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A Review of Human Cysticercosis and Diagnostic Challenges in Endemic Resource Poor Countries

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Abstract

Human cysticercosis is a neglected tropical parasitic zoonotic disease with high public health concerns. Infection of *Taenia solium* cysticerci in the brain commonly known as neurocysticercosis is a cause to over 29% of all epileptic cases in endemic countries. Unfortunately, this infection can go unnoticed for over 10 years. The objective of this review was to characterize the diagnostic approaches accessible in endemic poor resource countries. The review sought literature from library catalogues and public databases for studies on epidemiology and diagnosis challenges of human cysticercosis. The search key words included "*Taenia solium*, *T. solium* cysticercosis, human cysticercosis, neurocysticercosis and diagnosis". Most of the diagnostic procedures rely on serology. Neuroimaging tools which would confirm and thus enable the assessment of the burden of the disease in endemic countries are rarely used. Therefore assessing the estimate on prevalence and burden of the disease fallacious is owing to the low sensitivity of serological tools and the inhibition of humoral, cellular immune responses, inflammatory reaction and cytokines by the living cysticerci.

Keywords

***Taenia solium*, *T. solium* Cysticercosis, Human Cysticercosis, Neurocysticercosis, Diagnosis and Challenges**

1. Introduction

Human cysticercosis (HCC) refers to the infection by the larval form of *Taenia solium*, the pork tapeworm. Records on pork tapeworm date back to 1500 BC and it has been recognized as one of the earliest human para-

sites which possibly evolved before the domestication of pigs [1] [2]. HCC is one of the parasitic neglected tropical diseases (NTDs) with negative impacts to public health. HCC can take several forms, namely, neurocysticercosis (cysticerci in the brain), ocular cysticercosis (cysticerci in the eye), muscular cysticercosis, and on the skin where cysticerci manifest as tender lumps under the skin. Neurocysticercosis (NCC), an infection of cysticerci/ pork tapeworm larvae in the brain, is the most serious infection and it is said to be responsible for up to 56% of all cases of epilepsy in endemic resource poor countries [3]-[5]. The World Health Organization (WHO) puts the estimates at 29% [6]. Human cysticercosis is endemic in most resource poor countries [7] [8]. However, Portugal has endemic transmission of *T. solium* [9]. As a result of tourism and globalization, cases of HCC have been reported in industrialized countries particularly in Spain [9] and America [10]. Moreover, cases of HCC have been reported among Muslims [11] and Orthodox Jews [10] [12], communities that do not eat pork. The objective of this review was to characterize approaches in the diagnosis, if any, of HCC in endemic developing countries as an indicator to early detection of the problem. The prevalence and diagnostic challenges were as well reviewed. The review included reports, journal articles, books and theses on epidemiology and diagnostic approaches of HCC from various endemic regions and highlights the way forward.

2. Review Approach

The review was based on life databases (HINARI and AGORA), library catalogues and electronic databases such as PubMed, Google Scholar using the key words "*Taenia solium*, *T. solium* cysticercosis, human cysticercosis, neurocysticercosis and diagnosis". Only those articles or publications in English or Kiswahili language were considered however, final reporting was in English. 282 citation articles were screened and selected for review of their abstracts. A total of 98 publications were selected for full review. The inclusion criteria considered all articles that reported on the epidemiology of *Taenia solium* cysticercosis (TSC), prevalence, diagnosis and control of HCC. After reviewing the full texts, only 58 studies fully met the inclusion criteria.

3. The Epidemiology of Human Cysticercosis

Human cysticercosis is one of the neglected tropical diseases alongside echinococcosis, filariasis, rabies, brucellosis, anthrax, leptospirosis and several others [13]. The resurgence of cysticercosis is one of the most serious public health concerns not only in developing but also developed countries [14]. Although cysticercosis is one of the most important life-threatening cestode zoonoses worldwide, it is endemic mainly in remote or rural areas of developing countries where local people consume pork without any adequate meat inspections in the closed communities [15]. Recent trends in international tourism into remote or rural areas, the expansion of global business and increase of the number of trans-migrants from rural to urban areas as well as increase of immigrants and refugees; these amplify the risk of taeniasis and cysticercosis in developed countries and in none pork eating communities [13].

Human cysticercosisis endemic in China, Southeast Asia, India, Africa and Latin America [8]. Also, because of increasing tourism and migration of people harbouring tapeworms, HCC calls for broader attention [14] [16]-[18]. Humans acquire cysticercosis through ingestion of *T. solium* eggs from a faecally contaminated environment [19]. The invasive oncosphere (embryo) is then liberated from the egg by the action of gastric acid in the gut and crosses the bowel wall and may establish in muscles, central nervous system (CNS), eye and skin where it grows to about the size of 1 cm in 2 - 3 months [19]. The condition of having cysticerci in one's body is called cysticercosis. The disease causes morbidity, disability and pre-mature mortalities [20]. According to Tolan [20] those people with disability lose productive power subjecting them into economic hardships. On the other hand, the disease is debilitating and to people with neurological symptoms particularly epilepsy, experience socio-stigmatization, which often leads to social isolation. The diagnoses, treatment, epilepsy cases monitoring and the associated accidents like burns and drowning are some of the major concerns resulting from HCC [21].

The epidemiology of HCC is associated with residence in endemic areas, frequent travel to endemic areas and or household contact [13]. The fact that HCC may not occur in the absence of the intermediate host, the pig, it is usually clustered around human tapeworm carriers, consequently, it is focal in nature. People harbouring tapeworms who migrate from endemic areas can take the infection to non-endemic areas and infect others who do not normally consume pork. However, poor sanitation that is accompanied by free-range system of keeping pigs and social cultural settings remain the main drivers of the disease in endemic countries. About 20 million people suffer from TSC [22] with an annual fatality rate of approximately 50,000 people worldwide [20].

High incidences of HCC have been reported in Latin America, Asia and Africa. In some regions of Mexico, HCC prevalence reaches 3.6% in the general population [20]; in Asia 3.2% [23] and in the Caribbean (Haiti) 2.8% [24]. In western Africa the prevalence of HCC ranges from 1.3% - 2.4% [22]. Likewise, over 30% of people with epilepsy (PWE) in sub-Saharan Africa have been reported to have NCC [25]. In East Africa, the epidemiology of NCC is poorly understood, as there are very few studies focusing on the disease in humans. Most focus has been on the disease in pigs, referred to as porcine cysticercosis. In Tanzania recently, the prevalence of neurocysticercosis to people with epilepsy has been shown to range from 14% - 56% [4] [5] [26] [27]. HCC, however, is far more wide spread than studies on epileptic people indicate [4] [5].

Diagnosis of Human Cysticercosis

The detection of human cysticercosis is one of the keys to the management of the disease [28]. Identification of *T. solium* proglottids or eggs, which have both low sensitivity and specificity, in human faeces is confirmatory of infection by the adult stage of the parasite [28]. Deoxyribonucleic acid (DNA) based technologies are sensitive and specific [29], but their use is not common. On the other hand, the diagnosis of HCC can be achieved through enzyme-linked immunosorbent assay (ELISA), Cysticercus IgG Western Blot Assay, computed tomography (CT) scan and magnetic resonance imaging (MRI) (**Table 1**). CT scan and MRI are highly efficient, however, they are very expensive and not available or inaccessible in most endemic areas where accurate serological tests become indispensable [5] [30] [31]. Also the tools are few and so spread far apart in a country with few experts, and that people have to travel long distances to get help thus increasing expenses even if medication is free. But also that they are old models, at the end of their life span, are frequently broken taking months or years to get repaired and working again. Thus increasing the suffrage and expenses for the people who visit hospitals for a scan but only to be told that the machine is out of order, you have to wait for some months, and come again! Reason: expertise for repair is not resident in the country but overseas; so it takes time to bring them to the developing world!!

Challenges Facing Early Detection of Human Cysticercosis

With regard to **Table 1**, over 60% of the detection methods is serological tests. According to Zoli *et al*. [22] the prevalence of *T. solium* cysticercosis in humans might remain underestimated because of lack of awareness by medical carders and the inadequate neuroimaging diagnostic facilities in the public health sector. Generally, neuroimaging facilities, CT scan and MRI, are the best tools for diagnosing HCC, particularly neurocysticercosis [36]. But the tools are limited by scarcity of CT scanners, while MRIs are virtually non-existent in HCC endemic poor resource countries [36]. Therefore, serological tests such as the antigen/antibody enzyme-linked immunosorbent assay (ELISA) and immunoblots are being used to screen people with cysticercosis in endemic resource poor countries [36]. The fact that serological and immunoblots are used for screening, and taking into account their considerable variable sensitivity and specificity [36], the true prevalence estimates of the disease will remain speculative. Yet, cysticerci infection can go unnoticed for over four years until the cysticerci degenerate, die and calcify when the immune system is elicited [54]. Infection by *T. solium* metacestodes in humans (with or without signs), commonly referred to as HCC, may occur as early asduring childhood [8] [55]. At 2 to 10+ years after the cyst, particularly neurocysticerci, degenerates with thick cystic fluid and thickened capsule; the cyst no longer suppresses the host immune response and its antigens leak from the bladder wall [56]. Intense inflammation is provoked around the degenerating cyst in which most patients bearing this stage of infection develop clinical signs and symptoms such as seizures, occasional focal neurological signs, headaches, nausea, vomiting, lethargy from increased intracranial pressure and altered mental status [56]. Nevertheless, infected persons may develop nervous signs in adulthood without any particular association with sex or race, with the pig-raising populations or pork handlers being at a higher risk [57].

Despite the problems related to awareness and neuroimaging diagnostic tools in endemic poor resource countries, this review shows that the *T. solium* cysticerci inhibit IFN-γ and IL-2, and to a lesser degree IL-4 production [57] [58]. Live metacestodes (larvae) also secrete cysteine and serine proteases that deplete CD4+ cells (T helper cells) that send signals to other types of immune cells, including CD8 killer cells that destroy and kill the infection [58]. The elucidation of these molecules provides insights into the mechanisms by which *T. solium* metacestodes evade host immunological attack and are able to survive long periods of time [58]. Yet, even if one develops neurological symptoms in early stages, it is difficult to link them to infection by cysticerci. Therefore infection by *T. solium* cysticercosis in humans might have high public health consequence than it is estimated.

Table 1. Various diagnostic approaches for HCC from endemic countries/regions.

Test	Case	Country/Region	Source
Sero-Screening, CT Scan	Neurocysticercosis	Nepal	[32] [33]
CT Scan, MRI and Biopsy	Multiple tonics-chronic seizures vs neurocysticercosis	United States of America	[34]
Sero-Screening	Epilepsy as indirect marker for neurocysticercosis	Laos, South-East Asia	[35]
Autopsy and Sero-Screening	Human cysticercosis	Central and West Africa	[22]
Sero-Screening, X-Ray and Autopsy	Human cysticercosis	Togo and Benin	[36] [37]
Sero-Screening and CT Scan	Human cysticercosis	Cameroon	[22] [38]
Sero-Screening	Human cysticercosis	Burundi	[39]-[41]
Sero-Screening, CT Scan and Autopsy	Human cysticercosis	Eastern and South Africa	[42]-[45]
X-Ray and Sero-Screening	Human cysticercosis	Zimbabwe	[46]-[48]
Sero-Screening	Human cysticercosis	Mozambique	[49] [50]
Sero-Screening	Human cysticercosis	Madagascar	[51] [52]
Sero-Screening	Human cysticercosis	Kenya	[53]
Serology and Cerebral Spinal Fluid (CSF)-Screening, CT Scan	Human cysticercosis/neurocysticercosis	Tanzania	[4] [5] [26] [27]

4. Conclusion

The literature reviewed has shown that limitations on facilities required for diagnosis of HCC, the unnoticed long-life of the parasite in the human body and low public awareness on the transmission drivers for the disease contribute to its persistence. However, even if neuroimaging tools were available, they are unaffordable and inaccessible to the common person from endemic developing countries. Furthermore, the inconsistence of the sero-screening technique(s) widely used in endemic poor resource countries undermines the resulting estimates on prevalence of the disease. This is because of the low sensitivity of the tools for the diagnosis of HCC. Efforts must therefore, be invested in developing cheap, easily accessible, reliable, sensitive, specific and environmentally stable tools for the diagnosis of *T. solium* cysticercosis in both definitive host, humans and intermediate host, pigs. Also awareness creation among the medical, veterinary and community development sectors and the general public on the epidemiology and risk factors of HCC is of paramount importance.

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