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Neurocysticercosis- An overlooked tropical disease

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Abstract

Introduction. Background: Neurocysticercosis (NCC), a parasitic disease caused by the pork tapeworm Taenia solium (T. solium), is a significant public health concern in endemic countries. It is estimated to contribute to roughly 30% of all epilepsy cases and leads to chronic morbidity in nearly 70% of affected patients. This study aimed to determine the prevalence of anti-cysticercus antibodies to T. solium in individuals with recent-onset seizures. We employed two serological techniques: Enzyme-Linked Immuno Sorbent Assay (ELISA) and Enzyme-Linked Immuno Transfer Blot (EITB). **Materials and Methods**. A total of 100 serum samples were collected: 50 from patients experiencing recent-onset seizures (cases) and 50 from age-matched healthy controls. All samples were analyzed for the presence of anti-cysticercus antibodies to T. solium. **Results**. Among the 50 cases, EITB detected anti-cysticercus antibodies in six patients (12%), while ELISA identified antibodies in three patients (6%). Notably, only two cases tested positive using both EITB and ELISA. In the control group, one individual was seropositive by EITB, and none were positive by ELISA. **Conclusion**. This study underscores the critical role of implementing high-quality screening methods, employing a vigilant diagnostic approach, and taking prompt preventive measures to mitigate the burden of morbidity associated with NCC.

Key word: enzyme-linked immuno transfer blot, enzyme-linked immunosorbent assay, magnetic resonance imaging, neurocysticercosis.

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Introduction

Globally, seizures are one of the most common and stigmatized ailments, recognized since antiquity and encountered periodically in medical practice. Approximately 10% of the general population experiences at least one seizure in their lifetime, with the highest incidence occurring in early childhood and late adulthood. Seizures occurring in adulthood require special attention because they are often due to identifiable causes. These causes commonly include trauma, central nervous system (CNS) infections, space-occupying lesions, cerebrovascular accidents, metabolic disorders, and drugs (1). In contrast, seizures beginning in childhood are more likely to be idiopathic.

Neurocysticercosis (NCC) accounts for approximately 30% of seizure cases in endemic countries (2). This condition is caused by Cysticercus cellulosae, the larval form of the cestode Taenia solium (T. solium), also known as the pork tapeworm. NCC affects 50 million people worldwide, with three-quarters of them living in poor countries, and 94% remaining untreated. About 50,000 people succumb to the disease every year (3).

NCC presents with varied clinical manifestations. Seizures, or epilepsy, are a common manifestation and a major cause of chronic morbidity in nearly 70% of patients (4). Diagnosing and managing NCC is challenging, as no single diagnostic test identifies all cases of cysticercosis. Although it is being reported more frequently in some areas, minimal data are available about the prevalence of epilepsy due to NCC in India.

In this context, this study was conducted to estimate the prevalence of anti-cysticercus antibodies to T. solium in the serum of patients with recent onset seizures using Enzyme-Linked Immunosorbent Assay (ELISA) and Enzyme-Linked Immunoelectrotransfer Blot (EITB). The study also compared the effectiveness of these methods in detection and examined the clinical profile and radiological findings in NCC seropositive patients.

Methods

This cross-sectional study was conducted in a 1300-bed tertiary care teaching hospital in Tamil Nadu, India, over one year, from November 2019 to October 2020. Written informed consent was obtained from all study participants. A total of 50 serum samples were collected from cases admitted with new-onset seizures, and 50 samples from age-

matched healthy controls were collected using a purposive sampling method. The control population was included to estimate the seroprevalence among the normal population, to rule out active infection, and to check for cross-reactions with other cestode infections. Samples were stored at -20°C until serological tests were performed. They were analyzed for the presence of anti-cysticercus antibodies to T. solium using ELISA (NOVATEC Immuno Diagnostics, Germany). Samples with absorbance values higher than 10% above the cut-off were considered positive, and those lower than 10% below the cut-off were considered negative. All samples were subjected to EITB, and those showing reactive bands to one or more glycoprotein antigens were considered reactive.

The study included cases of new-onset seizures (seizures occurring for the first time) among both sexes. Persons with epilepsy due to metabolic disorders, alcohol withdrawal seizures, epilepsy secondary to encephalitis or meningitis, post-traumatic epilepsy, pregnant women, and pediatric patients with febrile seizures were excluded from the study.

Ethics. Institutional ethical committee approval [REF. NO: 1601/MICRO/2019 dt: 20-11-2019] was obtained. Sociodemographic details, clinical, and radiological findings were recorded in a structured proforma.

Statistical Analysis. The collected data were entered into Microsoft Excel and analyzed. Mean and standard deviation were used for continuous variables, and the Fisher's exact test was used for categorical variables.

Results

The mean age of the study population was 24.5 years with a standard deviation of 12.2 years. The mean age of the cases was 22.42 years with a standard deviation of 11.6 years, and the mean age of the control group was 26.7 years with a standard deviation of 12.5 years. There was no significant difference in the mean age between the two groups (p-value = 0.081, Independent sample t-test).

Out of the 50 patients with recent onset seizures, 15 had Complex Partial Seizures (CPS) and 35 had Generalized Tonic-Clonic Seizures (GTCS). Among them, 28% had symptoms for less than a week, 22% for one week to one month, 40% for one to six months, and 8% for six months to one year. Thirteen patients (26%) were on antiepileptic drugs, and the remaining 37 (74%) were not on antiepileptic drugs.

Of the 50 cases, four (8%) had granulomatous lesions and four (8%) had ring-enhancing lesions on MRI. Of these eight MRI-positive cases, two were detected by both EITB and ELISA, and four were detected by EITB. Of the remaining 42 normal MRI cases, only one was positive in ELISA.

Of the 50 cases, six (12%) tested positive by EITB and three (6%) tested positive by ELISA (Table 1). Only two cases were detected by both EITB and ELISA. In the control group, one tested positive for EITB and none tested positive for ELISA. This signifies that the findings in ELISA and EITB were statistically significant (p-value = 0.035, Fisher's exact test) (Table 2).

Table 1

Distribution of EITB & ELISA positive among cases and controls

Age (in yrs)	Cases			Controls		
	Total	EITB* Positive No (%)	ELISA& Positive No (%)	Total	EITB Positive No (%)	ELISA Positive No (%)
05-14	15	1(6.6)	0(0)	11	0(0)	0(0)
15-24	16	3(18.8)	2(12.5)	10	0(0)	0(0)
25-34	12	1(8.3)	1(8.3)	12	0(0)	0(0)
35-44	3	1(33.3)	0(0)	13	1(7.7)	0(0)
45-54	3	0(0)	0(0)	2	0(0)	0(0)
>55	1	0(0)	0(0)	2	0(0)	0(0)
Total	50	6(12)	3(6)	50	1(2)	0(0)

*ELISA. Enzyme Linked Immuno Sorbent Assay. &EITB. Enzyme Linked Immuno Transfer Blot

Table 2

Comparison of EITB and ELISA among cases

ELISA*	EITB&		Total	P-value
	Positive	Negative		
Positive	2	1	3	0.035 (Fishers Exact Test)
Negative	4	43	47	
Total	6	44	50	

*ELISA. Enzyme Linked Immuno Sorbent Assay. &EITB. Enzyme Linked Immuno Transfer Blot

Out of the six EITB-positive cases, only two had adequate toilet facilities, and four did not have adequate toilet facilities. Among the EITB-positive cases, four participants were on a mixed diet and two were on a vegetarian diet. According to the Del Brutto scoring, one seizure case was classified under a definitive diagnosis of NCC, and five were classified under a probable diagnosis.

Discussion

The clinical manifestations of central nervous system (CNS) infection in humans depend on the number of lesions, location and immunological reaction against the parasites. Parenchymal brain cysts primarily present with seizures, though headache, focal signs, and cognitive deficits are not unusual. Ventricular and subarachnoid cysts manifest as space-occupying lesions, with or without hydrocephalus, and often present with headache and intracranial hypertension (5,6).

After gaining access to the CNS, cysticerci undergo different stages of involution. The first is the vesicular stage (viable stage), characterized by a transparent membrane, clear vesicular fluid, and an invaginated scolex, which may remain viable for years or enter the next stage due to the host's immunological attack. The second is the colloidal stage, where the vesicular fluid becomes turbid, and the scolex shows signs of hyaline degeneration. The third is the granular

stage, where the cyst wall thickens, the scolex transforms into mineralized granules, and the cysticercus is no longer viable. The last is the calcified stage, in which the remnants of the parasite appear as a mineralized nodule. Due to considerable individual differences, the duration of each stage has not been defined. Pathological studies have shown that different stages of involution may present in the same individual (7).

Parenchymal brain cysticerci elicit a scarce inflammatory reaction in the surrounding tissue, whereas the meningeal form shows a severe inflammatory reaction and may disseminate to distant sites where the parasite may lodge. Ventricular cysticerci also show severe inflammatory reactions (6).

The most common hematological change in neurocysticercosis is peripheral eosinophilia, reported in 37% of cases (6). Further, non-specific abnormalities in the cytochemical composition of CSF have also been reported in these cases.

Neuroimaging techniques (CT and MRI) provide a description of the number, location, stage of involution, and degree of the host's inflammatory reaction against the parasites (8). The sensitivity of conventional MRI for detecting calcified lesions is poor compared to CT (9).

Diagnosis by antigen detection is restricted by the amount of circulating larval antigen released by the parasites, unlike the antibody responses enhanced by the host's immune system. Hence, antigen detection is more likely associated with active disease and is used to monitor therapeutic response (10).

Semipurified somatic parasite or cyst fluid antigens are mostly used in antibody detection ELISA assays. The performance of these tests is generally poor, with suboptimal sensitivity and cross-reactions with other common cestode infections such as hymenolepiasis or hydatid disease (10). False negative results are due to the local production of antibodies in the CNS without a parallel increase in peripheral blood or immunotolerance to parasites without anticysticercal antibody production. Some authors advocate that antibody detection by ELISA in CSF is more specific and substantially more sensitive than in serum (11).

EITB is the best serological test, targeting antibodies to seven larval-specific antigens and does not necessarily indicate active disease. The sensitivity of serum EITB ranges from 94 to 98%, and specificity is 100%. A limitation of this assay is false negative results in many persons with single cysticercus granuloma due to insufficient antigenic stimulus (10). Persons with calcified lesions are less likely to test positive for EITB than those with active disease. Hence, using EITB alone may underestimate taeniasis-cysticercosis infection in such cases. Another limitation of EITB is that it may show seropositivity in persons exposed to the adult parasite without developing cysticercosis, in those with infection outside the brain, and it may persist up to one year after successful treatment (12).

The seroprevalence of cysticercosis among the normal population is 10%. In this study, 2% seropositivity was noted among the control group. Among eight MRI-positive cases, only six were detected by serological techniques. This shows that using serological techniques (EITB & ELISA) alone will underrate the diagnosis of neurocysticercosis compared to neuroimaging techniques. A similar finding was observed in a study by Arroyo et al. in Peru (13).

In endemic areas, screening for specific coproantigen by ELISA and PCR improves the detection of Taenia solium carriers among healthy individuals (14). They are mostly asymptomatic and do not seek medical assistance. Since Taenia carriers are foremost in the local transmission of the disease, detecting such carriers is essential to any control program. Poor sanitation facilities, consuming uncooked vegetables, and undercooked meat contribute to seropositivity.

Unlike antibody assays, antigen detection tests are useful in assessing the efficacy of treatment response, owing to the death of all parasites resulting in a rapid fall in antigen levels. Resolution of extensive NCC may require several courses of antiparasitic therapy.

The limitations of the study were the small sample size and the need to study the seroprevalence of anti-cysticercal antibodies among healthy controls involving larger populations.

Conclusion

In this study, 2% seropositivity was noted among the control group. Among the eight MRI-positive cases, only six were detected by serological techniques. Anti-cysticercus antibodies were also observed in the control group. Relying solely on serology for diagnosis may result in overlooked cases of neurocysticercosis. Therefore, a comprehensive diagnosis of neurocysticercosis requires a combination of serological tests and neuroimaging techniques. This study underscores the importance of high-quality screening, vigilant diagnostic strategies, and prompt preventive measures to reduce the morbidity associated with NCC.

Author contribution statement

Reachel Reena Durairaj: Conceptualization, Methodology, Formal analysis, Data curation, Writing- Original draft preparation, Writing- Reviewing and Editing. **Poongodi Santhana kumarasamy**: Conceptualization, Methodology, Formal analysis, Data curation, Writing- Original draft preparation. Visualization, Validation, Writing- Reviewing and Editing.

Ethics statement

The authors declare that the present study was conducted under the strictest ethical conditions.

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None.

Conflict of interest

The authors declare no conflicts of interest

Availability of data

The datasets generated and /or analyzed during current study available from the corresponding author on reasonable request.

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