



Review article

Newcastle disease virus in poultry animals

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ABSTRACT

Newcastle disease virus (family *Paramyxoviridae*; genus *Avulavirus*), poultry disease is extensively spread in Asia, Africa, USA and Canada. In literature, strains of Newcastle disease virus are worldwide reported and causing a huge loss to the poultry industries. The present review discusses about Newcastle disease virus and mentioning about its clinical trial-based studies and also discussed about surveillance-based studies and vaccination. In this literature there should be more focus area on the techniques to make a vaccination successful and make any permanent cure for it. Also, we have checked the mortality rate of different states so that we should perform our techniques in those countries. In addition, this literature includes bioinformatics approach study various strains of Newcastle disease virus.

Keywords: Newcastle disease virus, *Paramyxoviridae*, *Avulavirus*, surveillance, vaccination.

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INTRODUCTION

One of the most severe disease is reported in birds and also reported in poultry animals i.e. Newcastle disease virus. This is extremely contagious virus and is mainly caused through virulent strains of avian paramyxovirus type 1. In literature, this disease is mainly reported and appeared in these forms (i.e. lentogenic, mild; mesogenic, moderate and velogenic, very virulent) [1, 2]. Out of three forms, lentogenic strains are commonly reported and may cause severe disease outbreaks. Now, Newcastle disease virus may be considered as pathogenic disease and is totally similar to avian influenza in terms of clinical diagnosis and this disease is included in the list of World Organization for Animal Health (OIE) Terrestrial Animal Health Code. In addition, Newcastle disease virus also called as minor zoonosis (disease of animals that infect humans) and cause diseases in human are also reported i.e. conjunctivitis but the condition of disease in human is self-limiting [3]. In general, clinical signs may totally vary from one virus strain to another and it is entirely dependent on aspects such as strain of the virus, specie of infected birds and its age, susceptibility to other organisms, immune status etc. some strains may directly attack on nervous, respiratory and digestive system and its major signs related to disease are also reported as mentioned in the literature [4, 5].

The single-stranded, non-segmented enveloped RNA virus: Newcastle disease virus belongs to family *Paramyxoviridae*. It is a widespread and deadly virus that affects more than 250 bird species

throughout the world. So, this is one of the most devastating diseases of poultry animals which is infected through virulent strains of APMV-1 and now it is also reported to the OIE [6, 7]. In this regard, there is an urgent needed of vaccination for these poultry species for controlling the severity of Newcastle disease virus. One of the trials related to Newcastle disease virus is conducted in United States of America (Saint Louis, Missouri and Buffalo, New York with clinical trial no. NCT04613492 completed in year 2025) and Mexico (worked in Live recombinant Newcastle disease virus based vaccine against COVID-19 with clinical trial no. NCT04871737 completed in year 2022).

In the literature, Newcastle disease virus was affected in all age groups of birds and highest incident rate was observed in winter season followed by rainy and summer season. The major symptoms or clinical signs were observed i.e. depression, head edema, paralysis, sneezing, nasal discharge etc. In some cases, there is sudden decline in egg production and few of them dead without any clinical signs due to Newcastle disease virus [8, 9]. In India, first case of Newcastle disease virus was revealed and described in 1928 and now this disease is endemic especially for India. In 1993, outbreaks of Newcastle disease (six isolates) were also reported in many farms of Tamil Nadu, India. This disease is mainly spread through contaminated water and air and also spread through sick bird products (e.g. feathers, eggs, intestines etc.). Lot of efforts were taken

by the farmers in order to control the burden of disease i.e. proper hygiene (kept clean; chicken droppings are swept; apply a disinfectant regularly), housing (ventilated house; avoid overcrowding; easy washing and sweeping); isolation (keep animals in a controlled environment) etc ^[10, 11].

Newcastle disease virus genome is mainly composed of transcriptional units (6 no.) which encodes several viral proteins i.e. nucleocapsid protein (NP), phosphoprotein (P), matrix (M) & fusion (F) protein, hemagglutinin-neuraminidase (HN) protein and large polymerase (L) protein ^[12]. In addition, two accessory proteins (V and W) are mainly produced through RNA editing of the P gene. In general, Newcastle disease virus replicates (*in vivo*) as mentioned in the literature and stimulate mucosal immunity. So, Newcastle disease virus may be considered as one of the most superlative vectors where its genome (~15 kb) is manipulated and may reproduce the uninterrupted genome into a transcriptional plasmid for molecular engineering. So, enormous production of virus especially Newcastle disease virus yield is revealed and described in case of chicken embryos ^[13, 14].

Although Newcastle disease virus mainly affected on domestic poultry animals but showed some minor threat to humans especially reported some rare infections i.e. conjunctivitis and mild flu-like symptoms. In preclinical studies related to animal model studies where Newcastle disease virus may consider them as an effective oncolytic agent (e.g. cancer) and also showing its ability to replicate more effectively in human cancer cells as compared to nonneoplastic cells ^[15]. Some of the clinical studies data related to Newcastle disease virus as mentioned below-

MEDI 9253 (recombinant Newcastle disease virus which encoding interleukin-12), developed by AstraZeneca especially for the treatment of solid tumors. These studies were now in Phase I Clinical studies (no. D7880C00001) trial in order to evaluate its safety, tolerability, pharmacodynamics, and determining its efficacy rate of MEDI9253 in combination with durvalumab (FDA approved, immunotherapeutic agent) applied in adult participants with selective type of advanced/metastatic solid tumors. These studies were doing in United States of America and completed in year 2025.

Another studies were conducted related to live recombinant Newcastle disease virus based Vaccine against COVID-19 (SARS-CoV-2 Infection). These studies were conducted under Phase I trial and using administration of a recombinant vaccine (3 different doses and two administration routes i.e. Intranasal and Intramuscular Route) against SARS-CoV-2 based on a viral vector (Newcastle Disease virus) in human healthy volunteers in Mexico City. These studies were completed in June 2022.

One of the studies was withdrawn from human clinical

trials conducted in March 2006 and completed in the same year (June 2006). In this trial, two major sub-strains of NDV (oncolytic and another non-oncolytic) were used in Hadassah Medical Organization, Jerusalem, Israel. In Oncolytic NDV (MTH-68H) preferentially replicates in cancer cells and therefore, intravenously administration or by injection directly into an afferent artery may result in direct lysis of tumour cells. These studies were conducted and applied in patients with different types of cancer worldwide. These studies were showing effective results in preclinical (animal model) studies and Phase I trial. But in phase 2 trial, patient number exceeds with different types of cancer, no cure can be provided by this treatment.

The preclinical studies reported the different strains of Newcastle disease virus worldwide that displayed tumouricidal activity against different types of cancer cells in animal model studies. Among these, mechanism of one of the strains reported in Malaysia (i.e. NDV AF2240) is still unclear. To see if cytokine-related apoptosis-inducing NDV AF2240 may be used to treat breast cancer, researchers looked into it ^[16].

Surveillance based studies were conducted in order to observe and quantified the bird's mortality rate. As per the literature, frequent mortality rate of birds (e.g. peafowls) was recorded (year 2009-2011) and documented in these regions of India (i.e. Haryana, Delhi and Uttar Pradesh). As per the survey, it may be revealed that birds of inconsistent age groups (mortality rate) were revealed and showed drastic symptoms as mentioned in the literature such as wing immobility, circling and alteration in respiratory distress. So, these clinical evidences and indicators totally resembled across these geographical orientations of India. In this regard, deceased birds were necropsied and tissue specimens from visceral organs (such as the lungs, trachea, brain, intestines, spleen, and bursa of Fabricius) were taken and dissolved in glycerol saline for viral isolation and genetic analysis. In literature, pooled samples (lungs, trachea, swabs etc.) of distinct tissues specimen were tested through RT-PCR. In contrast, isolation of virus from samples using standard protocols ^[17, 18].

Samples were prepared in the form of suspension (inoculated into embryonated chicken eggs through the allantoic route) and these samples were dismissed in phosphate buffered saline (PBS, pH 7.2). Observation studies should be conducted through candling method where we determining the allantoic fluids through haemagglutination activity ^[17, 18]. Finally, determination of Newcastle disease virus within the allantoic fluids was also confirmed through haemagglutination inhibition test and RT-PCR ^[19, 20].

EFFECT OF VACCINATION ON NEWCASTLE VIRUS

The major approach is to control or reduce the burden of disease through vaccination and providing maternally acquired antibodies to the descendants in order to prevent the transmission rate

particularly vertical ones and also safeguard the breeder congregation from infection. Recently, none of the vaccines provide hundred percent protections against this Newcastle disease virus. The major reason of failure (in case of genetic and antigenic dissimilarities) is reported in field isolates but some companies may develop some vaccines (autogenously) which is mainly generated through ubiquitous virus isolates but these are less productive in case of memory (B and T cell) retort, mucosal immunity, and extended time scale immunity. Hence, immunological strategies were created to generate newer type of vaccines which are highly demanded to provide a wider spectrum of protection against these diseases. So, viral vectored vaccines should be considered as one of the most alternate approach to control the burden of Newcastle disease virus infection.

In contrast, attenuated poultry vaccines have been developed through genetically modified based technology pertaining to use in the form of vaccine vectors for controlling the burden of poultry diseases. Among these viruses, Newcastle disease virus may be considered as one of the most appealing vaccine vector for animal diseases. According to the literature, genome of Newcastle disease virus can be exploited through reverse genetics machinery pertaining to develop vaccines (live attenuated, bivalent) in case of economically supreme poultry diseases [21, 22]. Regarding vaccination, recombinant viral vaccine may be giving more importance or attention by various researchers as compared to conventional vaccine because of inducing both humoral and cell mediated immune responses. This type of immunity is required for these poultry diseases which is responsible for causing major losses to the poultry industry [23].

BIOINFORMATICS STUDIES (NEWCASTLE DISEASE VIRUS)

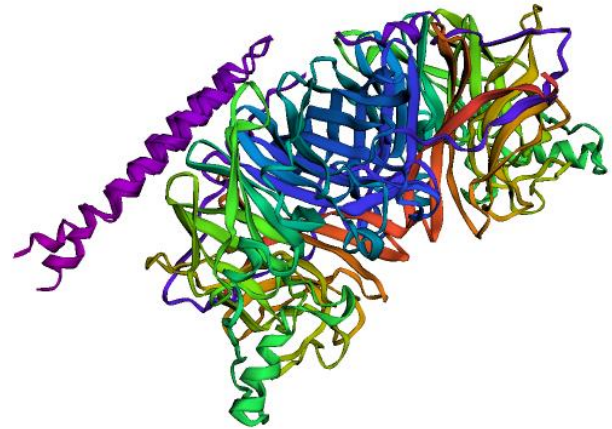
Bioinformatics is the application of tools of computation and analysis to capture and interpret biological data .it is a necessity in management of data in modern biology and medicine. The prime tools of a used by bioinformaticians worldwide are computer software programs and the internet. Bioinformatics is an evolving discipline, and expert bioinformaticians now use complex software programs for retrieving, sorting out, analyzing, predicting, and storing DNA and protein sequence data [20-23]. Traditional and modern approach of bioinformatics includes the study of its phylogeny, crystal models, genomics, proteomics etc. This section includes the phylogenetic tree and distance among its clades, crystal models and various models used study of NDV. The crystal model as shown in

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Fig 1 which is derived via python code. The pictorial data of virus gives brief about its structure. The aim to retrieve phylogenetic tree is to understand the evolutionary relationships among organisms.

Figure1: Structure detection of Newcastle disease virus



by tool used in the bioinformatics study. This picture depicts the actual structure of virus.

CONCLUSION

Since last many years' poultry farming developed with a very high rate and shows their side effects by causing infectious disease such as NDV. One of the poultry diseases (i.e. NDV) where this disease causing huge loss of money in terms of economic rate. Initially the huge failure is reported in field isolates but there are many companies who develops several kinds of vaccines and tend to control the transmission of disease due to the cause of virus which is mainly generated through ubiquitous virus isolates but these are less productive in case of memory (B and T cell) retort, mucosal immunity, and extended time scale immunity. In this regard, deceased birds were necropsied and tissue specimens from visceral organs were taken for viral isolation and genetic analysis. As per the survey it has been found that if these kinds of diseases can't be controlled via vaccination or any other method so it will definitely cause a pandemic in any country and that should be uncontrollable. The current research field setting is further complicated by the introduction of antigenic variations and highly virulent strains of NDV. Nowadays there is no permanent treatment to cure this kind of disease but many treatments should be going on to make it successful.

CONFLICTS OF INTEREST

The authors have no conflicts of interest to declare.

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