2022-06-27

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Journal of Advanced Veterinary Research

Received: 02 April 2022, Accepted: 07 June 2022

Journal of Advanced Veterinary Research
(2022) Volume 12, Issue 3, 324-328

Review Article

Current Trend and Future Perspectives of Paratuberculosis in Tanzania

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Abstract

Paratuberculosis prevalence, economic and public health significance in animal populations is well documented in most of the developed countries. In African countries however, information on paratuberculosis is sparse mainly due to lack of surveillance and research on the disease. In Tanzania, the disease was first reported in Kilimanjaro in year 1960 and up until year 2014, different cases have been reported in almost all agro ecological zones of the country, but there is no epidemiological information to link the cases. This creates an impression that the disease is absent in Tanzania. However, it is recently realized that in any African country that has done some surveillance, the disease has been confirmed to be present. The aim of the present review is to revisit the trend of paratuberculosis in Tanzania from 1960 when the disease was first reported to the current situation in year 2022. Attempt is made to highlight the possible link between the cases and suggest future strategies to enable the country grips with the disease. It is anticipated that this review is going to raise awareness on paratuberculosis in Tanzania and catalyze the institution of paratuberculosis surveillance and control programs in Tanzania.

KEYWORDS
Ecosystem, Johne's disease, One health, Paratuberculosis, Tanzania

INTRODUCTION

Johne's disease (JD, or Paratuberculosis) is a debilitating, granulomatous, enteric disease resulting in emaciation, persistent diarrhea, and eventual death of an infected animal (Sweeney *et al.*, 2012). Paratuberculosis is caused by *Mycobacterium avium* subspecies paratuberculosis (*M. paratuberculosis*). Paratuberculosis is prevalent all worldwide (Collins, 2003; Whittington *et al.*, 2019), and mainly affects domestic ruminants including cattle, sheep, goats, camelids, and buffaloes as well as wild ruminants (Dennis *et al.*, 2011; Sweeney *et al.*, 2012). In livestock, the disease is more prevalent in dairy cattle (Lombard, 2011) compared to other susceptible animals largely because of intensive research in dairy cattle, and confinement of animals which support transmission of the disease (Motiwala *et al.*, 2004).

Major economic impact of paratuberculosis is due to reduced production. Losses are largely caused by decreased milk production, progressive weight loss and decrease slaughter value, and early culling of infected animals (McKenna *et al.*, 2006; Whittington *et al.*, 2019; Wiszniewska-Łaszczych *et al.*, 2020). In a survey conducted across US dairy herds in 1996, estimated an annual average economic loss due to paratuberculosis was US$200–250 million (Ott *et al.*, 1999). Furthermore, *M. paratuberculosis* has been associated with Chrohn's disease in humans therefore has acquired another dimension of public health concern (Sechi and Dow, 2015; Agrawal *et al.*, 2021).

In Tanzania and most African countries, the disease occurrence, distribution, and prevalence in animal populations is not well established mainly because of lack of surveillance programs on the disease. In Tanzania reports available involve isolated cases that are distributed in time and space. Paratuberculosis was first reported in Tanzania in year 1960 as reviewed by Nyange *et al.* (1983). Subsequent reports indicate that the disease was widespread in larger part of the country (Nyange *et al.*, 1983; Batamuzi *et al.*, 1984; Matovelo *et al.*, 1994; Manjurano *et al.*, 2002). The last report on the disease in Tanzania is more than 8-years (Mpenda and Buza, 2014a; Mpenda and Buza, 2014b), which may create an impression of absence of the disease in Tanzania.

Seroprevalence reports in cattle and goats from Arusha Municipality indicated clearly presence of the disease (Mpenda and Buza, 2014a;Mpenda and Buza, 2014b). This is consistent with realization that in any African country which has done some surveillance the disease has been confirmed (Okuni, 2013). The aim of this review is two folds: To revisit paratuberculosis history in Tanzania focusing on different cases and reports, try to make a link between reported cases in different parts of the country at different times and suggest future strategies for controlling the disease in Tanzania, and to review the possible role of wildlife res-

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ervoirs and persistence of paratuberculosis in domestic animals.

Historical perspective of paratuberculosis in Tanzania

In Tanzania, paratuberculosis was first reported in 1960 at Marangu farm and Lyamungu Coffee Research Station (TACRI) in Kilimanjaro region (Nyange *et al*., 1983). Three years later (1963), incidences of paratuberculosis were reported in other government established farms, including Mbimba and Mitalula in Mbeya region and Seatondale in Iringa (Southern highlands), Chambesi in Coast region (Eastern zone), Livestock Training Institute (LITI)-Tengeru in Arusha (Northern zone) and Mpwapwa in Dodoma (Central zone). The possible source of these incidences was not established, and information to whether disease spread from infected farms in Kilimanjaro to these farms in different part of the country or the infection pre-existed in these farms is lacking. Importantly, these reports indicated presence of the disease in most of the agroecological zones of the country.

Following the disease outbreaks in1960-1963, strict quarantine measures were imposed (Nyange *et al*., 1983). However, despite of these quarantine measures, cases of disease were reported in the same or different farms. For example, paratuberculosis was reported in 1965 at Marangu farm and Lyamungu coffee research station for second time, and other cases were reported at LITI - Mpwapwa in 1967, 1971 and 1972. The disease was then reported at Ubena prison farm, Morogoro in 1968, Uyole Agriculture Centre (UAC)-Mbeya, 1972 (Nyange *et al*., 1983; Batamuzi *et al*., 1984), and Kitengule ranch in Kagera (lake zone), 1972 (Tanzania, Ministry of Agriculture report, 1972). Nyange *et al*., (1983) confirmed 2 cases out of 5 clinically ill animals among the stock of Jersey cattle imported from New Zealand in 1976 at Livestock Training Institute (LITI)-Tengeru in Arusha using clinical and post-mortem examination. A follow up work by Batamuzi *et al*. (1984), further confirmed that paratuberculosis at LITI- Mpwapwa, which had acquired animals from LITI - Tengeru. ten- years later, Matovelo *et al*. (1994) reported paratuberculosis at Sokoine University of Agriculture (SUA) farm, involving a Boran cattle purchased from Kilimanjaro region, Northern Tanzania in 1987.

Manjurano *et al*. (2002) identified *M. paratuberculosis* in feces from Kitulo dairy farm using Ziehl Neelsen (ZN) staining and microscopic examination. A significant association between diarrheic animals and presence of organisms in feces was noted (Manjurano *et al*., 2002). In a seroprevalence study, paratuberculosis was detected using ELISA in cattle (Mpenda and Buza, 2014a) and goat (Mpenda and Buza, 2014b) samples collected in urban and peri-urban Arusha in 2010 and 2011. Some of the seropositive cattle came from LITI-Tengeru, a farm from which the disease was reported some 31 years ago before the seroprevalence study.

Possible linkage between paratuberculosis cases in Tanzania

Although the actual origin of paratuberculosis in Tanzania cannot be unequivocally established, it is most likely that the disease was introduced in one or multiple foci through importation of infected dairy cattle from countries where the disease is prevalent (Nyange, 1983). This is mainly supported by the fact that earlier cases of the disease in Tanzania occurred in imported dairy cattle breeds. The disease has now been reported in almost all the agroecological zones of Tanzania including the Northern Zone, Eastern Zone, Central zone and the lake Zone. In some farms, only one report is recorded but in others, the disease has been reported in more than one occasion, which suggests persistence of the causative agents, amongst other reasons. It is well established that paratuberculosis is an intractable disease once introduced in an area therefore hard to control and/or eliminate (Collins, 2003; Lombard, 2011; Whittington *et al*., 2019; Agrawal *et al*., 2021;). Based on the available paratuberculosis reports in Tanzania, it may be hypothesized that these cases are linked and the disease is endemic in Tanzania. Seroprevalence reports of the disease in cattle (Mpenda and Buza, 2014a) and goats (Mpenda and Buza, 2014b) in Arusha, more than 38 years after the last case was reported is an example, which corroborate on the presence of paratuberculosis in Tanzania.

Reasons on the persistence of paratuberculosis in domestic animals in Tanzania

The mode of transmission of the disease plays a major role in the maintenance of the disease within a herd or flock. Although the epidemiology of paratuberculosis is not well established, the main mode of the disease transmission in cattle is the fecal-oral route (Sweeney, 1996; Corbett *et al*., 2019; Garvey, 2020;). Young animals, that are mostly susceptible because of immature immune system, get infected by ingesting *M. paratuberculosis* on contaminated teats during suckling or through contaminated feedstock such as milk, colostrum and contaminated grazing pasture (McKenna *et al*., 2006; Whittington *et al*., 2019; Garvey, 2020). Other routes of transmission have been documented such as through semen, the uterus, artificial insemination, and embryo transfer procedures (Collins, 2003; Whittington *et al*., 2019; Garvey, 2020). For instance, through meta-data analysis it was found that 9% of fetuses born from sub-clinically infected cows and 39% of fetuses born from clinically infected cows were infected with *M. paratuberculosis* (Sweeney *et al*., 2012; Whittington *et al*., 2019; Whittington and Windsor, 2009). The various transmission mechanisms ensure persistence of the infection over generations.

Prolonged incubation

Mycobacterium paratuberculosis infection is characterized by prolonged pre-clinical period (Whittington *et al*., 2019; Garvey, 2020). Most animals get infected as calves or neonates, but clinical signs are observed when they are adults (Collins, 2003; Sweeney, 1996; Whittington *et al*., 2019). For example, in cattle clinical cases are most observed in 2 to 4 years with incubation period as long as 14 years (Sweeney, 1996; Corbett *et al*., 2019; Garvey, 2020). During this incubation period, infected animal sheds organisms in feces intermittently for long time to the level that most available diagnostic test cannot detect, but enough to cause infection to susceptible hosts (Corbett *et al*., 2019; Whittington *et al*., 2019). This lead to contamination of environment and subsequent pathogen transmission to naïve animals undetected, which perpetuates the infection cycle. This leads to the iceberg concept of *M. paratuberculosis* infection, which states that "for every clinical animal born in the herd or flock an additional of 15-20 animals are infected" (Whitlock and Buergelt, 1996). Therefore, once clinical animals are found in an area, numerous sub-clinical infected animals are present, and this helps to maintain *M. paratuberculosis* in the herd or flock.

Survival of M. paratuberculosis in the environment

M. paratuberculosis persist in the environment for long time posing the risk of infecting animals in the vicinity and as a consequence the environment becomes a reservoir of infection to naïve animals (Whittington *et al*., 2005; McKenna *et al*., 2006; Eppleston *et al*., 2014; Ramovic *et al*., 2020). This was demonstrated in one study in which *M. paratuberculosis* was recovered for up to 12 months from soil inoculated with *M. paratuberculosis* (Rowe and Grant, 2006). Other studies demonstrated the ability of *M. paratuberculosis* to survive in a variety of harsh microenvironment. It was shown that bacillus can survived up to 55 weeks in dry fully shaded environment with the survival decreased with increased in exposure to solar radiation (Whittington *et al*., 2005; 2019). Moisture and lime applied on pastures and soil has no effect on the survival of *M. paratuberculosis* in the environment (Whittington *et al*., 2005), suggesting that *M. paratuberculosis* can persist in dry soil and harsh environment.

Furthermore, it has been demonstrated that *M. paratuberculosis* can survive in water dams and sediments for prolonged time. For instance, *M. paratuberculosis* was recovered up to 48 weeks in shaded water and/or sediment dams, although survival time decreased to 36 weeks in semi-exposed locations to solar radiations (Whittington *et al*., 2005). Furthermore, *M. paratuberculosis* has been reported to survive in harsh and high temperature environment (Stabel *et al*., 1997). Also, findings demonstrate that *M. paratuberculosis* tend to move slowly through soils and remain on grass and on the upper layer of pasture soils (Salgado *et al*., 2011); suggesting that *M. paratuberculosis* can move to distant places from shedding point with running water. The ability to survive in the environment for a long time enables the pathogen to persist in a locality. Therefore, even if the infected flock is eliminated, *M. paratuberculosis* may still be there to infect newly introduced flock.

Mixed housing and grazing of large and small ruminants

Co-grazing and or co-housing of different paratuberculosis susceptible species has an influence on the disease incidences in respective species based on research conducted in New Zealand (Verdugo *et al*., 2014). Verdugo *et al*. (2014) found that the risk of infection was increased 3-4 times in each species when beef cattle and sheep were co-grazed. Similarly, the risk of infection in deer increased three times when co-grazed with beef cattle but conversely, co-grazing of sheep and deer reduced disease incidences in the two species (Verdugo *et al*., 2014).

In Tanzania, as many other African countries, the co-grazing of cattle, sheep and goats is a common practice and may play a major role on the epidemiology of paratuberculosis. Although the effect of co-grazing goats and cattle on incidences of paratuberculosis is not yet reported, it is possible that goats may have similar effect as sheep (Fridriksdottir *et al*., 2000; Rangel *et al*., 2015). We reported paratuberculosis seropositive cattle and goats from the same flock in urban and peri-urban Arusha where co-grazing and co-housing of the two species in commonly practiced (Mpenda and Buza, 2014a; Mpenda and Buza, 2014b). Although the exact mechanisms by which co-grazing of different species influences the disease incidence is yet clearly established, goats can potentially increase shedding of *M. paratuberculosis* in two ways; first the preclinical period in goats is shorter compared to cattle (Collins, 2003), and this increases the chances of animal shedding infectious *M. paratuberculosis* in a farm. Secondly, because of shorter gestation period (5 months) as compared to cattle (9 months), goats can produce twice as many offspring in a given time therefore ensuring availability of many *M. paratuberculosis* susceptible kids that will grow up to become shedders.

Possible role of wildlife reservoirs

The interface between livestock and wildlife can serve as hotspot for bi-directional paratuberculosis transmission between livestock and wild animals (Simpson, 2002; Stevenson *et al*., 2009; Cunha *et al*., 2020). For example, *M. paratuberculosis* was detected in rabbits from farms that had previous history of clinical paratuberculosis (Greig *et al*., 1999; Beard *et al*., 2001), and through molecular genotyping strains identified in rabbits were similar to those found in cattle (Greig *et al*., 1999). Paratuberculosis has been reported in wild ruminants such as buffalo (Karthikeyan *et al*., 2019; Martucciello *et al*., 2021) and wild boar (Kim *et al*., 2012). Also, infection has been reported in wild non-ruminants, such as rabbit (Greig *et al*., 1999), foxes (Beard *et al*., 2001), mice (Florou *et al*., 2008), rats (Florou *et al*., 2008) and stoats (Beard *et al*., 1999), which inhabits grazing areas of livestock.

In Tanzania grazing pastures particularly, dairy farms are infested with various types of wildlife including rabbits, rats, mice, rats, wild boars and others may play a role in maintaining *M. paratuberculosis*. For example, different Mycobacteria species were detected in 7.3% of small mammals trapped in different cattle farms in Morogoro (Durnez *et al*., 2011). In pastoral areas such as the Ngorongoro Crater, sharing of pastures between wildlife and livestock may help maintain the *M. paratuberculosis* through cross-infection.

The role wildlife reservoir for persistence of disease in domestic livestock has been demonstrated in African setting in other Mycobacterial infections such as bovine tuberculosis (bTB) caused by *Mycobacteria bovis* (Mtb) (De Garine-Wichatitsky *et al*., 2013). For instance, it has been shown that wild animals act as reservoir of Mycobacterium bovis (Mtb) at the livestock-wildlife interface in Ruaha National Park (RNP), protected area bordering with endemic grazing land, in south-central Tanzania (Clifford *et al*., 2013) and similar situations have been reported in other African countries (Michel *et al*., 2006; Munyeme *et al*., 2009; Tschopp *et al*., 2010).

Lack of paratuberculosis certification and free animal movements

In Tanzania, information available do not provide original source of *M. paratuberculosis* infection; however, one report clearly indicated link between importation of cattle from New Zealand and clinical cases of paratuberculosis at LITI-Tengeru in Arusha (Nyange *et al*., 1983). Since then, in Tanzania here is no laws or regulation governing importation of animals into the country, particularly with regard to paratuberculosis. As a result, the country will always remain at the risk of introduction of infected animals.

Furthermore, since the first cases of paratuberculosis involved dairy cattle that were imported in the country for the purpose of multiplication and distribution to other farms in different parts for the purpose of genetic improvement of milk production, the disease may have been spread through this channel. For example, the Kitulo and other dairy farms in Iringa and Mbeya where the disease was relatively recently reported (Manjurano *et al*., 2002) are still the source of heifers sold to other farms in Southern highlands of Tanzania and the country as a whole. These well-intentioned dairy cattle multiplication projects may have inadvertently played a role in the spread of paratuberculosis to various parts of the country.

The way forward

Since currently no information on the extent of paratuberculosis in Tanzania, there is need to conduct a nationwide surveillance to map the distribution of the disease in susceptible livestock in the country. Results from this surveillance should be informative for formulation of disease control strategies as is practiced in other countries such as USA, Australia, and New Zealand. The key ingredients in most paratuberculosis control programs in ensuring imported animals are disease free while at the same executing a systematic elimination of infected animals through the test and slaughter policy. In this regard, there is need to establish a legislation that will require all imported cattle, sheep and goats to be free from paratuberculosis. A test and slaughter policy will help eliminate the disease in infected farms, herds or flocks.

Livestock owners should be educated on the economic and public health impacts of the disease and be encouraged to willingly present their animals for paratuberculosis test as well to adopt management practices that minimize chances of cross-infection between animals. Compensation for slaughtered animals is recommended to increase compliance.

Although seropositive cattle and goats were found in Arusha, no paratuberculosis cases has been reported from this area for more than 34 years. This may be due to a number of reasons; the veterinary extension officers may be overlooking the clinical signs of paratuberculosis because the disease is not known to be prevalent in the country. Alternatively, the genotype of circulating *M. paratuberculosis* may have been altered to result in reduced virulence as the consequence of circulating in locally available breeds. On the other hand, it may be that the locally available livestock breeds are relatively resistant to *M. paratuberculosis*. Therefore, training of extension staff on diagnosis of the disease is needed to identify clinical cases as well as lesions during meat inspection. On the research front, there is need to study the epidemiology of the disease in the country, taking into account of the local situation in terms of susceptibility of locally available cattle, goats, sheep and wildlife, the management system, livestock movements and all other factors that influence the epidemiology of the disease. The Veterinary laboratory Agencies should build capacity for diagnosis of paratuberculosis and also include the disease in active surveillance programs.

Genotype characterization of circulating *M. paratuberculosis* strains will be informative on possible vaccine for use in Tanzania. Furthermore, the genotype information will be informative on the possible source of the prevailing strains in Tanzania, the spreading pattern from one area to the other and the cross-species infection including the possible role of wildlife in the epidemiology of the disease.

In view of the possible link of *M. paratuberculosis* with human Chrohn's disease, is important to obtain information on risks associated with consumption of products from susceptible animals. *M. paratuberculosis* is known to be shed in milk from infected animals and is also known to survive pasteurization. Quantification of *M. paratuberculosis* in milk before and after pasteurization will help obtain information on risks associated with consumption of milk. Cattle and goat intestines soup is a favorite serving in many parts of Tanzania. Incidentally, these tissues are the main sites of *M. paratuberculosis* localization. It will therefore be interesting to quantify the viable *M. paratuberculosis* in intestinal soup that is served to customers.

ACKNOWLEDGMENTS

Gratitude to Ms. Milian Marcus of the Sokoine University of Agriculture Library who assisted in locating various literatures in the archive.

CONFLICT OF INTEREST

The authors declare that they have no conflicts of interest to disclose.

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