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Needs of exploring the burden of recent onset seizures due to neurocysticercosis and challenges in southeast Asia focusing on scenario in Malaysia

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ABSTRACT

Seizures due to neurocysticercosis (NCC) is a neglected human-to-human transmitted disorder and an emerging problem worldwide. A substantial portion of recent onset seizures is known to be attributed to NCC in *Taenia solium* (*T. solium*) endemic areas where populations which neither raise pigs nor eat pig meat are also at risk. High prevalence of NCC causing epilepsy has been reported in the underdeveloped areas of Southeast Asia (SEA) however, only fragmentary information on its incidence is available in countries like Malaysia. In Malaysia *T. solium* infection was previously thought to be infrequent due to Muslim population majority and the religious prohibition of consuming pork, but it is not totally absent. There is an evident lack of knowledge and awareness of the actual burden, routes of transmission, and the impact of NCC in this region. The problem is assumed to be more prevalent particularly in cities because of the frequent inflow of possibly *T. solium* infected individuals or carriers among those who migrate from neighboring endemic countries to Malaysia. The issue of imported cases that are likely to be emerging in Malaysia is highlighted here. An accurate quantification of regional burdens of epilepsy due to NCC in Malaysia is warranted considering the disease emergence in its neighboring countries. It is suggested that the importance of NCC be recognized through quantification of its burden, and also to collect epidemiological data for its subsequent elimination in line of World Health Organization's mission for control of cysticercosis as a neglected tropical disease. In this review the need as well as a strategy for neuro-care center screening of epilepsy cases, and various issues with possible explanations are discussed. It is also proposed that NCC be declared as a reportable disease which is one of the eradicable public health problems in SEA.

1. Introduction

Today it is a well-documented fact that neurocysticercosis (NCC), the *Taenia solium* (*T. solium*) metacestode larval infection in central nervous system (CNS) is an important cause of acute epilepsy in humans, particularly in the tropics [1–4]. Currently, there is no sufficient evidence available in order to project NCC's global prevalence. However, a recent meta-analysis which summarized the proportion of NCC among persons with epilepsy (PWE) suggested that in endemic communities nearly one-third of PWE are living with *T. solium* cystic lesions in their brain [5].

Though the magnitude of NCC burden in endemic countries is high, its neurological involvement is being recognized only recently as an important but neglected cause of epilepsy [6]. As per WHO estimation of 50 000 deaths due to *T. solium*, neural involvement was assumed to be the major reason [7], making NCC the single most important cause of acute epilepsy in developing countries. It is prevalent in Latin America, a major part of Asia (including China and the Southeast Asia), Eastern Europe, and most of Africa [2–4] with seroprevalence rates

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reaching up to 25% in general populations in areas known to be endemic for *T. solium* [8].

In addition, NCC is also emerging in geographical areas which were never known to be endemic for this parasite [9,10]. Controlled studies using CT scans in Ecuador, Honduras, and Peru have demonstrated strong association between NCC and seizures, with up to 30% of seizures attributable to NCC [2–4]. This rate was similar to studies from other endemic countries which have estimated prevalence of NCC among PWE to be between 25 and 50% [11,12]. There were also reports revealing NCC prevalence in apparently healthy communities in previously unexplored provinces as in the case of Port-au-Prince in Haiti; 2.8% of general population were identified to be clinical cases of NCC [13]. These reports are making governments in many other never explored countries realize the potential endemicity of this infectious disease.

In developed countries, NCC is diagnosed more frequently among immigrant populations [14,15]. As reported in western countries, it occurs in small outbreaks [16]. NCC has been found in 10% of new-onset seizure patients in California [17,18]. More than 1000 new cases are being detected in the United States every year [19]. Surprisingly, its prevalence is also on the rise in Muslim countries; especially in the Gulf region because of the heavy reliance on laborers from highly endemic neighboring countries [20–22]. Hence, NCC is no more limited to tropical regions, religion and/or economic status of the affected communities. This situation reinforces the urgent need for a global initiative of screening programs and regulations which warrant compulsory reporting of new cases.

In the SEA region, the potentiality of human to human transmission of *T. solium* infections is of concern in this review. Among the known *T. solium* endemic regions in Asia, particularly Bali in Indonesia is reported to be of high importance due to the risk of transmission of infection to tourists [23]. However, the likelihood that Malaysia might also be sub-endemic for this disease which is not yet explored. Indigenous cases of *T. solium* taeniasis/cysticercosis were initially thought to be infrequent in Malaysia. However, this problem might be more prevalent in future since there is an increase in tourism and population movements. The proportion of infection might be less compared to neighboring endemic countries in Asia or other endemic tropical countries; however that likelihood of underestimating its prevalence in this country should be addressed. In this review, the need for screening PWE in order to estimate the cysticercal burden of recent onset seizures in SEA and challenges of the present time are discussed. Also a strategy is suggested for neurocare center screening from among epilepsy cases for an etiological confirmation and a compulsory reporting of NCC in this region.

2. The need to screen recent onset seizures patients for cysticercal etiology in SEA

NCC is known to be one of the major preventable causes of adult onset epilepsy in tropical developing countries that is presently a public health threat crossing international boundaries. SEA is an endemic region for NCC with widespread economically underdeveloped areas. It has been reported that pork consumption in SEA has considerably increased over the last decades [24]. There are many small-holder farming communities with inadequate hygiene practice, poor pig management, and lack of meat inspection as well as control. Given that there is evident lack of knowledge and awareness of the actual burden, routes of transmission, and the impact of NCC in SEA, there is an urgent need to screen epileptic patients for NCC in order to fill this gap of information.

The burden of *T. solium* taeniasis/cysticercosis either in general communities or in epileptic patients has been documented in Indonesia [25–30], Thailand and Myanmar [31–41], Lao People's Democratic Republic (Lao PDR) [42–45], Cambodia [46–51], Vietnam [52–58], Taiwan [59], and Philippines [60–62]. Thus many of countries in SEA are known to be endemic for taeniasis/cysticercosis. However only recently some proposals being raised to pay attention on the prevention and control of this NTD [63,64]. Other than the SEA region, *T. solium* taeniasis and particularly NCC as a major contributor of recent onset seizures in other major countries in Asia are widely documented in India [65–76], China [77–84], Nepal [85–99]. A recent review on cysticercosis/taeniasis endemicity in SEA describes a country-wise prevalence picture [60].

In SEA, as in other parts of the globe, there is continuous migration towards cities or international destinations according to season, crop harvest time, or other routine activities. SEA is a target for travel and immigration from neighboring countries for various reasons that include but not limited to trading, technological collaboration development, education, and employment. For example, there is a large immigrant population working in Malaysia – legally and illegally. Some of the immigrants may be tapeworm carriers and they work in Malaysian cities as cooks and food handlers or vegetable/fruit sellers. Most of the time, immigrants from neighboring countries obtain employment without undergoing thorough/any health screening or treatment. This is the main reason for the possible dissemination of infection into urban communities. Some of these workers might be domestic helpers in the urban cities of Malaysia. They may not be aware of the underlying infection and they can spread the disease to the local population. This problem is not confined to the inflow of migrants to Malaysia as outbound travel of local population to other countries is also increasing again for the various reasons. A large segment of the Malaysian populations consists of descendants of immigrants and they maintain close contacts with their places of ancestry. Often they travel to places in neighboring SEA countries endemic for NCC where they might be acquiring this parasitic infection.

In Malaysia, recent case reports indicated an emergence of NCC as diagnosed in major medical centers [100–104]. The most recent one was a pediatric case of seizure which underwent surgery for excision of the live worm [101]. These studies indicated a possible inflow of immigrants being one of the reasons for the NCC caused recent onset of acute epilepsy (AE) in Malaysia. An epidemiological study in a rural province of Sabah, Malaysia Borneo indicated evidence of exposure to the parasite in the local population (cysticercosis antibodies = 2.2%) [105]. In a recent screening study by our group, a positive anti-cysticercus antibody in serum has been detected in 3.5% (20 of 572) of indigenous communities in peninsular Malaysia [64]. A personal communication with Neurocare Division of University of Malaya Medical Center in Kuala Lumpur (Malaysia) revealed 3 cases of confirmed NCC in recent time, of which 2 were detected among Malaysians, and one case was in an Indian nationality (unpublished observation by Devaraj Pancharatnam). Besides that, few clinically and radiologically suspected cases attending neuromedicine clinics were also available in hospital record

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