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Infectious laryngotracheitis in avian species: A review

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Abstract
Infectious laryngotracheitis (ILT) is an acute, highly contagious upper-respiratory infectious disease of chicken, which was first described in the USA in 1925. ILT is an important respiratory disease of chicken that affects poultry industry worldwide. The causative agent for Infectious Laryngotracheitis is a pneumotropic virus of the family Herpes viridae, genus Iltovirus. The main transmission routes are ocular and respiratory. The virus is shed in respiratory secretions, so easily transmitted by inhalation or mechanically transmitted by people and fomites. Chickens are the primary host for infectious laryngotracheitis. The disease is characterized by conjunctivitis, sinusitis, oculo-nasal discharge, respiratory distress, bloody mucus, swollen orbital sinuses, high morbidity, considerable mortality and decreased egg production in birds. gross lesions lesions such as catarrhal to hemorrhagic tracheitis, fibrinopurulent to caseous exudates or cheesy or caseous plugs in the larynx and trachea are seen. Microscopic changes in tracheal mucosa include the loss of goblet cell and infiltration of mucosa with inflammatory cells. The disease is diagnosed on the basis of clinical signs, gross lesions, histopathology and molecular diagnostic tests.

Keywords: Diagnosis, epidemiology**,** infectious laryngotracheitis, poultry, prevention

Introduction
Infectious Laryngotracheitis (ILT) is an important respiratory disease of chicken that affects poultry industry worldwide. It is caused by Gallid herpes virus 1 (GaHV-1), a member of the Herpes viridiae family. The most characteristic signs are observed in adult birds, although disease affects all ages of birds [1]. The main transmission routes are ocular and respiratory. Infectious laryngotracheitis virus (ILTV) infects laryngeal and tracheal epithelial cells causing lesions in the trachea of chickens, which can lead to mucous build up, tracheal hemorrhaging, suffocation and death in the birds. ILT is characterized by cough, rales, bloody mucus excretion, marked dyspnea and decrease in egg production [2]. The morbidity and mortality rates can reach upto 70% in the acute form of disease. Organ mostly affected includes conjunctiva and the respiratory tract and most consistently observed in larynx and trachea [1].

Etiology
The causative agent for Infectious Laryngotracheitis is a pneumotropic virus of the family Herpes viridae, genus Iltovirus. Taxonomically, this virus is classified as a Gallid herpes virus 1 [3]. Conjunctiva and tracheal mucosa are the major sites of ILTV replication, where replication occurs during first week of infection leading to inflammation, serous or mucoid discharge and respiratory distress [4, 5, 6].

Epidemiology
Infectious laryngotracheitis (ILT) is an acute, highly contagious upper-respiratory infectious disease of chicken, which was first described in the USA in 1925 [7, 8] but some reports suggest that it may have existed earlier [9]. Presently, ILT has been reported in most of the countries worldwide and remains an important viral disease of poultry. The name ILT was adopted in the year 1931 by the special committee of poultry diseases of American Veterinary Medical Association, earlier it was referred as avian diphtheria [10].
Related respiratory and immunosuppressive diseases such as Mycoplasma gallisepticum, Mycoplasma synoviae, infectious coryza, mycotoxicosis, Chicken anaemia virus, Reticuloendotheliosis virus and Marek's disease possibly aggravate the impact of ILT in the field [11]. The trend of poultry farmers toward high flock density, shorter production cycles, raising of multi-age and multipurpose chicken within same geographical area, and improper vaccination and breach in the biosecurity have contributed to the increased ILT outbreaks many parts of the world [12, 13].

In recovered birds, Infectious laryngotracheitis virus can establish a carrier state. Like other herpes viruses, ILTV can also establish latency in the trigeminal ganglion of the central nervous system after 7 days of acute infection [14]. These viruses can be detected by tracheal organ culture and detection of ILTV DNA in the trigeminal ganglion by PCR of live recovered birds [4]. Certain factors such as stress, rehousing and onset of laying have also been shown to induce virus shedding from latent carrier birds [15].

Pathogenesis

The main transmission routes are ocular and respiratory. The virus is shed in respiratory secretions, so easily transmitted by inhalation or mechanically transmitted by people and fomites. Chickens are the primary host for infectious laryngotracheitis [4] but it may affect pheasants. Starlings, sparrows, crows, pigeons and ducks seem to be resistant to the virus [10]. Chickens of all ages are susceptible to the infection by the laryngotracheitis virus, but birds older than three weeks are more sensitive [16].

The initial replication of the virus takes place in the epithelium of the conjunctiva, respiratory sinuses, larynx and upper respiratory tract to a greater extent [17]. At the primary replication sites, the virus titre peaks between 4 and 6 days post-infection [18, 19]. The cytolytic affect of ILTV results in severe damage to tracheal and conjunctival epithelial lining leading to haemorrhages and other clinicopathological manifestations in birds [20, 21, 17].

Clinical signs

The severity of the disease is influenced by the virulence of the virus, stress conditions, co-infections with other pathogens, flock density, immune status of the flock and age of the bird [22]. The incubation period of the disease varies between 6 and 14 days [23, 24]. The clinical course of ILT varies from 11 days to 6 weeks depending on the form of the disease (mild or severe) [25]. The disease is characterized by peracute, acute and chronic forms.

In peracute form, there is rapid spread and high mortality. The birds die within 3 days of onset of disease. The clinical signs are characterized by dyspnea and gasping with an extension of the head and neck of the birds. There will be coughing, rattling, and gurgling sounds when the birds try to expectorate bloody mucus from trachea [26, 13]. The clotted blood can be seen in cages, feed turfs, walls and floor of the poultry houses [27].

Clinical signs associated with acute form of the disease include gasping, depression, nasal discharge and purulent conjunctivitis with frothy exudates in the inner canthus of the eye [9]. The morbidity may reach 100% and the mortality varies from 10 to 30%. Varying level of egg production is noticed in layer flocks, some flocks may experience the complete cessation of egg production, which they may recover to the normal level in due course of time [28, 29].

The clinical signs associated with less severe chronic forms of the disease include swelling of the infraorbital sinuses, closed eyes, persistent nasal discharge, mild tracheitis unthriftiness, coughing, moist rales, head shaking, squinting eyes, drop in egg production [30]. The mortality is usually less than 2% and morbidity is upto 5% in this form.

Gross lesions

The gross lesions may be found in conjunctiva, sinuses and upper respiratory tract and vary with the severity of the disease [31, 32]. In trachea, characteristic hemorrhages and mucus plugs are observed [27, 33, 34]. The involvement of lungs and air sacs in ILT are rare. However, congestion of the lungs and thickening of air sacs with caseous exudates in the lumen are sometimes seen [35]. Lesions such as muco-fibrino acute rhinitis and sinusitis, occlusion of paranasal sinuses by caseous exudate, facial swelling, and muco-fibrino tracheitis have been observed in concurrently infected cases [36]. Pneumonic changes of congestion, consolidation and red hepatisation were noticed in some of the severely affected birds [37].

Microscopic lesions

Microscopic changes in tracheal mucosa include loss of goblet cell, infiltration of mucosa with inflammatory cells, cell enlargement, lose of cilia, and become edematous. Multinucleated giant cells (syncytia) are formed and lymphocytes, histiocytes, and plasma cells migrate into the mucosa and submucosa after 2-3 days. Cell destruction and desquamation occurs later resulting in mucosal surface either covered by a thin layer of basal cells or lacking any epithelial covering. Due to severe epithelial destruction and desquamation with exposure and rupture of blood capillaries hemorrhage may occur in such cases [38].

Inclusion bodies generally are present only in the early stages of infection, they are found in epithelial cells by 3 days post infection mostly [26, 39, 40], but as a result of the necrosis and desquamation of epithelial cells, they start disappearing.

Diagnosis

Infectious laryngotracheitis in chicken can be diagnosed on the basis of clinical signs such as conjunctivitis, gasping, open mouth or extended head respiration, expectoration of bloody mucous, dyspnoea, and from gross lesions lesions such as catarrhal to hemorrhagic tracheitis, fibrinopurulent to caseous exudates or cheesy or caseous plugs in the larynx and trachea on necropsy. The suspected cases are then subjected to laboratory diagnosis by conventional and molecular diagnostic tests. In conventional methods, histopathology, virus isolation by embryonated chicken eggs and cell culture, immunofluorescence (IF), immunoperoxidase (IP) assay, and serology were done [41, 42, 26, 43, 44].

Humberd *et al*. [45] developed Infectious Laryngotracheitis Virus (ILTV) specific nested polymerase chain reaction (PCR) and tested its ability to detect ILTV DNA by performing nested PCR on formalin-fixed, paraffin-embedded tissues from 35 cases of respiratory disease. Of the 35 cases, 12 were considered ILT suspects clinically. Eleven cases were diagnosed as ILT, the remaining 24 were diagnosed as non specific tracheitis by histopathologic examination. Histopathologically positive samples were also confirmed by direct fluorescent antibody test and virus isolation. Of the 11 ILT-positive cases, 10 were positive by nested PCR in this case. In addition, ILTV DNA was also detected in 7 of the 24 samples diagnosed as NST upon histopathologic examination.

Timurkaan *et al*. [30] carried out study to describe gross, pathological and immunohistochemical findings in broilers inoculated with low virulent strain of Infectious Laryngotracheitis Virus (ILTV). They identified antigens of ILTV in laryngeal and tracheal cross sections between 3 and 9 days post infection in the infected chickens. Their study revealed that the antigen was mostly localised in the non ciliated epithelial cells of larynx and trachea.

Sellers *et al*. [33] utilized immunohistochemistry and a nested

infectious laryngotracheitis polymerase chain reaction to confirm the presence of Infectious Laryngotracheitis Virus (ILTV) nucleic acid in fixed tissues of birds exhibiting mild infectious laryngotracheitis. They also inoculated 2-wk-old specific-pathogen-free (SPF) birds with field material, which exhibited the mild signs observed in broilers in the field.

Callison *et al*. [46] described the development and validation of a real-time (ReTi) PCR assay using a Taqman® labeled probe for the detection and quantitation of infectious larygotracheitis virus (ILTV) in chickens. They collected a total of 246 tracheal swab samples collected from natural outbreaks of the disease which were tested by virus isolation and the ReTi ILTV assay.

Chacon *et al*. [47] diagnosed infectious laryngotracheitis in layer hens in a region in Brazil which experienced outbreak, characterized by respiratory signs, decrease in egg production and increased mortality. The disease was differentially diagnosed from other respiratory diseases by nested-PCR and virus isolation. Infectious Bronchitis virus was detected in one farm and Mycoplasma synoviae was detected in some farms.

Diallo *et al*. [48] diagnosed a naturally occurring dual infection of layer chickens with fowlpox virus and gallid herpesvirus 1 (Infectious Laryngotracheitis Virus) using a multidisciplinary approach including virus isolation, histopathology, electron microscopy and polymerase chain reaction (PCR). The histopathology of tracheas from dead birds revealed intra-cytoplasmic and intra-nuclear inclusions suggestive of poxvirus and herpes virus involvement which was further confirmed by electron microscopy and PCR.

Islam *et al*. [49] conducted research work for the isolation and characterization of infectious laryngotracheitis virus in layer chickens. The study was conducted on 25 field samples collected from suspected layer chicken of five commercial farms. The samples were cultivated into 10-12 days old embryonated chicken eggs through chorioallantoic membrane route for isolation of virus. The field viruses were characterized by physico-chemical properties, serological and pathogenicity testing.

Preis *et al*. [50] found pathological, immunohistochemical and molecular findings in commercial laying hens and in backyard chickens naturally infected with infectious laryngotracheitis virus. The disease was histopathologically diagnosed in commercial layers. Histopathologically, lesions were characterized by the formation of synctial cells with eosinophilic intra nuclear inclusion bodies in hyperplastic epithelium, followed by lympho-plasmacytic infiltrate in the lamina propria of the upper respiratory tract, primary and secondary bronchi, and conjunctiva. IHC showed 70% (21/30) positive signals in the larynx and trachea characterized by yellowish brown granular staining in the cytoplasm of synctial cells adhered to the mucosa or desquamated.

Sivaseelan *et al*. [37] evaluated the tissue tropism and pathobiology of Infectious Laryngotracheitis virus in natural cases of chickens. Symptoms manifested by affected birds and the gross lesions from post- mortem examination were recorded by them. The study showed that ILT virus, possesses greater affinity towards the middle portion of the trachea and conjunctiva, and lesser towards larynx and other portions of the trachea.

Couto *et al*. [36] described the natural concurrent infections associated with Infectious Laryngotracheitis in layer chickens. They subjected samples of nasal turbinates, sinuses, pharynx and trachea from 31 chickens to histopathological analysis, which showed 22.6% of chickens had lesions suggestive of co- infection, either by GaHV-1 or Mycoplasma. Through PCR analysis they found the presence of at least two respiratory pathogens in 61.2% of chickens.

Kaboudi *et al*. [51] used histopathological and molecular techniques to diagnose Infectious Laryngotracheitis in 48 layer and broiler flocks. Birds were showing respiratory signs such as dyspnoea, bloody mucus excretion and decrease in egg production. Lesions suggestive of ILT, such as epithelial necrosis, sero-fibrinous and sero- hemorrhagic exudates, synctia and intranuclear inclusion bodies were observed. ILTV virus was detected by conventional PCR, using specific primers for the gB gene of ILTV.

Prevention and Control

For intensive broiler production, the short growth cycle and high level of biosecurity measures on farms is recommended to reduce the need for prophylactic vaccination. Vaccination for ILT is not as successful as for other disease, but is an excellent preventive measure for use in outbreaks and in epidemic areas, if ILTV is diagnosed early in an outbreak, unaffected birds may be vaccinated, protecting them before they are exposed to the disease [12].

Several types of vaccines are available to prevent ILT. These vaccine types include vaccine of chicken embryo origin (CEO) and tissue culture origin (TCO). CEO is attenuated by successive passages in embryonated eggs and that can be applied in water, in eye drops, or with a spray [52, 53, 54]. TCO strain is attenuated by multiple passages in cell culture and is applied individually in eye drops [55, 56]. A new generation of vectorized vaccines has been developed recently using the fowlpox avipoxvirus (FPV) and the Meleagrid herpesvirus 1 of turkeys (HVT) [6, 12].

Treatment: To date, no drug has shown efficacy in reducing the severity of lesions or relieving symptoms of ILTV. Antibiotics have no effect against the virus, but may control possible secondary bacterial infection [10].

Eradication: Eradication of virus from intensive poultry production sites appears to be highly feasible due to several biologic and ecologic properties of the virus such as high degree of host-specificity of the virus, the relative fragility of ILTV infectivity outside the chicken, and antigenic stability of ILTV genome [57]. Also, the chicken is the primary host species as well as the reservoir host. As all ILTV strains are antigenically homogeneous a single LTV vaccine produces cross-protective immunity for all ILTV strains. So disease can be eradicated.

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