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Human and porcine *Taenia solium* infections in Mozambique: identifying research priorities

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Abstract

The objective of this paper is to critically review and summarize available scientific and lay literature, and ongoing studies on human and porcine cysticercosis in Mozambique to identify knowledge gaps and direct immediate and long-term research efforts. Data on the spatial distribution and prevalence of the disease in human and swine populations are scarce and fragmented. Human serological studies have shown that 15–21% of apparently healthy adults were positive for cysticercosis antibodies or antigen, while in neuropsychiatric patients seroprevalence was as high as 51%. Slaughterhouse records indicate a countrywide occurrence of porcine cysticercosis, while studies have shown that 10–35% of pigs tested were seropositive for cysticercosis antibodies or antigen. Current research in Mozambique includes studies on the epidemiology, molecular biology, diagnosis and control of the disease. Future research efforts should be directed at better understanding the epidemiology of the disease in Mozambique, particularly risk factors for its occurrence and spread in human and swine populations, documenting the socio-economic impact of the disease, identifying critical control points and evaluating the feasibility and epidemiological impact of control measures and development of local level diagnostic tools for use in humans and swine.

Keywords: cysticercosis, neurocysticercosis, epidemiology, immunodiagnosis, *Taenia solium*, Mozambique

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Introduction

Cysticercosis is considered to be a neglected zoonosis – a disease transmissible from animals to humans that draws little attention as it has largely been controlled in the developed world, even though it continues to have serious social and economic impacts in the developing world (World Health Organization [WHO], 2006). Nevertheless, it has been identified as one of six infectious diseases deemed potentially globally eradicable (Centers for Disease Control, 1993). Cysticercosis in humans is caused by the cysticercus larval stage of the tapeworm *Taenia solium*, after direct ingestion of eggs or consumption of food or water contaminated with eggs. Humans act as definitive hosts when infection by adult *T. solium* tapeworm in the small intestine causes the disease taeniosis. Pigs are intermediate hosts and develop *T. solium* cysts in their muscles and brain after ingestion of the parasite's eggs from human feces (Rey, 2008). Cysticercosis is typically a disease of the poor in developing countries, associated with lack of appropriate sanitation, free-ranging and scavenging pig production systems and inadequate or absent pork meat inspection.

T. solium cysts located in the brain lead to neurocysticercosis (NCC), which has been identified as the cause of 30–50% of epilepsy cases in developing countries (Bern *et al.*, 1999; Correa *et al.*, 1999; Román *et al.*, 2000; Mafojane *et al.*, 2003; Fisher *et al.*, 2005; WHO, 2006). This is strongly supported by a recent World Health Organization-commissioned systematic review of studies reporting the frequency of NCC worldwide that estimated the proportion of NCC among people with epilepsy of all ages to be 29.0% (95% CI: 22.9–35.5%) (Ndimubanzi *et al.*, 2010). In Africa, the prevalence of epilepsy has been estimated to be double that of developed countries (Commission on Tropical Diseases of the International League Against Epilepsy, 1994; Correa *et al.*, 1999; Román *et al.*, 2000). Winkler *et al.* (2009) estimate that 2–3 million people in sub-Saharan Africa have NCC-related epilepsy.

There are multiple prevention and control options for *T. solium* taeniosis and cysticercosis. They require food safety measures to avoid the consumption of contaminated meat. This can be achieved through the treatment of infected animals, condemnation of infected carcasses, thorough cooking of meat, and appropriate legislation regarding animal husbandry and commercialization (WHO, 2003). Food safety measures are also required to prevent ingestion of water and vegetables contaminated with *T. solium* eggs (Murrell, 2005; Willingham and Engels, 2006). Self-infection and human to human transmission can be avoided by good personal hygiene. The prevention of pig infection requires proper sanitation for human waste (i.e. no open human defecation) and improved swine husbandry to prevent access to human feces (Soulsby, 1982; Schantz *et al.*, 1993).

Proper case management based on standardized criteria and guidelines for early diagnosis and treatment (especially in peripheral health-care structures) combined with reporting and surveillance will help to understand the extent of the problem and the identification of transmission foci (WHO, 2003). The identification and treatment of individuals who are direct sources of contagion, and their close contacts, combined with hygiene education and better sanitation, will interrupt or reduce the cycle of direct person-to-person transmission, an approach that has been successfully applied to other contagious diseases (WHO, 2003).

Human tapeworm infection can be treated with either praziquantel or niclosamide (Willingham and Engels, 2006). Niclosamide has been the drug of choice because of concern that praziquantel treatment could lead to neurological symptoms (headache, seizures) when viable cysts are affected by the drug in those tapeworm carriers co-infected with non-symptomatic NCC (Flisser *et al.*, 1993).

A single dose of oxfendazole is effective for treatment of infection in pigs and cysticerci in the muscles of treated pigs disappear in 3 or more months (Gonzalez *et al.*, 1996; Liu *et al.*, 2003; Sikasunge *et al.*, 2008). Additionally, infection in pigs may be preventable by immunization as an experimental vaccine against *T. solium* in swine currently being tested in field trials may prove to be a control option in the future (Lightowlers, 2010).

Improvement of sanitary conditions of humans and animals along with awareness of parasite transmission cycle and hygienic behavior help in the prevention and control of cysticercosis (WHO, 2003). Most developed countries have controlled *T. solium* infection by improving sanitation and controlling domestic pig raising (Schantz *et al.*, 1993; Gilman *et al.*, 1999). However, each of these options presents unique challenges in the developing world where intervention measures for control are urgently needed.

Mozambique is located on the eastern coast of southern Africa. The country is divided into 11 provinces and has a total population of approximately 21.7 million people (Instituto Nacional de Estatistica, 2007). It is ranked 172nd of 182 countries in the UN Human Development Index (United Nations Development Program, 2010), with approximately 70% of the population in rural areas (Instituto Nacional de Estatística, 2007). Only 36% of the population in the country has access to safe drinking water, and less than 45% has access to sanitary facilities (Instituto Nacional de Estatística, 2007). There are 24 physicians per 100,000 people (Ministério da Saúde, 2007). Primary health care is delivered through rural health centers that typically cover an area of 8 km^2, but may cover more than 50 km^2 through mobile health-care agents (Ministério da Saúde, 2002). Some centers have basic medical laboratory services, such as fecal examination for parasite infection. Secondary health care is delivered by district hospitals, to which more complex cases are referred. Staffed by one or two general physicians, they cover populations of 50,000–900,000 and provide basic laboratory services and simple radiology. Provincial hospitals provide tertiary care, while quaternary care is provided by hospitals in Nampula (North), Beira (Central) and Maputo (South).

In pigs, cysticercosis causes economic losses associated with decreased productivity and decrease in the commercial value of infected animals as it makes pork unsafe for consumption (Garcia *et al.*, 2003). The last livestock census in Mozambique (2003) estimated the national pig population to be 1.4 million (Direcção Nacional de Pecuária, 2004). Swine production is present in all 11 provinces, with the central region home to the largest population (51%) followed by the south (37%) and north (12%) (Direcção Nacional de Pecuária, 2004). The smallholder sector, essentially comprised of free-ranging indigenous small black pigs, accounts for the majority of production (65%) (Direcção Nacional de Pecuária, 2004), with the number of pigs per family ranging from 2 to 10 (Penrith *et al.*, 2004). The majority of pigs are slaughtered in the backyard, without formal meat inspection. Slaughter inspection regulations do exist (Ministério da Coordenação Económica, 1975), but inspection services are carried out only in large urban centers. At the village level, meat may be informally inspected by rural animal health service providers. Traders regularly examine and palpate the tongues of pigs before purchase, with palpable cysts resulting in lower purchase price or refusal to purchase. However, much pork is consumed without meat inspection, which constitutes one of the important risk factors. There are currently no porcine cysticercosis surveillance or control programs in Mozambique.

The combination of swine husbandry and sanitation practices in Mozambique provides ideal conditions for endemic taeniosis in humans, and cysticercosis in humans and swine (Vilhena *et al.*, 1999; Mafojane *et al.*, 2003; Dorny *et al.*, 2004; Pondja *et al.*, 2010). The objective of this paper is to summarize and critically review the available scientific and lay literature, and ongoing studies on human and porcine cysticercosis in Mozambique to identify gaps in knowledge and to direct immediate and long-term research efforts. Ultimately, the paper is intended to raise awareness of national and regional stakeholders about the importance of this disease, and define research priorities in terms of the epidemiology, impact, diagnosis, treatment and control of *T. solium* infections.

Human cysticercosis status in Mozambique

The first human case of NCC in Mozambique was reported in 1968, as an incidental post-mortem finding in association with rabies (Serra, 1968). Studies of healthy adults conducted between 1994 and 2008 in Tete Province and Murrumbala, Marengo and Angónia districts used an enzyme-linked immunosorbent assay (ELISA) and found antibodies to *T. solium* cysts in 15–21% of the population (Vilhena and Bouza, 1994; Vilhena *et al.*, 1999; Afonso *et al.*, 2001; Vilhena, 2002; Noormahomed, 2005; Assane, 2009).

Researchers found that 20.8% (n=269) of children from 6 months to 15 years of age living in orchards around Maputo irrigated with water from sewage canals had antibodies to *T. solium* detected by ELISA (Noormahomed *et al.*, 2003), but fecal examination of the same population identified *Taenia* spp. eggs in only one child. A positive correlation was identified between having antibodies to *T. solium* cysts and age, with the risk of being positive increasing with age in children.

Studies in patients presenting with epileptic and neuropsychiatric symptoms found that the prevalence of individuals with antibodies to *T. solium* cysticercosis varied between 8 and 51% (Vilhena *et al.*, 1999; Noormahomed, 2005; Assane, 2009). Most recently, Assane (2009) conducted a study in Angónia District, Tete Province, to evaluate the association between epilepsy and NCC. Of 2023 individuals screened with a *T. solium* cysticercosis antigen ELISA, 15% were positive. Of these, 47% had a history of epilepsy and 43 (57.3%) out of 75 individuals positive for cysticercus antigens with associated epilepsy had brain lesions identified as *T. solium* cysts on computerized tomography scan (CT scan).

Capacity for *in vivo* diagnosis of human cysticercosis in Mozambique includes *T. solium* adult and egg detection, and *T. solium* larval cyst antigen and antibody ELISA available at the Medical and Veterinary Faculty laboratories at Eduardo Mondlane University. CT scanning is available in the three quaternary hospitals, and magnetic resonance imaging in Maputo Central hospital. Different methods for sample collection, storage, antigen preparation and blood or sera testing make it difficult to compare study results. Differences observed between studies can be attributed to differences in testing and sampling protocols, in addition to other factors such as differences in populations under study. Moreover, there is evidence that different antigenic patterns (Ito *et al.*, 2003; Sato *et al.*, 2006) and genetic populations (Nakao *et al.*, 2002) of *T. solium* exist, raising questions regarding the accuracy of tests using *T. solium* adult or metacestode antigens produced outside of Africa. However, according to the limited number of studies available, up to 20% of the general population in Mozambique may suffer from cysticercosis of the muscle or brain at one point in their life, and cysticercosis may be the cause of up to half of the neuropsychiatric symptoms observed in patients in Mozambique (Vilhena and Bouza, 1994; Vilhena *et al.*, 1999; Afonso *et al.*, 2001; Vilhena, 2002; Noormahomed, 2005; Assane, 2009).

Porcine cysticercosis status in Mozambique

The first description of porcine cysticercosis in Mozambique was in 1954 (Travassos Dias, 1954). Subsequent studies using slaughterhouse records demonstrated the presence of cysticercosis in all provinces, with prevalence estimates varying between 15 and 35% of carcasses examined (Abreu *et al.*, 1960; Cruz e Silva, 1971).

A study in Tete province using a porcine cysticercosis antibody ELISA found a 15% seroprevalence in swine (n=387) (Afonso *et al.*, 2001), and an immunoblot and antibody ELISA serology in Inhambane province with the same antigen showed a 10% seroprevalence (n=20) (Vilhena, 2002), but the number of samples was small. In Murrumbala and Zambézia provinces, 10 pigs were examined post-mortem and two were found to be infected with *T. solium* cysts (Vilhena, 2002). More recently, Pondja *et al.* (2010), in a cross-sectional study in Angónia district, found evidence of *T. solium* cysts on tongue palpation in 13% of animals examined (n=661), while 35% of these pigs were positive for porcine cysticercosis by antigen ELISA. The study identified increasing age and free-range production as the most frequent risk factors for porcine cyticercosis (Pondja *et al.*, 2010).

Capacity for *in vivo* pre-mortem diagnosis of porcine cysticercosis in Mozambique includes *T. solium* antigen and antibody ELISA available at the Veterinary Faculty, Eduardo Mondlane University and tongue palpation for cysts in rural areas. Post-mortem diagnosis is made by detecting *T. solium* cysts during meat inspection in major urban centers. Similar issues as discussed in the previous section with regard to sample collection, storage, antigen preparations and blood or sera testing in the diagnosis of cysticercosis in humans also pertain to its diagnosis in animals, and make reliable diagnosis of the disease in the veterinary sector problematic. Mozambique is a large country and there is a lack of information about the occurrence of porcine cysticercosis in many parts of the country, but in Tete province's Angonia district 35% of swine are infected (Pondja *et al.*, 2010). These findings suggest that porcine cysticercosis could be a public health problem in Mozambique.

Gaps in knowledge

Little is known about risk factors associated with human and porcine cysticercosis in Mozambique. Pondja *et al.* (2010) found that increasing pig age and free-range pig husbandry were the two main risk factors associated with porcine cysticercosis in Angónia district, Tete province. However, the full range of human and porcine cysticercosis risk factors needs to be identified and validated, and populations and geographic areas at risk targeted as priorities for further research and the foci of surveillance activities. Some studies have been conducted on the prevalence of human and porcine cysticercosis, providing evidence that NCC is an endemic public health threat. This threat may be increasing as swine population densities, particularly pigs under free-range production, increase. Yet, information on the nationwide prevalence of human and porcine cysticercosis, and human taeniosis, is lacking.

The socio-economic impacts of cysticercosis in Mozambique are not well understood. It is estimated that the number of epileptics may reach 4% of the population in rural areas, but the proportion of those due to NCC remains unknown (Yacubian, 2008). In the few regions where studies on human cysticercosis were conducted, the disability-adjusted life years as a measure of impact were not evaluated. Likewise, the economic impacts of cysticercosis in the public health and livestock sectors are not known. Documentation of the full impact of the disease along the swine value chain is necessary for public and animal health decision makers to understand its importance, and to allocate appropriate human and financial resources for its control and treatment. By documenting the epidemiology of taeniosis and cysticercosis, the value chain of swine and swine meat production, as well as the public health impact of the disease, the risk factors associated with maintenance and spread of *T. solium* in humans and livestock can be identified, leading to targeted control and preventive measures.

Although cysticercosis has been successfully controlled in the developed world, its control remains a challenge for poor countries such as Mozambique. Critical control points in the life cycle of *T. solium*, and along the swine value chain, need to be identified and tested for impact on taeniosis in human populations, and cysticercosis prevalence in human and swine populations. Research into the individual and cumulative effects of sanitation, swine production, communication, treatment and vaccination measures and the feasibility of their implementation and sustainability in Mozambique is necessary.

Research and surveillance need to be supported by reliable, appropriate diagnostic tools and protocols for taeniosis and cysticercosis in humans and swine. The existence of different genetic populations creates a challenge for the production of recombinant *T. solium* antigens, and emphasizes the need to validate the accuracy and reproducibility of tools for the serological diagnosis of cysticercosis in Mozambique (Ito *et al.*, 2003). A low-cost bed-side test for cysticercosis in rural areas would allow for screening of rural patients presenting with neurological symptoms, and referral of potential NCC patients to tertiary and quaternary hospitals for definitive diagnosis and treatment. Although there is awareness of the existence of NCC in Mozambique's medical community, protocols for the diagnosis, treatment and monitoring of cysticercosis cases are necessary. Such protocols should take into account existing human and infrastructure resources in the country, and the organization of the national health-care system. Likewise, low-cost pen-side serological tests for cysticercosis in swine would allow for targeted veterinary surveillance and control measures in high-risk areas.

Cysticercosis research priorities in Mozambique

In developing countries, resources for randomized large-scale epidemiological studies and surveillance are generally not available, particularly in the case of neglected zoonoses. Therefore, it is important to develop tools for identifying and analyzing populations that are at high risk of cysticercosis in Mozambique. Preliminary cysticercosis risk maps have been developed based on swine and human populations and they suggest that the central north and northeast areas of the country might be at higher risk of transmission of this disease (Pondja *et al*., 2009). However, targeted epidemiological studies are needed to validate these maps in predicted high- and low-risk areas. In addition, further research to understand cysticercosis risk in terms of production, marketing and consumption is necessary to improve their predictive value. If cysticercosis risk maps with a high degree of accuracy can be developed for Mozambique, they will be an important tool for targeting public health and veterinary cysticercosis surveillance and further research into cysticercosis control.

Control measures that are appropriate for Mozambique need to be developed and verified. In this context, an applied research approach with communities in areas of high pig population densities and proven high cysticercosis burdens would be appropriate to test the individual and cumulative impacts of different control measures on the incidence of human taeniosis, pig cysticercosis and, in the long term, human cysticercosis. Control measures tested should include improved human sanitation (i.e. ending open defecation), improved swine husbandry, detection and treatment of human patients with taeniosis, public health education campaigns and the prevention of cases in swine using chemical prophylaxis and/or vaccination. However, any research into the impact of cysticercosis control on disease incidence must also study the institutional feasibility of these measures in terms of national policy, cost, available infrastructure and community compliance, and their sustainability in the long-term.

Public and animal health decision-makers allocate resources according to their best understanding, based on available information, of the importance and impact of diseases. Therefore, in order to achieve cysticercosis control, an accurate understanding of the economic, public health and livestock production impacts of the disease is necessary. Human health and swine production parameters in communities with high and low human and porcine cysticercosis prevalences should be compared with corresponding information from cysticercosis-free communities, if possible.

Finally, ongoing research, surveillance and clinical care for cysticercosis must be supported by diagnostic tools and protocols that are appropriate for Mozambique. There is a need to validate the accuracy of diagnostic tools being produced at Eduardo Mondlane University for human and porcine cysticercosis, and to adapt these tools to field situations. A temperature stable bed-side test for human cysticercosis would allow rural health center staff to screen patients presenting with neurological symptoms to determine whether they have cysticercosis. The capacity for bed-side testing needs to be accompanied by standard operating procedures for referral of suspect patients to appropriate secondary or tertiary care facilities for definitive diagnosis and treatment. Likewise, pen-side testing for swine would allow community level veterinary practitioners to identify and treat pigs with cysticercosis. A reliable test for human taeniosis would also be helpful for identifying sources of eggs in populations, and assessing interruption of transmission in control programs. This capacity needs to be accompanied by public health communication regarding the dangers of swine cysticercosis and safe pork slaughter and preparation techniques.

Conclusions

Evidence indicates that cysticercosis is an important, but neglected, zoonotic disease in Mozambique. Up to 35% of the swine in some areas, 21% of humans, and half of the people presenting with neuropsychiatric symptoms may have cysticercosis.

Ongoing research on cysticercosis in Mozambique is making important strides toward understanding cysticercosis epidemiology, risk and diagnosis. However, critical knowledge gaps exist, including risk factors, nationwide prevalence, appropriate control methods and the economic, human health and livestock production impacts of cysticercosis. In addition, further work is needed to develop diagnostic tools appropriate for Mozambique.

There is a need to fill in the gaps of current research efforts with value added investments to address top research priorities. These include – epidemiological studies to strengthen and validate risk maps that can then be used in targeting research and surveillance; identification and validation of disease control measures that are feasible and sustainable in Mozambique; documenting the economic, health and production impacts of the disease so as to provide the necessary evidence for public and animal health decision making in terms of resource allocation and control policies; and the development and validation of diagnostic tools such as bed- and pen-side tests for local-level diagnosis, accompanied by diagnostic and treatment protocols to maximize community awareness and disease prevention and increase the entry of potential NCC patients into the health-care system for appropriate treatment and care.

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