of normal unaffected intestine. Degenerative changes begin with congestion of blood vessels followed by diffuse oedema. Later the epithelial cells of the villi become enlarged, with pale vacuolated cytoplasm and an indistinct homogenous deposit in place of the striated border. The degenerative process progresses down the villi in regular manner that many villi are equally affected. At this stage necrotic tissue is clearly differentiated from normal by a clear sharp line. In some cases stroma of the villi are sloughed off. There is fibrin with amorphous basophilic deposits in the majority of blood vessels [35].

Other significant changes include dissolution of the nuclei, with nuclear material flowing out of the individual cells in the form of irregular deposits that disappear when all layers of the intestine, from mucosa to serosa, are affected in the final stage of the degenerative process. a proliferation of the epithelial cells of the crypts to replace necrosed cells in the intestinal tract. There is also production of connective tissue in the inflammatory area and a decreased number of goblet and epithelial cells. In the lumen of an affected intestine, disintegrated necrotic villi, degenerated epithelial cells, goblet and inflammatory cells can be found, leaving the intestinal villi shortened and flattened with a reduced absorptive surface. Large numbers of gram-positive rod-shaped bacteria can be seen in the sloughed epithelium [38].

DiagnosisA presumptive diagnosis may be made from the case history, clinical signs, lesions and staining fresh smears of upper part of the intestinal tract with Gram stain showing an abundant number of clostridia organisms [15].

Isolation and identification of *C. perfringens*strains is carried to assure of infection and to evaluate the efficacy of treatment. For isolation several media are available such as sheep blood agar supplemented with neomycin or tryptose-sulfite cycloserine agar. Most of isolates ferment lactose, glucose, maltose hydrolyze gelatinand reduce nitrate. This bacterium is non-motile, indole and catalase negative. Loops of the intestinal mucosa were taken under aseptic conditions from slaughtered birds, incubated anaerobically at 37°C for 72 hours in cooked meat broth. Samples were then subjected to heat shock for spore select ion and then cultured onto blood agar plates. Preliminary identification of *C. Perfringens* was made based on Colony morphology (Circular-to stellate and smooth), presence of a distinctive double zone of hemolysisand Gram staining organism (Grampositive short, plump rods with blunt ends) [40].

Enzyme LinkedImmunosorbent Assay technique for screening, a difference in the number of *C. perfringens* and the amount of toxin present when comparing sick and healthy birds was demonstrated. A polymerase chain reaction method for quantification of *C.Perfringens* and for the detection of the alpha-toxin gene within *C.perfringens* isolated from the gastrointestinal tract of Chickens has also been reported [33].

Differential Diagnosis Coccidiosis is a known predisposing factor of NE and can occur prior to or simultaneously with the disease and thus it must be differentiated from NE. Outward signs of coccidiosis in chickens include droopiness and listlessness, loss of appetite, loss of yellow color in shanks, pale combs and wattles, ruffled, unthrifty feathers, huddling or acting chilled, blood or mucus in the feces, diarrhea, dehydration and even death. Moreover, decreased feeding and watering, poor weight gain and feed conversion efficiency are also common findings. Survivors of severe infections recover in 10-14 days, but may require even more time to recover to normal production [41].

Ulcerative enteritis (UE) is another clostridial enteric disease that must be differentially diagnosed from NE. UE will present with ulcers in the small intestine that often perforate the intestinal wall and produce peritonitis and intestinal adhesions that is caused by *Clostridium colinum*. Lesions are characterized by multiple ulcers throughout the intestinal tract, including ceca and foci of necrosis and inflammation in the liver [42].

Histomonias is must also be differentiated from NE. Gross pathology of histomonias is includes necrotic liver lesions with depressed centers and well-defined edges, as well as cecal lesions composed of necrotic mucosa, with blood and other debris. The observation of living organisms by phase contrast microscopy can assist in diagnosing histomoniasis[43].

Treatment with antibiotics such as penicillin, amoxicillin, ampicillin, erythromycin, dihydrostrepto-mycin and tetracycline provided a satisfactory clinical response. Penicillin's are known to be particularly active against C. perfringens. Resistance to penicillin is very rare. Three days is the minimum duration of treatment, however longer applications may be required

[44]. A low frequency of resistance was detected against erythromycin and tiamulin with 5 and 20%, respectively. Spectinomycin, neomycin and colistin showed the highest incidence of resistance with 74, 94 and 100%, respectively [45].

Control and Prevention Necrotic enteritis prevention is usually associated with management practices that minimize the effects of the predisposing factors that contribute to disease development.Reducing the inclusion of dietary ingredients that may lead to NE, such as fish meal, oats, barley and rye, has been a note worthy solution in decreasing NE incidence [46]. The use of antibiotic growth promoter (AGP) in feed has also played an important role in the control of NE. The introduction of AGP in the diet assists with coccidiosis management and modifies the intestinal microbial populations, which both result in a reduction in the incidence of NE[19, 46]. Other methods used to control coccidiosis, such as vaccination with live Eimeria vaccines, may also have an indirect effect on the incidence of NE [19].

Vaccination has been an effective way to prevent humans and animals from many infectious diseases. It can enhance specific immunity of the organisms to viral and bacterial diseases. Vaccines have also been successfully applied to control numerous clostridial diseases in livestock animals. Therefore, vaccination against NE disease is proposed to provide an alternative treatment for NE in poultry especially when more convincing evidence was revealed that the toxin NetB is responsible for the disease. Vaccination strategies have been put forward for the control of NE mainly in broiler chickens [47]. Prior to the discovery ofNetB, the earlier vaccination focused on toxins that may not be associated to NE by and large, for example, a-toxin. Thus, the vaccines developed only had limited success in controlling NE. while the partial protective effect of a-toxin based vaccine may be due to the association of a -toxin protein with cell membrane that can have immune interaction to perform such protection[48].

The most important step forward to developing vaccines to immunize the birds against NE occurred following the discovery of NetB toxin. A recombinant NetBC. Perfringens (rNetB) was constructed and attenuated as a vaccine by Keyburn *et al.* [47]. The birds immunized with rNetB were significantly protected against NE challenged with a mild dose of virulent bacteria, while the effectiveness of the vaccination was not so when a more robust challenge was performed. Alternatively, when the birds were immunizedwith a combination of rNetB, bacterin and cell free toxoid, significant protection against moderate and severe challenge was observed. It was suggested that invitro levels of NetB produced by virulent C.Perfringens isolates were too low to produce strong immune response in the birds and thus the combined vaccination of birds with rNetB and other cellular or cell-free antigens may be necessary [49].

Clostridium perfringens recombinant proteins as vaccine candidates using the Montanide ™ISA 71 VG adjuvant in an experimental model of NE. When the broilers were immunized with purified clostridialrecombinant NetB toxin, pyruvate: ferredoxin oxidoreductase (PFO), a-toxin, or elongation factor-Tu, significantly reduced gut lesions were observed. Furthermore, birds immunized with NetB toxin exhibited significantly increased body weight gains and greater NetB toxin antibody titers [50].

Economic Impact for the commercial poultry industry, controlling the levels of C. perfringens is an important issue because of the economic cost of infected flocks. It has been estimated that, worldwide, C. perfringens costs the international poultry industry in excess of $US 2 billion per year [6].

Commercial broiler flocks with clinical and subclinical necrotic enteritis infection and production performance in 2.5 years time period the farmer's profit on average was reduced by 33 % when comparing flocks with high and low levels of the disease. Impaired feed conversion, reduced live weight at slaughter and increased condemnation percentage were major causes of production losses associated with *C. perfringens* infection. Subclinical clostridial enteritis has also been associated with impaired feed conversion and retarded growth in a pen trial [7].

Costs to broiler producers associated with SNEwere estimated recently by using published information on impacts on body weight and feed conversion rate (FCR) associated with SNE and costs and revenues associated with broiler production. SNE was estimated to result in a 12% reduction in body weight and a 10.9% increase in FCR compared with healthy birds. For the purposes they considered scenarios involving hypothetical flocks of 20, 000 birds raised to final body weights ranging from 4.63 to 7.94 lb. SNE is a major economic cost to the broiler production industry due to poor growth and feed conversion efficiency of broiler chickenflocks, higher condemnation of livers or rarely the whole carcasses at the slaughter house and an increased risk of microbial contamination of poultry meat [51].

Public Health SignificancePublic health significance C. perfringens type A and type C, in addition to producing toxins which can induce NE in poultry, also produce enterotoxins at the moment of sporulation which can produce foodborne illness in humans. Two distinct diseases are induced by these subtypes; type A C. perfringens produces diarrhea and type C C. perfringens produces necrotic enteritis in humans [39].

High percentages of *C. perfringens* positive carcasses have been reported following processing and outbreaks of type A food poisoning traced to consumption of chicken have been reported. Although type C food poisoning is a much more severe disease in humans and type C *C. perfringens* can be found in poultry, it is not considered to be a major foodborne concern because of the very low prevalence of the disease in humans. Of concern is the potential for incidence of *C. perfringens*-induced foodborne illnesses to increase with the worldwide trend of removing growth enhancing antibiotics from poultry rations. The removal of these compounds, most of which have anti-clostridial activity, has led to an increase in clinical and SNE and hepatitis in broilers and will, no doubt, also increase the carriage of *C. perfringens* on broiler carcasses throughout processing [33].

CONCLUSION

Necrotic enteritis is a complex, multifactorial disease with many unknown factors influencing its occurrence and the severity of outbreaks. This disease has become economically significant problems in poultry production system especially in developing countries. Moreover, only certain C. Perfringens strains are capable of inducing necrotic enteritis under specific conditions that predispose to the disease such as: feed withdrawal, IBD, coccidiosis and high levels of dietary fish meal, wheat and barley. Also factors such as high stocking density, poor litter conditions, poor hygiene and high ammonia level and other stressful situation may reduce the resistance of the birds and increases their susceptibility to infections. Few tools and strategies are available for prevention and control of C. perfringens in poultry. The most cost-effective control will probably be achieved by balancing the composition of the feed. Vaccination against the pathogen and the use of probiotic and prebiotic products has been suggested, but are not available for practical use in the field at the present time.

Based on the above conclusion the following recommendations are forwarded:

- Cost-effective alternatives, a combination of measures that include avoiding predisposing factors and combating the pathogen it have to be sought and more research should be urgently done on this matter.
- Bio security measures such as hygiene and sanitation of poultry farms, equipment like feeding trough, water tanker and personnel disinfectants and liter management should be the first line for control and prevention of necrotic enteritis.
- Dietary ingredients such as fish meal, wheat, barley and high fiber litter should be reduced.

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