Recent Advances in Diagnosing of Human Cysticercosis

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Kostadin Kanchev[1] and Saba Mehnaz[2]

ABSTRACT

Cysticercosis in humans is a parasitic disease caused by Cysticercus (C.) cellulosae, the larval stage (known as metacestode) of the Cyclophyllidean tapeworm Taenia (T.) solium. It is a highly prevalent infection in India, China, the Southern part of the African continent, South America, the Central American region of North America, and a few Eastern European countries. T. solium (neuro cysticercosis, NC) causes a zoonotic disease complex. According to many authors NC is considered as one of the most important food-borne zoonotic diseases respectively, caused by helminth parasite. Accurate and prompt diagnosis is essential for early detection and effective treatment of the disease. Diagnostic approaches including: Direct Detection of metacestodes and tissue lesions in CNS and soft tissues; Various Imaging Techniques like: CT, MRI, Ultrasonography (US) and X-ray; Classical and Rapid Serology tests and Molecular techniques. Neuroimaging by CT or MRI is critical in the diagnosis of neurocysticercosis. MRI is more expensive but is becoming more accessible in developing countries often provides a clearer picture of cysticerci and has greater sensitivity for multiple lesions. Serological testing provides important confirmatory data for patients with suspicious lesions on CT or MRI. Serological testing has improved, with a sensitivity of 98% and a specificity approaching 100%. The electro-immune-transfer blot (western blot) assay using lentil lectin purified glycoprotein antigens (LLGP-EITB) is preferable to the ELISA for the identification of anti-cysticercal antibodies in human serum. Low molecular weight metacestode secretion proteins, and especially glycoproteins, have shown the best performances in NC diagnosis assays. The LAMP (loop-mediated isothermal amplification technique) test would be a very useful tool to contribute to reducing the incidence of cysticercosis in developing countries, except when the cysticerci are calcified, because in that case no circulating antigens are available. Ideally both ways are used, combining the advantage of the higher sensitivity of MRI with CT detection of calcium. Identifying of human cysticercosis is possible by collecting and analyzing laboratory results and clinical/epidemiological data strictly following Del Brutto's revised diagnostic criteria.

Key words: human cysticercosis diagnosing, neuro cysticercosis, Cysticercus cellulosae, Taenia solium metacestode

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[1] Department of Infectious pathology, HTCFAO, Faculty of Veterinary Medicine, University of Forestry, Sofia, Bulgaria
[2]Department of Parasitology, Faculty of Veterinary Science, University of Agriculture, Faisalabad, Pakistan
***Corresponding author:** kkanchev@ltu.bg

1. INTRODUCTION

Cysticercosis in humans is a disease caused by infestation with *Cysticercus* (C.) *cellulosae*, the larval stage (known as metacestode) of the tapeworm *Taenia* (T.) *solium* (Linnaeus 1758). It is a highly prevalent infection in India, China, the Southern part of the African continent, South America, the Central American region of North America, and a few Eastern European countries (WHO 2020). The *T. solium* metacestode is located in subcutaneous space, intermediate host internal organs (Chatuthanai et al. 2022) and muscles, but more often invades the central nervous system (CNS), resulting in a medical syndrome known as neurocysticercosis (NC). Separate intramuscular *C. cellulosae* cysticercosis without the involvement of the central nervous system is very rare (Dwipayana et al. 2022). Metacestodes affect predominantly the central nervous system (97.46%), followed by ocular localization (1.4%), rarely subcutaneously, and soft tissue infection (1.14%) (Gnanamoorthy and Suthakaran 2019). NC, a leading cause of adult-onset seizure disorder, is a major global public health concern from parasitic origin in many endemic areas. NC may cause neurological manifestations such as epileptic seizures and/or chronic prolonged headaches (Li et al. 2019). The intensity of presented clinical signs and their frequency depends on the size, number of growing cysts, predilection site, and inflammatory stage of the cyst in the brain (Mlowe et al. 2022). Parasite subcutaneous tissue location may provoke the formation of palpable nodules, on the other hand, diffuse intra-muscular cysticercosis may present as myalgia, or pseudo-hypertrophy (Gnanamoorthy and Suthakaran 2019). Clinical symptoms of pulmonary cysticercosis include cough, sputum production, constitutional disorders, pulmonary nodule/s, and pleural effusion (Savigamin et al. 2022).

T. solium (neuro cysticercosis) causes a zoonotic disease complex. According to many authors NC is considered as one of the most important food-borne zoonotic diseases respectively, caused by helminth. Annually, NC causes approximately 28,000 deaths and more than three million people are at risk of infection (Despommier et al. 2019). NC is becoming an emerging or re-emerging disease in industrialized countries from endemic areas. The presented problem is a result of the increased global traveling due to business trips or tourism (Chun-Seob et al. 2019). NC is one of the leading causes of human epilepsy in many hyper-endemic regions in Latin America, Asia, and sub-Saharan Africa. In endemic regions, NC accounts for 10%–12% of all hospitalizations in hospital neurology departments. The World Health Organization (WHO) reports an estimated 2.5–8.3 million cases of NC annually with a disability-adjusted life year burden of 2.8-5.0 million people and 3%–6% population in endemic regions, but as for all neglected tropical diseases these values are likely to be underestimated (Jobanputra et al. 2020; Butala et al. 2021).

C. cellulosae metacestodes are rounded or oval cysts, up to 15 mm in diameter, whitish, filled with transparent fluid, and possesses a single invaginated scolex (bearing hooks and four suckers typical for *T. solium*) which can be seen as small eccentric solid granule. Occasionally, large, irregular, fluid-filled, and round or lobulated cysts, similar to a bunch of grapes known as racemose cysticercus (*Cysticercus racemosus*).

This infection thrives in areas with poor sanitary facilities, overcrowding, poor personal hygiene, and places, where pigs are reared commonly. Note that cysticercosis is acquired from the fecal-oral route (ingestion of eggs). This may happen when humans drink water or eat fresh vegetables or fruits contaminated with tapeworm eggs or put contaminated feces fingers in their mouths. People who live with someone who has a tapeworm infection in their intestines have a much higher risk of getting cysticercosis than other people. When the egg is ingested, the embryo (oncosphere) inside survives the action of gastric hydrochloric acid in the stomach and enters the small intestine. The egg hatches and the larva penetrate the intestinal wall and enters the bloodstream of the intermediate host. Eventually, the oncosphere penetrates into one of many tissues (e.g., striated muscles, heart, brain, eyes) and encysts there into a cysticercus-type metacestode, grows, develops, and creates a space-filling lesion within 2–3 months. Parasite life

cycle maintenance between humans and pigs is attributed to poor sanitation, unhygienic practices in food preparation, inadequate hygienic measures of the slaughter house personnel, improper handling of infected pig carcasses. *T. solium* cysticercosis positive pig carcasses are not properly treated (buried or incinerated), and poor pig husbandry practices in which pigs are left to scavenge on human feces and eat feeds and drinking water contaminated by *T. solium* infective eggs (Kungu et al. 2015).

2. DIAGNOSTIC APPROACHES FOR HUMAN CYSTICERCOSIS EVALUATION

2.1. DIRECT DETECTION OF METACESTODES AND TISSUE LESIONS IN CNS AND SOFT TISSUES

NC is usually revealed during necropsy and confirmed by further biopsies (postmortem). Ophthalmologic examination is of great use in cases of ocular cysticercosis. When cysticerci are located in muscles or subcutaneous tissue, palpation, biopsies, and fine-needle aspiration cytology are employed, with rapid onsite evaluation. A technique known as fine-needle aspiration (FNA) of a viable cysticerci cyst yields clear fluid and bladder wall fragments in a clear acellular background, whereas aspirates from necrotic lesions contain bladder wall fragments, including calcareous bodies and detached from rostellum single hooks. This approach is effective in cases of subcutaneous cysticerci. Diagnosis of cysticercosis is made on fine needle aspiration cytology (FNAC) only when fragments of metacestode tegument and parenchyma are identified, which were absent in the present case. Even to suspect a parasitic infection characteristic cell type host inflammatory reaction consisting of eosinophils, neutrophils, palisading histiocytes, and giant cells must be present in the aspirate from suspicious subcutaneous nodule (Koteeswaran et al. 2013). Cytochemical evaluation of cerebrospinal fluid is also of great help in extra parenchymal cysts, showing various stages of inflammatory cell reaction (increase of lymphocytes, proteins, and hypoglycorrhachia) that are important to perform prognosis before antiparasitic treatment.
Differential diagnosis (DD) from other pathogens and pathological conditions should be made necessary. All presented parasitological methods enable early parasitic infection detection, particularly when lesions are found in anatomically approachable superficial sites.

2.2. IMAGING TECHNIQUES

CT and MRI are key tools for the imaging diagnosis of NC, since they allow revealing the number, size, evolutionary stage, and specific location of the lesions (Nepal and Ojili 2021). Cysticerci of *C. cellulosae* have variable appearances in neuroimaging studies. Inside the brain parenchyma, metacestodes show different visual characteristics according to their evolutionary stage: cystic-like lesions without amplification (vesicular cysticerci), contrast based hyper enhancemented cystic or nodular lesions (colloidal and granular cysticerci), and small globular calcifications (calcified cysticerci).
The same parasites in the subarachnoid space may be present as multiple confluent cysts (racemose cysticerci) or may appear as focal or diffuse arachnoiditis that most often involves the Sylvian fissure or the basal brain cisterns, which is typical to the picture of obstructive hydrocephalus. Intra-ventricular metacestode cysts appear as lesions with different signal properties than the ventricular fluid, distorting the normal structure of the ventricular system and leading to asymmetric hydrocephalus. Some of the present cysts may contain parasite scolices (Pineda-Reyes and White 2022).
Spinal cord-located cysticerci appear as nodular or cystic lesions if they are present intramedullary or as focal or diffuse spinal arachnoiditis with or without cysts into the spinal subarachnoid space (Yang et al. 2022). Lesions in the ventricles and the cisterns (Garcia et al.

2020) are better visualized by using volumetric balanced steady-state gradient echo sequences (FIESTA, BFFE, or CISS).
Ultrasonography (US) and MRI findings allow for identifying intramuscular cysticerci even if solitary cysts are present. Imaging techniques have improved the detection of scolices and visualization of cysts in extra parenchymal spaces (Del Brutto et al. 2017; Nash et al. 2020). High-resolution ultrasonography is very helpful in settling down the exact DD: Lipoma US findings are hyperechoic lesions with no evidence of cystic-like pathological changes. Neurofibromas are hypoechoic structures near the nerve, which are proximally and distally visualized by the US. Schwannomas respectively are hypoechoic lesions present eccentric to the nerves (Jeyakumar et al. 2022). High-resolution ultrasonography is the first choice in intra-parenchymal stages of cysticercosis in humans and various animal species inside abdominal or pleural cavities especially effective for rapid and inexpensive diagnosis in the acute migration phase (Kanchev 2013). Neuroimaging techniques are more helpful than serology in providing data about the number, size, predilection site, and stage of lesions, also in peri-lesion inflammation type and response (Garcia et al. 2020).
X-ray is not so sensitive and accurate IT method due to the visualization of already formed calcified foci (Maquera-Afaray et al. 2014). Radiography is a possible choice for visualization of cysticercus in predilection sites of parasites in internal organs parenchyma or skeletal muscles.
Computed tomography (CT) is more sensitive test in detection of calcified lesions but magnetic resonance imaging (MRI) is more accurate for the detection of the metacestode scolex, edemas, small parenchymal foci and abnormalities, lesions inside posterior fossa, and the involvement of the subarachnoid spaces and ventricles in infection with the parasite. The fluid attenuation inversion recovery (FLAIR) technique is particularly very helpful for identifying associated tissue edema and cysticercus scolex (Clinton et al. 2018).
The advent of CT changed the landscape of NC diagnosis by revealing many clinical cases with mild disease, much more benign than the severe cases seen before, which were limited to those that could be detected by old, less-sensitive techniques. The introduction of MRI improved imaging definition and added the capacity to present images in different visual planes (Garcia et al. 2020). Imaging diagnosis of human cysticercosis needs precise CT or MRI scans and further image reliance by qualified and experienced radiologists. DD: cysticercosis must be differentiated from cystic-formed tumors that bear debris of neoplastic cells in the interior area of the cystic compound resembling a scolex (pseudo-scolices). Warning of patients with a single intra-parenchymal brain cyst (Del Brutto 2022).
The complexity of NC clinical signs and the difficulties in diagnosing, and identifying human cysticercosis is possible by collecting and analyzing laboratory results and clinical/epidemiological data strictly following Del Brutto's revised criteria (Table 1).

2.3. IMMUNO-DIAGNOSTIC TESTS

2.3.1. CLASSICAL SEROLOGY DIAGNOSIS

Neuroimages may be highly compatible with NC diagnosis. In many cases, the diagnosis is not conclusive. Serology plays a major role in confirming the diagnosis (Deckers and Dorny 2010).
Antibody detection is most frequently used because of its higher sensitivity, while antigen detection is very effective in cases where live parasites are available. The enzyme-linked immunosorbent assay (ELISA) for the detection of anti-cysticercal antibodies has been used for NC diagnosis and is still used in many countries where more advanced tests are not available. Recent studies have documented reliability problems with the use of ELISA, because of the involvement of crude and semi-purified antigenic extracts in reaction, which makes this test

unreliable for cysticercosis diagnosis. The electro-immune-transfer blot (western blot) assay using lentil lectin purified glycoprotein antigens (LLGP-EITB) is preferable to the ELISA for the identification of anti-cysticercal antibodies in human serum. This test has a sensitivity of 98% in patients with more than one cysticercus and no cross-reactivity with antibodies induced by other infections appears. Unfortunately, LLGP-EITB sensitivity drops down to about 50%-70% when patients have a single parasite cyst or they are calcified (Del Brutto 2022). Several studies, as well as the Pan American Health Organization, have recognized LLGP-EITB as the gold standard for NC. LLGP-EITB has 100% specificity and is confirmed overall sensitivity of 98%. The introduction of monoclonal antibodies-based antigen detection by ELISA is an encouraging approach for cysticercosis diagnosis (Ferrer and Perteguer 2022).

Table 1: Diagnostic criteria and degrees of diagnostic certainty for diagnosing of NC (described and revised by Del Brutto et al. 2017)

Absolute criteria:	Neuroimaging criteria:	Clinical/exposure criteria:	Degrees of diagnostic certainty:
• Histological demonstration of the parasite from a biopsy of a brain or spinal cord lesion • Visualization of subretinal cysticercus • Conclusive demonstration of a scolex within a cystic lesion on neuroimaging studies	Major neuroimaging criteria: • Cystic lesions without a discernible scolex • Enhancing lesions • Multi lobulated cystic lesions in the subarachnoid space • Typical parenchymal brain calcifications Confirmative neuroimaging criteria: • Resolution of cystic lesions after cysticidal drug therapy • Spontaneous resolution of single small enhancing lesions • Migration of ventricular cysts documented on sequential neuroimaging studies Minor neuroimaging criteria: • Obstructive hydrocephalus (symmetric or asymmetric) or abnormal enhancement of basal leptomeninges	Major clinical/exposure: • Detection of specific anticysticercal antibodies or cysticercal antigens by well-standardized immunodiagnostic tests • Cysticercosis outside the central nervous system • Evidence of a household contact with *T. solium* infection Minor clinical/exposure: • Clinical manifestations suggestive of neurocysticercosis • Individuals coming from or living in an area where cysticercosis is endemic	Definitive diagnosis: • One absolute criterion. • Two major neuroimaging criteria plus any clinical/exposure criteria • One major and one confirmative neuroimaging criteria plus any clinical/-exposure criteria • One major neuroimaging criteria plus two clinical/exposure criteria (including at least one major clinical/exposure criterion), together with the exclusion of other pathologies producing similar neuroimaging findings Probable diagnosis: • One major neuroimaging criteria plus any two clinical/exposure criteria • One minor neuroimaging criteria plus at least one major clinical/exposure criteria

Antigen detection is limited to patients with clinically presented infection and is possible for patients with multiple cysts, predominantly those located in the subarachnoid space or the ventricular system (Del Brutto 2022). The seven LLGP antigens used in the LLGP-EITB assay belong to three families, with low-molecular-weight antigens associated with active disease and appearing a few weeks or months after infection (Donadeu et al. 2017). Heavier-molecular-weight antigens appear first and are the latest to disappear after the patient is healed and all the parasites have died. Patients have circulating antibodies for months or years after successful therapy (Garcia et al. 2020).

Several studies have shown that the detection of low molecular weight proteins with subunits in 150kDa and 120kDa in blood serum or cerebrospinal fluid (CSF) is a good target for the diagnosis of active NC stages (Corstjens et al. 2014). High antigen levels are associated with extraparenchymal NC, whereas low or undetectable antigen levels are associated with the intraparenchymal type of cysticercosis (Chun-Seob et al. 2019). Serodiagnosis is able to differentiate those two types of NC which is crucial in low-living standard countries, where neuroimaging is not practically available outside of major hospitals. ELISA kits vary from US$5 to US$30 per sample, whereas EITB tests range from US$22 to US$100 but can cost as much as US$347 per sample (Butala et al. 2021). Low molecular weight metacestode secretion proteins, and especially glycoproteins, have shown the best performances in NC diagnosis assays. Thus, 14- and 18-kDa antigens and 8kDa–30kDa protein fraction have been described as the best alternative for developing an antibody detection system ruled at detection of NC (Ferrer and Perteguer 2022).

Recent progress in NC serodiagnosis has resulted in two different types of antigenic platforms:

- Chimeric protein fused with defined molecules with different epitope specificities
- Multi-antigen print immunoassay that uses different antigens as a mixture (Hancock et al. 2006).

Detecting circulating blood parasite antigens is a difficult task because, unlike antibodies, antigens are limited in amount and can't be multiplied by the host immune system (resulting in decreased sensitivity), closely related helminths share many diagnostic epitopes (resulting in frequent cross-reactions). Antigen levels are used to monitor the efficacy of antiparasitic treatment (Garcia et al. 2020).

Diagnosing the acute NC is important because it allows treatment with specific chemotherapeutics especially anthelmintics, while chronic-phase or acephalic budding cysticercosis in the brain ventricles requires surgical techniques or symptomatic therapy for the control of intractable seizures (Chun-Seob et al. 2019). Based on the HP10 monoclonal antibody, a lateral flow assay (HP10-Ag-LFA) for the diagnosis of extraparenchymal neurocysticercosis (EP-NC) has been developed and successfully tested with CSF and serum samples, providing an encouraging field test for rapid identification of endemic human cysticercosis. The monoclonal antibody-based B158/B60 Ag-ELISA has been used for human cysticercosis diagnosis in several epidemiological studies (Kabululu et al. 2020). Some difficulties (biochemical purification, requirement of large parasite amounts, reproducibility) restrict their uses. Biotechnological approaches have been used to solve the insufficiency of *T. solium* parasitic material for the preparation and purification of diagnostic antigen applicants. Many genes have been studied for that purpose. Paramyosin, sHSP, TSA18/HP6, F18, TS14, TS18, T24, 50-kDa glycoprotein, TsAg5, and other molecules were cloned and expressed in prokaryotic and eukaryotic systems and evaluated with collections of serum and CSF samples. The recombinant products were checked by ELISA, western blot (WB), EITB, or multiplex bead-based assay, with good sensitivity and specificity for NC diagnosis. Three other new recombinant antigens of *T. solium* metacestode have been described for the immunodiagnosis of cysticercosis, TsF78 (filamin), TsP43 (peroxidase), and TsC28 (collagen XV), with diagnostic performances. Proteins with 8-kDa have been chemically synthesized (Ts18, Ts18 var1, Ts18 var3, Ts18 var4, Ts18 var6, TsRS2 var1 Ts14, Ts18 var8, and TsRS1) and evaluated successfully for cysticercosis testing by ELISA. Of all these proteins, TsRS1 has 100% sensitivity and 100% specificity, when tested with cysticercosis-positive sera (previously reactive with the 8-kDa proteins) on WB, and Ts18 var1 and Ts18 var3 show 97% sensitivity and 100% specificity were selected for a future diagnostic antigen mixture. Recently, NC41 synthetic peptide was evaluated for NC diagnosing with high diagnostic performance (Ferrer and Perteguer 2022).

2.3.2. RAPID SEROLOGY DIAGNOSIS

2.3.2.1. ANTIBODY DETECTION TESTS

Several tests have been developed targeting antibodies against the previously described recombinant T24H (rT24H) glycoprotein in serum for the diagnosis of cysticercosis. The rT24H-MICT test uses the same technology as rES33-MICT; therefore, the advantages and disadvantages are similar. The up-converting phosphor T24H lateral flow reporter assay (UCP-rT24H LFA) uses up-converting phosphor (UCP) particles as a detection method. Results are read using a multi-lane reader after chromatography and when the strips are dry. In this format, this test is reported to detect a low level amounts of antibodies. Ease of use is reduced by the requirements for sample dilution, washing, conjugate application, and strip analysis. This limits its use to begin at the clinic level. The rT24H antigen has been used in other test formats with reported sensitivity and specificity as follows; Multi-antigen print immune assay (MAPIA), 97%-99%, and EITB 94%-99%, respectively (Mubanga et al. 2019).

Quick ELISA™ is adapted for serodiagnosis of cysticercosis based on the recombinant T24H and GP50 glycoproteins, as well as the synthetic peptide sTs18var1. It is suitable for surveillance of cysticercosis. The Quick ELISA™ is a high-throughput quantitative assay that can be performed on a benchtop but can also be automated. It is suitable for field studies but requires a basic laboratory due to; the number and type of samples, the buffers used, which require a cold chain, and equipment such as the absorbance reader, which requires electricity. Performance of rGP50 in other test formats, sensitivity, and specificity; EITB 90% and 100%, ELISA 95% and 94%, MAPIA 93% and 100%, is close to the minimum requirement of 90% and 98% respectively. Reported false positives for rGP50 have not been associated with any specific parasite infections. The performance, sensitivity, and specificity of Ts18var1 in other reported test formats are; EITB, 97%, and 100%, ELISA 95% and 85%, other ELISA 90% and 90%, RAPID ELISA 97% and 100%. No cross-reactivity has been reported in other test formats of rGP50 and sTs18var1. Quick ELISA appears to be a good test for use in a peripheral laboratory.

All antibody detection tests meet the minimum performance requirements for the diagnosis of cysticercosis with a sensitivity of 90% and a specificity of 98% proposed by WHO in the target product profiles for human cysticercosis, only tests based on sTs18var1 do not meet the requirements. Quick ELISA rT24H showed the best performance among the antibody detection tests, but for the detection of NC, sensitivity falls down when the cysticerci count is low (Lee et al. 2011).

2.3.2.2. ANTIGEN DETECTION TESTS

Rapid Slide/Latex Agglutination test has been standardized and evaluated for the detection of *T. solium* metacestode antigen in cerebrospinal fluid (CSF) and serum. It uses latex particles that have been sensitized from manufactured rabbits' hyperimmune antiserum against cysticercosis. Agglutination is performed on a glass slide where the latex suspension is added to a serum or CSF sample. A positive test is seen by agglutination. Cross-reactions with tuberculous meningitis have been reported in both serum and cerebrospinal fluid. One healthy control out of 25 serum samples tested positive. Test results were below the performance requirements proposed for cysticercosis and NC. Nevertheless, the simplicity of the test format makes it easy to diagnose a single case. Preparation of the latex suspension and sensitization of the latex particles is relatively easy, and they can be stored at 4°C for further use. This test can be used at the clinical level for

serum, with the limitation being the expertise required to obtain CSF by lumbar puncture (Mubanga et al. 2019).

Another RDT reported for NC is HP10 LFA. The target analyte is the HP10 antigen in CSF, which is a circulating surface as well as an excretory-secretory antigen in *T. saginata, T. hydatigena, T. solium, and Echinococcus granulosus*. The primary objective of this analysis is a post-treatment follow-up in patients with extra-parenchymal NC as well as supportive diagnosis.

whereas imaging is less sensitive for extra-parenchymal NC. The HP10 antigen was used in an ELISA format for the diagnosis of NC using CSF and serum with a sensitivity and specificity of 91.3%-100%, and 84.8%-98%, respectively. The diagnostic efficiency meets the proposed requirements for the diagnosis of cysticercosis. Further evaluation is required in patients with multiple parasite infections. The biggest limitation of this test is the sample type. Although the test is easy to perform, the lumbar sampling procedure is invasive and requires experience.

The results show that there is the development of RDTs for NC. Most of the serological tests developed are based on the same antigens, only changing the test formats. The tests developed, despite their limitations, are potentially able to be used as intervention mapping and monitoring tools, especially when integrated with conventional tests. Further evaluation of most of these tests is needed to provide sufficient information on their applicability in endemic areas, especially in low-resource settings. It is also necessary to determine the added value of these tests to the health outcomes of individuals. Further research is needed on the effect of test format on diagnostic outcomes (Mubanga et al. 2019).

2.4. MOLECULAR DIAGNOSIS

A new quantitative PCR (based on the highly repetitive Tsol13 sequence) was recently designed, showing high sensitivity and specificity for the diagnosis of subarachnoid and ventricular NC and for the assessment of response to antiparasite treatment (O'Connell et al. 2020). PCR systems have also been used to detect *T. solium* DNA in samples such as brain biopsy material, blood and urine samples (Goyal et al. 2020). On the other hand, CSF next-generation sequencing-based pathogen analysis has been reported for successful diagnosis and monitoring of NC patients (Garcia et al. 2020).

The LAMP (loop-mediated isothermal amplification technique) test would be a very useful tool to contribute to reducing the incidence of cysticercosis in developing countries, except when the cysticerci are calcified, because in that case no circulating antigens are available (Rodriguez et al. 2012). The LAMP technique requires further work with symptomatic patients to demonstrate its utility in the diagnosis. Cox1 sequence technique has ability to perform species differentiation between Taenia species (*T. solium, T. saginata* and *T. asiatica*), combined with its greater capacity to detect positive samples. The used protocols have been shown to be able to detect the different stages of cysticercus and have greater sensitivity than multiplex PCR (Avendano and Patarroyo 2020).

T. solium DNA detected by PCR or deep genomic sequencing using cerebrospinal fluid (CSF) of patients with subarachnoid NC. There are no reports of its use in parenchymal NC cases, much less in patients with a single brain lesion, where most diagnostic problems are available. Cell-free *T. solium* DNA has been demonstrated in the urine and serum of patients with NC, and recent data suggest that monocyte gene expression and serum mass spectrometry profiles can be used to identify NC cases. Unfortunately, molecular biology assays are not directly applied to routine case assessments (Garcia et al. 2020).

3. CONCLUSIONS

The diagnosis of cysticercosis is usually based on imaging tests and established criteria. Neuroimaging by CT or MRI is critical in the diagnosis of neurocysticercosis. Ideally both ways are used, combining the advantage of the higher sensitivity of MRI with CT detection of calcium. Because it is often not practical to biopsy cysticerci, consultation with a neuroradiologist is extremely helpful. CT scans of the cysts appear as hypodense images containing a small hyperdense nodule that represents the parasitic scolex. Calcium can sometimes be seen. The inflammation around the dead and dying parasites will provide the so-called ring enhancement in the presence of contrast material. In the natural history of neurocysticercosis, dead and dying cysts become calcified. MRI is more expensive but is becoming more accessible in developing countries often provides a clearer picture of cysticerci and has greater sensitivity for multiple lesions. Serological testing provides important confirmatory data for patients with suspicious lesions on CT or MRI. Serological testing has improved, with a sensitivity of 98% and a specificity approaching 100%. For patients with a single lesion, sensitivity is much lower, possibly because of the small amount of parasite antigen available to the host immune system. In the acute care setting, ELISA requires considerable interpretation because antibody titers can remain high long after the parasites have died. Clinical practice guidelines that outline specific diagnostic criteria were updated in 2017.

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