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https://dx.doi.org/10.4314/nvj.v45i1.4 **ORIGINAL ARTICLE**

Rabbitry and Emerging Rabbit Haemorrhagic Disease Virus in Nigeria: A Concern for Food Safety and Security

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SUMMARY

For many decades, small-scale livestock, including rabbit production, has been a veritable pro-poor poverty alleviation venture in Africa. With the rising population and increasing demand for food, the need to introduce and expand small-scale rabbit farms for long-term sustainability cannot be over-emphasized. While increasing the production and commercialization of domestic rabbit production is desirable, the intensification of livestock also comes with some animal health problems. One of these is the emergence of Rabbit Haemorrhagic Disease (RHD) caused by Rabbit Haemorrhagic Disease Virus (RHDV). The virus causes sudden death in rabbits, and does not yet pose any public health risk. Symptoms of RHD may include: loss of appetite, lethargy, high fever, seizures, jaundice, bleeding from natural orifices, difficulty in breathing and sudden death. The first known outbreak of RHD in Nigeria was reported in September 2020 at rabbit farms in Kwara and Oyo States,in Nigeria. Despite several intervention strategies, the disease has continued to spread across the country. In this review, we search literature on the current state and knowledge of RHD as it affects rabbits and the economic impact on livelihood and animal health implication of this emerging viral disease on rabbit farms in Nigeria.

Key words: Rabbitry, Haemorrhagic Disease, Food safety, Livelihood, Nigeria.

INTRODUCTION

In a developing country like Nigeria, population growth is expeditiously on the increase. This calls for increase in the production of livestock to meet the demand for food by the populace (Mailafia *et al*., 2010). Rabbit production can contribute to available protein to feed the populace and income for the farmers. Rabbitry can be a lucrative business if managed properly (Abu *et al*., 2008). Rabbit farming does not require a lot of capital and space to set up, and is well adapted to domestic rearing. Recently, numerous micro-organisms have been recognized as the cause of emerging diseases in lagomorphs. The most current emerging disease of rabbit is RHD caused by the RHDV2, a new variant that causes similar fatal viral hepatitis to classical RHDV strains (Gleeson and Petritz, 2020).

Rabbit haemorrhagic disease virus (RHDV) is a lagovirus with mortality potential of 80–90% in farmed and wild rabbits. The disease is a highly contagious, acute and fulminating, it has been reported in wild and domesticated European rabbits (*Oryctolagus cuniculus*) (Abrantes *et al*., 2012). RHDV is a single-stranded positive-sense RNA virus that belongs to the family *Caliciviridae*, genus *Lagovirus* (Abrantes *et al*., 2020). RHDV was first observed in China in 1984, but was thought to have originated in Europe, and has now have been confirmed in Europe, the Mediterranean, Africa, Asia, North America. Outbreak was recently reported in southwestern Nigeria. The first laboratory-confirmed RHDV outbreak that was reported to the Office International des Epizooties (OIE) from Nigeria was recorded on the 13th of October 2020 (OIE, 2020).

Currently, (RHDV2) GI.2 strains are present in several North and Sub-Saharan African countries. Considerable economic losses due to (RHDV) GI.1 have been observed in industrial and traditional African rabbitries (Ben Chehida *et al*., 2021). Outbreaks of RHD have only been recorded in some African countries such as Egypt, (Ghanem and Ismail 1992; Magouz *et al*., 2019), Tunisia (Bouslama *et al*., 1996), Morocco (Lopes *et al*., 2019) and the Republic of Benin (Kpodekon and Alogninouwa 1998; OIE, 2015). In Tunisia, it was first detected in Southern Tunisia in 1989, but was not confirmed until 1992 (Bouslama *et al*., 1996). The GI.2 was noticed for the first time in Africa in 2015, with the first outbreak in Kairouan, Tunisia. Later, it was followed by outbreaks in industrial rabbit farms in different places, causing considerable economic distress (Chakroun *et al*., 2015). In the same year, a GI.2 outbreak was reported in Benin (OIE, 2021) and, in 2016, multiple outbreaks were recorded in Côte d'Ivoire (OIE, 2021). In 2017, Morocco reported its first outbreak (Lopes *et al*., 2019), and Egypt in 2018 (Erfan *et al*., 2020). The outbreak was first reported in 2020 in Nigeria (Happi *et al*., 2020; OIE, 2021; Daodu *et al*., 2021), Ghana (Ambagala *et al*., 2021) and Senegal (OIE, 2021). Continuous monitoring and surveillance of Rabbit Haemorrhagic Disease (RHD) will reduce the likely impact of the disease on animal health, livestock production and the economy.

RABBIT FARMING FOR FOOD AND LIVELIHOOD

Rabbit farming has a minimum economic risk and is less expensive when compared with poultry or cattle farming. It requires minimum space, which is more suitable to the rural agro-ecology of Nigeria (Amin *et al*., 2011). It is a veritable way of alleviating animal protein deficiency in Nigeria (Ajala and Balogun, 2004). Rabbit meat has high

nutritional value, but in developed countries, despite its outstanding dietetic properties, it continues to be considered for rural usage or limited to ethnic groups (Dalle Zotte, 2014).

Across the globe, China is the major rabbit meat producer with 735,021 tonnes/year, followed by Italy (262,436), Spain (67,775), Egypt (56,338) and France (52,955) tonnes/year (FAOSTAT, 2012). Currently, rabbits are systematically raised on a large scale, with the global rabbit meat production reaching 1.8 million metric tonnes per year. This production is concentrated, in decreasing order, in Asia (48.8%), Europe (28.4%), Americas (18.1%), and Africa (4.7%) (FAOSTAT, 2012).

Rabbit Farming offers numerous advantages, which are derived from its attributes. These advantages make rabbit farming profitable for farmers. They have a very short gestation period of 27-33 days and can re-breed immediately after littering such that the does (female rabbits), if well managed under simple conditions, can produce at least 5litters/year with an average of 6 kids/litter, that is 30kids/doe/year (Odinwa *et al*., 2016). Rabbit farmers have various reasons for keeping rabbits, some for income, others consumption while many more for hobby or pet (Osei *et al*., 2012; Serem *et al*., 2013). Baruwa (2014) reported that the purpose of rabbit production in Nigeria ranges from 40% consumption and 60% for income generation. However, domestic consumption was more important for keeping rabbits than income generation in Nigeria (Abu *et al*., 2008; Oseni *et al*., 2008). The proportion of individuals rearing rabbits as a hobby was lower than those doing so in southern Ghana (Osei *et al*., 2012). One of the major problems of rabbit production in Nigeria is high cost of concentrates, relatively smaller weight gain during the dry season, non-readily available market as most Nigerians lack inadequate knowledge on the advantages of consuming rabbit meat (Nworgu, 2006). A renewed interest in the production of rabbits by utilizing cheap and unconventional feedstuffs such as cassava peel, maize cob and groundnut shell will result in increasing meat production in Nigeria (Owen and Amakiri, 2010). Moreki and Seabo (2012) suggested that in Botswana, rabbits are kept mainly in backyard, indicating that intensive systems of production have not yet been embraced. Rabbits are kept mainly under intensive production system in Ghana, usually on backyard and non-commercial basis for home consumption in the rural areas (Osei *et al*., 2019). The development of intensive rabbit rearing in Egypt is considered due to the hot weather, especially where there are no opposing factors of social, cultural or religious nature regarding the breeding technology (Ali and Abdel-Wareth, 2014). In Botswana, rabbits are usually fed mainly on garden and kitchen waste which may or may not be supplemented with compounded diets (Moreki and Seabo, 2012). Majority of the farmers (57.2%) fed their rabbits on locally available forages with minimal concentrate supplementation in Kenya (Serem *et al*., 2013). While feeding is a major husbandry input in rabbit production, infectious diseases are the major challenges for a successful operation either for livelihood or as a hobby.

RABBITRY AND INFECTIOUS DISEASES CHALLENGE

The rabbit breeding industry has witnessed a considerable increase in rabbit meat production despite the common occurrence of various infectious disease like viral, bacterial and

parasitic. Viral infections seem to have the highest impact on their health (Kwit *et al*., 2019).

Rabbits are infected with various infectious diseases such as protozoan disease (coccidiosis, Encephalitozoon cuniculi, Toxoplasmosis); mycotic (Dermatophytosis, Aspergillosis); viral (myxomatosis, papillomatosis coronavirus); parasitic : ectoparasites (fleas, lice, mites, warble flies), endoparasitic (intestinal worms, tapeworm) and bacterial (Pasteurellosis, Staphylococcus aureus, paratuberculosis, pseudotuberculosis, listeriosis, lyme disease) (Harcourt-Brown, 2002). Mycobacteriosis in rabbits is rare; however, infections with both non-tuberculosis and tuberculosis Mycobacterium have been reported in both wild and domestic rabbits (Wu and Holland 2015). Hepatitis E is an emerging zoonotic disease in humans, and certain strains have a high prevalence in wild, farmed, and laboratory rabbits (Purdy et al, 2017). A novel picornavirus has been detected in fecal samples of asymptomatic rabbits, demonstrating that they may act as hosts of kobuviruses (Gleeson and Petritz, 2020). A novel bocaparvovirus was recently identified in rabbits with and without diarrhea, which expands the number of parvoviruses detected in this order than can contribute to clinical gastrointestinal disease (Gleeson and Petritz, 2020).

Currently, one of the viral diseases with the highest impact on rabbits is the RHD also known as Rabbit plague or “bunny ebola”. The disease is caused by the etiological agent which belongs to the family caliciviruses, rabbit haemorrhagic disease virus (RHDV), a non-enveloped single stranded positive sense RNA virus, belonging to the genus *lagovirus* within the family *Caliciviridae*.

RHDV like other caliciviruses forms 28–32 nm diameter, non-enveloped, icosahedral virus particles that harbor a 7.4 kb positive or sense oriented single-stranded RNA genome that encodes a 257 kDa polyprotein. Its genome is a linear single-stranded (SS) RNA of 7437 nucleotides and the capsid is built from a single structural protein VP60 (Hukowska-Szematowicz *et al*., 2012).

RHDV is environmentally stable, highly infectious, and transmissible by close contact or by contact with fomites such as contaminated fur, clothing, or cages. Indirect arthropod vectors, including blow flies or flesh flies, have also been implicated in the spread of RHDV (McIntosh *et al*., 2007).

The disease is characterized by pale liver with areas of necrosis, multifocal petechial hemorrhages in multiple organs which may be the reason for describing it as rabbit Ebola. Pathological lesions include: congested and edematous lungs, pulmonary edema with tracheal foam, splenomegaly, and hemorrhagic lesions affecting the liver and lung. Clinical signs appear after an incubation period of 1 to 3 days and typically include pyrexia (> 40°C), anorexia, dullness, prostration, nervous signs, vocalization, dyspnea, convulsion, bloody nasal discharge, mucus in feces, and paralysis and cyanosis of the mucous membranes. Death typically occurs within 12 to 36 hours after the onset of fever (Embury-Hyatt *et al*., 2012; Ambagala *et al*., 2021). Introduction and persistence of RHD, an infectious disease with high mortality rate is a threat to food safety and security in underdeveloped countries like Nigeria.

EPIDEMIOLOGY OF RABBIT HAEMORRHAGIC DISEASE VIRUS

A detailed knowledge of the epidemiology of any disease is key to the management of the disease. RHDV is specific for European rabbits (*Oryctolagus cuniculus*), while RHDV2 has a broader host range, affecting both European rabbits and some species of hares (*Lepus* species). Probably all ages are susceptible to infection but young rabbits less than 4 weeks of age rarely develop lethal disease. This age-based protection is lost between 4 and 12 weeks of age (Robison *et al*., 2002). There is no gender predisposition. Young rabbits may be more susceptible to an emergent virulent variant of Rabbit Calicivirus (RCV) (Dalton *et al*., 2012). According to the OIE in 2021, the transmission of RHD may occur through direct contact with infected animals through the oral, nasal or conjunctival routes. Exposure to an infected carcass or hair of an infected animal and indirectly through fomites, including contaminated food, bedding and water. Mechanical transmission through flies and other insects can also occur. Also, importation of infected rabbit meat serves as a means of transmission. RHD, caused by classic RHDVa, has high morbidity of up to 100% and mortality of 70% to 90% in adult rabbits. Young rabbits between 6 to 8 weeks old are less likely to be infected, and kits younger than 30 days old are not infected (Percy *et al*., 2007; Kerr *et al*., 2013; OIE, 2019). The newly emerged RHDV2 causes disease and death in animals as young as 15 to 20 days old, which has not previously been seen in RHD outbreaks and represent a major clinical difference between RHDV1 and RHDV2. RHDV2 seems to have a more variable mortality of (5% to 70%) and has been confirmed as a cause of fatal disease in rabbits previously vaccinated against RHDV1, demonstrating the distinct antigenic profiles between the two viruses. Mortality rates from early outbreaks of RHDV2 averaged 20-30%, leading to be classification as a mildly pathogenic calicivirus (Capucci, 2017).

Within a proposed new classification system, all lagoviruses are reclassified into a single species, *Lagovirus europaeus*, and the causative viruses of RHD are all grouped within genogroup I (*L. europaeus* GI). *Lagovirus europaeus* GI.1 (or RHDV/RHDVa) viruses are only pathogenic for adults, while *L. europaeus* GI.2 (RHDV2 or RHDVb), causes clinical disease in both adults and kittens. (Neimanis *et al*., 2018).

Outbreaks can be seasonal, often occurring during cooler months when the virus is more stable in the environment, but they can occur at any time of the year. The virus can be found mainly in the liver which has the highest virus titre, followed by the spleen and serum. Urine, faeces and respiratory secretions, are believed to contain the virus. Rabbit meat contains virus due to its high blood supply (Abrantes et al., 2012; OIE, 2019).

According to Nigerian news report https://www.pmnewsnigeria.com/2020/18/rhd-virus-hits-nigeria-government-urged-on-actions, the virus was imported from the neighboring Republic of Benin to Nigeria in 2013. “Then, in October 2019 another outbreak was recorded when infected rabbits were again imported from the Republic of Benin. The disease was contained in the affected farms by destroying the rabbits and complete fumigation of the farms”. In June 2020, another outbreak of RHD was recorded in Nigeria, which has already killed over 5,000 rabbits across the country. Even though these reports may suggest RHD, it was not investigated, diagnosed and reported to OIE. However, RHD was first reported in 2020 in Nigeria based on the description of the case in Kwara State (Daodu *et al*., 2021). Official disease report to OIE was based on confirmatory diagnosis of cases from Ibadan, Oyo State of the same epidemiological incursion to Nigeria (OIE, 2020).

CLINICAL AND LABORATORY DIAGNOSIS OF RABBIT HAEMORRHAGIC DISEASE VIRUS

RHDV is characterized by sudden death in

apparently health rabbits, and in-contact rabbits. Affected rabbit, may die in one to three days, sometimes clinical signs are longer in the peracute form of RHD. The acute form, initially displays signs of malaise and rabbits die within 12 to 36 hours from the onset of pyrexia (temperatures above 40.1°C). Depression, anorexia, lethargy and general malaise are seen this form. Other possible signs include: dyspnea, cyanosis, congestion of the palpebral conjunctiva and circulatory shock with severe hypotension, ataxia, recumbence, paddling, paralysis, opisthotonos, convulsions and vocalization: described as crying or squealing/screaming.

In the subacute to chronic form, affected animals show a protracted clinical disease with severe jaundice, anorexia and lethargy. Death, if it occurs, usually happens one to two weeks after the onset of clinical signs, and is generally a result of liver dysfunction, lethargy, anorexia, weight loss and severe jaundice. In some animals concurrent underlying diseases such as rhinitis may become clinical. Surviving animals shed the virus for a protracted period.

Subclinical form, a proportion of infected animals remain subclinical and may shed virus for up to two months (Rocchi and Dagleish, 2018).

Pathologically, the infection is characterized by necrotizing hepatitis, with gross morphological impacts on liver and spleen, hemorrhage in other tissues, and occasionally jaundice (icterus). The distinguishing diagnostic feature is massive hepatic necrosis report on RHDV2 for North American lagomorphs that massive hepatocellular dissociation and necrosis or apoptosis, and pulmonary congestion, epistaxis, edema in the lung, hemorrhage in the lung and acute renal tubular injury. (Lankton *et al*., 2021).

The virus has not been successfully grown *in vitro;* however, the diagnosis can be confirmed by negative-contrast electron microscopy of liver tissue. Specific antibodies can be detected by ELISA or by hemagglutination inhibition (Nowland *et al*., 2015). Rabbit hemorrhagic disease virus has not yet to be grown in cell culture, but high concentrations of the virus occur in tissues of infected rabbits and easily can be detected by immunofluorescence or immunohistochemical staining with specific antibodies. Antigens from infected tissue or from capsid protein expressed *in vitro* can be used to detect antibodies from surviving animals, using ELISA. Some strains of rabbit hemorrhagic disease virus hemagglutinate human erythrocytes, a property that can be used for a simple antibody detection test. RT-PCR assays for the detection of viral nucleic acid are routinely available, it is the most common diagnostic assay for RHDV (Balasuriya *et al*., 2017).

Histopathological examination shows coagulative necrosis of hepatocytes on the periphery of lobules, nephrosis, disseminated intravascular coagulation (DIC) with thrombi, particularly in small renal and large pulmonary blood vessels. In rabbits that survive beyond acute infection, signs of liver regeneration may be present (e.g., connective tissue and bile duct proliferation; large, pale-staining binucleate hepatocytes) (Mayer *et al*., 2013).

CONTROL AND PREVENTION OF RABBIT HAEMORRHAGIC DISEASE (RHD)

Disease control in rabbit relies mainly on vaccination and biosecurity measures. Such measures are difficult to implement in wild populations of rabbits (Abrantes *et al*., 2012). A quick response is vital for containing outbreaks of RHD in disease-free regions. Veterinarians who encounter or suspect rabbit hemorrhagic disease or European brown hare syndrome should follow their national and local guidelines for disease reporting. Non-infected countries may impose restrictions on the importation of live lagomorphs, meat and other animal products (e.g., Angora wool) from endemic areas (CFSPH, 2020). All rabbit colonies with this disease should be

quarantined and depopulated, and the environment thoroughly cleansed and disinfected (Nowland *et al*., 2015).

Vaccines are available for RHDV, and they are made from virulent virus grown in rabbits and inactivated. The recently characterized nonpathogenic form of RHDV could be a suitable live vaccine if cultivation problems can be solved. Recently, recombinant virus-like particles (VLPs) have been developed for RHDV and are effective immunogens (Carter *et al*., 1998).

Vaccination with an adjuvanted killed vaccine derived from infected rabbit liver is thought to be effective (Deng *et al*., 2019). Manufacturer recommendations for vaccination should always be followed. A single shot is generally given at 10 to 12 weeks, along with an annual booster. Earlier vaccination may be necessary in some circumstances, but maternal immunity may interfere, and a second dose would be advisable. Antigenic variants of RHD virus can overcome vaccination (Mayer *et al*., 2013).

CONCLUSION AND RECOMMENDATION

RHD is currently causing a lot of devastation to small scale farmers making livelihood from rabbitry in Nigeria. Hence, it is important to educate farmers on the disease and encourage them to report any suspicion or outbreaks to relevant animal health authority. Coordinated surveillance should be carried out by espousing protocols of detection and management of viruses for containment and control of the disease through biosecurity. Government should find a way to compensate farmers as in the case of Highly Pathogenic Avian Influenza (HPAI). Further research and molecular characterization of RHDV to identify the strains of the virus in Nigeria for possible vaccine production is a long-term measure for the control of the disease in Nigeria and the sub-regions.

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