Occurrence of Foot-and-Mouth Disease Virus Serotypes in Uganda and Tanzania (2003 to 2015): A Review and Implications for Prospective Regional Disease Control

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Abstract

Endemic foot-and-mouth disease (FMD) presents a global economic challenge to the livestock industry. The progressive control pathway for FMD (PCP-FMD) specifies successive steps through which a country/region can reduce FMD virus circulation and impact. These steps are reliant on understanding and obtaining knowledge on FMD epidemiology, to inform development of appropriate disease interventions like vaccination and quarantine programs. Currently, Uganda and Tanzania are in the early stages of the PCP-FMD.

This review was undertaken to determine FMDV serotype distribution in Uganda and Tanzania between 2003 and 2015. The paper also presents the vaccine strains used in both countries for the same period viz avis the circulating topotypes. The review highlights four (O, A, SAT 1 and SAT 2) and five (O, A, SAT 1, SAT 2 and SAT 3) serotypes that occurred in Uganda and Tanzania respectively in the thirteen year period. Observations revealed that reported circulating serotypes O and A in the two countries belonged to similar topotypes, East African 2 (EA-2) and AFRICA respectively. The SAT 1 viruses in Tanzania belonged to topotype I and differed from the Ugandan SAT 1s that belonged to topotype IV. Similarly, the SAT 2s in both countries belonged to different topotypes: IV in Tanzania and I in Uganda. This review additionally, underscores the spatial distribution of FMDV serotypes in Uganda and Tanzania and highlights regions in both countries that had high serotype diversity.

The paper recommends definitive disease diagnoses, molecular serotype characterisation and matched vaccination deployment for improved disease control.

Keywords: control, East Africa, epidemiology, foot-and-mouth disease, serotypes

1. Introduction

1.1 Foot-and-Mouth Disease

Foot-and-mouth disease (FMD) is a highly infectious and economically important livestock disease (James & Rushton, 2002; Food and Agricultural Organisation [FAO], 2018). The notifiable disease is caused by the foot-and-mouth disease virus (FMDV), a member of Aphthoviridae genus and the family of Picornaviruses (Thompson & Bastos, 2004). The virus has seven serotypes; O, A, C, SAT 1, SAT 2 and SAT 3 and Asia 1 (Jamal & Belsham, 2013). Foot-and-mouth disease is spread through contact of susceptible non-infected animals with those that are infectious. Fomites such as clothes, cars tyres and farm tools can be important agents for virus transmission (Kitching, 2005). Some studies have documented FMD spread through aerosols and wind currents and, have recorded virus transmission of 250 km over sea and 60 km over land (Donaldson, Gloster, Harvey, & Deans, 1982; Donaldson & Alexandersen, 2002; Kitching, 2002). Clover hooved animals including livestock
and wildlife species are mostly affected, with cases of the FMD virus having been isolated from cattle, sheep, goats, pigs, and some wildlife species (Anderson et al., 1979; Bengis, Thomson, Hedger, De Vos, & Pini, 1986; Thompson, 1994; Vosloo, Bastos, Sangare, Hargreaves, & Thomson, 2002; Ayebazibwe et al., 2010a; Miguel et al., 2013). Wildlife species such as buffalo, deer, gazelles, elands, Wildebeests, impalas, Hartebeests, waterbucks and giraffes, and elephants have been cited to have a role in FMD epidemiology in eastern and southern Africa (Anderson et al., 1979; Vosloo et al., 2002; Vosloo, Bastos, Sahle, Sangare, & Dwarka, 2005; Bengis, 2005; Ayebazibwe et al., 2010a; Miguel et al., 2013). As early as 1979, Anderson et al. (1979) documented the recovery of the FMDV from over 50% of oesophageal-pharyngeal samples from selected wild animals in Kenya. The wildlife species included buffalo, elands, gazelles, impala, giraffes, water bucks and wildebeests. Additionally, serological evidence of infection after exposure to the virus was detected from samples from buffalo, elands, gazelles, wildebeest and topi. Although buffalos have been implicated for spreading FMD because of their carrier status, no experimental evidence has been established to this effect (Anderson et al., 1979; Sutmoller & Casas, 2002; Kitching et al., 2007). On the other hand, domesticated animals such as goats, sheep that hardly show clinical signs of FMD when infected, and have been implicated in some of the major global outbreaks that happened in the United Kingdom and Denmark in early 2000s (Sutmoller & Casas, 2002; Kitching, 2002).

The World Health Organisation for Animal Health (OIE) has classified FMD to be among the most important notifiable diseases. Foot-and-mouth disease outbreaks require quick intervention because of the potentially rapid rate of disease spread and substantial negative economic impacts on livestock stakeholders (OIE, 2017). Losses such as reduced meat and milk yields, loss in draught power, control and treatment costs, and lack of or low sales during outbreaks are some of the negative impacts of FMD (Domingo et al., 1990; Domingo, Baranowski, & Escarmís, 2002; James & Rushton, 2002; Baluka, 2016; Casey-Bryars et al., 2018). Annual funds spent on vaccination in Africa, have been estimated at US $ 830 million (James & Rushton, 2002) while the total cost burden in Africa has been estimated at more than US $ 6.5 billion per year (FAO, 2018). Countries that usually suffer from FMD outbreaks, have been shown to have low Gross Domestic Products (GDPs) compared to those where FMD has been eradicated (Jamal & Belsham, 2013). The observation of such trends could be attributed to the high costs of controlling the disease and the incurred losses due to disease.

The FMDV exists as seven serotypes, namely; O, A, C, Asia 1 and Southern African Territories (SAT) 1-3 (Stanway, Brown, Christian, Hovi, & Hypia, 2005; Jamal & Belsham, 2013). These FMDV serotypes are grouped according to the nucleotide differences within the viral protein 1 (VP1) gene coding region (Jamal & Belsham, 2013). This coding region has also been commonly used to infer antigenic diversity among the different serotypes (Knowles & Samuel, 2003; Fry et al., 2005). The independent FMD virus serotypes are subdivided into topotypes which are further divided into lineages and sub-types still based on the VP1 sequence diversity (Jamal & Belsham, 2013; WRLFMD). Globally, serotype O is the most predominant serotype and has been reported to have 11 geographic topotypes in circulation (Jamal & Belsham, 2013). Within this serotype, topotypes East Africa (EA-1-4) have been found in circulation in eastern Africa, with EA-2 being the most prevailing topotype in Uganda and Tanzania (Knowles, Samuel, Davies, Midgley, & Valarcher, 2005; Balinda et al., 2010a; Kasambula et al., 2012; Wekesa et al., 2013, Kasanga et al., 2015). Serotype A viruses have been clustered into three main topotypes, AFRICA, ASIA and EURO-SA which comprise over 26 different subtypes globally. The topotype that has been documented in circulation in East Africa is the AFRICA topotype and specifically genotypes I, II, IV and VII (Kasanga et al., 2015; Bari et al., 2014). The SAT serotypes have been predominantly found in Africa and were first isolated in South Africa. The SATs have been closely associated with wildlife-livestock interfaces and each SAT serotype has been isolated from the African buffalo in East African region (Vosloo et al., 2005; Ayebazibwe et al., 2010a; Kalema-Zikusoka, Bengis, Michel, & Woodford, 2005; Wekesa et al., 2014). Serotype SAT 1 has 13 topotypes (I-XIII) and four of these have been in circulation in East Africa. These topotypes have been observed to have unique and distinct geographical distributions across the different countries in East Africa (Vosloo et al., 2002). The SAT 2 serotype comprised of fourteen documented topotypes (I-XIV) whereas SAT 3 has five topotypes (I-V). Serotype C has not been reported in circulation in East Africa since 2004 when it was last detected in Kenya (Sangula et al., 2010). The serotype is distributed into three topotypes EURO-SA, ASIA and AFRICA. Serotype Asia 1, is predominant in the Asian continent and has only one topotype in circulation, and has never been detected on the African continent (WRLFMD).

1.2 Global Distribution of FMDV Serotypes

The global distribution of FMDV has been influenced by factors such as: livestock density, grazing systems, animal movements, animal husbandry and livestock trade patterns, wildlife reservoirs and low capacities for
Foot-and-mouth disease has been endemic both in Uganda and Tanzania since 1953 and 1927 respectively, with outbreaks reported more than once each year (Kivaria, 2003; Ayebazibwe et al., 2010b; Kasanga et al., 2012). Christensen et al. (2004) documented an increase in FMD cases in Uganda between 2000 and 2003. The same study reported 1 to 15 annual cases between 1996 and 1999; 1 200 to 3 100 annual cases between 2002 and 2003; 27 000 cases in 2003 and an additional 18 000 cases in the first six months of 2004. Between 2001 and 2008, 311 outbreaks were recorded in 70% of the districts in Uganda (Ayebazibwe et al., 2010b). In Tanzania, 878 outbreaks were reportedly occurred between 2001 and 2006, with variable numbers reported. The reports showed that most outbreaks occurred at locations close to international borders (Ayebazibwe et al., 2010b; Kivaria, 2003).

### 1.3 Control of FMD in Uganda and Tanzania

In most of the continents, mainly in sub-Saharan Africa, eradication of FMD may be considered as a long term objective (Kitching et al., 2007). Ideally, FMD control and eradication in endemic settings should involve vaccination of livestock twice a year, control of livestock movement and assessment of the risks associated with introduction of FMD in disease free areas (Thomson et al., 2003; Bruckner et al., 2002; Jori et al., 2009, Maree et al., 2014). The use of FMD vaccines has been commonly used in Uganda to prevent spread of FMD outbreaks (Ministry of Livestock Animal Industry and Fisheries [MAAIF], 2009) with annual expenses of FMD vaccines estimated at US $58 000 to $1 088 820 (Muleme et al., 2012). However, lack of routine vaccinations and reports of delayed and inadequate vaccination campaigns have been cited in causing disease spread to other areas (MAAIF, 2009). Issues with FMD laboratory diagnosis and poor reporting systems have increased the risk of disease spread and led to poor disease control options (MAAIF, 2009). In Tanzania, very low levels of vaccinations have been reported as most farmers do not vaccinate their animals (Railey, Lembo, Palmer, Shirima, & Marsh, 2018; Hasler et al., 2017). The Animal Health Strategy and Vision for Tanzania emphasizes improved epidemiological surveillance, better response to outbreaks and improved laboratory diagnostic networks in order to eradicate FMD (Maziku, Mruttu, & Gebru, 2016). The trivalent FMD vaccine used then in Uganda contained strains for serotypes O, SAT1 and SAT 2 (Namatovu et al., 2015), while in Tanzania the multivalent vaccine commonly used consists of serotype O, A, SAT-1 and SAT-2 (Balinda et al., 2010a; Sallu et al., 2015). Vaccination against FMD especially in endemic areas remains complex because of multiplicity of antigenic types and subtypes given that there is limited cross protection between serotypes or topotypes within the given serotypes (Kitching et al., 2007). Issues such as poor knowledge of circulating strains, vaccine expense and the short time of protection elicited by the vaccine (often as little as 6 months) hinder the success of vaccination schemes in endemic countries (Kitching et al., 2007; Maree et al., 2014). Although the restriction of livestock and product movement is a control strategy emphasized by both countries, especially in Uganda (Kasambula et al., 2012), it still lacks proper enforcement (East African Community [EAC], 2004; Balinda et al., 2010b), making disease control difficult.

#### 1.3.1 Progressive Control Pathway—FMD

The progressive control pathway for FMD was introduced by the FAO/OIE/EU-FMD to enable countries that are still endemic with FMD to develop strategies centred around existing information on the FMD status in the countries. The initial stages of the pathway, in which Uganda and Tanzania are in, are critical because comprehensive information on FMD is collected so as to move from stage 0 to 1 (FAO, 2011; FAO, 2018). The
pathway has five steps through which a region/country should go until they reach a status of free without vaccination. For countries in stages 1-4 vaccination is one of the major control strategies and thus basic information on serotypes and even topotypes in circulation in that region are important (FAO, 2011). With the recent start of the PCP-FMD implementation in East Africa in 2012, one of the vital requirements in the initial stages is the need for better understanding and knowledge on FMD epidemiology in a given country/region. Since Uganda and Tanzania are still in the initial stages of the PCP-FMD, where vaccination plays an important role in FMD control, this review aims to provide important information that can be used to develop effective vaccination strategies based on the spatial and temporal distribution of FMD serotypes in both countries between 2003 and 2013.

2. Review Methodology

2.1 Data Base Search

The methodology used was adapted from Khan, Regina Kunz, Kleijnen, and Antes (2003). Relevant questions were framed for the review, after which relevant work was identified, the quality of the selected studies was assessed, evidence from the reviewed articles summarised and finally information from the compiled evidence interpreted.

The PubMed Central, Google scholar, Science Direct databases were searched using key words “foot-and-mouth disease” OR “foot and mouth disease” AND “Tanzania” and “foot-and-mouth disease” OR “foot and mouth disease” AND “Uganda”. The search included theses, books, conference proceedings as well as project reports. A total of 59 items were found relevant to the topic, the years (2003-2015) and the defined geographical study area. Abstracts were exported to Mendeley and were later viewed to determine if they met the selection criteria on whether to be included in the study or not. Additionally, Government reports and other relevant documents were retrieved in both hard and soft copy.

2.2 Selection Criteria

Studies in which analysed samples were collected before 2003 and after 2015 were not included in this paper. This was done in order to have a more comprehensive picture of what had transpired in eleven years before the PCP-FMD was implemented in East Africa and shortly after its implementation. The review only considered studies where FMD diagnosis was either performed using cell culture, loop-mediated isothermal amplification (LAMP), antigen-enzyme Linked Immuno-sorbent Assays (Ag-ELISA) or polymerase Chain reaction (PCR). This is because the above mentioned laboratory methods are able to detect for the presence of FMDV in an appropriate sample and are serotype specific (OIE, 2012). The criteria included articles on buffalo but excluded articles on other wild animals. It also included articles on other livestock species including cattle. In the end, a total of 39 articles were selected for consideration.

2.3 Data Retrieval

Articles whose abstracts had been included for the study were then retrieved in full text format and reviewed by the first author as to whether they met the inclusion criteria. All articles reviewed in the study were in the English language. Qualitative data were compiled on country, year, serotypes, topotype, accession number, location from which samples were collected and referenced (Table 1).

Table 1. Foot-and-mouth disease viruses used in study

| S/N | Country | Year | Virus name | Serotype | Topotype/ Lineage | Accession Number | Location | Reference |
|-----|---------|------|------------|----------|------------------|-----------------|----------|-----------|
| 1   | Uganda  | 2003 | O/UGA/7/03 | O        | NM               | EU919243        | Unknown  | Chitray, de Beer, Voslou, & Maree, 2014 |
| 2   | Uganda  | 2003 | O/UGA/5/03/Masaka | O | NM | AY349955 | Masaka, Central region | Sahle, 2004 |
| 3   | Uganda  | 2003 | O/UGA/7/03/Hoima | O | NM | AY349956 | Hoima, Western region | Sahle, 2004 |
| 4   | Uganda  | 2003 | O/UGA/4/03/Jinja | O | NM | AY349954 | Jinja, Eastern region | Sahle, 2004 |
| 5   | Uganda  | 2003 | O/UGA/3/03/jinja | O | NM | AY349953 | Jinja, Eastern region | Sahle, 2004 |
| 6   | Uganda  | 2004 | U20B/04 | O | EA-2 | HM756621 | Hoima, Western region | Balinda et al., 2010a |
| 7   | Uganda  | 2004 | U17B/04 | O | EA-2 | HM756620 | Hoima, Western region | Balinda et al., 2010a |
| 8   | Uganda  | 2004 | U14B/04 | O | EA-2 | HM756619 | Hoima, Western region | Balinda et al., 2010a |
| 9   | Uganda  | 2004 | U13B/04 | O | EA-2 | HM756618 | Hoima, Western region | Balinda et al., 2010a |
| 10  | Uganda  | 2004 | UGA/12/2004 | SAT 2 | 1 | GU323179 | Kiboga, Central region | Namatovu et al., 2013 |
| 11  | Uganda  | 2004 | UGA/11/2004 | SAT 2 | 1 | GU323178 | Kiboga, Central region | Balinda et al., 2010b |
| 12  | Uganda  | 2004 | UGA/09/2004 | SAT 2 | 1 | GU323177 | Kiboga, Central region | Balinda et al., 2010b |
| Country | Year | Code | Area | Reference |
|---------|------|------|------|-----------|
| Tanzania | 2004 | TAN/2/2004 | O | EA-2 | KF561679 | Kibaha, Pwani | Kasanga et al., 2012 |
| Tanzania | 2004 | TAN/1/2004 | O | EA-2 | KF561678 | Bagamoyo | Kasanga et al., 2012 |
| Tanzania | 2004 | TAN/2/2004 | O | EA-2 | KF561706 | NM | Reeve et al., 2016 |
| Tanzania | 2008 | TAN/11/2008 | A | AFRICA/G-I | KF561690 | Iringa | Kasanga et al., 2012 |
| Tanzania | 2008 | TAN/12/2008 | A | AFRICA/G-I | KF561691 | Iringa | Kasanga et al., 2012 |
| Tanzania | 2008 | TAN/18/2008 | O | EA-2 | KF561684 | Morogoro | Kasanga et al., 2012 |
| Tanzania | 2008 | A/TAN-CVL-155 | A | AFRICA/G-I | KF947815 | Rukwa | Sallu et al., 2015 |
| Tanzania | 2009 | TAN/1/2009 | O | EA-2 | KF561696 | Morogoro | Kasanga et al., 2012 |
| Tanzania | 2009 | TAN/11/2009 | A | AFRICA/G-I | KF561694 | Kibaha, Pwani | Kasanga et al., 2012 |
| Tanzania | 2009 | TAN/10/2009 | O | EA-2 | KF561686 | Njombe | Kasanga et al., 2012 |
| Tanzania | 2009 | TAN/5/2009 | O | EA-2 | KF561685 | Morogoro | Kasanga et al., 2012 |
| Tanzania | 2009 | O/TAN-CVL-040 | O | EA-2 | KJ947823 | Mwanza | Sallu et al., 2015 |
| Tanzania | 2009 | O/TAN-CVL-013 | O | EA-2 | KJ947830 | Mara | Sallu et al., 2015 |
| Tanzania | 2009 | O/TAN-CVL-006 | O | EA-2 | KJ947832 | Tabora | Sallu et al., 2015 |
| Tanzania | 2009 | O/TAN-CVL-004 | O | EA-2 | KJ947826 | Kagera | Sallu et al., 2015 |
| Tanzania | 2009 | O/TAN-CVL-011 | O | EA-2 | KJ947808 | Mara | Sallu et al., 2015 |
| Tanzania | 2010 | O/TAN-CVL-037 | O | EA-2 | KJ947806 | Tabora | Sallu et al., 2015 |
| Tanzania | 2010 | O/TAN-CVL-046 | O | EA-2 | KJ947827 | Tabora | Sallu et al., 2015 |
| Tanzania | 2010 | O/TAN-CVL-015 | O | EA-2 | KJ947828 | Mara | Sallu et al., 2015 |
| Tanzania | 2010 | O/TAN-CVL-006 | O | EA-2 | KJ947830 | Mara | Sallu et al., 2015 |
| Tanzania | 2010 | O/TAN-CVL-013 | O | EA-2 | KJ947829 | Mara | Sallu et al., 2015 |
| Tanzania | 2010 | O/TAN-CVL-014 | O | EA-2 | KJ947833 | Mara | Sallu et al., 2015 |
| Tanzania | 2010 | O/TAN-CVL-012 | O | EA-2 | KJ947825 | Mara | Sallu et al., 2015 |
| Tanzania | 2010 | O/TAN-CVL-040 | O | EA-2 | KJ947805 | Iringa | Sallu et al., 2015 |
| Tanzania | 2010 | O/TAN-CVL-019 | O | EA-2 | KJ947811 | Rukwa | Sallu et al., 2015 |
| Tanzania | 2010 | O/TAN-CVL-010 | O | EA-2 | KJ947836 | Dar Es Salaam | Sallu et al., 2015 |
| Tanzania | 2010 | O/TAN-CVL-004 | O | EA-2 | KJ947826 | Kagera | Sallu et al., 2015 |
| Tanzania | 2010 | O/TAN-CVL-018 | O | EA-2 | N/A | Mtwara | Sallu et al., 2015 |
| Tanzania | 2010 | O/TAN-CVL-018 | O | EA-2 | N/A | Zanzibar | Sallu et al., 2015 |
| Tanzania | 2010 | O/TAN-CVL-071 | O | EA-2 | N/A | Morogoro | Sallu et al., 2015 |
| Tanzania | 2010 | O/TAN-CVL-017 | O | EA-2 | N/A | Rukwa | Sallu et al., 2015 |
| Tanzania | 2010 | O/TAN-CVL-034 | O | EA-2 | N/A | Tabora | Sallu et al., 2015 |
| Tanzania | 2010 | O/TAN-CVL-047 | O | EA-2 | N/A | Tabora | Sallu et al., 2015 |
| Tanzania | 2011 | KJ947819 | A | AFRICA/G-I | KIgoma | Sallu et al., 2015 |
| Tanzania | 2011 | KJ947813 | A | AFRICA/G-I | Tabora | Sallu et al., 2015 |
| Tanzania | 2011 | KJ947821 | A | AFRICA/G-I | Mtwara | Sallu et al., 2015 |
| Tanzania | 2011 | KJ947837 | A | AFRICA/G-I | Dar es salaam | Sallu et al., 2015 |
| Tanzania | 2011 | A/TAN-CVL-160 | A | AFRICA/G-I | Dar es salaam | Sallu et al., 2015 |
| Tanzania | 2011 | A/TAN-CVL-289 | A | AFRICA/G-I | Kigoma | Sallu et al., 2015 |
| Tanzania | 2011 | TAN/CVL-036 | O | EA-2 | N/A | Tabora | Sallu et al., 2015 |
| Tanzania | 2011 | TAN/CVL-109 | O | EA-2 | N/A | Dar es salaam | Sallu et al., 2015 |
| Tanzania | 2011 | TAN/CVL-031 | O | EA-2 | N/A | Coastal region | Sallu et al., 2015 |
| Tanzania | 2011 | TAN/CVL-039 | O | EA-2 | N/A | Mwanza | Sallu et al., 2015 |
| Tanzania | 2011 | TAN/6/2011 | SAT2 | NM | MF592599.1 | Arusha | Casey-Bryars et al., 2018 |
| Tanzania | 2011 | O/TAN-CVL-015 | O | EA-2 | KJ947828 | Mara | Sallu et al., 2015 |
| Tanzania | 2011 | TAN/4/2011 | SAT2 | NM | MF592598.1 | Arusha | Casey-Bryars et al., 2018 |
### 3. Results

#### 3.1 Temporal Serotype Distribution

Five FMDV serotypes; O, A, SAT 1, SAT 2 and SAT 3, were detected in Uganda, whereas four serotype O, A, SAT 1 and SAT 2, were detected in Tanzania between 2003 and 2015 (Balinda et al., 2010a; Balinda et al., 2010b; Kasanga et al., 2012; Kasanga et al., 2012; Kasanga et al., 2012; Kasanga et al., 2012; Kasanga et al., 2012; Kasanga et al., 2012; Kasanga et al., 2012; Kasanga et al., 2012; Kasanga et al., 2012; Kasanga et al., 2012; Kasanga et al., 2012; Kasanga et al., 2012).
Kasanga et al., 2012; Kasambula et al., 2012; Sallu et al., 2014; Namatovu et al., 2015; Kasanga et al., 2015; Dhikusooka et al., 2015; Dhikusooka et al., 2016).

3.1.1 Serotype O
Between 2003 and 2015, serotype O was reported in 10 out of the 13 years in both Uganda and Tanzania. In 2005, 2006, 2008 and 2009, 2010 in Uganda, all the outbreaks were associated with only serotype O. From 2003 to 2015, alongside one other serotypes, serotype O was cited again in all the outbreaks that occurred in the country (Figure 1 and Table 1), making it the most predominant serotype in Uganda between 2003 and 2015. The situation was closely similar in Tanzania, where serotype O outbreaks were reported annually except for 2013, 2014 and 2015. It was also observed that in Tanzania, serotype O occurred alongside at least one other serotype (SAT 1 and SAT 2) (Figure 2). This review suggests that serotype O was accountable for most of the outbreaks in Uganda stretching from south western Uganda to Kaabong in far eastern part of Uganda (Figures 1 and 3). While, in Tanzania, the distribution of serotype O was evenly spread across the country and occurred in the regions of Mwanza, Kagera, Mara, Shinyanga, Tabora, Arusha, Tanga, Dar es Salaam, Mtwara, Lindi, Ruvuma, Iringa, Morogoro, Pwani, Mbeya, Njombe and Rukwa. The review revealed that the serotype O viruses that were published between 2003 and 2015 from both countries, all belonged to topotype EA-2.

3.1.2 Serotype A
The observations from this review indicated that serotype A was detected in Uganda in 2013 and 2014, while in Tanzania it was detected in 2008, 2009 and 2012. Additionally, the findings from this review reveal that serotype A was detected only in the western and central parts of Uganda in the districts of Kiruhura and Wakiso. There were no outbreaks of serotype A detected in the eastern and northern parts of Uganda. However, in Tanzania, although the serotype occurred a few times, it was distributed throughout the regions of the country in the regions of Kagera, Mara, Arusha, Kigoma, Tabora, Rukwa, Njombe, Iringa, Dodoma, Morogoro, Pwani, Mtwara and Dar es Salaam (Figure 3). We additionally observed that the Ugandan and Tanzanian FMD serotype A all belonged to genotype 1 (G-1) within the AFRICA topotype, to which the vaccine strain A/K5/1980 that was being used belonged.

3.1.3 Serotype SAT 1
The SAT 1 viruses in Uganda was detected in 2011 and 2015 in cattle from Kasese and Kiruhura, districts respectively. The serotype was also detected in buffalo in 2007 from Lake Mbuuro National Park in Mbarara district. From these findings, the review shows that in Uganda, the SAT 1 viruses were found only in the south western region of the country and there was no detection of SAT 1 viruses in the central, northern and eastern regions. In Tanzania, SAT 1 viruses were detected every year from 2003 up to 2014. The SAT 1 viruses were distributed only along the eastern part of Tanzania and were found in the regions of Mara, Manyara, Morogoro and Dar es Salaam. We further observed in this review that all the Tanzanian SAT 1s belonged to the topotypel also called North-Western Zimbabwe (NWZ) whereas the SAT 1s of Uganda belonged to topotype IV also known as East Africa-1.

3.1.4 Serotype SAT 2
Serotype SAT 2 was detected in samples from Ugandan samples collected in 2004, 2013 and 2014 from the districts of Kiboga in the central and Isingiro and Kiruhura in the western region of the country. No SAT 2 viruses were detected in the eastern and northern regions of Uganda. In Tanzania, SAT 2 was confirmed in all the nine years from 2003 to 2012. The review highlighted that the distribution of SAT 2 in Tanzania was approximately correlated to the distribution of wildlife reservoirs (Figure 3). More than half of the regions that harboured a national park or game reserve had recorded an outbreak by SAT 2. Detected SAT 2 viruses were from the regions of Kagera, Mara, Arusha, Tabora, Rukwa, Mbeya, Singida, Manyara, Kilimanjaro, Morogoro, Pwani, Kigoma, Iringa, and Njombe. It was further observed that the SAT 2 FMDV from Uganda and Tanzania belonged to different topotypes, I and IV respectively.

3.1.5 Serotype SAT 3
Between 2003 and 2015, this serotype was never detected in Tanzania but was isolated in Uganda in 2013 from Kasese district near the Queen Elizabeth National Park, 16 years after it was last isolated from an African Buffalo.
3.2 Spatial Distribution

From this review, it was observed that between 2003 and 2015, the western and central regions of Uganda registered more outbreaks than the northern and eastern regions. The serotype diversity was highest in western Uganda with five serotypes (O, A, SAT 1, SAT 2 and SAT 3) documented. The central region followed with three serotypes namely, O, A, and SAT 2 and, the eastern region and northern regions had only serotype O in circulation. The outbreaks in the northern region were observed in the districts around the Lake Kyoga basin. The west Nile region had no outbreaks recorded for the entire study period (Figure 3).
In Tanzania, between 2003 and 2015, there was a wide distribution of multiple serotypes (Figure 3). Regions such as Kagera, Pwani, Morogoro, Arusha and Iringa registered more outbreaks than other regions during the eleven years. The highest serotype diversity was realised in Morogoro, Mara and Pwani which had all the four serotypes, (O, A, SAT 1 and SAT 2). Rukwa, Iringa, Arusha, Dar es Salaam, Njombe and Tabora regions followed with three serotypes each (Figure 3). Other areas like Geita and Katavi did not have any FMD outbreaks reported according to the reviewed publications.

4. Discussion

Inadequate documentation and characterisation of the occurrence of FMD outbreaks in Uganda and Tanzania creates deficiency of information for effective disease control within the East African region (Namatovu et al., 2013; Dhikusooka et al., 2015). In this review, using the available literature, occurrence of the different serotypes in Uganda and Tanzania was determined. From published literature, differences in the topotypes of circulating serotypes in each country was demonstrated.

4.1 Serotype O

Previous studies have shown serotype O to be the most prevalent serotype circulating both in Uganda and Tanzania (Balinda et al., 2010a; Kasambula et al., 2012; Kasanga et al., 2015; Salu et al., 2014) which is in agreement with the observations from this review. In Uganda, serotype O was detected from the south western part of Uganda to the far-east in Kaabong district, illustrating its wide distribution across the country. Other studies in Uganda have demonstrated the dominance of this serotype (Balinda et al., 2010a; Kasambula et al., 2012; Kerfua, Isubikalu, Ademun-Okurut, Muwani, & Masembe, 2013; Namatovu et al., 2015) in the different regions. In Tanzania, the distribution of serotype O was fairly even across the country, as supported by previous studies. Salu et al. (2014) observed that serotype O was wide spread in Tanzania and was responsible for most of the outbreaks between 2003 and 2008. Kasanga et al. (2012) similarly reported that serotype O was widespread throughout Tanzania except for some of the central parts of the country.

Although topotype EA-2 was found dominant in Uganda and Tanzania, this is contrary to what has been observed previously in the 1980s and 90s when topotype EA-1 was circulating in both countries (Vosloo, 2002; Balinda et al., 2010a). The disappearance of topotype EA-1 remains mysterious but probably shows that the topotype may be approaching extinction in the two countries or its detection overlooked. However, the predominant circulation of the topotype EA-2 in Uganda and Tanzania has implications for FMD control because the current vaccine strain (O/KEN/77/78) in use belongs to EA-1. Earlier studies by Kitching et al. (2007) have
argued that wide antigenic differences between the vaccines and circulating strains may result in a failure of the vaccine to generate protective antibodies. Thus the need for constant vaccine evaluation studies.

4.2 Serotype A

This paper demonstrated the rare detection of serotype A in both countries for the period covered by the review. Namatovu et al. (2015) highlighted the infrequent detection of this serotype in Uganda. Before its detection in 2013, the serotype has been last documented in 2002 (Namatovu et al., 2015). While in Tanzania, serotype A was regularly detected in the northern parts of Tanzania from 1954 up to 1971, but disappeared for over 30 years until its detection in 2008 in Iringa (Kasanga et al., 2012). The reason for the rare appearance of serotype A is still not well understood but its appearance and disappearance has been highlighted in the Asian continent as well (Kitching, 2005). Casey-Bryars et al. (2018) observed that serotypes were spreading over landscapes by waves and the distribution patterns were not random. The authors argued that certain serotypes were dominant during outbreaks for a specific time, after which they did not appear immediately (Casey-Bryars et al., 2018). This could be the same case for serotype A virus outbreak patterns in both Uganda and Tanzania. Never the less, more research is required in understanding the serotype A patterns in both countries in order to inform better control strategies. The spatial distribution of serotype A in Uganda demonstrates its confinement to the western and central parts of Uganda, suggesting certain epidemiological factors may be playing a role. The similarity in serotype A, lineages between the two countries may be indicative of FMDV serotype A spread between the two countries given the proximity between the south western region of Uganda and the northern regions of Tanzania. Despite the few years in which serotype A was detected in Tanzania, its distribution in the country was roughly even throughout. This could mean that the serotype easily spread across the different regions in the country probably due to factors such as uncontrolled animal movement, poor uptake of vaccination programs, and lack of biosecurity measures in place among others

Previous studies have shown that older Ugandan serotype A viruses isolated in the 60s belonged to genotype G-VII of AFRICA topotype to which the vaccine strain K35/1980 belongs (Namatovu et al., 2015). Although, the recent viruses belong to same topotype as the vaccine strain, Namatovu et al. (2015) highlighted antigenic differences between them that could affect the efficacy of the vaccine. Additionally, previous research has also shown that serotype A is a highly diverse serotype that is constantly evolving. This constant evolution is able give rise to new variants that may not be so closely antigenically related (Kitching, 2005; Kasanga et al., 2015; Sallu et al., 2014). Consequently these variants may complicate the control of FMD by vaccination.

4.3 Serotype SAT 1

The observed trend of the high detection of SAT 1 in Tanzania compared to that in Uganda, may highlight differences in surveillance and reporting systems, SAT 1 incursions or/and submission of samples for diagnosis. One of the challenges in comprehending the epidemiology and risk of FMD in endemic settings, is the low submission of samples both to the regional and world reference laboratories (Namatovu et al., 2013). Other reasons for the observed disparity in the frequency of reported SAT 1 occurrence in Uganda and Tanzania may be due to underreporting or limited appropriate diagnostic tools in Uganda (Dhikusooka et al., 2016; Kerfua et al., 2018).

Previously conducted studies have also shown that SAT 1 Ugandan isolates were significantly different from other SAT 1s from Tanzania and Kenya (Dhikusooka et al., 2016), suggesting that the SAT 1 virus strains from Uganda strains are most likely geographically confined to Uganda (Sangula et al., 2010). This could explain the observed differences in topotypes presented. All the Tanzanian SAT 1s belonged to the toptype I (NWZ) (Kasanga et al., 2015), whereas those of Uganda belonged to toptype IV (East Africa-1). According to Sangula et al. (2010), SAT 1 viruses in East Africa have evolved from two independent lineages from South Africa. Ugandan viruses were found to be related to West African and Sudanese viruses while Tanzanian and Kenyan SAT 1 viruses were found to be closer to each other (Kasanga et al., 2015). These observations could aid in explaining the spatial distribution of Tanzanian SAT 1s which were found in the eastern part of the country that is close to Kenya (Figure 3).

The TAN/155/71 vaccine strain that belongs to the toptype I (NWZ) has been consistently used in controlling FMD spread in the region. Since the vaccine strain belongs to a different toptype from the Ugandan strain, there may be no cross protection between these strains thus a lot of implications for FMD control. This indicates the need for more studies in Uganda on vaccine evaluation in order to ascertain the protection elicited by the TAN/155/71 vaccine strain.

Dhikusooka et al. (2016) reported silent manifestation of clinical signs in the cattle from which the SAT 1 viruses were isolated. This kind of scenario presents challenges to the clinical based reporting systems (Namatovu et al.,
where most reported FMD cases in Uganda and Tanzania were shown to rely on clinical manifestations of the disease instead of laboratory diagnosis (Muleme et al., 2012; Kerfua et al., 2018).

4.4 Serotype SAT 2

The occasional detection of SAT 2 in Uganda may be attributed to limited outbreak surveillance and may not reflect the true representation of the situation in the country. It may also be that SAT 2 viruses were rare in Uganda during the reviewed period. However, in Tanzania, the observed widespread and frequent occurrence of SAT 2 could be attributed to regular sample diagnosis or/and the presence of high numbers of wildlife reservoirs. In this review, it was observed that the distribution of SAT 2 in Tanzania was roughly correlated to the distribution of wildlife reservoirs (Figure 2). In Uganda, though, the distribution of SAT 2 viruses was mostly confined to western region of Uganda. However, the eastern part of the country that has three major national parks harbouring buffalos (Mt Elgon, Kidepo and Pian Upe), did not have SAT 2s detected. The association of SAT 2 outbreaks with wildlife-livestock interphases were observed in studies carried out in the southern and eastern Africa, and the African Buffalo has been connected with the SAT carrier status, and implicated in virus exchange with cattle (Woodsbury, 1995; Vosloo et al., 2005; Kasanga et al., 2012; Ayebazibwe et al., 2010a; Jori et al., 2016). However, other studies have shown that it’s not always the case that buffalos are responsible for SAT 2 incursions (Brito et al., 2016). Nevertheless, reasons for this distribution pattern of SAT 2 in Tanzania and Uganda still remain poorly understood (Kasanga et al., 2012; Sallu et al., 2014).

According to Balinda et al. (2010b), the 2010 SAT 2 Ugandan viruses were different from viruses that were isolated in years of 1975, 1995, 1998 and 2002. We suggest that the viruses could have evolved along different lines and raises questions on whether they could have emerged from different buffalo populations. However, the limited number of SAT 2 FMD virus sequences from Uganda limits the comprehensive phylogenetic analysis of FMDVs SAT 2 from both cattle and buffalo. Furthermore, disparity in topotypes of the SAT 2 FMDV from Uganda and Tanzania either implies that SAT 2 viruses are not spreading between country or that there may be under reporting of SAT 2 incursions in Uganda. According to Balinda et al. (2010b) and Namatovu et al. (2013), Uganda has reported two virus lineages of SAT 2 FMDVs. However, the most recent isolates have been observed to belong to a similar lineage as the vaccine strain (K52/84). Namatovu et al. (2015) further demonstrated that vaccine strain had significant genetic diversity with the most recent circulating SAT 2 virus, underscoring a need for vaccine matching studies to be carried out in both Uganda and Tanzania.

4.5 Serotype SAT 3

Previous SAT 3 isolates from Uganda were only from buffalo (Kalema-Zikusoka et al., 2005; Ayebazibwe et al., 2010a). The SAT 3 isolate was retrieved from a calf that had been grazing in the Queen Elizabeth National Park (QENP). The findings from the study by Dhikusooka et al. (2015), presents a new challenge for continued surveillance in the livestock wildlife interphase areas both in Uganda and Tanzania.

The SAT 3 isolate had a 19% nucleotide difference with buffalo FMD virus UGA/2/97 that was grouped in topotype IV. However, Dhikusooka et al. (2015), recommended that the isolated SAT 3 virus from Uganda should be categorised within a single topotype V. Currently, there is no vaccine strain that incorporates the SAT 3 serotype. This calls for further vaccine development and other strategic controls.

5. Conclusion

This review presents similarities and differences in the distribution of FMD serotypes in Uganda and Tanzania. It also highlights regions with the highest serotype diversity and those with the least diversity. In addition, this review has shown that there are differences between the circulating virus serotypes/topotypes and the vaccine strains currently in use in both countries. Although, underreporting of outbreaks and limited resources for diagnosis hinder the true picture of the serotype distribution in endemic countries, these findings still provide information important for strategizing control of FMD. For example, efforts for control can be specifically targeted to an area based on the prevalent serotypes and the serotype diversity.

This review recommends routine characterisation of circulating viruses, further research on FMD risk factors for certain serotypes, vaccine evaluation studies and implementation of harmonised regional FMD control programmes.

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