

# Prevention and control of neurocysticercosis and epilepsy

Emilia Virginia traces the link between neurocysticercosis and other central nervous system parasitic diseases and epilepsy in Mozambique

Cysticercosis, caused by a pork tapeworm larva, is a zoonotic and neglected tropical disease (NTD) that forms cysts in the tissues of pigs and humans. Its consequences span reducing the value of pigs, making pork unsafe to eat, and leading to neurological disease including epilepsy and death in humans.<sup>1-3</sup>

It occurs where pigs range freely, sanitation is poor, and meat inspection is inadequate. It is strongly associated with poverty and smallholder farming, constituting a serious public health and agricultural problem in endemic countries of Africa, Latin America, and Asia. In these countries, the prevalence estimates range from 13% to 54% in general population.<sup>1-3</sup>

In humans, when cysts of *T. solium* larva are located in the central nervous system (CNS), the disease is called neurocysticercosis (NCC). Other symptoms of NCC include severe headache, blindness, hydrocephalus, chronic meningitis, intracranial hypertension, dementia and some neuropsychiatric disorders.<sup>1,2</sup>

It is estimated that in 2010 there were 370,710 affected by NCC and that it was the cause of death of 28,114 individuals. Computed axial tomography (TAC) and magnetic resonance imaging (MRI) studies in children and adult epileptics found brain lesions consistent with NCC, varying from 18.8% to 47.3%.<sup>1,4</sup>

The diagnosis of NCC remains a challenge because of the poor specificity of clinical and neuroimaging findings with magnetic resonance imaging (MRI) and computed tomography (CT-scan) and suboptimum predictive values in immunodiagnostic tests, particularly in endemic settings. Further, neuroimaging is expensive and very limited in low-income countries (LICs).<sup>2,5,6</sup>

NCC may remain asymptomatic for years with seizures being the most common presentation of symptomatic NCC, affecting from 70% to 90% of infected patients. The incubation period of cysticercosis is extremely variable, and the proportion of infected cases that will develop NCC is unknown.<sup>1,5</sup>

## The relation between NCC and epilepsy

NCC is considered the main preventable cause of epileptic seizures and late-onset epilepsy in young adults from LICs.<sup>1,2</sup> Approximately 80% of individuals with

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Brain CT showing neurocysticercosis nodules

epilepsy live in low-income countries (LICs), where its incidence is also higher compared to the incidence in high-income countries (HICs). This high prevalence and incidence of epilepsy in LICs is most likely associated with the higher incidence of adverse perinatal events, head injuries, and some parasitic infections, such as cysticercosis, toxocariasis, onchocerciasis and toxoplasmosis. Though epilepsy is considered a primary health problem by the WHO, the epilepsy treatment gap is >75% in LICs, compared with <10% in HICs.<sup>7,8</sup>

On the other hand, epileptic seizures due to NCC disappear in most patients after an effective anti-parasitic treatment combined with a short course of antiepileptic drugs (AEDs) – usually in about a year and half. Symptomatic treatment of epilepsy without knowing the underlying cause will condemn the patient to take AEDs for life.<sup>1,2</sup>

## Mozambique profile

Mozambique is a low-income country located in the southeast Africa with nearly 28 million people, an adult literacy rate of 60.7% and about 69% of its population leaving in rural areas. It ranks 184 in human development index, indicating a huge unmet need in health care delivery, education and basic living standards.<sup>9</sup> The national health system covers only 50 % of the population; and only 36% of those have access to a health facility within 30 minutes of their homes. Furthermore, only 7.2% of public health facilities offer any services for mental health.



Community health education

In terms of mental health care, Mozambique has only 18 psychiatrists for the entire country. To address the gaps in mental health care provision, the Mozambique Ministry of Health created a cadre of psychiatric technicians, whose number rose from 66 in 2010 to 241 in 2014.<sup>10</sup>

As is in many other African countries, Mozambique lacks epidemiological data on human and porcine cysticercosis. Serological studies found a sero-prevalence to *C. cellulosae* antibodies and antigens ranging from 14.9%–20.8% in the apparently healthy, while in people with psychiatric disorders the sero-prevalence to *C. cellulosae* antibody ranged from 7.6%–51.4%. In a community-based study conducted in Angónia district, located in the central western part of the country, it was found that 57.3% of epileptic patients with positive serology for cysticercosis had brain lesions consistent with NCC based on CT scan examinations.<sup>8,11</sup>

The prevalence of epilepsy is estimated to be between 3% and 4% and it is the second leading cause of out-patients in psychiatric consultation, and of these 54% are children below 18 years.<sup>10,12</sup> However, the underlying causes of epilepsy in these individuals are not well defined.

### Integrating mental health with NTD work

In most endemic countries, NCC occurs in about 30% of patients with epilepsy. So from this data it is clear that an important fraction of patients with epilepsy are due to NCC. Knowing the underlying causes for epilepsy will allow treatment not only symptomatically, but also with anti-parasitic drugs, thus reducing the time that patient will be taking AEDs. This in turn will reduce the pressure over the health systems in terms of human, infrastructure and financial resources, and scarce resources to be allocated to other priority areas.

It is well documented that epilepsy has a negative impact on health and quality of life of the affected families and communities, which includes stigma, low sense of self-esteem and low confidence, as it is often viewed as a punishment leading to social marginalisation. Societal consequences include burns, head injury, lack of education, being unmarried or unemployed.<sup>13</sup>

### Work in Mozambique

Zambezi Province is one of Mozambique's most populous provinces (5.5 million people) and one of the most heavily affected by HIV-1. Until recently, the province lacked a Central Hospital and many people were essentially outside the health care system.

This province is endemic with various chronic diseases and Neglected Tropical Diseases (NTDs), including epilepsy, cysticercosis, onchocerciasis, toxocarosis, intestinal parasites and food- and water-borne parasites such as toxoplasmosis. Yet, we do not know to what extent the CNS parasitic diseases are responsible for the high rates of epilepsy, especially in rural areas.

Though the diagnosis of cysticercosis/NCC is complex and tools are not available for most of population the focus should be directed to preventive measures to interrupt the cycle of *T. solium* in humans and in pigs.

Based on that and with support from the Health Education Partnership Initiative (HEPI), a partnership formed between Universidade Eduardo Mondlane (UEM) and the University of California San Diego (UCSD), together with administrative support from Mozambique Institute for Health Education and Research (MIHER), the Zambezi Provincial Directorate and National Directorate for Mental Health, we developed an innovative strategy to scale up training of health professionals in diagnosis and management of epilepsy, its possible etiological causes and preventive measure. We visited and met

community leaders and population in general to raise awareness about cysticercosis/NCC. This interaction allowed easy expansion of epilepsy treatment to the most remote areas and also to demystify the beliefs and stigma around epilepsy.

We also worked with agricultural officers to raise knowledge about porcine cysticercosis so that they would incorporate in their everyday activities the sensitisation of the population to recognise infected meat pork and ways to avoid contracting the disease from eating infected pork.

From 2018 to June 2020 we carried out a number of activities that included: (1) training of health providers (nurses, physicians, non-physicians technicians) in clinical features of NCC and epilepsy and its management; (2) working with community leaders and the population to explain to them the concerns about NCC, ways of transmission and prevention as well as availability of symptomatic treatment; (3) work with agriculture officers and raise their awareness about porcine cysticercosis and how to recognise infected meat.

As a result, the number of new cases of epileptic patients attended to in the Health Units from the entire province rose from 1,800 in 2017 to 3,605 in 2018, and later to 5,558 in 2019.

In terms of healthcare provider training, we were able to train more than 300 from the entire province on treatment of epilepsy, prevention and promotion of health to avoid infection by *T. solium*. During this period, we visited all districts and met community leaders and population in general to tell them about NCC and epilepsy, treatment options and preventive measures. These visits and meetings resulted in interaction with more than 250,000 people from all districts.

### Conclusion

By sharing human resources to jointly address mental health and CNS parasitic diseases preventive and curative strategies we were able to rapidly scale up the gap in the treatment of epilepsy to all primary health care units in the province, while raising awareness about NCC as one of the its causative agent.

Further, it was possible to train healthcare providers working at the primary level to treat and promote preventive measures for cysticercosis and NCC.

Through this initiative we set the basis to develop research with the aim to access the burden of NCC and other CNS parasitic diseases and their role on the development of epilepsy and other neuropsychiatric manifestations in this region, which could be translated to actions in other settings with similar problems.

This innovative approach should be followed by other LICs with a view to preventing and controlling NTDs and mental health problems, allowing the achievement of sustainable development goals.

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*Infected meat*

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### References

1. Carpio A, Fleury A, Romo ML, Abraham R. Neurocysticercosis: the good, the bad, and the missing. *Expert Rev Neurother*. 2018;18(4):289-301.
2. Garcia HH, Nash TE, Del Brutto OH. Clinical symptoms, diagnosis, and treatment of neurocysticercosis. *Lancet Neurol*. 2014;13(12):1202-15.
3. Nhancupe N, Noormahomed EV, Afonso S, Svard S, Lindh J. Further evaluation of recombinant Tsol-p27 by enzyme-linked immunoelectrotransfer blot for the serodiagnosis of cysticercosis in pigs from Mozambique. *Parasit Vectors*. 2019;12(1):564.
4. Assane YA, Trevisan C, Schutte CM, Noormahomed EV, Johansen MV, Magnussen P. Neurocysticercosis in a rural population with extensive pig production in Angonia district, Tete Province, Mozambique. *Acta Trop*. 2017;165:155-60.
5. Nhancupe N, Salazar-Anton F, Noormahomed EV, Afonso S, Lindh J. Further characterization of Tsol-p27 as a diagnostic antigen in sub-Saharan Africa. *Exp Parasitol*. 2013;135(3):573-9.
6. Del Brutto OH. Diagnostic criteria for neurocysticercosis, revisited. *Pathog Glob Health*. 2012;106(5):299-304.
7. Levira F, Thurman DJ, Sander JW, Hauser WA, Hesdorffer DC, Masanja H, et al. Premature mortality of epilepsy in low- and middle-income countries: A systematic review from the Mortality Task Force of the International League Against Epilepsy. *Epilepsia*. 2017;58(1):6-16.
8. Saldanha V, Saldanha G, Reys RP, Benson CA, Noormahomed EV. Neurocysticercosis in Child Bearing Women: An Overlooked Condition in Mozambique and a Potentially Missed Diagnosis in Women Presenting with Eclampsia. *EC Microbiology*. 2018;14(11):736-40.
9. Noormahomed EV, Mocumbi AO, Ismail M, Carrilho C, Patel S, Nguenha A, et al. The Medical Education Partnership Initiative Effect on Increasing Health Professions Education and Research Capacity in Mozambique. *Ann Glob Health*. 2018;84(1):47-57.
10. Wagenaar BH, Cumbe V, Raunig-Berho M, Rao D, Kohrt BA, Stergachis A, et al. Outpatient Mental Health Services in Mozambique: Use and Treatments. *Psychiatr Serv*. 2016;67(6):588-90.
11. Noormahomed EV, Nhacupe N, Mascaro-Lazcano C, Mauaie MN, Buene T, Funzamo CA, et al. A cross-sectional serological study of cysticercosis, schistosomiasis, toxocarosis and echinococcosis in HIV-1 infected people in Beira, Mozambique. *PLoS Negl Trop Dis*. 2014;8(9):e3121.
12. Patel V, Simbine AP, Soares IC, Weiss HA, Wheeler E. Prevalence of severe mental and neurological disorders in Mozambique: a population-based survey. *Lancet*. 2007;370(9592):1055-60.
13. Kariuki SM, Matuja W, Akpalu A, Kakooza-Mwesige A, Chabi M, Wagner RG, et al. Clinical features, proximate causes, and consequences of active convulsive epilepsy in Africa. *Epilepsia*. 2014;55(1):76-85.