INFECTIOUS BURSAL DISEASE – A REVIEW

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SUMMARY: Infectious bursal disease is a highly contagious disease that accounts for significant economic losses in the poultry industry around the globe including Sri Lanka. The causative agent is Infectious Bursal Disease Virus (IBDV) in the genus *Avibirnavirus* of the family *Birnaviridae*. Among the two major serotypes of IBDV, clinical disease in poultry is caused by serotype 1, which is further classified into three pathotypes, classical virulent, antigenic variant and very virulent. Young chicken of three to six weeks of age are more susceptible for the disease and the clinical signs include exhaustion, prostration, dehydration, watery diarrhoea and ruffled feathers. The virus causes severe damage to lymphocytes in the Bursa of Fabricious of poultry. Consequent immunosuppression increases the susceptibility of the affected chicks to other diseases and cause unresponsiveness to vaccines. In spite of the control measures taken, IBD continues to be a major constraint in the poultry industry. This review extensively discusses the characteristics of the virus, its genome and the functions of each virus coded protein, circulating virus pathotypes and their emergence, host pathogen interactions, pathogenesis, and pathology of the disease. Further, we have reviewed and summarized the current information about the epidemiology of IBD in both local and global perspective, the available diagnostic techniques, prevention and control strategies and the challenges encountered in that process. Considering the enormous economic importance of IBD, this review is aimed to benefit the scientific fraternity, veterinary practitioners, veterinary students, researchers and diagnosticians, which will in turn help in the better and effective management and ultimately control of this disease.

INTRODUCTION

Infectious bursal disease (IBD) is a highly contagious immunosuppressive viral disease in young chickens (Nascimento *et al.,* 2017). It was first reported in 1962 in Gumboro, Delaware, United States of America, hence named as Gumboro disease (Cosgrove, 1962). By year 2000, IBD became a massive problem to the global poultry industry (Van den Berg *et al.,* 2000). Currently, infectious bursal disease virus (IBDV) continues as one of the major constraints for poultry farmers in all poultry producing regions of the world (Alkie and Rautenschlein, 2016) and it is a listed avian disease reported annually in the world animal health information system (WAHIS) of the World Organization of Animal Health (OIE).

The virus

Causative agent of Gumboro, IBDV belongs to the genus *Avibirnavirus* of the family *Birnaviridae* (Delmas *et al.,* 2019). It is a naked (non-enveloped) virus having a single capsid structure of icosahedral symmetry with a diameter of 58-60 nm (Dobos *et al.,*1979). The viral genome consists of two segments of double stranded RNA named as segment A and segment B (Müller *et al.,* 1979). Segment A, the larger of the two segments (~3.4 kb) contains two partially overlapping open reading frames (ORFs). The first ORF encodes the nonstructural viral protein VP5 (17 kDa) (Lejal *et al.,* 2000). The larger second ORF encodes a 110 kDa precursor polyprotein (PP), which is subsequently cleaved into three mature proteins VP2 (54.4 kDa), VP3 (32 kDa) and VP4 (28 kDa) (Birghan *et al.,* 2000). Segment B, the smaller of the two segments (~2.9 kb) codes for VP1 protein (97 kDa) (Tacken *et al.,* 2004). As a summery, segment A of the genome encodes four proteins (VP2, VP3, VP4, and VP5) while segment B encodes VP1 (Ture *et al.,*1998).

Functions of virus coded proteins

VP1 is the RNA-dependent RNA polymerase (RdRp) of IBDV (Tacken *et al.,* 2004)

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that mediates viral RNA replication (Müller and Nitschke, 1987).Virus proteins VP2 and VP3 are the two major structural proteins (Birghan *et al.,* 2000) of the virus constituting 51% and 40% of the virion, respectively (Dobos *et al.,* 1979).The single shelled capsid of IBDV is assembled by VP2 and VP3 proteins (Saugar *et al.,* 2005). VP2 contains the major antigenic sites (immuno dominant epitopes) responsible for induction of a protective humoral immune response through generating neutralizing antibodies (Fahey *et al.,* 1989). In addition, VP2 is an apoptotic inducer (Qin and Zheng, 2017). VP3 acts as a scaffold protein that binds both the viral double-stranded RNA and VP1 in viral morphogenesis (Mertens *et al.,* 2015). VP4 is a viral serine (S) protease (Birghan *et al.,* 2000) that works on cleavage of the PP (Jagadish *et al.,*1988, Lejal *et al.,* 2000). Further, VP4 act as a suppressor of the innate immunity (Qin and Zheng, 2017). VP5 is involved in the dissemination of the virus from infected cells (Lombardo *et al.,* 2000). The PP is considered as the main mediator of IBDV-induced immunosuppression and pathogenicity (Peters *et al.,* 2004).

Virus serotypes and pathotypes

Two serotypes (serotype 1 and serotype 2) of IBDV have been identified of which only the serotype 1 is capable of causing clinical disease in poultry (OIE 2016). The apathogenic serotype 2 has been isolated from chickens and turkeys (Van den Berg *et al.,* 2000). Serotype 1 strains of IBDV are further classified into 3 pathotypes (Van den Berg *et al.,* 2000), based on their virulence and pathogenicity as classical virulent, antigenic variant and very virulent (Ture *et al.,*1998). A recent global molecular epidemiological study on IBDV isolated from four continents revealed that 60% to 70% of circulating IBDV isolates were very virulent (vv) strains (Alkie and Rautenschlein, 2016).

Emergence of IBD pathotypes

Classical virulent strains of IBDV usually cause 20-30% mortality mostly due to the widespread bursal damage in infected poultry (Lukert and Saif, 2003). Historically, classical virulent strains were used as a source of commercially available vaccines against IBDV infections (Rosenberger *et al.,* 1985). In early 1980s, comparatively more virulent new antigenic variants producing rapid bursal damage and about 50% mortality emerged (Rosenberger *et al.,* 1985). The vaccines prepared from classical strains failed to control the disease caused by these newly emerged antigenically variant strains (Chettle *et al.,* 1989). However, the disease associated with IBDV was generally of mild to moderate severity until the year 1986. The widespread use of live and inactivated vaccines had proved effective, up to that time, in controlling the more serious manifestations of the disease (Cullen, 1994). However, by 1986 very severe outbreaks of IBD were reported from some European countries that induced more pronounced bursal lesion accompanied with very high (90%) mortality (Chettle *et al.,* 1989). The well tried vaccines which had been effective previously were ineffective in controlling these infections (Cullen, 1994). This disease was attributed to very virulent IBD (vvIBD) strains that are now accepted to have emerged in the late 1980s (Chettle *et al.,* 1989). Extensive usage of live vaccines in the field is thought to favor the emergence of new strains of IBDV that evaded vaccine-induced immunity. A high genetic mutation rate is one of the key features of RNA viruses (Withers *et al.,* 2005) such as IBDVs. In addition to the mutations in VP2 hyper variable region of IBDV, genetic reassortment events and homologous recombination within segments also contribute to the variation of IBDV (Islam *et al.,*2001, Wei *et al.,* 2006, He *et al.,* 2009, Jackwood, 2012). Further, some IBDV live vaccines maintain quasispecies nature, which in the face of selection pressure may favor the outgrowth of more virulent antigenic variants or mutants in the viral population (Jackwood and Sommer, 2002).

Host susceptibility

The domestic chickens are the only avian species susceptible to the pathogenic serotype 1 virus which causes clinical disease. Turkeys, ducks, guinea fowls and ostriches may be naturally and experimentally infected, however infections are apathogenic (Sharma *et al.,* 2000). The susceptibility is age related. Young chicks of 3 to 6 weeks of age undergoing maximal stage of bursal development have greatest susceptibility for the serotype I virus (Sharma *et al.,* 2000, Mahgoub, 2012). The disease is unusual in birds over 15 weeks of age (Cullen, 1994). In the case of vvIBDV infection, the age susceptibility is extended which covers the entire growing period in broilers (Ingrao *et al.,* 2013).

Transmission

Infected chickens excrete the IBDV in their feaces contaminating the poultry house environment.

The virus is resistant to many disinfectant and environmental factors and remains infectious for at least four months in the poultry house. Contamination of a rearing site with the IBDV enables significant horizontal transmission between flocks *via* ingestion of feed and water contaminated by the virus containing faeces (Alkie and Rautenschlein, 2016). Therefore when the poultry house becomes contaminated with IBDV, the disease tends to repeat in subsequent flocks. However, there has been no reports of vertical transmission of IBDV (Alkie and Rautenschlein, 2016). Indirect contact with any animate or inanimate contaminated vectors also transmit the disease (Howie and Thorsen, 1981). There is no egg transmission but the virus can survive on egg shell surface to serve as a surface contaminant (McLachlan and Dubovi, 2001). Darkling beetles and litter mites carry virus up to 8 weeks. Mosquitoes are a possible mode of transmission as strains of IBDV have been isolated from mosquitoes (Howie and Thorsen, 1981).

Pathogenesis and pathology

Following oral inoculation, initial viral replication occurs in gut-associated lymphoid cells. The secondary viral replication that occurs in the bursa of fabricius (BF) is responsible for high titer of virus and mortality. Therefore, Kaufer and Weiss (1980) showed that chickens can be protected from IBDV by bursectomy. The BF is the central immune organ responsible for the development and maturation of B cells and the generation of diverse antibody repertoire in young chickens (Nera *et al.,* 2015). IBDV affects lymphoid organs, primarily BF (Nascimento *et al.,* 2017). The specific tropism of IBDV to developing immature B lymphocytes in the BF has been well-documented (Alkie and Rautenschlein, 2016, Sharma *et al.,* 2000).

IBDV infection of B lymphocytes is cytolytic. That causes lymphocytic destruction in the BF and to a lesser extent in other lymphoid organs leading to direct immuno suppression. The massive depletion of the precursors of antibody producing B cells in the BF caused by IBDV-induced apoptosis is the major reason to cause severe immune-suppression and atrophy of the primary immune organ (Wang *et al.,* 2010). The immune-suppression is also partially due to the decreased phagocytotic activity of monocytes/macrophages (Sharma *et al.,* 2000, Lam, 1998) and the diminished response to mitogen activation of T cells (Rauw *et al.,* 2007, McNeilly *et al.,* 1999).

The disease

IBD is a highly contagious, severe and acute viral disease of young chickens around 3-6 weeks of age characterized by enlargement and extensive damages in the BF with high mortality (Eterradossi and Saif, 2008). Infection in younger birds is usually asymptomatic but causes permanent and severe damage to BF. Since the majority of field infections are subclinical, it causes more economical damage to the poultry industry due to resultant immunosuppression (Veterinary Epidemiological Bulletin Sri Lanka, 2013). The incubation period of IBD is about two to three days (Ley *et al.,*1983). The acute IBDV infection producing clinical manifestations lasts for only 3 to 4 days (Withers *et al.,* 2005). IBD is clinically characterized by self-vent pecking, profuse watery yellowish-white diarrhoea, tremor of the whole body, and characteristic spiking curve of mortalities. It is pathologically characterized by inflammatory enlargement of BF followed by atrophy, edematous to haemorrhagic BF, and ecchymotic haemorrhages on the lateral aspect of the thigh and pectoral muscles.

The disease distribution

Since the first discovery of classical IBDV strains over 55 years ago (Cosgrove, 1962), IBD had been reported in most parts of the USA by 1964 (Lasher and Davis, 1997). Subsequently, the IBDV has spread throughout the world including Europe, Asia, Africa, Middle East, Far East and Australia (Van den Berg *et al.,* 2000). In year 1992, 109 OIE member countries reported the presence of IBD. Since the initial discovery, complex evolution of the IBDV has taken place (Alkie and Rautenschlein, 2016) and it is currently found in virtually all major poultry producing areas of the world.

The first outbreak of vvIBD virus was reported in Europe in early 1990s (Brown *et al.,* 1994). According to an OIE survey done in 1990, vvIBD was distributed in all regions except Asia and Oceania. Since that time, there has been further spread of vvIBD and it became a serious problem in parts of Asia too (Cullen, 1994). Aricibasi *et al.* (2010) reported that vvIBDV strains have spread all over the world. Recent vvIBD pandemics across Asia, Africa and South America have heavily damaged the commercial poultry industry (Teshome *et al.,* 2015).

IBD in Sri Lanka

The first suspected occurrence of IBD in Sri Lanka was reported in 1986 (Ranasinghe *et al.,* 1986). Even though the clinical, post mortem and histopathological signs of the affected broiler chicks were strongly suggestive of the disease, it was not confirmed serologically in that particular flock due to previous immunization of the birds with IBD vaccines (Ranasinghe *et al.,* 1986). A sero-epidemiological survey carried out in 1991 revealed the presence of anti-IBD antibodies in chickens in 15 out of 17 districts surveyed (Wijewardena *et al.,* 1991). In 1995, a disease clinically resembling IBD was reported in Vavuniya and the serological studies had revealed that the birds had been exposed to natural IBD infection (Sellasamy, 1996). Among poultry diagnostic submissions to the Veterinary Research Institute, Gannoruwa, 18.3% out of 455 cases were serologically positive for IBD in 2002 (Bandara *et al.,*2003) while 27.8% out of 489 cases were serologically positive in 2003 (Kothalawala *et al.,* 2004). In another study, 182 serum samples out of 200 village chickens had antibodies against IBDV (Jayasundara *et al.,* 2010).

According to Sri Lanka Veterinary Epidemiological Bulletin, IBD was reported throughout the country with increasing incidence until year 2014. In 2014, 96,771 IBD cases were reported with 3,479 deaths. In comparison to year 2014, a noticeable decrease in the number of reported IBD cases was observed in year 2015 (52,911 cases with 1,788 deaths) and the majority of the reported IBD cases were from North Western Province. More recently, in year 2016 there were 248,403 cases with 3.87% fatality (Annual Report 2016, Department of Animal Production and Health). In Year 2017, IBD was observed in all districts of the country, reporting 163,713 cases with a 2.96% fatality rate (Annual Report 2017, Department of Animal Production and Health). In each year North Western was the predominantly affected province.

IBD diagnosis

Diagnosis of IBD takes in to account the disease history of the affected flock, typical clinical signs and necropsy lesions. During later stages of the disease it is difficult to confirm a diagnosis of IBD by examining only atrophied BF, as other diseases like Marek's and mycotoxicosis result in similar lesions (Veterinary Epidemiological Bulletin Sri Lanka, 2013). The diagnosis is therefore supported by laboratory tests such as detection of viral antigen in the BF using direct/indirect fluorescent antibody test (FAT) on sectioned tissues, immunoperoxidase staining of BF, use of IBD specific DNA probes labeled with ^{32}P, biotin or digoxygenin, reverse transcriptase PCR, agar gel precipitation test, virus neutralization test, antigen capture ELISA methods, direct detection of viral particles using electron microscopy, or later in the disease the measurement of specific antibody levels to demonstrate seroconversion (Van den Berg *et al.,* 2000). These methods are also used to monitor flock health and to measure the immune response to IBD vaccination (Cullen, 1994). The infection in chicks less than 3 weeks of age is usually subclinical due to the effect of maternal antibodies. Therefore diagnosis is made by histopathology, serology or virus isolation by inoculation of chorio-allantoic membrane of 9-11 day embryonated chicken eggs where the embryos die within 3-5 days post inoculation producing mottled liver and kidneys with congested lungs. In addition IBDV can be isolated on cell cultures such as chicken embryo fibroblasts, chicken embryo bursa, avian B lymphocytes, and other avian cell cultures and/or mammalian cell lines by serial passages where the virus produces plaques (Hossain *et al.,*2006).

Virus stability

IBDV is highly stable and persists in the poultry house despite application of thorough physical and chemical cleansing and disinfection procedures (Lukert & Hitchner, 1984, Sharma *et al.,* 2000). The virus remains viable for at least 6 months in dry litter and more than 1 year in unused dry chicken houses (Edgar and Cho, 1976). Its persistence in the environment, even after disinfection, makes the eradication unrealistic in the affected countries (Van den Berg, 2000). Because of the environmental stability of IBDV, its control through sanitation and isolation alone is not practical in commercial poultry production (Vakharia *et al.,*1994).

IBD vaccines

Major types of vaccines available to control IBD are, live attenuated vaccines, immune-complex vaccines, live recombinant vectored vaccines expressing IBDV antigens and inactivated oil-emulsion adjuvant vaccines (Muller *et al.,* 2012). Live attenuated, recombinant or immune-complex vaccines are used to achieve active immunization in young chickens whereas, passive protection is achieved by vaccinating the parents using a

combination of live and killed vaccines. Classical virulent strains are the basement of most commercially available conventional live IBDV vaccines (Mueller *et al.,* 2012). These vaccines are produced from virus strains that have been attenuated by serial passages in embryonated chicken eggs. The vaccine strains are classified as "mild", "intermediate" or "intermediate plus" ("hot") based on their increasing ability to overcome residual maternally derived antibodies (MDA) and to replicate and cause lymphocytic depletion in the BF (OIE 2016, Van den Berg *et al.,* 2000).

IBD vaccines available in Sri Lanka

Several commercial products of live vaccines and inactivated vaccines have been registered under the Veterinary Drug Control Authority (VDCA) of Sri Lanka. As of January 2019, there were 16 registered IBD vaccines, out of which 9 were live and 7 were killed vaccines. One was a mild vaccine strain, 13 were intermediate strains and 2 were intermediate plus (hot) strains (personnel communication with Registrar, VDCA). Vaccination of commercial poultry is done using intermediate strain vaccines. Intermediate plus vaccines are not allowed to be registered in Sri Lanka for sale. However, individual users can obtain a user permit with the recommendation of Range Veterinary Surgeon and the District Veterinary Investigation Officer incase intermediate plus vaccines are to be used. However, intermediate plus vaccines are allowed to use in the subsequent batches following confirmation of IBD for 3 cycles (Veterinary Epidemiological Bulletin Sri Lanka, 2013).

IBD control

Although identified more than 55 years ago, IBDV continues to be a major threat to the global commercial poultry industry (Muller *et al.,* 2012). The first essential for control of IBD is to maintain good hygiene and site security. This is especially important when vvIBD is present, as there is a relative deficiency of vaccine efficiency against the virulent disease. A thorough well planned disinfection procedure must be implemented in the infected site with disinfectants like Iodine, Peroxygen and Glutaraldehyde to prevent the infection in subsequent batches. There should be an adequate time between depletion and restocking of the poultry houses. Ideally, minimum of 2 week resting period for the poultry houses should be maintained between successive poultry flocks. All infected litter and carcasses of infected birds must be disposed properly away from the poultry operation (Veterinary Epidemiological Bulletin Sri Lanka, 2013). The control of IBD through depopulation of infected farms and disinfection of infected premises was practiced for long period in some countries but was considered ineffective and costly (Van den Berg *et al.,* 2000). However, the strict application of biosecurity measures and thorough cleaning and disinfection will play a critical role in reducing virus pressure and preventing the emergence of new IBD virus strains.

Vaccination has become the principle method of controlling IBDV and its success depends on the choice of vaccine strain, vaccination schedule, and the circulating field virus strains (Van den Berg, 2000). Conventional live attenuated IBDV vaccines are suitable for mass vaccination and they have induced robust immunity when applied in drinking water (Van den Berg *et al.,* 2000). The potential for reversion to virulence (Yamaguchi *et al.,* 2000), residual immunosuppressive effects (Rautenschlein *et al.,* 2005), as well as their role as genetic sources for the generation of assorted new viruses (He *et al.,* 2014) are major safety concerns. Strict biosecurity together with the use of conventional inactivated and live vaccines had been a success story for controlling IBD until the emergence of antigenic variants in early 1980s. These changes in the virus antigenicity and virulence made the task of controlling IBD by vaccination more challenging (Eterradossi *et al.,* 1992, Muller *et al.,* 2012). In addition, vaccination against the vvIBD strains encounters many challenges as they can breakthrough protective antibodies, and therefore require more efficient vaccination approaches (Khan, 2018).

Breeder vaccination program plays a crucial role in preventing and controlling of IBD in commercial birds. The main emphasis of vaccinating parent stock is to obtain chicks with sufficient amount of maternal antibodies to give protection against IBDV in the first 4 to 5 weeks of life (Kibenge *et al.,* 1988) in order to protect the chicks against economically devastating subclinical infection. In breeder vaccination programs, mild or intermediate live vaccines are administered to produce a primary response prior to the usage of inactivated vaccine near to point of lay (Cullen, 1994, Skeeles *et al.,* 1979) to stimulate high and uniform levels of antibodies in parent chickens, and subsequently in their off-spring through maternal transfer of antibodies (OIE, 2016).

Vaccination of commercial flocks against IBDV prevents the clinical disease as active immunity is achieved by administering live vaccines. Intermediate types of vaccines are more commonly used for commercial poultry in Sri Lanka. In some instances intermediate plus (hot) vaccines are administered to broiler chickens and commercial layer replacements (OIE, 2016). Vaccinating chicks with high maternal antibody levels may not develop anticipated immunity due to vaccine virus neutralization (Moraes *et al.,* 2005) by maternal antibodies, making the timing of vaccination very crucial (Hsieh *et al.,* 2010). Recombinant and immune-complex vaccines can be administered even in the presence of maternally derived antibodies, *in ovo* at 18 days of incubation or to one day old chicks (OIE, 2016).

Control of IBD depends upon an informed assessment, leading to the deployment of the most suitable vaccines, administered at the optimum times, combined with high standards of hygiene and strict disease security measures. Future immunization strategies against IBD need to develop protection against all pathogenic field strains while avoiding setting up selection pressures that might cause new variants to emerge.

Recommended vaccination schedule

Fantay *et al.* (2015) determined the appropriate time for administration of live vaccine as 18 days of post hatch. It could vary according to the management conditions at the particular farm (Fantay *et al.,* 2015, Moraes *et al.,* 2005). Therefore, ideally IBD vaccination of chickens whose parents had been vaccinated against IBD should not be done without determining maternal antibody titer (Fantay *et al.,* 2015). Furthermore, administration of a booster vaccine against IBD at pre-layer stage in order to increase the level of antibodies in their off-spring until being vaccinated is recommended (Fantay *et al.,* 2015).

According to OIE (2016), intermediate vaccine is administered as a coarse spray for day old chicks in order to protect chicken in the flocks that carry no or minimum levels of maternal antibodies. Second and third applications are administered if vaccinated chicks carry uneven maternal antibody levels or if there is a high risk of exposure to virulent forms of IBDV. Second dose is usually given at 10-14 days post hatch when 10% of the population is susceptible to IBD followed by a third dose 7-10 days later (OIE, 2016).

In spite of preventive vaccination programs practiced with the intermediate strains, IBD is being reported throughout the world. Strict bio security measures should be coupled with vaccination to control the disease. With the emergence of vvIBDV strains, controlling IBD by vaccination has been more challenging (Muller *et al.,* 2012). *In ovo* vaccination and live viral vector vaccines introduced recently have proved high efficacy even in the presence of high levels of maternally derived antibodies (Muller *et al.,* 2012).

Economic impact

IBD is economically very significant to the global commercial poultry industry through the mortality, impaired weight gain, immunosuppression and excessive condemnation of carcasses due to marked haemorrhage in the skeletal muscle (Zeryehun, 2017). Infected chickens less than 3 weeks of age may appear healthy without exhibiting clinical signs (Hitchner, 1971), but have a subclinical infection characterized by microscopic lesions in the BF (Winterfield *et al.,* 1972). Although rapid recovery from IBD is common in surviving chicks, the damage to BF is irreversible and results in immunosuppression. The greatest economic loss of IBD result from immunosuppression leading to increased susceptibility to other diseases and being unresponsive to costly vaccination programs (Withers *et al.,* 2005). It was found that both IBDV infected broiler and pullet flocks would respond poorly to live attenuated vaccines against viruses such as Newcastle disease and infectious bronchitis (Cullen, 1994) and Marek's disease (Kibenge *et al.,* 1988). IBDV infected broilers have greater tendency and severity of respiratory disease and consequent downgrading of carcasses at slaughter (Cullen, 1994). It was also shown that IBDV infected birds may become good propagators of other viral pathogens (Alkie and Rautenschlein, 2016). IBDV infected breeders may show lower egg production and poor chick quality (Cullen, 1994). Control of IBD imposes additional costs in vaccination, health screening and increased sanitation. In areas with emerging industries, scarcity of diagnostic facilities and lack of vaccines can result in serious losses and high costs (Cullen, 1994). IBD imposes a serious constraint to profitable production as highly virulent IBDV can cause high mortality in unprotected flocks (Alkie and Rautenschlein, 2016). Among susceptible chickens subclinical IBDV infection is not uncommon in the field, and may occur particularly when the affected flocks have maternal antibodies or

the involved IBDV strains are of low pathogenicity (Van den Berg *et al.,* 2000).

Future perspectives

Prevention of IBD related losses associated with immunosuppression and secondary infections will continue to be a specific focus in the field in future. The identification and characterization of new emerging IBDV strains remains a major reason for the development of new vaccination strategies. In this regard, new sequencing technologies and bioinformatics need to be used in the future to understand IBDV epidemiology and possibly to predict the distribution of certain strains in the field (Alkie and Rautenschlein, 2016). Edible vaccines to combat IBD hold promise in future and one of the strategies to develop cost-effective and clean vaccines is to express engineered IBD antigenic genes in edible plants or their seeds to induce immunity after their consumption (Khan and Maliga, 1999, Khan *et al.,* 2007). It has been shown that when IBDV VP2 gene expressing rice and certain grains were fed to chicks, neutralizing antibodies were produced and the birds were protected from vvIBDV strains (Wu *et al.,* 2007).

Conclusion

Choices to control IBD seem to be limited. While the emphasis is on prevention rather than cure, there is not much one can do with the infected flocks once an IBD outbreak had occurred in the farm. In addition, eliminating the sturdy and persistent IBDV particles from the farm is by no means an easy task (Zeryehun, 2017). With the intensive uses of live vaccines, the number of vvIBDV strains and their reassortants have continuously increased and these strains became epidemic and posed a great threat to the current poultry industry (Kurukulasuriya *et al.,* 2016) making the prevention and control of IBD more challenging. At present, the disease is controlled by the combined use of live virus and inactivated oil emulsion vaccines. But these vaccines are not always effective as they may not contain the required immunogens present in the variant strains circulating in that area (Zeryehun, 2017). Therefore attempts should emphasize on the identification of local viral strains present in the field to design cost effective vaccines. Further, vaccines prevent viral shedding more efficiently if they have been developed from strains homologous to currently circulating genotypes (Miller *et al.,* 2009). Finally, all these facts warrant complete molecular characterization of evolving IBDV strains.

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