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Non-Tuberculous Mycobacteria in Uganda: A Problem or Not?

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1. Introduction

1.1 HIV/AIDS

HIV/AIDS scourge has been and still is a devastating disease since its advent in the late 70's, claiming up to 25 million lives globally (WHO, 2010). The United Nations program on AIDS (UNAIDS) estimated that 39.5 million people were living with HIV/AIDS by the end of 2006, 63% of these were in Sub Saharan Africa. Furthermore, 4.3 million people were reported to be newly infected with HIV while 2.9 million had lost their lives to AIDS in 2006 alone (UNAIDS, 2010). It is also reported that young people of age 15 and above account for 40% of new infections (CWYF, 2007). Epidemiological models predict a growing trend of the disease most notably the alarming incidence of new infections in sub-Saharan Africa, Western Europe and Asia (UNAIDS, 2010).

1.2 HIV/AIDS in Uganda: Past and current situation

In many regards, Uganda is considered a global role model in awareness, prevention and control of HIV/AIDS (Aidsmap, 2006; Kaiser family foundation, 2005). The first cases of AIDS in Uganda were identified in Rakai district off the shores of Lake Victoria in 1982 (Serwadda et al 1985; MOH, 2006). AIDS was clinically characterized by wasting, this is why it is popularly known as 'slim disease' (Serwadda et al., 1985). Just as before, this disease is still characterized by opportunistic infections, notable are *Mycobacterium avium* complex infections which are usually the causes of fatality in victims (Serwadda et al., 1985; MOH, 2006). In the late 1980's a famous Ugandan Musician Philly Bongole Lutaaya paved the way for the awareness campaign by publically disclosing his sero-positive status at a time when the epidemic prevalence was up to 29% in peri-urban and urban areas of Uganda (Open Vision Club, 2004; Hooper, 1990; Hogle, 2002).

This campaign later evolved into the first ever control programme designed to educate the general population on measures of avoidance coined in the abbreviation ABC; 1) Abstinence, 2) being faithful to your partner and 3) the use of condoms (Hooper, 1990; Hogle, 2002). The success of this open campaign was characterized by a drastic fall in the incidence and prevalence of HIV/AIDS among young adults as well as pregnant women (Stoneburner, 2004; STI/AIDS, 2002). This prevalence has been kept at a record low in part due to this awareness, global funds and subsidies on anti-retroviral therapy in addition to a steady development in palliative treatment and counseling offered by nongovernmental organizations like 'The AIDS support organization' (TASO) (Hogle, 2002;UAC,2004;Ashemeire,2010). Unfortunately this effort together with the evolving life style trends today have bred an army of complacent and risk taking youth (Chinaview, 2008*)*, therefore the resilience of this control strategy is yet to be fully tested. Early age at first sex is reported to be among the key risk factors for HIV infection. In this regard, records from the ministries of health and Gender Labour and Social Development estimates age at first sex being 16.7 and 18.8 for girls & boys respectively in 2005 (MGLSD,2004; MOH,2006).

Furthermore, by age 17, half of young women are sexually active and 62.7% have already begun child bearing by the age of 19 (MOH, 2006). This explains the current prevalence estimated at 7% (UNAIDS, 2010) with the highest records of 17% and 18% in HIV/AIDS hot-spot districts of Mubende and Nakasongola, respectively (Anonymous, 2004 and Anonymous, 2008).

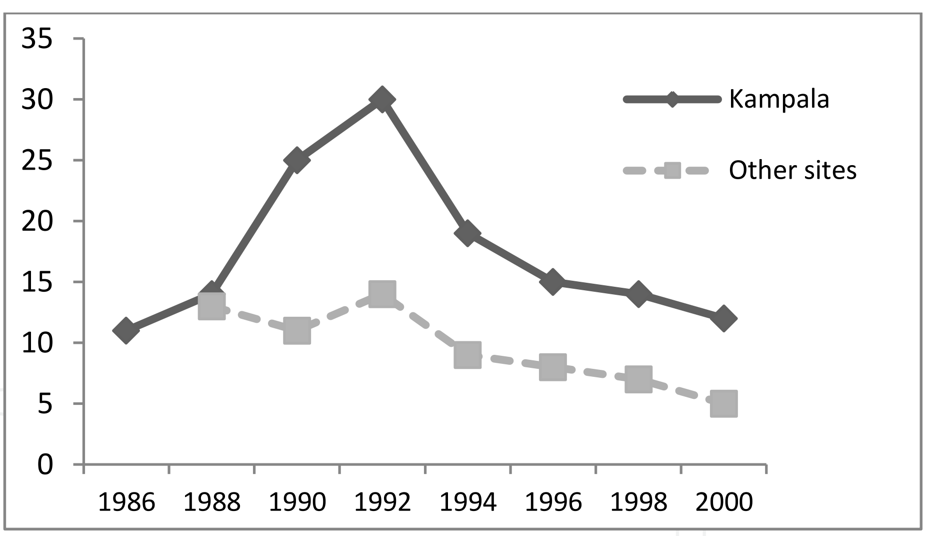

Fig. 1. Median HIV prevalence among pregnant women in Uganda (Hogle, 2002)

Likewise the Ministry of Health's indices in Uganda also indicate that to date this disease has affected approximately 7.4 % of the total national population and that 3.2% of the deaths that have occurred since its advent globally have been in Uganda (MOH,2006; UNAIDS, 2010). The socio-economic effects of AIDS on communities have recently been documented in a study conducted among public service officers with AIDS. It showed a significant increase in direct and indirect costs on HIV/AIDS related illness in addition to claiming the lives of family breadwinners. This has given rise to orphans who are left at the mercy of nongovernmental support groups (MOH report, 2010).

2. Mycobacterial infections in Uganda

Tuberculosis (TB) caused by *M. tuberculosis complex* group remains a major public health problem in Uganda. It is documented to be endemic in poor peri- urban and urban areas mainly due to; 1) congested living conditions (Banerjee, 1999; Tupasi, 2000; Asimwe et al., 2009), 2) high prevalence of HIV, malnutrition and use of immunesupressive therapy in use today (Cosivi, 1998; Asimwe, 2009). Uganda is ranked 16th among the countries with the highest burden of TB in Sub-Saharan Africa, with an estimated incidence rate of 559 cases per 100,000 per year (WHO, 2007). There are other pathogenic mycobacteria other than *M.tuberculosis* and *M.bovis* that have been documented in Uganda, and these include *M. ulcerans* and *M. leprae* (Giuseppe et al, 1997). *M. ulcerans,* the cause of Buruli Ulcer is a skin infection clinically characterized by a nodular skin lesion that busts open into a non healing ulcer (Giuseppe et al, 1997). In the 60's and 70's Buruli ulcer was reported in the Busoga District on the east side of the Victoria Nile, north of Lake Victoria (Barker, 1971). Although cases were known in the other parts of the country, it was unknown in the district before 1965. In this study Barker postulated that the outbreaks were related to the unprecedented flooding of the lakes of Uganda from 1962 to 1964 as a result of heavy rainfall (Barker, 1971). Leprosy in comparison to TB is an old disease documented in the Bible as affecting people even before Christ. It is caused by *M. leprae,* which damages the skin and the peripheral nervous system resulting in skin lesions and deformities, most often affecting the cooler places on the body for example, eyes, nose, earlobes, hands, feet, and testicles (Giuseppe et al, 1997). In Uganda, it was first documented in the South Eastern part in 1978 by a Christian based hospital (Kawuma, 1999). Currently, the prevalence of leprosy is 2.8 cases per 100,000 population, *with a case detection rate* of 2.5 per 100,000 (WHO, 2002&2004). In 2004, new cases were reported in Iganga, Hoima, Kabarole, Kyenjonjo, Rukungiri and Lira district. The latter had has as high as 86 new cases reported (Nation TB and Leprosy, 2004). Recent incidence reports on leprosy in Uganda showed a slight increase in the years 2004/05, but case detection rate continues to decline. It is therefore too early to envisage a Uganda free of leprosy.

At the beginning of the AIDS pandemic, Non-Tuberculous Mycobacteria (NTM) were reported as emerging pathogens responsible for opportunistic infections, found in almost half of HIV/AIDS infected patients, usually associated with CD4 cell counts B/100/ml and a survival of less than one year (Masur,1993). The species documented to cause opportunistic human infections are : *Mycobacterium avium, M. intracellulare, M. kansasii, M. paratuberculosis, M. scrofulaceum, M. simiae, M. habana, M. interjectum, M. xenopi, M. heckeshornense, M. szulgai, M. fortuitum, M. immunogenum, M.chelonae, M. marinum, M. genavense, M. haemophilum, M. celatum, M. conspicuum, M. malmoense, M. ulcerans, M. smegmatis, M. wolinskyi, M. goodii, M. thermoresistible, M. neoaurum, M. vaccae, M.palustre, M. elephantis, M. bohemicam and M. septicum* (Katoch, 2004). It has previously been estimated that up to one-quarter of all patients with AIDS will acquire this infection during their lifetime (Horsburgh, 1991). It is difficult to accurately describe the situation in Sub Saharan Africa since most of the data on which these inferences are made comes from northern Europe or North America (Horsburgh, 1989). Notably, these regions have experienced a gradual decline in the prevalence of TB and increase in mycobacterial infection caused by NTM's in the past several years (Claudio et al., 2008). It is still unclear if this trend is real or is the result of technologic developments in diagnostics (Claudio et al., 2008). Worse so, little has been done in developing countries especially in the sub Saharan Africa to capture this trend (Narang, 2008). Studies in 1990's in Kenya, Uganda, Tanzania, and the Ivory Coast (Gilks et al., 1995; Okello et al., 1990; Archibald et al., 1998; Lucas et al., 1993) concluded that disseminated NTM infections were relatively uncommon in Africa. On the contrary, recent studies in Zambia and South Africa using better diagnostic tools have actually reported a high prevalence of NTM infections in HIV/AIDS patients. These dismissed the previous notion and warned that the problem was bigger than previously documented (Clive, 2001; Buijtels, 2009).

3. Non tuberculous mycobacteria in the environment

The distribution of NTM and the incidence of NTM diseases is still an enigma in most parts of the world however; consistent reports show that NTM are widely distributed in nature. Therefore, the environment is regarded to the biggest reservoir and source of NTMs for animal and human hosts (Falkinham, 1996; Falkinham, 2009; Van ingen 2009). This is in resonance with earlier studies done in Ugandan environments, in which Stanford et al., in 1972 reported that areas around Kampala and Kyoga had 67%, 34% and 98%, 56% of NTM isolation from mud and grass respectively. Of the districts from which mud samples were taken, the isolation rate and the greatest variety of mycobacteria species recovered was from east Bunyoro (present day Kibaale District), southern Lango (present day Oyam, Apac and Dokolo districts) and northern Busoga (present day Kamuli district). Species isolated included *M. chelonae*, *M. fortuitum*, *M. avium* and others which were more prevalent in areas with surface water pH values between 5.5 and 5.7 (Barker et al., 1972). Subsequent studies showed that *Mycobacterium avium* complex (MAC) was the most prevalent in urban environments, these accounted for 43% of the recovered NTM from water and soil environments in Kampala, Uganda (Eaton et al., 1995).These were mostly recovered from water and soil with pH ranges (6.0, 6.0-6.9, and > 7.0) respectively. Meanwhile, the most recent studies in pastoral environments have shown that MAC accounted for 29% of NTM recovered in Mubende and Nakasongola (Kankya et al 2011). *M. gordonae, M. nonchromogenicum M. engbaekii, M. hiberniae, M. kubicae, M. simiae, M. arupense, M. terrae, M. parafortuitum* were some of the other NTM isolated from pastoral ecosystems of Uganda (Table 1). Water is considered to be the primary source of NTM infections in humans while domestic and wild animals may be reservoirs (Biet et al., 2005). In the highly mobile pastoral systems of Uganda, humans, livestock domestic and wildlife share open natural water sources. The sharing of these stagnant open water sources provides yet another NTM infection challenge at the human- environment-domestic/ wildlife interface (HELI) (Kankya et al 2010). Subsequent studies on these natural water sources and follow up of this water that was being used in households revealed a high prevalence of *Mycobacterium* species including those known to be pathogenic (Kankya et al., 2011). Host-environment interaction is a key element in colonization and maintenance of *Mycobacterium* in a niche (Falkinham 1996; Biet al , 2005). This is held true by the vast amounts of mycobacteria that were recently isolated from animal environments (Krizova et al., 2010; Ofukwu et al., 2010). Kankya et al 2011a also recovered a wide variety of NTMs from swine and cattle environments, which included *M. fortuitum peregrinum* complex, *M. avium* complex, *M. parafortuitum, M. hiberniae* and *M. engbaekii* (table 1).

Species	Host	Environmental source	Geographical location	Reported by
M. avium	Human, swine, cattle	Household & valley dam water, swine shelter, cattle kraal	Kampala, Karamoja, Mubende ,Kyoga,Toro and Nakasongola	Muwonge et al.,2011 under review, Kankya et al 2011;Oloya et al 2007; Eaton et al 1995; Stanford et al 1976
M. gordonae	Swine and human	Household & stream water	Mubende, Nakasongola,Kyoga, Toro and Kampala	Muwonge et al.,2011 under review, Kankya et al 2011; stanford et al 1976
M. avium subsp hominisuis	Swine and human		Karamoja and Mubende	Muwonge et al.,2011 under review;Oloya et al 2007a&b
M. intracellure	Swine, human, cattle	Household & valley dam water, swine shelter, cattle kraal	Mubende, Nakasongola and Karamoja	Muwonge et al.,2011 under review, Kankya et al 2011;Oloya et al 2007
M. fortuitum	Swine	Household & valley dam water, swine shelter, cattle kraal	Mubende and Nakasongola	Muwonge et al.,2011 under review, Kankya et al 2011;Oloya et al 2007
M. nonchromgenicum		Household, stream water	Mubende, Kampala, Kyoga and Toro	Kankya et al 2011; Stanford et al 1976
M. parafortuitum	Swine	Household water	Mubende and Nakasongola	Muwonge et al.,2011 under review, Kankya et al 2011
M. chubuense		Household water	Mubende and Nakasongola	Kankya et al 2011;
M. vanbaalenii		Household water	Mubende and Nakasongola	Kankya et al 2011;
M. engbaekii		cattle kraal	Mubende and Nakasongola	Kankya et al 2011;
M. kubicae		Household water	Mubende and Nakasongola	Kankya et al 2011;
M. simiae	Swine, human	Household water	Mubende, Nakasongola and Kampala	Kankya et al 2011; Muwonge et al.,2011 under review; Ssali, 1998
M. hiberniae		cattle kraal	Mubende and Nakasongola	Kankya et al 2011
M. terrae	Swine	Household water	Mubende and Nakasongola	Kankya et al 2011; Muwonge et al.,2011 under review
M. senuense	Swine	valley dam water	Mubende and Nakasongola	Kankya et al 2011; Muwonge et al.,2011 under review

Species	Host	Environmental source	Geographical location	Reported by
M. arupense		Household water	Mubende and Nakasongola	Kankya et al 2011
M. asiaticum	Swine		Mubende	Muwonge et al.,2011 under review
M. parascrofulaceum	Swine		Mubende	Muwonge et al.,2011 under review
M. bejali	Swine		Mubende and Nakasongola	Muwonge et al.,2011 under review
M. neoaurum	Swine, Human		Mubende,Kampala,Kyoga and Toro	Muwonge et al.,2011 under review; Stanford, 1976
M.duvalii	Swine, Human		Mubende, Toro, Kampala and Kyoga	Muwonge et al.,2011 under review; Stanford, 1976
M. smegmitis	Swine		Mubende	Muwonge et al.,2011 under review
M. salmonphilum	Swine		Mubende	Muwonge et al.,2011 under review
M. rhodesia	Swine		Mubende	Muwonge et al.,2011 under review
M. septicum	Swine		Mubende	Muwonge et al.,2011 under review
M. chelonae	Swine		Mubende Kampala,Kyoga	Muwonge et al.,2011 under review;Stanford, 1976
M. marinum	swine		Mubende	Muwonge et al.,2011 under review
M. komamatonse	Swine		Mubende	Muwonge et al.,2011 under review
Unidentified NTM	Cattle, human, swine	Valley dam water	Mubende, Karamoja and Kampala	Muwonge et al.,2011 under review; Oloya et al.,2007; Assimwe et al 2009

Table 1. Non-tuberculous mycobacteria isolated from Human, Animals and environments in Uganda

4. Non tuberculous mycobacteria in animals

The subject of NTM in humans and animals in the sub-Saharan Africa has received increasing attention in the recent past. Major concerns in the NTM transmission especially in immuno-compromised individuals has been associated with high levels of interactions occurring at the human-environment-livestock-wildlife interface.

4.1 Poultry

Avian tuberculosis is caused by *M. avium*, it is mostly known to occur in temperate zones and has been widely documented in North and South America and Australia (Barnes et al., 2003). In the United states Avian tuberculosis has been reported to be responsible the condemnation of 1870 per 100,000 birds slaughtered however the figures here were anticipated to be higher than this given that only visual inspection was used (Barnes et al., 2003). The incidence is reported to be low in South Africa while in Kenya it has only been documented in lesser flamingoes (Barnes et al., 2003). Uganda has 37 million chickens and about half a million turkey's. Unfortunately there has not been any studies done to document the prevalence of fowl tuberculosis despite the constant reports of clinical signs typical of this disease in poultry in the east and central region of Uganda (rural poultry farmers' personal communication).

4.2 Cattle

Bovine tuberculosis just like its human cousin *M. tuberculosis* has been given top priority in Uganda, simply because it is a well-documented zoonosis. Worldwide, the proportion of human cases caused by *Mycobacterium bovis* is estimated to be 3.1% of all forms of TB (Cosivi, 1998). In the most recent studies on the prevalence of bovine TB in pastoral areas of Uganda, tuberculin reactors were reported to be 6% of cattle in Mbarara district, an important dairy cattle area in the south west (Bernard et al., 2005), and a prevalence of 2·8% in nomadic cattle of Karamoja in the north east of the country (Oloya et al., 2006). Cattle herds in Uganda are concentrated along the cattle corridor that stretches from the south west to the north east through the central parts of the country. In another study done by Oloya (2007) in the same area gave the initial indication that Non tuberculous mycobacteria could be a public health force to reckon. This study found that NTMs were an integral part of bacteria isolated from disseminated tuberculous lesions and surprisingly these were almost equal in proportions (48.6:51.4) to *M.bovis* (Oloya et al 2007). Similarly a study done by Asimwe et al., 2009 on slaughtered cattle in Kampala revealed a similar pattern of isolation with *M.bovis* and NTMs accounting for 64.7% and 35.3% of the *mycobacterium* isolated from various tuberculous lymph node lesions respectively.

These finding further reaffirm the key role played by NTM in the tuberculosis pathogenesis. In two separate studies by Oloya et al., 2006 and Inangolet et al., 2007, shared water sources were identified as the responsible factor for a high prevalence of high avian reactors to the purified protein derivative (PPD) skin test.

The highest response to avian purified protein derivative (PPD) was observed in cattle 7-9 years old (figure 1) which was attributed to non specific immune response to environmental mycobacteria of the *Mycobacterium avium* complex prevalent in the natural water sources animals drink from. Therefore it is no longer disputable that NTMs are prevalent in cattle in Uganda but rather the effort should be on the role if any played by cattle in disseminating them to human populations.

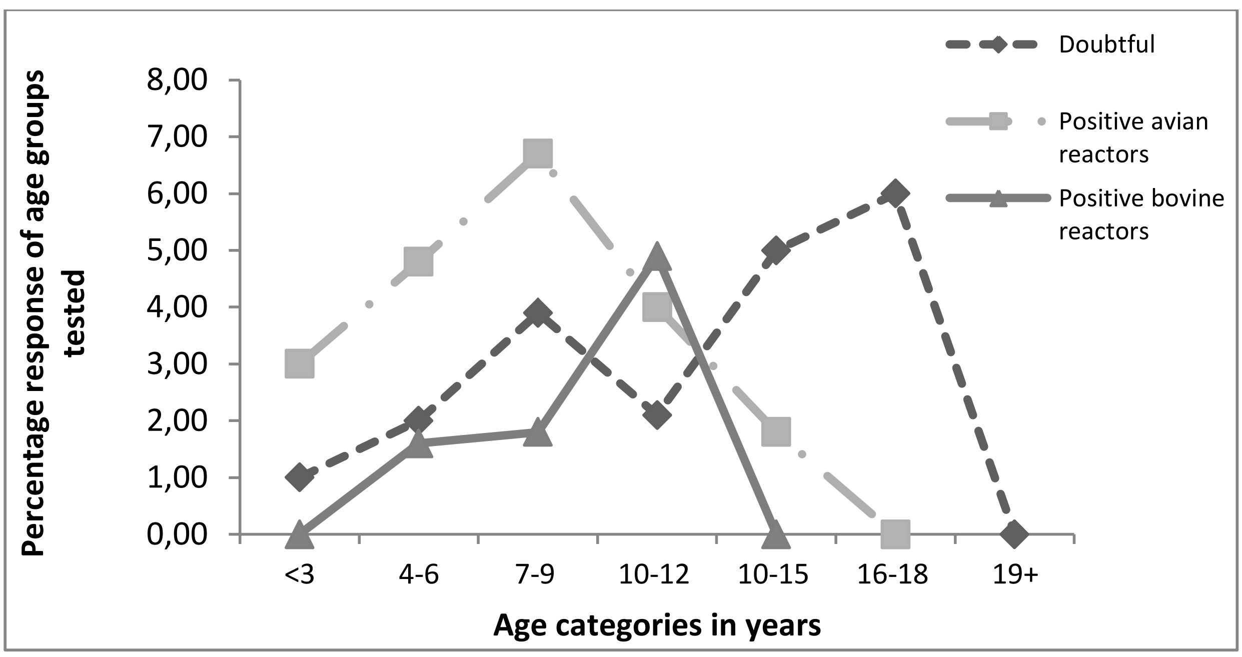

Fig. 2. Variation of skin reactions to comparative intradermal tuberculin test with age adapted from Oloya et al.,2006

4.3 Swine

Swine tuberculosis is a chronic infectious disease characterized by inflammatory reactions in various body parts but mostly in the digestive system. Calcification prone tubercles, inflamed lymph nodes and sarcoid-like granulomas are the most common features of this disease (Cvetnic, 2007; Coetzer, 2004; Ofukwu, 2010). The disease in swine is caused by *M. bohemicum, M. intracellulare, M. avium, M. hemophilum, M. malmose, M. szulgai, M. kansasii, M. scrofuleceum, M. tuberculosis, M.simiae, M. palustre, M. gordonae, M. terrae, M. xenopi and M. heckershornense* and other potentially pathogenic mycobacteria (PPM) (Jakko van Ingen, 2010, Cvetnic, 2007).

The only study in Uganda done on swine mycobacterial infection showed 9.3% and 3.1% prevalence based on necropsy examination and culture isolation, respectively (Muwonge et al 2010). A seasonal variation in prevalence of lesions typical of mycobacterial infections was also found in which lesions tended to increase after the rain season (figure 3).In a follow up molecular study on slaughter pigs in Mubende (Muwonge et al., 2011), *Mycobacterium avium* was the most prevalent *mycobacterium* specie accounting for 18% of the isolates from lymph nodes. Other species isolated included; *M. senuense, M. terrae, M. asiaticum, M. parascrofulaceum, M. bejali and M. neoaurum*, *M. simie, M. duvalii, M. smegmitis and M. parafortuitum,M.salmonphilum, M. rhodesia, M. septicum, M. chelonae, M. marinum,M. parafinicum, M. komamatonse and M. gordona* (Table 1).In general these findings are reflective of the NTMs load (infection/colonization) in swine reared in semi and free range systems, since the majority of the pigs in Uganda are reared in this system

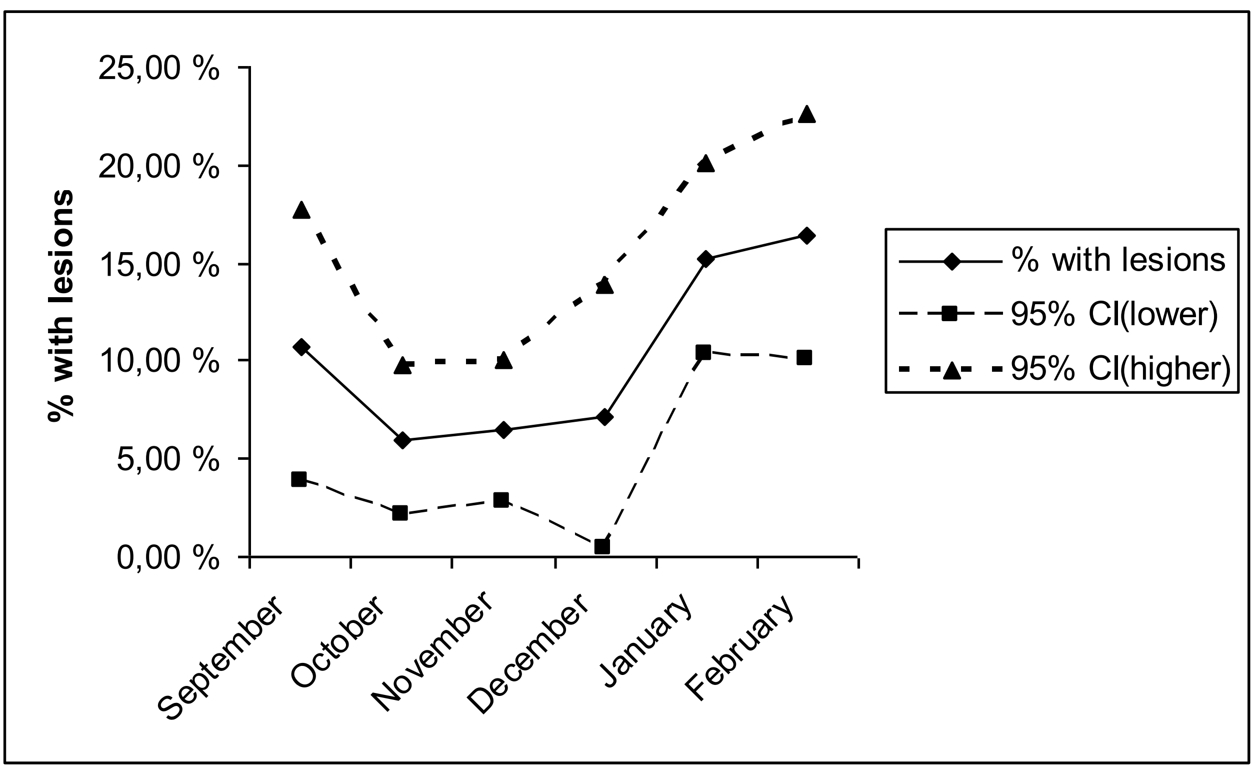

Fig. 3. Temperal occurrence of pathological lesions in slaughtered pigs in Mubende district (Muwonge et al., 2010)

5. Non-tuberculous mycobacteria in human

The absence of documented human to human transmission in the last 30 years has led to the conclusion that the environment is the source of NTM for human (Falkinham, 2009). In comparison to developed countries, NTM infections in humans are not well documented in Uganda. The few earlier studies did not show that disseminated *Mycobacterium avium* complex (MAC) infections was a problem in terminally sick AIDS patients unlike in the western world (Okello, 1990; Valadas, 2004; Chih-Cheng Lai, 2006). Subsequent studies further seem to support the absence of *M. avium* in HIV-infected Ugandans (Eaton et al., 1995). On the other hand Ugandan immigrants with AIDS in London had previously been diagnosed with symptomatic *mycobacterium avium* complex (MAC) infections (Nigel, 1993). These patients at the time of diagnosis had a CD4 count of $10X10^6$/L and some had been receiving treatment for extra pulmonary tuberculosis (Nigel, 1993). This disparity in prevalence at the time was explained by the speculation that temperate areas were preferential niches for NTMs and the superiority in diagnostics. It is now known that it was the latter, Nambuya et al., (1988) documented the prevalence of tuberculous lymphadenitis (which today is known to be caused by MTCs and NTM) but surprisingly they were unable to culture specimen to prove the cause. In 1998 Ssali et al reported for the first time presence of disseminated MAC and *Mycobacterium simiae* infections in HIV/AIDS patients in Mulago hospital in Uganda. This study showed that mycobacteriamia among febrile HIV-infected Ugandan adults accounted for 13% (Ssali et al., 1998). *M. avium* is also known to be one of the leading causes of infant lymphadenitis worldwide (Coetzer, 2004; Johansen, 2007; Van Ingen et al., 2009). This is in agreement with a study done in Uganda on the cause of cervical lymphadenitis. In that study the prevalence was highest among infants below 7 years of age and *M. avium* was the most frequently isolated NTM in this group (Oloya et al 2007). It is a common observation that NTM cause disease in individuals whose immunity has been compromised (Wolinsky, 1979; Wallace et al.,1990; von Reyn et al 1994; Falkinham et al 2009). Pneumoconiosis, cystic fibrosis, bronchiestasis , smoking and chronic alcoholism are some of the predisposing factors to NTM infections. The current technological advancements in diagnostics seem to indicate a possible further identification of more NTM zoonoses. In Netherland, Komjin et al., (1999) showed a close genetic relatedness between *M. avium* subsp. *hominissuis* isolated from swine and humans. Since then many scholars have continued to document more evidence re affirming the role pigs play in the transmission of mycobacterial infections to immunecompromised and immunecompetent indivuals. In 2007, Oloya et al isolated *M. avium* subsp.*hominissuis* from tuberculous lesions in cattle and T.B patients with cervical lymphadenitis in pastoral areas of Karamoja in Uganda. The molecular findings showed a very high genetic relatedness between animal and human isolates (figure 4 and 5). Although the true source of human infection is still a matter of dispute, these findings tend to point us to zoonotic scenario, with shared environment, in this case water, playing an important role. The true picture of human non tuberculous infections in Uganda is yet to be unveiled, but studies done elsewhere in Africa have indicated that this problem is bigger than previously documented (Buitjel, 2009).

5.1 Diagnostics and therapeutics

The greatest mistake in disease treatment arises when a physician is not well armed with facts about the cause of visible clinical signs, in other words a good diagnosis precedes a better treatment. Given the ubiquitous presence of NTMs in the environment and animal hosts, establishing the true causal relationship is highly dependent on representative sampling and stringent laboratory practices as contamination can easily occur. Another important problem is the overlapping of clinical manifestation of the disease caused by *M.tuberculosis* which makes the specific diagnosis of NTM disease practically impossible in poor health care settings. In Uganda, definitive NTM diagnosis in clinical setting is rarely done therefore, at the time of treatment commencement the only diagnosis available is presence/absence of acid fast rod like bacteria. This diagnosis is arrived at with the use of Ziehl-Neelsen (ZN) staining (Nation leprosy and tuberculosis programme). Literature on ZN staining indicates that the specificity is compromised by bacteria like *Rodococcus* that have the same acid fast characteristics thus giving some false positives (Coetzer, 2004). Definitive diagnosis on the other hand requires that a physician knows exactly which type of *Mycobacterium* is causing the clinical signs. This can be achieved using fast clinical diagnostic methods like; gene probes, Ino-lipa and *Mycobacterium* growth indicator (MGIT).

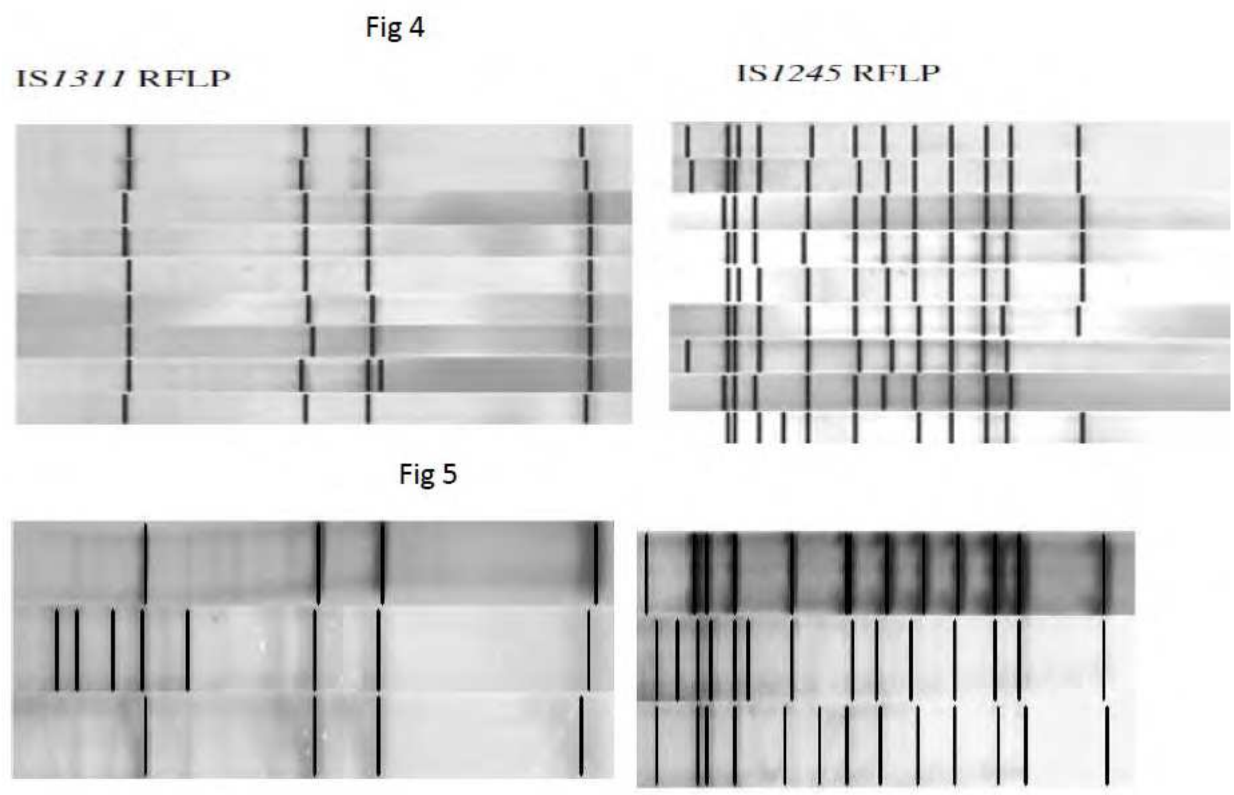

Fig. 4 & 5. Show the insertion sequences 1311 and 1245 of M. avium sub sp hominissuis isolated from humans with cervical lymphadenitis and cattle with disseminated tuberculosis respectively adapted from Oloya et al.,2007 a&b.

Most of these methods are available in Uganda however; they are mainly used for research and not routine clinical diagnostics. This is largely due to the fact that majority of people in Uganda cannot afford these extra costs to arrive at a definitive diagnosis. Fortunately, quick-cheaper, specific and sensitive diagnostic tools have been developed for example the ESAT-6 polymerase chain reaction primers which has been tailor-made to definitively diagnose *M. avium*, Serotyping methods using serotype specific sera for *Mycobacterium interacellulare scrofulaceum* (MAIS complex) and *M. avium* usually associated with AIDS patients can also be used in small and medium scale laboratories for definitive diagnosis (Kiehn et al., 1985; Singh et al., 2007; Wisselink et al 2010). NTM are generally resistant to the standard therapy Isoniazid, Rifampicin and Clarithromycin (Bum-Joon et al 2004). The reported resistance of *M. tuberculosis* (Asimwe et al., 2010) can be a contributing factor for the resistance in NTM due to constant exposure to these antibiotics as a result of lack of definitive diagnosis. There is optimism because of the consistent reported developments in medication which may improve on the treatment of NTMs for example dalfopristin, quinupristin and methoxy moieties of floroquinolones that are reported to have better effects (Lu et al., 2001; Braback, 2002; Singhai et al., 2010; Griffith et al., 2010). Their affectivity is however yet to be tested by the self prescriptive behavior common among Ugandans

5.2 Attitudes surrounding NTM

Uganda is blessed with a wide range of ethnic groups some with unique attitudes and perceptions with regard to prevention and control of infections (Nyanzi et al., 2005). Beliefs, myths, values, norms, taboos language, ritual and art are some of the cultural aspects that influence health of a given society. These cultural aspects describe the interaction between people, land and activities; they are also reported to influence the spread, control and prevention of diseases (Ntseane, 2004; Kyagaba, 2004). Tuberculosis, leprosy and Buruli ulcer are well documented simply because of the priority given to them by the Uganda health sector; this has negatively influenced the attitudes and perception of people towards the rest of NTMs that are regarded to be of less public health importance.

5.2.1 Socio-cultural attitudes in pastoral areas

In Uganda, studies done in rural areas have shown that there are many beliefs, attitudes and practices associated with NTM and other mycobacterial infections even when it is largely known that farming communities lack awareness with regards to mycobacterial infection, their epidemiology, and prevention and control strategies. Apart from mycobacterial infections due to zoonotic tuberculosis and classic tuberculosis; infections due to NTM have rarely been reported. Farming communities in Nakasongola and Mubende districts of Uganda lay their emphasis on the sharing of drinking water from open water sources with both domestic and wild animals as one of the major transmission route of NTM infection to humans and animals at the human-environment- livestock /wildlife interface (Kankya et al., 2010). Furthermore, attitude based studies have shown complacency in pastoral communities which is reflected in reports from service providers highlighted by statements like *''we teach community members that drinking un-boiled water is dangerous but they are stubborn as they continue to drink un-boiled water….many times they tell us that they have not died yet they have been drinking un-boiled water for decades"* commented; clinical officer Kiyuni Government Health Centre III, Mubende district Uganda (Kankya et al 2011 in press). Similarly in neighbouring sub county of Madudu residents said "*our grandparents and great grandparents used to drink un boiled water and milk and their cause of death was not as a result of drinking un boiled water and milk. We grew up drinking all these consumables raw, and that we have made it a cultural norm not to boil milk and water before consumption*" . Rural Africa is always punctuated with witchcraft, some communities have the belief that NTM infections can be caused by witchcraft (voodoo) and thus can be treated (Kankya et al 2011). Therefore families that have witches are believed to have the power to cause such diseases, and that this power can be inherited. Stigmatisation is probably one of the most important reason why these infections are under reported, rural communities are reported to say *"Some of us are sick and infected with mycobacterial infections such as tuberculosis, but we fear to disclose since these infections are associated with HIV/AIDS…''* (Kankya et al 2011). The affected individual would quickly be associated with HIV/AIDS. For the same reason, therefore affected individuals tend to shy away from seeking health services from the qualified health professionals. This aspect greatly impacts the health seeking behaviour (HSB) among the pastoral communities (Ashemeire, 2010).

5.3 Challenges and futures trends

The relative importance of mycobacterial diseases has been undergoing an evolution during the past few years, and further changes and modifications are expected to occur in the near future. The other concern especially in Africa has been the fact that non tuberculous mycobacteria diminishes the efficacy of the BCG (Brandt, 2002), the only available vaccine against tuberculosis. In a study done in Denmark it was shown in a mouse model that prior exposure to the Kalonga-Malawi environmental mycobacteria isolates resulted in reduction of efficacy or complete blockage of BCG activity (Brandt, 2002). This has however not yet been given its due attention in Uganda and therefore is anticipated to be a future challenge in the control of Tuberculosis especially in infants.

6. Conclusion

Non tuberculous mycobacterial infections have not been fully documented in Uganda because; 1) they are given less priority compared to TB regardless of the documented synergistic role they play in tuberculosis lesion development. 2) The dismissive attitude of communities, medical and veterinary fields as to their importance helps maintain their low priority status. With the wind of technological advancement in diagnostics and treatment blowing towards Africa, the increasing number of immune compromised individuals due to AIDS, it is anticipated that more infections due to NTM are likely to be discovered. Therefore the threat of NTM infections in Uganda is as real as the pandemic that precedes them.

7. Recommendations

1. NTMs are a force to reckon in the world today and therefore should be given priority by government, public, medical and veterinary fields.
2. The Ministry of Health and the available health marketing groups should put more emphasis on the campaigns geared towards a stigma free environment with regards to HIV/AIDS so as to improve the health reporting behavior among Ugandans

2a. The government should invest in disseminating free clean water sources like bore holes and piped spring water in rural areas to replace the valley dams which are reported to be the source of highly contaminated water.
2b. The government should improve the current waters sources for livestock and sensitize pastoral communities on the need to maintain them at reasonably high standards in a bid to reduce exposure to livestock.
3. The government should invest in research and innovation so that Ugandans develop tailor made diagnostic and therapeutic for Uganda and the great lakes region.

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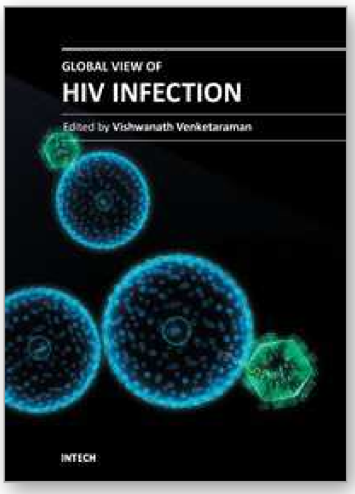

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