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Original Article *Virology*

First Rabbit Haemorrhagic Disease outbreak in Nigeria: Implications for the growing rabbit production industry

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ABSTRACT

The first outbreak of rabbit haemorrhagic disease (RHD) in Nigeria was reported in 2020 after over three decades of its existence in several parts of the world. In this study, we traced the timeline of the 2020 outbreaks of RHD in Nigeria, assessed the knowledge and practices of farmers about RHD and other infectious diseases of rabbits. A structured questionnaire was administered using Google Forms shared through the rabbit farmers' social media groups and other professional livestock platforms. Responses were obtained from 114 rabbitries across 15 States in Nigeria. Our findings revealed that the 2020 RHDV outbreak started in February, though its earlier introduction into Nigeria is possible. The responses indicated that 85.6% (3007/3514) of the rabbit population in Kwara, Ogun, Oyo and Osun States was lost to RHD between February - November 2020. The cases were confirmed as RHD based on clinical signs, necropsy findings and or reverse transcriptase-polymerase chain reaction results. The major clinical signs observed include sudden death (89.6%), uncoordinated movement (31.3%), paralysis (27.1%), epistaxis (22.9%) and melena (2.8%). Additionally, some (27.1%) of the farmers reported they suspected that RHD was introduced to their farm mainly 'after a co-farmer visited the rabbitry', 'after the introduction of new rabbit stock' (20.8%), and 'after a visit to another rabbitry' (12.5%). Our findings indicated snuffles, myxomatosis, coccidiosis, helminthiasis, mange, hairball, bloat, uterine tumours, overgrown teeth and ear canker as the commonest disease conditions encountered. Continuous surveillance and maintenance of an active reporting system for known and novel/emerging rabbit diseases in Nigeria are imperative.

Keywords: RHDV outbreak, rabbit diseases, massive mortality, Nigeria

1. Introduction

Rabbit haemorrhagic disease (RHD) is caused by the RHD virus (RHDV), which is a non-enveloped virus with a linear, positive sense ssRNA genome. It is a member of the genus *Lagovirus* of the family *Caliciviridae* [1]. The disease was first noticed in the Jiangsu Province of the People's Republic of China in 1984 among Angora breed of rabbit imported from Germany [2]. It was subsequently reported in Korea (1987), Italy (1989), Spain (1988), Portugal (1989) and later became endemic in Europe [3,4]. In the Americas, Mexico was the first country to report RHD in 1988 [5], while it was first reported in Africa in Egypt [6]. Among infectious diseases affecting rabbits, RHD is highly contagious and capable of being spread by contact with infected animals and excretion, fomites, fur and insects (fleas and mosquitoes) [7,8,9,10,11]. Importation of infected rabbit meat has also been identified as a means of the introduction of RHD to naïve geographical locations [12]. The disease is notifiable to the World Organization for Animal Health [13].

Four clinical forms of RHD exist: the peracute form involves sudden death of the animal without premonitory signs, while anorexia, apathy, palpebral conjunctival congestion and neurologic dysfunction (opisthotonus, excitement, paralysis and ataxia) are observed in the acute form. In addition, occasional respiratory abnormalities such as dyspnoea, tracheitis, cyanosis with lacrimation, ocular haemorrhages and epistaxis (foamy) could be observed [7,11,14]. The subacute form is known to elicit milder clinical signs, and affected rabbits often recover with the development of neutralizing antibodies [15], while the chronic form involves generalised icterus with anorexia, lethargy and possibly death 1-2 weeks later [11,16].

Disseminated intravascular coagulation resulting from haemorrhages and congestion of several organs has been described as the cause of death in RHDV-infected rabbits [17]. While early diagnosis of RHDV is crucial to preventing spread within rabbit populations, the unavailability of an appropriate cell culture system for the growth of the virus limits diagnostic options. Diagnosis is, therefore, largely

dependent on clinical signs, necropsy findings, haemagglutination test, competitive enzyme-linked immunosorbent assay and reverse transcriptase-polymerase chain reaction (RT-PCR) [18,19].

Rabbit haemorrhagic disease was first reported in Nigeria between June and September 2020 during an outbreak of haemorrhagic disease among domesticated rabbits in Kwara State [19]. Prior to the outbreak in Nigeria, the only West African countries that had reported RHD were the Republic of Benin, which shares a land border with Nigeria and where the disease was serologically detected [20,21], and Cote d'Ivoire where fatalities were recorded in both rabbits and hares [22]. Rabbit haemorrhagic disease has also been reported in the North African countries of Egypt, Tunisia and Morocco [6,23,24,25].

While it is difficult to trace the beginning of the Nigerian RHD outbreak from individual rabbit farmers, there is a paucity of data on the prevailing infectious diseases of rabbits in the country. Thus, this study was aimed at tracing the timeline of the RHD outbreak in Nigeria and how it spread. The knowledge and experience of rabbit farmers were also assessed.

2. Materials and Methods

2.1. *Study location*

The study was conducted in Nigeria immediately after the first Rabbit haemorrhagic outbreak in Nigeria in 2020.

2.2. *Questionnaire administration*

A pre-tested structured questionnaire was administered through a created Google Form. The link to the form was shared through the rabbit farmers' social media groups, academic and other professional livestock platforms (animal science and Nigerian veterinary medical association groups). The questionnaire was exclusively filled out by rabbit farmers in Nigeria. Information on socio-demography, knowledge, attitudes and practices of the farmers on rabbit management and diseases and the 2020 RHD outbreak was obtained. The link to the questions was opened for responses between September and November 2020.

2.3. *Data analysis*

The data obtained were entered into the Statistical Package for Social Sciences software (version 23, 2015) for descriptive data analyses. Inferential statistics were used to determine the level of association between rabbit management systems in Nigeria and the spread of RHD across States in the country during the outbreak period. The differences within and across variables were compared, and p-values < 0.05 were considered statistically significant.

3. RESULTS

A total of 114 rabbitries across 15 States of Nigeria were involved in this study (Table 1a). Overall, 3514 rabbits were documented in the rabbitries before the outbreak and mortalities started, while a total of 3,007 rabbits (85.6%) had been lost by the end of our investigation. Kwara, Ogun, Oyo and Osun States had the highest number of respondents that had experienced massive mortalities due to suspected and or confirmed RHD in their rabbitries between February and November 2020 (Table 1a; Fig. 1). However, follow-up interviews after November 2020 indicated persistent rabbit mortalities due to RHDV in Kwara, Ogun, Osun and Oyo States as well as the Federal Capital Territory (FCT). Rabbitries operating semi-intensive management systems had the highest mortality (47.1%), followed by those with intensive (41.5%) and extensive (33.3%) management systems.

Table 1a. Distribution of rabbitries with massive mortalities during the 2020 RHD outbreak in Nigeria

Variables	Number of respondents (%)	Mortality (%)	OR (95% CI)	p-value
State				
Kwara	44 (38.6)	24 (54.5)	2.4 (0.2-28.5)	0.5930
Ogun	25 (21.9)	12 (48.0)	1.0 (0.1-12.7)	1.0000
Oyo	14 (12.3)	5 (35.7)	1.1 (0.1-15.5)	1.0000
Osun	6 (5.3)	3 (50.0)	2.0 (0.1-35.8)	1.0000
Katsina	3 (2.6)	1 (33.3)	1	
Benue	2 (1.8)	1 (50.0)	2.0 (0.1-78.3)	1.0000
FCT	2 (1.8)	1 (50.0)	2.0 (0.1-78.3)	1.0000
Kano	1 (0.9)	1 (100.0)	x	1.0000
Lagos	7 (6.1)	0 (0.0)	x	0.3000
Edo	3 (2.6)	0 (0.0)	x	1.0000
Delta	3 (2.6)	0 (0.0)	x	1.0000
Ekiti	1 (0.9)	0 (0.0)	x	1.0000
Niger	1 (0.9)	0 (0.0)	x	1.0000
Kaduna	1 (0.9)	0 (0.0)	x	1.0000
Plateau	1 (0.9)	0 (0.0)	x	1.0000
Management system				
Intensive system	65 (57.0)	27 (41.5)	r	
Semi-intensive system	34 (29.8)	16 (47.1)	1.3 (0.5-2.9)	0.6714
Extensive system	15 (13.2)	5 (33.3)	0.7 (0.2-2.3)	0.7710

Key: OR- Odd ratio 95% CI- 95% Confidence interval r- Reference x- Not applicable

Table 1b. Characteristics of rabbitries with mortalities during the 2020 RHD outbreak in Nigeria

Variables	Number of respondents (%)
What were the clinical signs seen before death?	
Sudden death	43 (89.6)
Uncoordinated movement	15 (31.3)
Paralysis	13 (27.1)
Epistaxis	11 (22.9)
Bloody faeces	1 (2.8)
What was the duration of the mortality (days)?	
< 4	18 (37.5)
4-10	15 (31.3)
11-14	6 (12.5)
15-21	6 (12.5)
> 21	3 (6.3)
Indicate the recent percentage mortality in your rabbitry	
1-20	16 (33.3)
21-40	6 (12.5)
41-60	4 (8.3)
61-80	2 (4.2)
81-100	20 (41.7)
Do you still have an ongoing mortality?	
Yes	15 (31.3)
No	33 (68.8)
How do you think this disease was introduced to your farm?	
After a co-rabbit breeder visited my rabbitry	13 (27.1)
After introduction of new rabbit to my flock	10 (20.8)
I do not have any idea	8 (16.7)
After visiting another rabbitry	6 (12.5)
After feeding my rabbit with imported feed	5 (10.4)
After outbreeding	2 (4.2)
Heat stress	1 (2.1)
After rodents entered my rabbitry	1 (2.1)
After feeding them with green leaf (*Tridax procumbens*)	1 (2.1)
Airborne	1 (2.1)
What did you do during this mortality experience?	
I called my veterinarian	25 (52.1)
I gave them antibiotics	15 (31.3)
I did not do anything	4 (8.3)
I used organics	1 (2.1)
I separated the uninfected from infected rabbits	1 (2.1)
I changed their feed	1 (2.1)
I fumigated the rabbitry and its premises	1 (2.1)

Analysis of the responses of participants on the clinical signs observed among rabbits during the RHD outbreak revealed that sudden death was the most encountered (89.6%), followed by uncoordinated movement (31.3%), paralysis (27.1%), epistaxis (22.9%) and blood faeces (2.8%). In addition, 37.5% of the respondents reported that the RHD-associated mortality lasted < 4 days (Table 1b), while more than 40% of respondents claimed to have had 81-100% mortality due to RHD. A majority (27.1%) of the farmers whose rabbitries were infected with RHDV believed that it was introduced to their farms after the visit of a co-farmer, while 20.8% of them believed that the infection spread to their farms following the introduction of new rabbits in the flock. Other responses on likely sources of introduction of RHDV to the rabbitries include: 'I do not have an idea of the transmission' (16.7%) and 'after visiting another rabbitry' (12.5%) (Table 1b). While 52.1% (25/48) of owners of RHD-infected rabbitries claimed they invited a veterinarian when they observed the typical clinical signs and or mortalities, 31.3% (15/48) reported that they administered antibiotics to the rabbits, and 8.3% (4/48) claimed they did not do anything to control the outbreak.

More than 80% of respondents were managers or owners of rabbitries, while 69.3% (79/114) had ≥ 2 years' experience in managing rabbitries (Table 2). The majority of the respondents (94.7%, 108/114) raised rabbits for commercial, money-making purposes. In addition, across the States of Nigeria, snuffles/pasteurellosis, rabbit haemorrhagic disease and overgrown teeth were the diseases/conditions the rabbit farmers were most knowledgeable of and the ones most experienced in their rabbitries (Table 2).

Table 2: Knowledge of rabbit farmers on RHD and other diseases of rabbits in Nigeria.

Features	Number of respondents (%)
Role in Rabbitry	
CEO/Manager	96 (84.2)
Animal scientist	7 (6.1)
Veterinarian	11 (9.6)
Years of experience	
< 2	35 (30.7)
2-5	59 (51.8)
> 5	20 (17.5)
Reasons for raising rabbits	
Commercial (profit-making) purpose	108 (94.7)
As pet	1 (0.9)
Laboratory/experimental purpose	5 (4.4)
Which of the following diseases of rabbits have you heard of?	
Snuffles/Pasteurellosis	85 (74.6)
Rabbit Haemorrhagic disease	75 (65.8)
Overgrown teeth	66 (57.9)
Myxomatosis	43 (37.7)
Hairball	41(36.0)
Uterine tumour	40 (35.1)
Bloat	6 (5.3)
Coccidiosis	4 (3.5)
Helminthosis	3 (2.6)
Foot pressure sore	2 (1.8)
Mite infestation/Mange	2 (1.8)
Ear canker	1 (0.9)
Which of the following diseases have you experienced in your rabbitry before?	
Snuffles/Pasteurellosis	64 (56.1)
Overgrown teeth	44 (38.6)
Rabbit Haemorrhagic disease	43 (37.7)
Myxomatosis	25 (21.9)
Hairball	21 (18.4)
Uterine tumour	16 (14.0)
Bloat	6 (5.3)
Helminthosis	5 (4.4)
Mange	5 (4.4)
Coccidiosis	3 (2.6)
Ear canker	1 (0.9)

4. DISCUSSION

Analysis of data obtained from the rabbit farmers involved in this study showed that the RHD outbreak started in February 2020. However, it is possible that the disease might have emerged earlier but gone unnoticed due to poor knowledge of its clinical presentation among farmers, as well as the similar clinicopathologic features it shares with diseases like septicaemic pasteurellosis, poisoning, heat exhaustion and other causes of severe septicaemia with secondary disseminated intravascular coagulation [12].

Our investigation revealed that as of November, the 2nd, 2020, more than 85% (3007/3514) of the rabbit population in Kwara, Ogun, Oyo and Osun States had been lost to the RHD outbreak, most of which were diagnosed/confirmed by veterinarians through necropsy and or RT-PCR. This corroborates earlier reports that RHDV-infected rabbitries could experience an 80-100% mortality rate when RHDV GI.2 is involved [26,27] compared with RHDV GI.1 strains which only elicit such in adult rabbits and only subclinical infection in young kits [28]. Further, the significant differences observed in rabbit mortalities due to RHDV across the affected States of Nigeria (X^2= 10.42, p= 0.0012) might have resulted from differences in the duration of exposure of the rabbits to the virus.

Although there were no significant differences in RHD mortality rates when rabbit management systems in Nigeria were compared, it was observed that rabbitries being managed semi-intensively were 1.3 times more likely to have been exposed to the virus than those under intensive management systems. This could be due to the fact that semi-intensively managed rabbits are usually placed on non-commercially formulated feed such as *Tridax procumbens* which could be contaminated by faeces and urine of wild hares and rabbits that may be shedding the virus.

Further, the major clinical signs observed, including sudden death (89.6%), uncoordinated movement (31.3%), paralysis (27.1%), epistaxis (22.9%) and bloody faeces (2.8%), were consistent with those previously reported for the peracute and acute forms of RHD [7, 11, 14, 29]. The duration of mortality (a few hours to > 21 days), as observed in this study, is consistent with all four clinical forms of RHD previously reported [11].

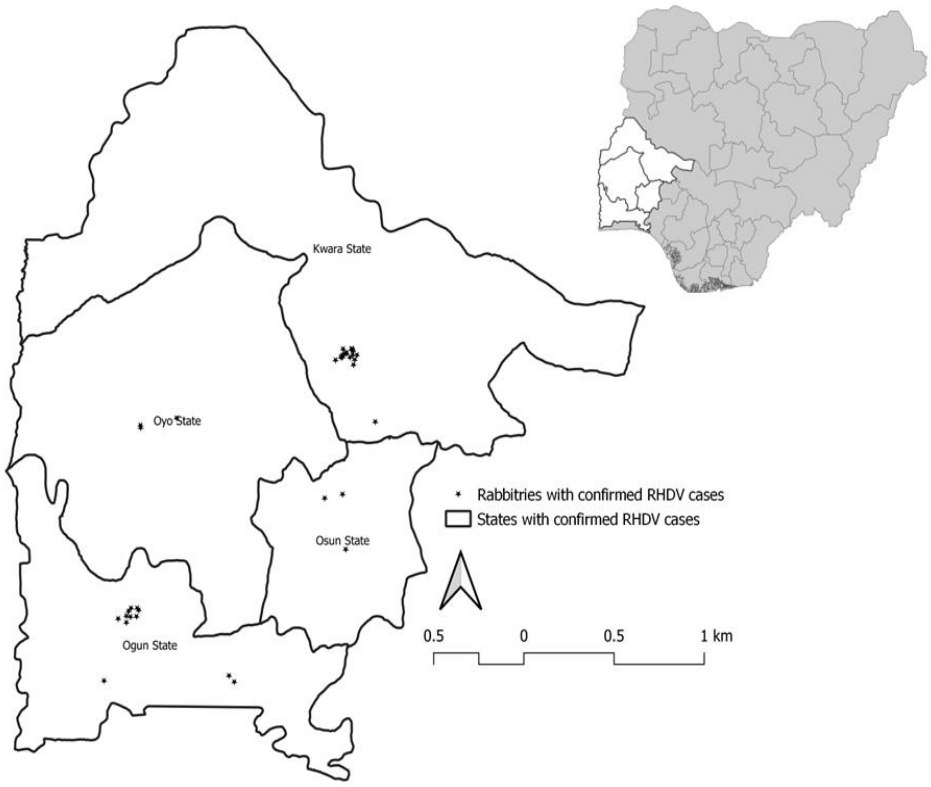

Figure 1: Map of Nigeria showing States with confirmed (necropsy/RT-PCR) cases of RHD. Black spots indicate the geo-location of respondents whose rabbitries were infected with RHDV.

Moreover, our findings revealed that more than 40% of rabbitries with RHD recorded > 80% mortality rate among their rabbit stock. Considering the route of spread of RHD to farms, 27.1% of respondents revealed that they noticed disease-specific signs and mortalities on their farms 'after a co-farmer visited the rabbitry', 20.8% 'following introduction of new rabbit stock', 12.5% 'after a visit to another rabbitry', and other indirect transmission means. According to Cooke [10] and Abrantes et al. [11], RHDV is a highly contagious virus that spreads through contact with infected animals (excreta, exudate and tissue), fomites (farm implements, fur, beddings, feed, footwear, clothes, cages) and or mechanically by insects. Thus, biosecurity and good farm practices are essential for the prevention of RHD since vaccination is currently not practiced in Nigeria, and there is no treatment for RHDV-infected rabbits.

While RHDV is one of the major causes of peracute and acute disease with high mortality in rabbit populations worldwide [30], respondents in this study displayed a high level of awareness of other diseases of rabbits compared to RHD. They opined that the frequently experienced disease conditions in rabbitries in Nigeria, in descending order, were snuffles/pasteurellosis, myxomatosis, overgrown teeth, uterine tumour, hairball, bloat, helminthiasis, mange, coccidiosis and ear canker, while RHD was recently experienced.

The results of this study suggest that rabbit rearing is now a thriving livestock enterprise in Nigeria as > 94% of the rabbit farmers reported that they reared them for commercial, profit-making purposes. This indicates a progressive switch from the traditional practice of subsistence rabbit farming which was common in the 1990s in Nigeria to modern, commercial-scale operations. In fact, more than 55% of respondents in this study reared their rabbits in cages and placed them on commercially formulated feed. Thus, the growing level of awareness and commercialization of rabbit farming in Nigeria indicates a need for stakeholder engagement through training workshops on profitable and sustainable rabbit production, their health and management in Nigeria. Also, since there are no approved vaccines for rabbit diseases in Nigeria, appropriate policy on rabbit vaccine development and their use in-country should be given priority consideration. According to Alboghdady and Alashry [31], RHD and other infectious diseases are regarded as limiting factors in rabbit production.

In addition, our study indicated that there is a high rate of replacement of local breeds of rabbits with exotic/imported ones with the aim of maximizing profit. This practice could be the major route of the introduction of RHDV to Nigeria which has porous borders at several

locations across the country. For instance, Kwara State, from where the first RHDV isolate in Nigeria [19] was obtained, shares an international border with the Republic of Benin which has a history of RHD [20, 21]. Although the origin of the RHDV detected in the Republic of Benin could not be traced due to lack of genetic evidence, the Nigerian isolate (RHDV/NGR/ILN/001) has been shown to be 98.57% genetically identical to RHDV 2 isolate (MN061492.1/RHDV2-NL2016) from the Netherlands [19], indicating its likely Dutch origin. More RHDV sequence data from other West African countries are required to establish the molecular epidemiology and relatedness of RHDVs in the sub-region and their possible source of introduction.

Conclusion

Considering the highly contagious nature of RHDV, its introduction to clean rabbitries in Nigeria can be prevented by the implementation of biosecurity measures, including sanitation, quarantine of new rabbit stock and their screening for RHD before introduction to farms, and avoidance of the use of imported rabbit feed and rabbit products, including meat and fur. The virus can be eradicated by depopulation and thorough disinfection of infected rabbitries. Lastly, the findings of this study underscore the need for continuous surveillance for RHD and maintenance of an active reporting system for known and unknown diseases of rabbits in Nigeria.

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Conflict of interest

The authors declear no conflict of interest in the conduct and presentation of the result

Research Ethics committee permission

Ethical approval for this study was obtained from the Kwara State Ministry of Agriculture and Rural Development (VKW-714/1/182).

Authors' Contributions:

O.B.D. and O.C.D. conceived and planned the experiments. O.B.D., O.C.D. and D.O.O. carried out the experiments. O.B.D., J.O.A., O.O.O. and D.O.O. planned and carried out the simulations. O.B.D., O.C.D., O.O.O. and I.D.O. contributed to sample preparation. O.B.D., D.O.O. and C.A.M. contributed to the interpretation of the results. O.B.D. took the lead in writing the manuscript. All authors provided critical feedback and helped shape the research, analysis and manuscript.

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