The performance of a point-of-care test for the diagnosis of Neurocysticercosis in a resource-poor community setting in Zambia – a diagnostic accuracy study

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Summary

Background Neurocysticercosis (NCC) is the main cause of epilepsy in *Taenia solium* endemic rural communities. NCC diagnosis is difficult due to unavailability and unaffordability of serologic assays and neuroimaging. This study aimed to assess the performance of a cheap, novel *T. solium* lateral-flow point-of-care (TS POC) test for the diagnosis of NCC in a community setting.

Methods A diagnostic accuracy study with prospective data collection, using a two-stage design was conducted in Sinda district of the Eastern province of Zambia between December 2017 and June 2019. Eligible participants were tested with the TS POC test. Thereafter, participants with a TS POC CC+ result and a subset of participants with a TS POC CC– result were subjected to serological testing for reference assays, and cerebral computed tomography (CT) for the reference diagnosis of NCC.

Findings A total of 1249 participants were tested with the TS POC of which 177 (14%) were positive. Of the 151 TS POC CC+ and 82 TS POC CC– participants with cerebral CT examination, 35 TS POC CC+ and 10 TS POC CC–, respectively, had NCC. The sensitivity of the TS POC CC strip was 26% (uncertainty interval [UI] 15–41) for any type of NCC, which was similar to that estimated for the rT24H-EITB (23%, UI 8–48) and the serum antigen ELISA (30%, UI 11–58). The specificity was 88% (UI 85–90) for the TS POC, 89% (UI 79–94) for the rT24H-EITB, and 82% (UI 71–89) for the antigen ELISA. For NCC with active stage lesions, sensitivity was >99% (UI 58–>99) for the TS POC, 76% (UI 40–94) for the rT24H-EITB and 76% (UI 39–94) for the antigen ELISA.

Interpretation The TS POC CC had a promising sensitivity for diagnosis of participants with active NCC lesions within a community-based setting. Accuracy for NCC at any stage was limited for all tests (TS POC, rT24H-EITB and antigen ELISA). With further development the TS POC CC may enable a better detection and faster referral of NCC patients who may benefit from antiparasitic treatment.

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Research in context

Evidence before this study

Neurocysticercosis (NCC), caused by the larvae of the tapeworm *Taenia solium*, is a common cause of acquired epilepsy in low-income and middle-income countries. However, the disease remains asymptomatic in the majority of people, which makes an epidemiological assessment difficult. While anthelmintic medication for the treatment of NCC is available, many people go undiagnosed due to a lack of access to serological testing and neuroimaging facilities. Considering these challenges, the World Health Organization (WHO) has acknowledged the need for an affordable and user-friendly point-of-care (POC) test to facilitate the diagnosis of NCC. WHO has also outlined specific target product profile requirements for such a test.

We searched Pubmed on December 29, 2023, using the following terms ("neurocysticercosis" OR "cysticercosis") AND ("point-of-care" or "diagnostic test"). The search yielded 50 results; among those were the evaluation of the same novel lateral-flow point-of-care test in a hospital-based setting which yielded excellent results for patients with viable lesions. Another recently published study was a proof-of-concept study using a dipstick assay for cysticercosis antigen detection in urine samples of patients with subarachnoid NCC with high antigen levels. A further recently published study assessed an immunochromatography-based test kit to detect anti-*T. solium* IgG antibodies in human serum and found that this kit may be useful for follow-up monitoring of patients, post-treatment. These studies, however, were laboratory-based case–control studies whereas our study was community-based and cross-sectional.

Added value of this study

We assessed the accuracy of a novel lateral-flow *T. solium* point-of-care (TS POC) test for the diagnosis of NCC in a community setting - in comparison with the current standard reference tests. We found that the TS POC test performance was excellent in patients with active NCC lesions that can be treated with anthelmintic medication but had limitations in patients with inactive lesion. Furthermore, the TS POC test performance was similar to that of the rT24H-EITB and the antigen ELISA—for NCC at any stage, as well as for NCC with at least one viable lesion.

Implications of all the available evidence

The TS POC test has great potential for diagnosis and treatment of people with active NCC in low-resource settings. However, in settings where a considerable number of individuals are asymptomatic or have calcified lesions only, both the TS POC test and the reference tests show limitations. Considering the findings from this current study and the prior study utilizing the same TS POC test, it can be inferred that the TS POC test is well-suited for clinical settings supporting the detection of NCC lesions that can be treated with anthelmintic medication.

Introduction

Neurocysticercosis (NCC) occurs when the metacestode larvae of the pork tapeworm *Taenia solium* settle in the central nervous system. NCC can be asymptomatic but often presents with epileptic seizures, acute or chronic headache or focal neurologic deficits.[1,2] Infections occur when ingesting *T. solium* eggs through consumption of contaminated water, food or directly hand-to-mouth. *Taenia solium* is endemic in areas in Asia, sub-Saharan Africa and Latin America, where poor sanitation and hygiene prevail and where free-range rearing of pigs is practiced.[3] NCC has significant biomedical, public health, veterinary public health, socioeconomic, and environmental impact.[4] Studies showed that knowledge about the disease is limited even among health care personnel and practices that interrupt the life cycle of the parasite are hardly ever followed.[5,6] In Zambia, NCC is considered the main cause of epilepsy in rural communities where a high prevalence of *T. solium* infections was found.[7,8]

NCC diagnosis on clinical grounds alone is extremely difficult due to the lack of specificity of the neurologic signs/symptoms.[9,10] In resource-poor communities, NCC diagnosis is even more challenging because of a lack of neuroimaging equipment, skilled medical personnel, and appropriate serologic tests.[11] Some serologic assays have been developed for NCC but most of them have insufficient sensitivity (especially for patients with one cyst in the brain) and specificity.[12,13] The current assay of choice for clinical diagnosis and epidemiologic studies of NCC is the enzyme-linked immunoelectrotransfer blot (EITB), which makes use of lentil lectin-purified glycoprotein extracts of *T. solium* cysticerci. This assay has a sensitivity of 98% and

specificity of 100% for individuals with two or more viable or degenerating cysts[14,15] but accuracy of tests depends often on the laboratory and the test cannot easily be transferred from one laboratory to another. Despite the high sensitivity and specificity, this test is expensive and not easily applicable in resource-poor communities.[16]

The need for a simple to use highly sensitive and specific point-of-care test for NCC has led to the development of several rapid diagnostic tests, none of which have been evaluated in the population in which they are intended to be used.[17] For the diagnosis of symptomatic NCC patients, a minimum agreed target product profile with sensitivity of 98% and specificity of 90% have been defined.[18] The Centers for Disease Control and Prevention (CDC, Atlanta, GA, USA) collaborating with the Department of Neurology, Center for Global Health, Technical University of Munich (TUM, Munich, Germany) recently developed a two-strip single-cassette, point-of-care (TS POC) test for simultaneous detection of *T. solium* antibodies for taeniosis (TS POC T) and cysticercosis (TS POC CC) in humans. In a hospital setting in Tanzania, among patients with neurological signs/symptoms associated with NCC, the TS POC CC strip yielded good performance results for patients with active NCC lesions, which are treatable, and results were comparable to those of the current reference tests.[19] However, for epidemiological assessments of NCC and for the detection of people with (a)symptomatic NCC, a highly accurate test is necessary that should be evaluated in a community setting.

The aim of this study was to assess the diagnostic accuracy of the TS POC CC for diagnosis of NCC in a community setting. As an additional objective, the performance of the TS POC CC test strip was compared to currently used serological reference tests for detection of NCC.

Methods

The study was part of the SOLID project "Evaluation of an antibody detecting point-of-care test for the diagnosis of *T. solium* taeniosis and (neuro) cysticercosis in Tanzania and Zambia". The TS POC test was assessed in two different settings, in a community setting in Zambia and in a hospital setting in Tanzania.[11] The evaluation of the TS POC test for the detection of taeniosis and cysticercosis have been reported elsewhere.[20–22] We report here the results from the community-based study in Zambia (see below for details on the study site), focusing on the performance for NCC diagnosis.

Study endpoints

The primary endpoints were the sensitivity and specificity of the TS POC CC test strip for any type of NCC on neuroimaging defined as either active or inactive NCC. Secondary endpoints were the sensitivity and specificity of the TS POC CC to detect active NCC. Exploratory endpoints were the sensitivity and specificity of other serological tests (rT24H-EITB and serum Ag ELISA) for the detection of NCC.

Study design

The study was a prospective diagnostic accuracy study with a two-stage design and has been described in detail elsewhere.[11] Briefly, after obtaining written informed consent, all eligible participants were tested with the TS POC test (index test; stage 1). Those participants with a TS POC CC+ result and a subset of participants with a TS POC CC– result (every fifth) were subjected to blood and stool sampling for *T. solium* cysticercosis and taeniosis analysis, clinical examination, and cerebral computed tomography (CT; (stage 2)). Fig. 1 below depicts the study flow.

Study area

The study was conducted in Sinda district in the Eastern province of Zambia (Fig. 2). The area is well known for its high *T. solium* endemicity, the presence of free-roaming pigs and low sanitation levels.[23] Four Neighborhood Health Communities (Mtore, Butao, Chinzure, and Ndaula) comprising 40 different villages in the catchment of Mtandaza Rural Health Centre were selected based on their willingness to participate, proximity to the Rural Health Centre, and ease of accessibility.

Participant recruitment

A minimum sample size of 1200 participants was determined prior to the study for the assessment of the diagnostic accuracy of the TS POC test. Details on the sample size calculation can be found elsewhere.[11] The recruitment was conducted between December 2017 and June 2019. Participants were eligible if they were living in the study area, were 10 years of age or older, not pregnant and not severely ill.

Participant sampling

All participants with TS POC CC+ and TS POC T+ (i.e., TS POC T+CC+, TS POC T–CC+, TS POC T+CC–) test result were selected for sampling (further serological testing), clinical examination, and CT examination. Twenty percent of TS POC T–CC– participants were selected for sampling; among which half were selected for CT examination by tossing a coin, resulting in a final 10% of the TS POC T–CC– group that was selected for CT examination (Fig. 1). All those selected for a diagnostic CT examination were also examined neurologically and were administered a questionnaire on past medical history and specifically on epileptic seizures/headache at the Rural Health Center by a study doctor.

Index test—the TS POC

The TS POC is an antibody-detecting prototype test comprising two test strips in one cassette for diagnosis

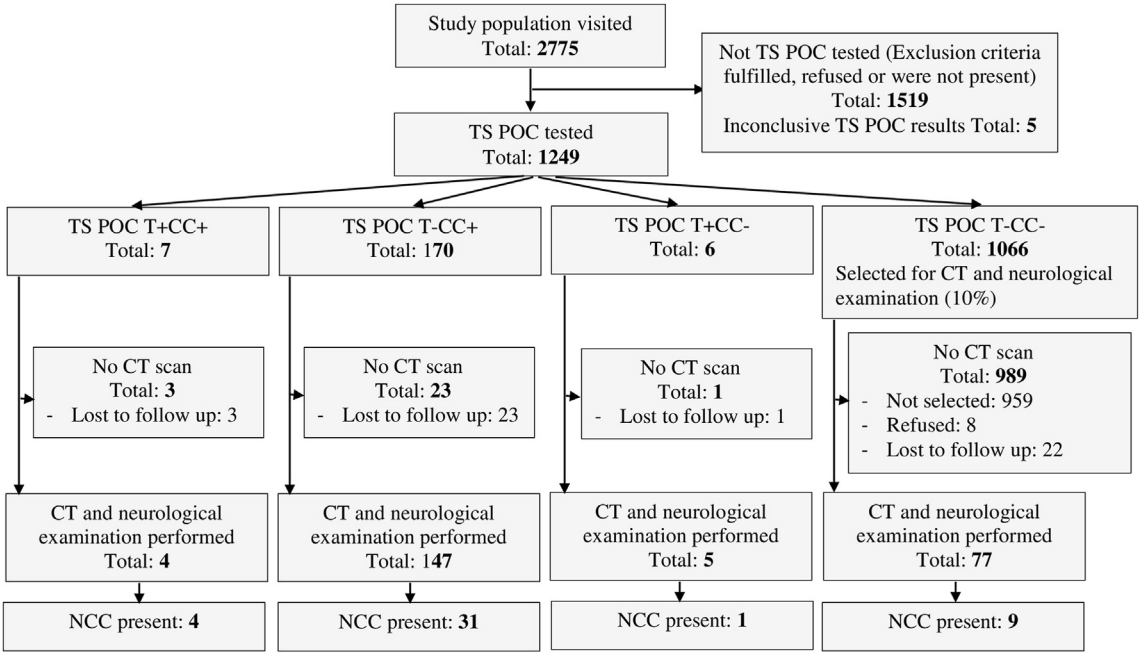

Fig. 1: Flowchart of the study to assess the performance of the TS POC CC test strip (index test) for the detection of NCC.

of taeniosis (TS POC T) and cysticercosis (TS POC CC). The test is an in-house produced standard lateral flow assay (LFA) based on two recombinant proteins, rES33 and rT24H.[24,25] The detailed information on how the TS POC test was performed and read is available in Mubanga et al.[21] The current study evaluates the TS POC CC test strip only.

Neurocysticercosis reference standard

Neurocysticercosis diagnosis was made following the principles of the revised Del Brutto criteria.[26] Details on neuroimaging procedures, classifications, and diagnostic criteria for NCC can be found in the Supplement (Text S1). Further on, stage of NCC was categorized as active (i.e., at least one lesions in vesicular, colloidal-vesicular or granular-nodular stage) and inactive (calcified stage).[27,28]

Fig. 2: Study area Sinda district.

Data analysis

The sensitivity and specificity were determined using survey-weighted generalized linear models.[29,30] The index test was included as outcome variable and the reference standard as predictor variable. Point estimates and confidence intervals were determined using the ggeffect package.[31] Weights were determined using the two-phase function[29] including the TS POC result combination as stratum identifier in phase two. This approach is used to account for the two-phase design and assumes that the reference standard is missing at random given the TS POC result combination of both test strips. Indeterminate index test results (n = 5) were excluded from the analysis.

Evaluation of disease progression

For several participants, the time between POC testing and the CT scan was longer than initially anticipated. In order to evaluate if the delay in CT would have an impact on our estimates for sensitivity and specificity, a subset analysis was performed using only participants who had a CT examination within two months after the TS POC test. Additionally, participants who had a CT examination more than two months after the TS POC

test were retested (Re-POC) using the TS POC CC test result at the time of the CT examination. To explore the time-lag effect, the analyses were repeated using the retest result (for subjects who were retested), or the original result (for those who were TS POC CC tested only once) as index test result.

Serological reference tests for cysticercosis

As part of the exploratory endpoints, the diagnostic accuracy measures were also determined for serum antigen ELISA and recombinant rT24H-EITB relative to any type of NCC and active NCC as reference standard, using only study subjects for whom all serological test results were available and a CT examination was performed.

Three serological reference tests for the diagnosis of cysticercosis were performed, the LLGP-EITB,[15] the rT24H EITB,[25,32] and the B158/60 serum antigen ELISA.[33,34] The chosen reference tests are the recommended tests for cysticercosis diagnosis.[26] Procedures for the reference tests have been described elsewhere.[20] As the LLGP-EITB tests reagents did not meet the internal quality control threshold (colour was very faint), the results of this test were not used in the analyses.

Trial registration and ethical consideration

The SOLID study was registered in the Pan African Trials Registry (PACTR201712002788898). All participants were informed about all parts of the study before inclusion, and all signed an informed consent form. For illiterate individuals and for underage participants (<18 years), a guardian signed the informed consent form after assent was given. All study partners obtained ethical clearance for the SOLID project: University of Zambia Biomedical Research Ethics Committee (UNZABREC 005-07-17), Technical University of Munich, Klinikum rechts der Isar, Ethical Committee (299/18S), Institute of Tropical Medicine, Belgium (IRB/AB/ac/112 Ref 1177/17), and University of Antwerp, Belgium (EC UZA 17/31/352). The reporting of this study followed the STARD checklist.

Role of the funding source

The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

Results

Population characteristics

A total of 1249 participants were tested with the TS POC test and had valid results (Fig. 1). The median age was 28 years (interquartile range from 18 to 44 years). More females (714; 57%) than males (535; 43%) participated in the study (Table 1).[20]

Parameter	Number (%)
Sex	
Female	714 (57)
Male	535 (43)
Age group in years	
≤20 years	409 (33)
21–40 years	466 (37)
41–60 years	256 (20)
61–80 years	98 (8)
>80 years	20 (2)
Age in years	
Median (IQR)	28 [18, 44]

IQR, Interquartile range.

Table 1: **Baseline characteristics of participants included in the study (n = 1249).**

Sensitivity and specificity of the TS POC test for the diagnosis of neurocysticercosis

Of the 1249 participants tested with the TS POC test, 177 (14%) were positive and 1072 (86%) were negative on TS POC CC. Within the TS POC CC+ groups (TS POC T+CC+ and TS POC T–CC+), 26 participants were lost to follow-up. From the TS POC T–CC– group only 77 of the 107 (72%) participants who were selected for CT examination had it performed (8 refused and 22 were lost to follow-up). A total of 233 (151 TS POC CC+ and 82 TS POC CC–) participants underwent cerebral CT examination of which 45 (35 TS POC CC+ and 10 TS POC CC–) had NCC (Fig. 1, Table 2). The Positive and negative predictive values were 23% and 88% respectively. The radiological description of the NCC lesions is shown in Table S1. Eight TS POC CC+ and zero TS POC CC– participants had active NCC. The number of NCC lesions in participants ranged from one to 24.

Detailed results of the clinical examinations are published elsewhere.[35] In summary, of the 45 participants with NCC, seven were symptomatic (reported epileptic seizures) (of which six were TS POC CC+; four with active NCC).

The results of the logistic regression with inverse probability weighting for the primary endpoints showed that the sensitivity of the TS POC CC for the diagnosis of NCC was 26% (UI 15–41), the specificity was 88% (UI 85–90). For the secondary endpoints, the sensitivity and specificity of the TS POC CC for the detection of active NCC were >99% (UI 58– >99) and 87% (UI 85–89), respectively.

When only considering the subgroup of participants for whom the CT was performed within two months of the initial POC test, the sensitivity and specificity of the TS POC CC were 18% (UI 8–38) and 87% (UI 83–90), respectively, with a positive predictive value of 22% and a negative predictive value of 81% (Figure S1, Table 3).

Number of participants TS POC tested	1249	
TS POC test result	TS POC CC+	[a]TS POC CC–
Number of participants with index test result	177	1072
Number of participants with CT examination result	151	82
Number of participants with NCC (%)	35 (23) [PPV]	10 (12)
Number of participants without NCC (%)	116 (77)	72 (88) [NPV]
Secondary endpoint		
Number of participants with active NCC (%)	8/35 (23)	0/10 (0)

CT, computed tomography; NCC, Neurocysticercosis; NPV; negative predictive value; PPV, positive predictive value; TS POC CC+, *T. solium* point-of-care cysticercosis positive; TS POC CC–, *T. solium* point-of-care cysticercosis negative. [a]The TS POC CC– are underrepresented in the subset of participants with a reference standard result as only 10% from the TS POC T–CC– group were selected for CT examination.

***Table 2*: Number of participants with Neurocysticercosis lesions according to TS POC test result.**

A total of 151 (65%) participants had a second TS POC test performed and 59 (39%) of those remained CC positive and 30 (21%) remained CC negative. Forty-two (28%) that were CC positive at first TS POC tested CC negative in the Re-POC, while 10 (7%) that were CC negative at first TS POC tested CC positive at Re-POC (Table S2).

Sensitivity and specificity of other serological tests for the diagnosis of neurocysticercosis

Of the 1249 participants tested with the TS POC test, 189 (15%) had a CT examination and both reference test results available (Figure S2). Among those with reference tests available, 30/124 (24%) TS POC CC+ and 4/65 (6%) TS POC CC– had NCC. The sensitivity of the rT24H-EITB (23%, UI 8–48) and the serum antigen ELISA (30%, UI 11–58) was comparable to that observed for the TS POC CC (Fig. 3). For NCC with active stage lesions, the point estimate of the sensitivity was higher for the TS POC CC (>99%, UI 58– >99) than for the rT24H-EITB (76%, UI 40–94) and the antigen ELISA (76%, UI 39–94, Fig. 4).

Discussion

In this study, we evaluated the diagnostic accuracy of the TS POC test, more precisely its CC strip, for the diagnosis of NCC in a resource-poor community setting in Zambia. Although there is a large uncertainty around the sensitivity estimate for active-stage NCC lesions, the TS POC CC performed well, with a sensitivity above 99%. These results are in line with a previously published assessment of the diagnostic accuracy of the TS POC CC for NCC in neurologically symptomatic patients attending district hospitals in Tanzania, which found a sensitivity of above 99% for patients with active-stage NCC lesions.[19]

	TS POC CC+	TS POC CC–
Number of participants with CT examination ≤ two months and both reference test results available (N = 72)	40	32
Participants with NCC	9 (22) [PPV]	6 (19)
Participants without NCC	31 (78)	26 (81) [NPV]

CT, computed tomography; NCC, Neurocysticercosis; NPV; negative predictive value; PPV, positive predictive value; TS POC CC+, *T. solium* point-of-care cysticercosis positive; TS POC CC–, *T. solium* point-of-care cysticercosis negative.

***Table 3*: Number of participants with Neurocysticercosis lesions according to CT examination performed less within two months of the TS POC test.**

The TS POC CC had only a limited accuracy for NCC at any stage, with a diagnostic accuracy that was comparable to that of the rT24H-EITB and the serum antigen ELISA. The sensitivity of the TS POC CC was much lower than the preliminary laboratory evaluation, which was conducted on serum of symptomatic patients with NCC lesions who were also serologically positive for cysticercosis (data unpublished). Among the reasons why the TS POC CC as well as the reference tests performed poorly (for any stage NCC) compared to these preliminary analysis is that the preliminary analyses were conducted in a diagnostic case–control study. Studies using a case–control design are prone to bias, as the selection of (extreme) disease positive (cases) and disease negative (controls) samples can result in inflated estimates of the diagnostic performance, known as spectrum bias.[36] As an example, to evaluate the diagnostic performance of the rT24H-EITB and the serum antigen ELISA test for the diagnosis of NCC, symptomatic patients with active-stage lesions were selected.[9] However, we conducted a community based, diagnostic cohort study to evaluate the test under real-life conditions. This included less severely ill patients, e.g., some without typical neurological signs/symptoms, patients with fewer lesions and patients with only calcified lesions who were also serologically negative in the two reference tests. In our population, most participants were asymptomatic, and many had only calcified NCC lesions—a sample that is representative for a community-based setting and not for case-control-based laboratory evaluations. Therefore, our estimates are more realistic for the study population than those from the preliminary laboratory evaluation.

Previous estimation of the performance of the rT24H-EITB for NCC diagnosis in a community-based setting revealed a sensitivity of 67% (2/3) for a single viable cyst, 80% (4/5) for multiple viable cysts and a specificity of 98%, though this was based on very few data points.[37] We found a very similar (slightly higher) point estimate with sensitivity of 76% with the rT24H-EITB for NCC with at least one viable lesion. The performance of this test for active NCC in our setting had a lower point estimate than the TS POC CC, though the uncertainty intervals were wide and overlapping. In contrast to our study, in the hospital-based TS POC test evaluation, the antigen ELISA and the rT24H-EITB also had a sensitivity of >99% for active-stage NCC.[19] The LLGP-EITB, despite being the current assay of choice

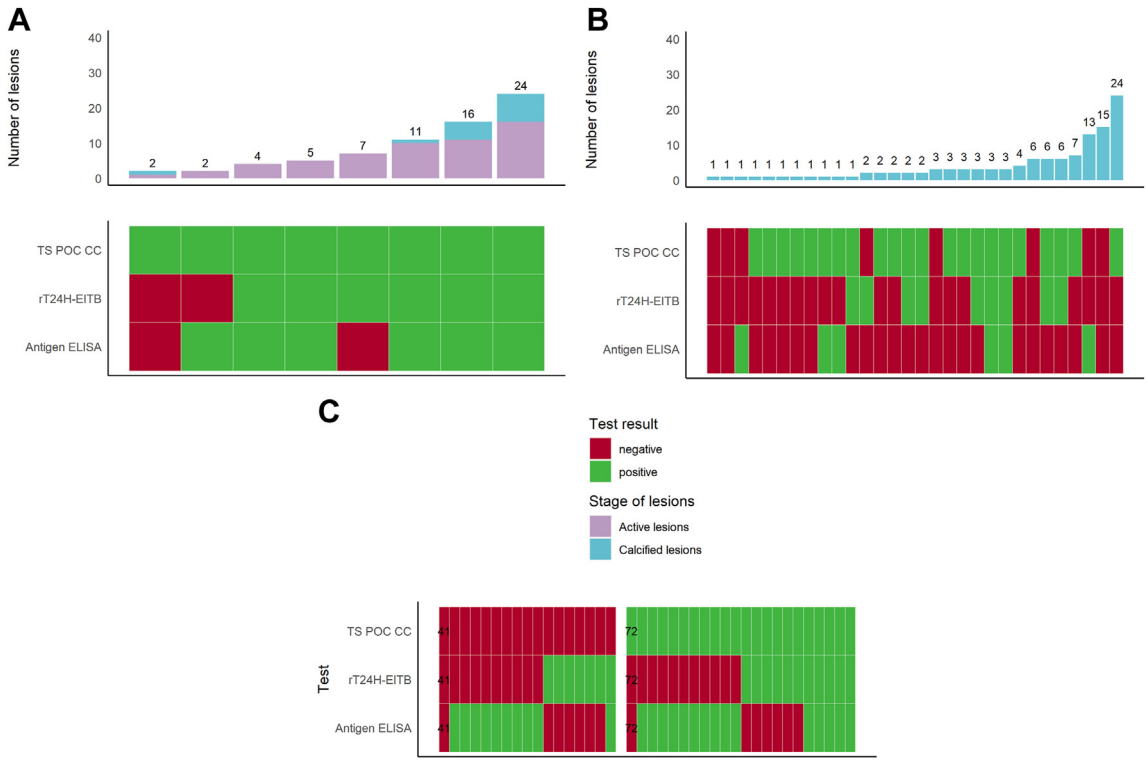

Fig. 3: TS POC CC results and serological reference tests by NCC status (disaggregated by A: active-stage NCC, B: only calcified stage lesions, C: No NCC); numbers on the bars indicate the number of NCC lesions. Each column represents one participant unless indicated differently by a number in the box. EITB, Electroimmunotransfer blot; ELISA, Enzyme linked immunosorbent assay; rT24H, Recombinant protein for *Taenia solium*; TS POC CC, *Taenia solium* point-of-care cysticercosis test. Note that the POC negatives are underrepresented in this figure.

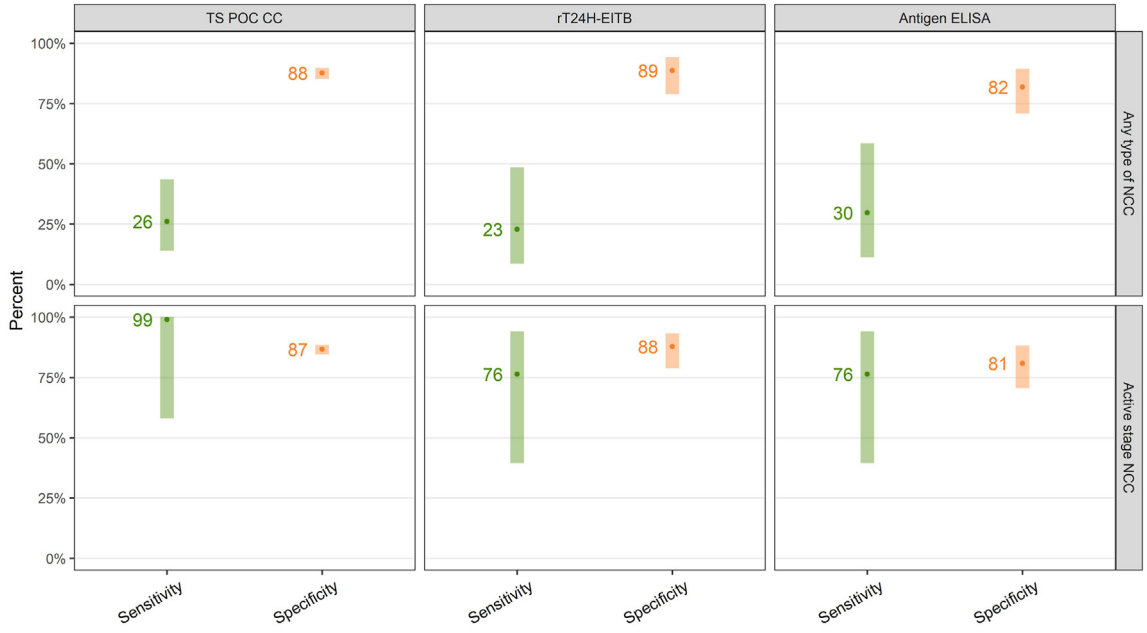

Fig. 4: Comparison of the performance of TS POC CC and serological tests for the diagnosis of NCC and active NCC. EITB, Electroimmunotransfer blot; ELISA, Enzyme linked immunosorbent assay; rT24H, Recombinant protein for *Taenia solium;* TS POC CC, *Taenia solium* point-of-care cysticercosis test.

for clinical diagnosis and epidemiologic studies of human cysticercosis, did not meet the quality control check and therefore data were not analysed.[20] It is difficult to exactly pinpoint the contributing factors behind this low performance of the LLGP-EITB test.

The agreed target profiles for NCC should be used to identify people with clinical signs suggestive of NCC. For human NCC, a POC test is recommended if it can identify symptomatic patients with viable cysts who need to be referred for confirmation by neuroimaging.[18] These patients are of particular interest as they may benefit from anthelmintic treatment with albendazole (and praziquantel).[38,39] Whilst the mid-point estimate of the TS POC CC met the sensitivity target for active NCC, the lower bound of the uncertainty interval was below the target profile threshold. TS POC CC test also fell short of the specificity target. Specificity as a target, however, is challenging, as the TS POC CC as well as the reference tests, are CC- and not NCC-specific tests. This means that CC cannot be ruled out if only neuroimaging is performed, as cysts may also be present in other organs. As a selector for neuroimaging, a highly sensitive test would suffice if there is no serological test to differentiate between patients with NCC and those with CC at other sites. We used CT imaging, but since this is not 100% sensitive for the detection of active NCC lesions, it may have had an impact on the sensitivity and specificity of the diagnostic tests.[9,40] Cross reactions with other pathogens also cannot be ruled out and would have had an effect on the specificity of the test. Improvements to the performance of the TS POC CC test could include the detection of low-titre antibodies by titration and optimisation of antigen and reagents combinations and work on improving the specificity as described by Mubanga et al.[20]

With regards to the TS POC CC and Re-POC, which was performed more than two months after the initial TS POC, 29% of the TS POC CC+ and 7% of the TS POC CC– at first TS POC changed results between the first and the second TS POC test. In the assessment of the temporal effect of diagnostic accuracy, we found a considerable proportion of people with a different Re-POC result compared with the initial TS POC CC result. It is not possible to evaluate if this change was due to seroconversion/seroreversion or because of test reproducibility issues (e.g., different reviewer of the test or different setting in which the Re-POC was performed). Another reason could be that the people who had a negative result had lower antibody levels on average, which are more difficult to detect and would be more likely to give a different result on repeated testing. Overall, it seems that there was no large effect of the prolonged time between the index test and the CT examination on TS POC CC test performance. The findings on potential sero-conversion/sero-reversion seem to be similar to those of a community-based study that showed over 40% seroconversion for serum antigens and about 39% for serum antibodies within a year of follow-up.[41]

This study also had some limitations. Seropositivity for CC was lower than anticipated in the sample size calculation, which meant there were only few people with NCC in our study area, resulting in wide confidence intervals around the sensitivity estimates. The low sensitivity of TS POC test to detect NCC also contributed to the few NCC cases in our sample. Another limitation of our study is the risk of bias due to dropout, which is a common problem in community-based studies. Despite regular follow-up, a substantial number of participants selected for CT examination were lost to follow-up. In this type of study design, the number of dropouts may be higher, especially if the reference tests (i.e., serological reference tests and CT imaging) are not performed at the same time as the index test (i.e., TS POC CC).[42]

In conclusion, this is the first study evaluating the performance of a TS POC CC test for diagnosis of NCC in a resource-poor community setting. For individuals with NCC with active-stage lesions, the TS POC CC showed promising results. Of course, neuroimaging remains the corner stone for assessing and detecting NCC at any stage. For symptomatic patients the test may be suitable for neuroimaging triaging needed for treatment decisions. The TS POC CC had a low sensitivity to detect any type of NCC in communities, which limits the use of the test for epidemiological assessment of disease burden. However, the TS POC CC test had comparable sensitivity to serological reference tests, hence the limitations of these tests should be considered when using them to detect NCC in communities. As the test was promising to detect all people with active lesions, irrespective of presence/absence of neurological signs/symptoms, it may be considered as a rule out test in the context of mass drug administration. Further large scale studies in endemic areas are needed to consolidate these results.

Contributors

Conceptualizations: GZ, DS, CM, VS, IVD, CT, PD, PM, KEM, SG, ASW, SG.
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Data sharing statement

The study data set is available at https://mediatum.ub.tum.de/1731900 and can be accessed upon request from the corresponding author.

Editor note

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Declaration of interests

We declare no competing interests.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.eclinm.2024.102893.

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