Mohamed et al, 2017;1(2):72–77.
https://doi.org/10.24911/IJMDC.1.2.6

A REVIEW ARTICLE

Parasites in central nervous system

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ABSTRACT

Parasites are different organisms that can be classified into single-cell organisms and multicellular organisms. Complications caused by parasites affect both children and adults in high number. Some parasites cause diseases with symptoms and other cause no symptoms. Parasites can be present in unusual places such as in central nervous system (CNS). The parasitic infections of CNS are sources of mortality and morbidity.

Keywords: CNS parasites, malaria, Schistosoma.

Introduction

Central nervous system (CNS) infections are significant as they affect the health of CNS [1]. It was reported that 25% of individuals in the world were infected with parasites, where these infections are more prevalent in developing agricultural and rural areas in the tropical and subtropical countries [2]. Human parasites may exist in an abnormal location in the body such as CNS. All over the world, parasitic diseases of the CNS are considered sources of mortality and morbidity. Parasites are a variety of organisms which can be classified into protozoa the single cell organism and metazoan the multicellular organisms [3]. The protozoans are either obligate parasites or free-living [4]. Protozoa are the most eukaryotic cells distributed in the world, and they are essential pathogens for both humans and animals [5], where they cause very mild to severe, life-threatening diseases [6]. Helminths cause diseases by the physical disruption of tissues where they migrate and stimulate intensive inflammatory response [7]. A large number of parasites infect humans and sometimes many of them migrate to the CNS and cause diseases [8]. Neurological disabilities caused by parasitic infections include infection with malaria, Taenia solium, Schistosoma, Toxoplasma gondii, and Soil-transmitted helminths [9].

Infection of CNS includes cysticercosis, echinococcosis, schistosomiasis, and toxoplasmosis. Malaria also causes CNS disorders [10]. Some parasites cause diseases with symptoms, whereas the others only cause few symptoms [3]. These disorders involve variety of vectors, causative organisms, and have several modes of transmission as well as endemic areas [3]. Seizures and epilepsy are related to parasitic brain infections using encephalopathy, diffuse encephalitis, or intra-cerebral location of the parasite [11]. Most of the seizures that caused by the parasitic disease is a result of neurocysticercosis and malaria [9]. The complication caused by the parasitic infections affect millions of adults and children in low- and middle-income countries, these complications include cognitive, neurological, and mental health complications [3]. Although the previous complications occur in endemic areas of parasites, sporadic cases appear in non-endemic regions [3]. Our continent Africa is considered to be the home of malaria [3] and two species of Schistosoma (*Schistosoma mansoni* and *Schistosoma haematobium*) represent a problem in Egypt as they transmit via the Nile River valley [12]. Also, there are increasing speed in the international travel which may cause transmission of these parasites. Schistosomiasis associated with travel has been reported [13,14]. For the previous reasons, in the present review, we focused on two examples of parasites that cause CNS diseases, malaria as an example of protozoa and Schistosoma as an example of metazoan.

Methods

In this review, we used the Internet to get articles related to the current subject. We searched scientific websites such as research gate, Google Scholar, and PubMed. The research process involved the use of different keywords to obtain the recent and more articles about the subject, the keywords used are “CNS parasitic diseases, neurological diseases, and parasites of CNS.” Several articles were obtained including original articles and review. We reviewed nine articles published between the year 2005 and 2016. Only one article published in 2005, while the other articles were more recent.

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Received: 3 January 2017 | **Accepted:** 15 April 2017

Discussion

Infection of CNS is a significant health problem which increased the number of cases recently [15]. Parasites are a large group of variety organisms. They can be divided into protozoa the single cell organisms and metazoa the multicellular helminths [3].

Parasites of the central nervous system

Malaria

Malaria is one of the most infectious diseases in the developing countries [16]. It is a worldwide most common and important parasitic disease, almost 3.2 billion persons were at risk of malaria in 2015 and it was estimated that annually there are 300–500 million new cases and 1.5–2.7 million deaths [3,17].

The highest incidence of malaria in sub-Saharan Africa which is the home of 89% of malaria cases and 91% of malaria deaths [3]. African children and Asian adults are the most affected persons by malaria with a higher percent in children where >90% of cases are children with £5 years of age [3]. However, during 1979–1998 in the USA, there were 118 deaths [18]. Malaria is responsible for most of the seizures that caused by parasitic disease [9], coma may follow generalized seizures [19].

The primary symptoms of malaria are general symptoms such as abdominal discomfort, headache, fatigue, irregular fever as well as muscle aches, while orthostatic hypotension, vomiting, and nausea are frequently occurring [3]. The mechanism of neurocognitive problems caused by malaria is not fully identified [9]. However, the suggested injury mechanisms involving parasite toxin, metabolic derangements, anoxia, vascular leakage, stroke and increased intracranial hypertension [11].

Five species of malaria infect human, almost all severe morbidity and mortality of malaria are associated with Plasmodium falciparum species [20], and it is responsible for most of the malaria cases (80%) as well as deaths from malaria (90%) [21]. Plasmodium falciparum also is responsible for acute seizures and most common CNS infections [8]. It is responsible for most of the CNS infections that result in wide range of neurological complications [6]. This species is a fatal parasitic infection worldwide, and most death caused by this species occurs in young children in sub-Saharan Africa [17].

It does not infect brain directly. However, coma can result from severe infection [9]. Plasmodium falciparum cause cerebral malaria which is the most severe complication of malaria and it can cause acute encephalopathy [9,22]. Children, pregnant women, immunosuppressed persons and non-immune individuals are the most categories to develop cerebral malaria [23].

Cerebral malaria also can obstruct microvasculature in the brain by means of sequestration [24]. Cerebral malaria caused by the sequestration of erythrocytes which are infected with malaria, almost in 2% of cases [25]. This erythrocytic stage is responsible for the occurrence of cerebral malaria [6].

When RBCs are infected with Plasmodium falciparum merozoites, these merozoites produce a protein to the surface of the infected RBCs; these infected blood cells adhere to the walls of microvasculature by a unique interaction between the cells and the vascular endothelium, this process known as cytoadherence [26]. Cytoadherence leads to the occurrence of few methods such as the release of endothelial microparticles, apoptosis of host cells and endothelial activation that occur in the brain; the endothelial activation process has an essential role in the pathogenesis of cerebral malaria [27].

The sequestration of red blood cells is caused by the presence of the parasite-derived protein on the cells [26]. Plasmodium falciparum erythrocyte membrane protein 1 was thought to be the dominant virulence factor of cerebral malaria [28]. By increase in the number of attached infected cells, the mass increases in size and causes impairment in the perfusion of blood, hence hypoxia occurs resulting in a coma [24]. The cytoadherence process causes a decrease in blood flow and as a result of this obstruction in microcirculation occurs [29].

More serious sequestration of infected RBCs makes the obstruction of blood flow irreversible, so hypoxia spreads widely and ischemic injury occurs and finally death [30]. The severity of the disease can be evaluated by the ratio between the decreased level of Ang-1 or increased Ang-2 in the serum, where Ang-1 and Ang-2 are two endothelial regulators [31].

There is a difference between symptoms in adults and children [29]. Cerebral malaria results in encephalopathy and coma [25] and other several neurological diseases including seizures, opisthotonus, nystagmus, and conjugate gaze palsy [32]. The symptoms of cerebral malaria include the most severe manifestation in young children which is the impairment of consciousness accompanied by coma [33], coma occurs suddenly with seizure then fever develops [6].

The children patient also expresses common symptoms such as metabolic acidosis, brainstem signs, anemia, brain swelling, intracranial hypertension, hyperpyrexia, hypoglycemia, shock, retinal changes, and electrolyte imbalance [23]. 30% of children experience brainstem dysfunction [34,35], while ocular bobbing, sixth nerve palsies, and nystagmus are occasional symptoms [36].

In adult patients, they suffer icterus, hypoglycemia, alteration in mental status, and disseminated intravascular coagulation [25]. In children, seizures are most commonly occurring after the sudden onset of coma, whereas in adults a seizure is related to gradually developed coma [37]. Seizures represent 80% of African children of cerebral malaria symptoms [34,35]. With parasitemia, the risk of seizures increases [38].

Seizures in Africa are the frequent reason for admission to hospitals [39,40], where one-third of seizures cases in the

emergency room in Africa are because of malaria [40]. It was found that seizures represented 15.8% of the total admissions and 69% of those were due to Plasmodium falciparum malaria [39]. Seizures occur in 25% of cerebral malaria [8].

Cerebral malaria develops long-term cognitive impairment in one of four infected children [41]; long-term cognitive disability also can be resulted from severe malarial anemia [42]. Cerebral malaria also can cause behavioral problems and epilepsy in long-term [43]. The association with epilepsy was reported in the endemic region in Africa [44]. In a prospective study on children by van Hensbroek et al. [45], they found that 5 in 466 out of 490 survivors had seizures at 1 month and another at 6 months and 18 months, this suggested that development of epilepsy in the short term was infrequent.

Carter et al. [46] found that active epilepsy was noted in 6.4%, 4.6%, and 1.1% in children with a history of cerebral malaria with complicated seizures, uncomplicated cerebral malaria, and a control population, respectively. This can be attributed to the predisposing of cerebral malaria with complicated seizures to epilepsy. By usage of suitable treatment, the mortality rate caused by cerebral malaria becomes 15–25% [25].

Schistosoma

The infection of helminths to the CNS occurs worldwide, especially in tropical and subtropical countries with high prevalence [47]. It is a significant public health problem in the developing countries [17]. Schistosoma is a severe public health problem especially in tropical areas where 200 million persons approximately got infected with it, and 20 million of them suffer severe illness. Also, it is one of the most prevalent parasites causing a parasitic disease [47]. Schistosomiasis is endemic in sub-Saharan Africa, the Middle East, South America, Asia, and the Caribbean Islands [48]. After malaria and amebiasis, schistosomiasis is the third-leading endemic parasitic disease in the world [2].

In Egypt, the distribution of Schistosoma species and prevalence differs between governorates and regions [2]. It was found that prevalence of *S. mansoni* was 4.3% and it was unusual in Upper Egypt, while in Lower Egypt it was endemic and ranged from 17.5% to 42.9% [49]. *S. haematobium* was endemic in Upper Egypt and ranged from 4.8% to 13.7% with a mean of 7.8%, while it was rare in the Lower Egypt [49]. Each year worldwide, up to 300 million people experience schistosomiasis, which is caused by five species [4].

The human disease commonly manifests as dermatitis [50,51]. Maturation and migration of Schistosoma eggs lead to Katayama syndrome which also known as acute schistosomiasis; this syndrome causes an immune-mediated hypersensitivity reaction [52]. The presence of systemic illness and eosinophilia as well as fever leads to acute encephalitis which occurs in 2–3% of acute schistosomiasis cases [53]. The symptoms include myalgias, fever with urticarial swellings, eosinophilia, and bloody diarrhea [54]; these symptoms are not common in endemic areas but when exist they last for several weeks [4].

A small percent of schistosomiasis patients give rise to Neuroschistosomiasis [36]. More recently, in a study in sub-Saharan Africa, it was reported that spinal schistosomiasis caused 1–5% of nontraumatic spinal cord injuries and 4.3% of schistosomiasis adults hospitalized in China had CNS involvement [55,56]. Schistosoma reaches to CNS by accident [47], three of five species have been involved in CNS invasion [51].

The migration of Schistosoma eggs or worms to the spinal cord or brain results in neuro-schistosomiasis, this happens after infection with *Schistosoma mansoni*, *Schistosoma haematobium*, or *Schistosoma japonicum* [9]. The three species of Schistosoma cause complication for CNS where the eggs cause infarction or granuloma formation. Schistosoma japonicum affects the brain, whereas *Schistosoma haematobium* and *Schistosoma mansoni* affect the spinal cord [3].

Schistosomiasis is considered an under-recognized cause of acute encephalopathy in the tropics [57]. Epilepsy can be caused by schistosomiasis [58]. In Egypt, schistosomiasis due to *Schistosoma mansoni* of the spinal cord is considered the primary cause of the parasitic invasion of the spinal cord [59]. Neurological involvement usually occurs within weeks or months after infection when eggs migrate via the vascular system to the spinal cord or the brain. Symptoms may occur as a result of the mass effect of the egg or from granuloma formation around the egg [51].

The spinal cord involvement results in hemiparesis, while in case of brain involvement, there is either acute phase (schistosomal encephalopathy) or chronic phase (cerebral schistosomiasis or pseudotumoral encephalic schistosomiasis) [53]. In the chronic phase, the pathogenesis is explained by the passage of eggs of Schistosoma to CNS where they stimulate space-occupying granulomatous reactions [53,60].

Posterior fossa and spinal cord are the most common sites involved in pathogenesis when the parasite enters to the CNS through Batson's plexus [4]. Intracranial pressure increases by granuloma formation mass and intracranial hemorrhage can be produced by erosion of vascular walls [4]. The clinical symptoms of cerebral schistosomiasis include focal neurologic deficits, fever and seizures [48]. The pathogenesis, manifestations and outcome of the disease differ according to the phase and clinical forms [53].

Clinical manifestations of schistosomiasis depend on the species that caused the infection and they can appear at several stages during the parasitic life cycle [4]. Symptoms include urticarial rash; pulmonary infiltrates, fever and cough; it is often accompanied by moderate peripheral eosinophilia [3]. However, cerebral schistosomiasis is common without symptoms, but it may exist with signs

of space-occupying lesions including seizures, visual and oral disturbances, headache, and papilledema [10].

Conclusion

Malaria and Schistosoma are two parasites that infect the CNS. Malaria is very prevalent in sub-Saharan Africa; it is responsible for most of the seizures cases that occurred due to parasitic diseases. Five species of malaria infect human: Plasmodium falciparum is the species that is responsible for most of the CNS infections. Cerebral malaria causes encephalopathy, coma, and opisthotonus. Schistosoma prevalence in Egypt varies between governorates. The neuro schistosomiasis occurs as a result of the migration of Schistosoma eggs or worms to the spinal cord or brain. The three species of Schistosoma result in CNS complications. Schistosomiasis causes acute encephalopathy and epilepsy. Hemiparesis is caused by infection of Schistosoma to the spinal cord, while brain infection causes the acute phase schistosomal encephalopathy and the chronic phase cerebral schistosomiasis.

Conflict of Interest
None

Funding
None

Consent for publication
Not applicable

Ethical consideration
Not applicable

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References

1. Sundaram C, Shankar SK, Thong WK, Pardo-Villamizar CA. Pathology and diagnosis of central nervous system infections. Pathology research international. 2011;21:1-4. https://doi.org/10.4061/2011/878263
2. Youssef AI, Uga S. Review of Parasitic Zoonoses in Egypt. Tropical Medicine and Health. 2014;42(1):3-14. https://doi.org/10.2149/tmh.2013-23
3. Carpio A, Romo ML, Parkhouse RME, Short B, Dua T. Parasitic diseases of the central nervous system: lessons for clinicians and policy Makers. Expert Review of Neurotherapeutics. 2016;16(4):401-414. https://doi.org/10.1586/14737175.2016.1155454
4. Walker MD., Zunt JR. Neuroparasitic Infections: Cestodes, Trematodes, and Protozoans. Semin Neurol. 2005;25(3):262-277. https://doi.org/10.1055/s-2005-917663
5. Zarlenga DS, Trout JM. Concentrating, purifying and detecting waterborne parasites. Vet Parasitol. 2004;126:195-217. https://doi.org/10.1016/j.vetpar.2004.09.001
6. Lim CZF, Bhantooa D, Balgobin D, Bissoonauth N, DRamburran DK, Lu F. Parasitic Encephalitis Caused by Plasmodium Falciparum, Trypanosoma Brucei and Toxoplasma Gondii. Ann Infect Dis Epidemiol. 2016;1(1):1005.
7. Graeff-Teixeira C, Da Silva AC, Yoshimura K. Update on eosinophilic meningoencephalitis and its clinical relevance. Clin Microbiol Rev. 2009;22:322–348. https://doi.org/10.1128/CMR.00044-08
8. Nash TE. Parasitic diseases that cause seizures. Epilepsy Curr; 2014;14:29-34. https://doi.org/10.5698/1535-7511-14.s2.29
9. John CC, Carabin H, Montano SM, Bangirana P, Zunt JR, Peterson PK. Global research priorities for infections that affect the nervous system. Nature. 2015;527:S178-S186. https://doi.org/10.1038/nature16033
10. Abdel Razek AA, Watcharakorn A, Castillo M. Parasitic diseases of the central nervous system. Neuroimaging Clin N Am. 2011;21:815–841. https://doi.org/10.1016/j.nic.2011.07.005
11. Vezzani A, Fujinami RS, White HS, Preux PM, Blumcke I, Sander JW. et al. Infections, inflammation and epilepsy. Acta Neuropathol; 2016;131:211–234. https://doi.org/10.1007/s00401-015-1481-5
12. CDC - Schistosomiasis - Epidemiology & Risk Factors [Internet] 2012. [cited 2017 January 31]. Available from: https://www.cdc.gov/parasites/schistosomiasis/epi.html
13. Steinmann P, Keiser J, Bos R, Tanner M., Utzinger J. Schistosomiasis and water resources development: systematic review, meta-analysis, and estimates of people at risk. Lancet. Infect. Dis. 2006;6:411-425. https://doi.org/10.1016/S1473-3099(06)70521-7
14. Chitsulo L, Engels D, Montresor A, Savioli L. The global status of schistosomiasis and its control. Acta Trop. 2000;77:41-51. https://doi.org/10.1016/S0001-706X(00)00122-4
15. Sgarbi N. Central nervous system infections: new diagnostic tools. Rev. Argent. Radiol. 2015;79(1):12-31. https://doi.org/10.1016/j.rard.2014.11.005
16. Talisuna AO, Bloland P, D'Alessandro U. History, dynamics, and public health importance of malaria parasite resistance. Clin Microbiol Rev. 2004;17(1):235–254. https://doi.org/10.1128/CMR.17.1.235-254.2004
17. Shih RY., Koeller KK. Bacterial, Fungal, and Parasitic Infections of the Central Nervous System: Radiologic-Pathologic Cor¬relation and Historical Perspectives.RadioGraphics. 2015;35:1141–1169. https://doi.org/10.1148/rg.2015140317

18. Stoppacher R, Adams SP. Malaria deaths in the United States: case report and review of deaths, 1979-1998. Journal of forensic sciences. 2003;48(2):404-408. https://doi.org/10.1520/JFS2002272
19. White NJ, Pukrittayakamee S, Hien TT, Faiz MA, Mokuolu OA, Dondrop AM. Malaria. Lancet. 2014;383:723–735. https://doi.org/10.1016/S0140-6736(13)60024-0
20. Beales PF, Brabin B, Dorman E, Gilles HM, Loutain L, Marsh K, et al. Severe falciparum malaria. Trans R Soc Trop Med Hyg. 2000;94:S1-S90. https://doi.org/10.1016/S0035-9203(00)90300-6
21. Lou J, Lucas R, Grau GE. Pathogenesis of cerebral malaria: recent experimental data and possible applications for humans. Clin Microbiol Rev. 2001;14(4):810–820. https://doi.org/10.1128/CMR.14.4.810-820.2001
22. Idro R, Jenkins NE, Newton CR. Pathogenesis. Clinical features, and neurological outcome of cerebral malaria. Lancet Neurol. 2005;4(12):827–840. https://doi.org/10.1016/S1474-4422(05)70247-7
23. Newton CR, Hien TT, White N. Cerebral malaria. Jb Neurol Neurosurg Psychiatry. 2000;69(4): 433–441. https://doi.org/10.1136/jnnp.69.4.433
24. Dondorp AM, Pongponratn E, White NJ. Reduced microcirculatory flow in severe falciparum malaria: pathophysiology and electron-microscopic pathology. Acta Tropica. 2004;89: 309-317. https://doi.org/10.1016/j.actatropica.2003.10.004
25. Mohanty S, Taylor TE, Kampondeni S, Potchen MJ, Panda P, Mishra SK et al. Magnetic resonance imaging during life: the key to unlock cerebral malaria pathogenesis? Malar J. 2014;13:276. https://doi.org/10.1186/1475-2875-13-276
26. Newbold C, Craig A, Kyes S, Rowe A, Fernandez-Reyes D, Fagan T. Cytoadherence, pathogenesis and the infected red cell surface in Plasmodium falciparum. Int J Parasitol. 1999;29: 927-937. https://doi.org/10.1016/S0020-7519(99)00049-1
27. Gillrie MR, Lee K, Gowda DC, Davis SP, Monestier M, Cui LW, et al. Plasmodium falciparum Histones Induce Endothelial Proinflammatory Response and Barrier Dysfunction. Am J Pathol. 2012;180: 1028-1039. https://doi.org/10.1016/j.ajpath.2011.11.037
28. Dzikowski R, Deitsch KW. Genetics of antigenic variation in Plasmodium falciparum. Curr Gent. 2009;55: 103-110. https://doi.org/10.1007/s00294-009-0233-2
29. Snow RW, Guerra CA, Noor AM, Myint HY, Hay SI. The global distribution of clinical episodes of Plasmodium falciparum malaria. Nature. 2005;434(7030):214-217. https://doi.org/10.1038/nature03342
30. Maude RJ, Dondorp AM, Abu Sayeed A, Day NPJ, White NJ, Beare NAV. The eye in cerebral malaria: what can it teach us? Trans R Soc Trop Med Hyg. 2009;1;103(7):661-664.
31. Lovegrove FE, Tangpukdee N, Opoka RO, Lafferty EI, Rajwans N, Hawkes M, et al. Serum angiopoietin-1 and-2 levels discriminate cerebral malaria from uncomplicated malaria and predict clinical outcome in African children. PloS one. 2009;20;4(3):e4912.
32. Bartoloni A, Zammarchi L. Clinical aspects of uncomplicated and severe malaria. Mediterranean journal of hematology and infectious diseases. 2012;4(1):26. https://doi.org/10.4084/mjhid.2012.026
33. Clark IA, Alleva LM. Is human malarial coma caused, or merely deepened, by sequestration? Trends Parasitol. 2009;25:314-318. https://doi.org/10.1016/j.pt.2009.04.003
34. Crawley J, English M, Waruiru C, Mwangi I, Marsh K. Abnormal respiratory patterns in childhood cerebral malaria. Trans R Soc Trop Med Hyg. 1998;92(3):305–308. https://doi.org/10.1016/S0035-9203(98)91023-9
35. Marsh K, English M, Crawley J and Peshu N. The pathogenesis of severe malaria in African children. Ann Trop Med Parasitol. 1996;90(4):395–402. https://doi.org/10.1080/00034983.1996.11813068
36. Thakur K and Zunt J. Neurologic Parasitic Infections in Immigrants and Travelers. Semin Neurol. 2011;31(3):231-244. https://doi.org/10.1055/s-0031-1287651
37. Jain K, Sood S, Gowthamarajan K. Modulation of cerebral malaria by curcumin as an adjunctive therapy. The Brazilian Journal of Infectious Diseases. 2013;31;17(5):579-591.
38. Idro R, Ndiritu M, Ogutu B, Mithwani S, Maitland K, Berkley J, et al. Burden, features, and outcome of neurological involvement in acute falciparum malaria in Kenyan children. Jama. 2007;23;297(20):2232-2240.
39. Waruiru CM, Newton CR, Forster D, New L, Winstanley P, Mwangi I, Marsh V, Winstanley M, Snow RW, Marsh K. Epileptic seizures and malaria in Kenyan children. Transactions of the Royal Society of Tropical Medicine and Hygiene. 1996;1;90(2):152-155.
40. Asindi AA, Ekanem EE, Ibia EO, Nwangwa MA. Upsurge of malaria-related convulsions in a paediatric emergency room in Nigeria. Consequence of emergence of chloroquine-resistant Plasmodium falciparum. Tropical and geographical medicine. 1993;45(3):110-113.
41. John CC, Bangirana P, Byarugaba J, Opoka RO, Idro R, Jurek AM, et al. Cerebral malaria in children is associated with long-term cognitive impairment. Pediatrics. 2008;1;122(1):e92-99.
42. Bangirana P, Opoka RO, Boivin MJ, Idro R, Hodges JS, Romero RA, et al. Severe malarial anemia is associated with long-term neurocognitive impairment. Clinical Infectious Diseases. 2014;24;59(3):336-344.

43. Birbeck GL, Molyneux ME, Kaplan PW, Seydel KB, Chimalizeni YF, Kawaza K, et al. Blantyre Malaria Project Epilepsy Study (BMPES) of neurological outcomes in retinopathy-positive paediatric cerebral malaria survivors: a prospective cohort study. The Lancet Neurology. 2010;31;9(12):1173-1181.
44. Ngugi AK, Bottomley C, Kleinschmidt I, Wagner RG, Kakooza-Mwesige A, Ae-Ngibise K, et al. Prevalence of active convulsive epilepsy in sub-Saharan Africa and associated risk factors: cross-sectional and case-control studies. The Lancet Neurology. 2013;31;12(3):253-263.
45. van Hensbroek MB, Palmer A, Jaffar S, Schneider G, Kwiatkowski D. Residual neurologic sequelae after childhood cerebral malaria. The Journal of pediatrics. 1997;31;131(1):125-129.
46. Carter JA, Neville BGR, White S, Ross AJ, Otieno G, Mturi N et al. Increased prevalence of epilepsy associated with severe falciparum malaria in children. Epilepsia; 2004;45:978–981. https://doi.org/10.1111/j.0013-9580.2004.65103.x
47. Othman AA, Bruschi F, GANNA AA. HELMINTH PARASITIC INFECTIONS OF THE CENTRAL NERVOUS SYSTEM: A DIAGNOSTIC APPROACH. J. Egypt. Soc. Parasitol. (JESP). 2014;44(1):55– 70. https://doi.org/10.12816/0006446
48. Betting LE, Pirani C Jr, de Souza Queiroz L, Damasceno BP and Cendes F. Seizures and cerebral schistosomiasis. Arch Neurol. 2005;62(6):1008–1010. https://doi.org/10.1001/archneur.62.6.1008
49. El-Khoby T, Galal N, Fenwick A, Barakat R, El-Hawey A, Nooman Z, et al. The epidemiology of schistosomiasis in Egypt: summary findings in nine governorates. Am J Trop Med Hyg. 2000;62: 88–99. https://doi.org/10.4269/ajtmh.2000.62.88
50. van de Beek D, de Gans J, Tunkel AR and Wijdicks EF. Community-acquired bacterial meningitis in adults. N Engl J Med. 2006;354(1):44–53. https://doi.org/10.1056/NEJMra052116
51. Pittella JE. Neuroschistosomiasis. Brain Pathol. 1997:7(1):649–662. https://doi.org/10.1111/j.1750-3639.1997.tb01080.x
52. Showler AJ, Wilson ME, Kain KC, Boggild AK. Parasitic diseases in travelers: a focus on therapy. Expert review of anti-infective therapy. 2014;1;12(4):497-521.
53. Ferrari TC, Moreira PR. Neuroschistosomiasis: clinical symptoms and pathogenesis. The Lancet Neurology. 2011;30;10(9):853-864.
54. Stuiver PC. Acute schistosomiasis (Katayama fever). British medical journal (Clinical research ed.). 1984;21;288(6412):221.
55. Scrimgeour EM. Non-traumatic paraplegia in northern Tanzania. Br Med J (Clin Res Ed). 1981;10;283(6297):975-978. https://doi.org/10.1136/bmj.283.6297.975
56. Chen MG. Assessment of morbidity due to Schistosoma japonicum infection in China. Infectious diseases of poverty. 2014;14;3(1):6.
57. Carod-Artal FJ. Neuroschistosomiasis. Expert review of anti-infective therapy. 2010;1;8(11):1307-1318.
58. Toovey S. Manson's Tropical Diseases. Travel Medicine and Infectious Disease. 2009;1;7(5):328.
59. Badr HI, Shaker AA, Mansour MA, Kasem MA, Zaher AA, Salama HH, et al. Schistosomal myeloradiculopathy due to Schistosoma mansoni: report on 17 cases from an endemic area. Annals of Indian Academy of Neurology. 2011;14(2):107. https://doi.org/10.4103/0972-2327.82796
60. Ferrari TC, Gazzinelli G, Corrêa-Oliveira R. Immune response and pathogenesis of neuroschistosomiasis mansoni. Acta tropica. 2008;31;108(2):83-88.