

Brain Swelling and Death in Children with Cerebral Malaria

Article by Dave Raynier C. Paguntalan
Health Science, Texila American University, Guyana
E-mail: dave.p@tau.edu.gy

Abstract

Introduction

Cerebral malaria is the most severe neurological impediment of infection and it is caused by Plasmodium falciparum idro et al. The article was aims to determine the main pathogenic processes and causes of death of children infected with cerebral malaria, by using clinical observations and pathologic findings, among children admitted with cerebral malaria who fulfil the world health organization criteria for cerebral malaria (WHO). The article further emphasises in regard using treatment challenges facing the children affected by cerebral malaria.

Using Artesunate in the treatment of cerebral malaria was found to be infective in complete eradication of the parasite that causes the disease. The article proposes that an enlargement in brain volume caused by the pressure exerted within the brain of children infected with cerebral malaria will be considered as the main cause of death. The article looks forward for its contribution to the population affected with malaria by inputting new scientifically proven knowledge that enhances new drug development.

The article begins with general introduction and proceeds by mentioning the aims and problems and the importance of the study. So, to address the stated problem the article uses an observational study design on children suffering from cerebral malaria. The article bases on numerous literature reviews, this supports the significance of the research. The comparison statistical analysis which was done on children with cerebral malaria who survive verses who lived.

The study was carried out in Queen Elizabeth Central hospital in Blantyre Malawi, from 2009 to June 2011.

Review of literature

As it is stated on the world malaria report, 2014 countless efforts in treatment, prevention and control of malaria has been done but yet difficult to eradicate. According to Dondrop, 2005 pathophysiology of cerebral malaria was not fully understood and the processes are vary in adults and children.

Although some articles discuss the features of the parasite life cycle considered as exceptional to *plasmodium falciparum* which is attach to endothelial cells and uninfected red cells (Sherman *et al*, 2003) in various organs including brains (Taylor *et al*, 2004). However, in contradiction other researches based on an autopsy-based study states 25% of children qualified for a cerebral malaria falls short to have histologic evidence of sequestration at autopsy. According to the research done by Newton *et al*, the swelling in brain and injury in cerebral malaria patients can be caused due to intracranial factor on top of its immediate effect of the intravascular sequestration. The relevance of the study was more pronounced as most of the literature reviewed couldn't discuss the pathophysiology of diseases and diseases associated with cerebral malaria and the cause of death.

Brown *et al*, documented in their study that the breakdown of BBB is caused by sequestration in areas of the parasite. Some researches done in intracranial pressure in childhood cerebral malaria shows an elevated opening CSF pressure Waller *et al*. He further finds out brain swelling and the compression of brain stem in brain swelling is seen in children die from sudden respiratory arrest.

As part of the exclusion strategy malarial retinopathy was used in distinguishing malaria to non-malaria coma according to an autopsy study of children dying with cerebral malaria in Malawi (Bear *et al*, 2006) in addition of the WHO criteria stated by WHO, 2000 which was good because as it is a new finding proven to do so.

It is also supported by other research Newton *et al*, as the pressure created with in the brain is very important disease-causing factor in children with cerebral malaria. But other researches show the death due to cerebral malaria can not only limited to brain swelling because in addition of the neurological

problem's other diseases such as anaemia, respiratory distress, hypoglycaemia and complications of pregnancy also has an impact, according to Murphy and breman.

Article summary

African Child death due to cerebral malaria ranges from 15 to 25%, the disease development and its possibility of causing death is not well understood. This article carries an observational study in combination with pathological finding aimed to find out the relationship between brains enlargements as a result of the pressure created with in the brain could be the cause of death.

Magnetic resonance imaging (MRI) is used to investigate the role of the enlarged brain to the disease development of the deadly cerebral malaria in Africa.

Children who have retinopathy were considered as positive for cerebral malaria with cerebral malaria and were included in the research. Detailed clinical data, MRI scan and Electroencephalogram images data on and after admission was collected.

The result of the article indicates Although 348 children were admitted only 168 manage to fulfil the inclusion criteria of cerebral malaria given by WHO. A total of 25 children which is 15% were recorded as dead, 21 out of 168 which is 84% were having brain swelling on admission. Meanwhile 39 out of 143 survivors. The MRI of children with cerebral malaria who died shows an increase in brain volume as compared than those who survive.

Finally, the article concludes with the finding of an increase in brain volume experienced in the cerebral malaria patients.

Article structure

The article was structured in a chronological order of the abstract, introduction, Method, Results, Discussion and Conclusion.

The article's abstract summaries in short and precise form. It covers concisely the background of the study, states the problem and article objective. Later the methods and instruments used to achieve the proposed problem were stated.

The authors Introduces generally about the epidemiology of the disease and acknowledge what has covered and achieved so far and what the article will contribute in detail. it includes numerous reviewed literatures up on the area, this support the research and shapes where it is heading. Besides, the hypothesis and the objectives of the study were stated.

Method: the researcher used an observational study design on the diseased children. An inclusion and exclusion criteria were implemented. In addition, Retinopathy examination was taken as distinguishing criteria for the malarial from the none malarial diseased children. It includes the recording the clinical findings, MRI Scans and EEG images of the patients on admission.

The result of the article was compiled in a tabular format, and the figures were discussed in a graphical interpretation of the collected data. This simplifies readers understanding of the outcome and its interpretation and summaries the overall findings of the research.

The article was properly referenced and this motivates readers who intend to read further and helps in article evaluation. Meanwhile the availability of the article only in a PDF format hinders the reader for a quick evaluation process due to the file.

The article was well aligned, punctuated and justified. The English used in the introduction and method was not difficult readers but as it goes to the result section, discussion and data interpretation it requires knowledge of the subject matter. The article data of the result was well coordinated and proper sign box was placed at the bottom of the table for it simplifies readers interpretation of the collected data. Tables and figures were labelled properly, and they are linked with the result and discussion efficiently. That means correct figure was used for the corresponding statement properly.

The article conclusion and discussion were placed under one category. Although the necessary information was there but separation of the two would be more beneficial.

Article critique

Authority

The article is authorised and published under the New England journal of Medicine. The New England journal of medicine is published by the Massachusetts medical Society and is among the most prestigious

peer-reviewed medical journals. This can show the credibility of the study. The authors of the article are listed below with their qualifications.

- Karl B. Seydel, M.D., Ph.D., Samuel D. Kampondeni, M.B., Ch.B., wrote 9 publications, Michigan state university, East Lansing, Department of Radiology
- Clarissa Valim, M.D., D.Sc., Harvard university, Cambridge, wrote 56 publications. Her publications have got 6279 views, 1071 citations for the last 3 months
- Michael J. Potchen, M.D., Board certified Radiologist with CAQ's in Neurology, American Board of Radiology, University of Rochester Medical Center School of Medicine and Dentistry
- Danny A. Milner, M.D., Brigham and Women Hospital, Boston, Pathology, Infectious Diseases. Featured in 41 publications.
- Francis W. Muwalo, A.D.I.T., Blantyre Malaria Projects. Biostatistics, information systems (Business informatics), Programming Languages. Featured in 1 Publication.
- Gretchen L. Birbeck, M.D., MPH. Professor- Department of Neurology, Epilepsy (SMD). Professor- Centre for Human Experimental Therapeutics. Professor- Department of Public Health Sciences (SMD) University of Rochester Medical Centre, School of medicine and Dentistry, featured in 118 publications.
- William G. Bradley, M.D., Ph.D., Professor, Radiology, UC San Diego
- Lindsay L. Fox, M.D.,
- Simon J. Glover,
- F. R. C. Ophth.,
- Colleen A. Hammond, A.S., Michigan State University, East Lansing. Neurology, Neuroradiology, Radiology. He featured in 8 Publications.
- Robert S. Heyderman, F.R.C.P., Ph.D.,
- Cowles A. Chilingulo, B.Sc.,
- Malcolm E. Molyneux, F. Med. Sci., and
- Terrie E. Taylor, Osteopathic Medical doctore, Researcher, Michigan State University, publishes 191 publications.

Review on the author

The article was written by well-known and experienced authors. The leading author was Dr. Karl Boynton Seydel, he is an osteopathic medical specialist. He has published about 56 publications.

Accuracy

The article was published recently in 2015 though the research was carried out 3 years earlier, from the year 2009 to 2012. A number of articles have been written in the study area of malaria, but the article is one of its types to cover the area accurately. The article inclusion and exclusion criteria, avoids sample bias.

The introduction of new medical diagnostic equipment such as MRI and EEG add more value to the article, as it has not done previously, which will contribute to a more reliable images and measurement figures. In addition, the article referred to two radiologist and two neurologist readings of MRI and EEG respectively with unawareness of each other and medical condition of the patients, this reduces informed bias. The article uses specific Statistical tests for reliability analysis, for the clinical characteristics and MRI and EEG. Reliability analysis was done for the Radiologic readings. P value of the likelihood ratio test was applied in comparing of models which don't have specific marker. Generally, the article implements proper statistical tests to avoid any form of bias. This indicates the accuracy of the article.

Currency

The research study was done at the Queen Elizabeth central Hospital in Blantyre, Malawi from January 2009 to June 2011. And it is published by the New England Journal of medicine in 2015; 372; 1126-37 Doi: 10.1065/NEJMoa1400116. It is a current research done in that particular topic recently.

Relevance

The article will be an asset in unlocking new research doors and will contribute in the development of new malarial drugs as the authors manage to associate the proposed objective. The article holds valuable information which can be utilized by pharmaceutical, academic, research institutes; but it still will limit

readers with no research background. This will be due to the vast statistical analysis and interpretations provided. The article will add awareness to the World health organization on how to set their plan in eradicating this deadly disease that affects African countries. It is also a good reference for pharmaceutical companies in developing an appropriate medication and reduces the mortality and morbidity overwhelming the African children. Understanding of the nature and cause of death in patients affected with cerebral malaria also will lead health sectors in setting up the treatment plan.

In general, the article discovers an additional broadened understanding on the pathogenesis of cerebral malaria and how it causes death.

Objectivity

The article was funded by National Institutes of Health and Welcomes Trust U.K. The article states the problem associated with cerebral malaria and the importance of the study relaying on previously done well referenced researches. The objective of the researchers was provided as it is finding out association of brain swelling and causes of death of children infected with cerebral malaria. The study was carried out in an area where there is high prevalence of cerebral malaria among children in Africa.

The article was supported by referring many related articles and underlines their limitations as well as their contribution.

The article used an observational study on 348 children. It states the inclusion and exclusion criteria for cerebral malaria. The sample participants were known, although the distribution of sample was not proportional among the compared participants.

The article succeeded in eliminating any possible cofounder such as misdiagnosing patients for cerebral malaria. It diligently follows the research processes, inclusion and exclusion criteria and other protocols. For example, it targets children aged > 5 months and it includes patients with cerebral malaria according to the criteria given by WHO for cerebral malaria. This helps the article to focus only on the proposed study groups and avoid sampling errors. The article also manages in avoiding errors caused as a result of misdiagnosis the cerebral malaria patients. According to some researches patients with cerebral malaria must be diagnosed for the presence of retinopathy to be included in the research.

The article includes updated medical equipment that were used such as MRI and EEG and compare them with previously used instruments and their limitations. This assists in producing precise images and collect accurate data that helps in objectively developing the association of brain swelling among the died and survived patients. The data collected was statistically analysed and scrutinized. Finally, the article discusses the findings as 21 out of 25 which is 84% children were found to have severed increase brain volume on MRI Scan. In contrast only 27% were having brain volume increase from the survivors. It shows brain swelling is the main cause of death cerebral malaria patients.

Stability

The article is available as a stable source for an academic or further research journal. The original article can be found from the New England Journal of medicine website. And it can also be found from various other research websites, and journals.

<http://www.nejm.org/doi/pdf/10.1056/NEJMoa1400116>

Data analysis

Based the data collected regarding the clinical features of the admitted patients, the author manages to diagnose children infected with cerebral malaria before admission and rule out other diseases such as HIV. And the researcher tries to relate lactate increase in patients who died as compared to patients who survive. On admission the CSF opening partial pressure was higher in patient who died in comparison to those who survived. High parasitic infestation in the dyed patients than the survivors has also recorded; this shows an increase intracranial pressure and vascular degradation.

The article statistically analyses and compares the association of MRI and EEG among patients who survived and the patients who died. Severely increased brain volume was noted among patients who died 21 out of 25 (84%) as compared to the patients who survived 39 out of 143 (27%). An increased water retention has been observed in both the survived and died patients but the died patients have shown a relative increase. Higher parchy lesions which is described as discrete cerebral injury relate to venous

occlusion has been shown to be increased by 28% in Patients who died of cerebral malaria as compared to the 6% patients who survived the disease.

EEG findings shows that there is a slight increase in patient who died of seizure activity in than survived.

The graph indicates a decreased preopontine CSF is noticed in patients with severe increased brain volume who died as compared to the patients who survive.

Conclusion

It is also supported by other research Newton *et al*, 1991 as the pressure created with in the brain is very important disease-causing factor in children with cerebral malaria.

In the review it was concluded that children who died from cerebral malaria as a result of intracranial pressure and these evidences of severe brain swelling was proved using serial MRI scans. The decrease in brain swelling on the dyed children up on this further mri check-up shows strictly the relationship of brain swelling as the main cause of death.

It was concluded that *plasmodium falciporium* which brings about the brain swelling in children with cerebral malaria though the pathogenesis of cerebral malaria is incompletely understood. It was suggested that brain swelling increase in intracranial pressure are the main cause of death in Malawian children with cerebral malaria as proved by the study design. An it furtherly emphasised the article will contribute by adding knowledge not only on the eradication of the parasite but also reliving intracranial pressure which was observed to be the mail cause of mortality and morbidity. This contributes an insight in research and developing drugs that works in lowering the intracranial pressure alongside of cleansing of the causative parasites.

I argued in this article about the way it correlates the pathogenesis of the brain swelling which was not fully understood with the overall finding of the research. The article failed to provide enough information on the pathogenesis of cerebral malaria in relationship with brain swelling however it discusses extensively the association of brain swelling lead by intracranial pressure as the cause of death in the children.

Source

The Original article was taken from the New England Journal of Medicine, written by KB Seyde *et el*, published in March 19, 2015.

N Eng L J Med 2015;372;11126-37 DOI: 10.1056/NEJMoa1400116

References

- [1]. Beare N. A.V, Taylor TE, Harding SP, Lewallen S and Molyneux M, 2006. Malarial retinopathy: A newly established diagnostic sign in sever malaria.
- [2]. Brown H, Rogerson S, Taylor T, Tembo M, Mwenechanya J, Molyeux M and Turner G, 2001. Blood-brain barrier function in cerebral malaria in Malawian children.
- [3]. Dondorp A, Nosten F, Stepniewska K, Day N, White N. Artesunate versus quinine for treatment of severe falciparum malaria: a randomised trial. Lancet 2005; 366:717-25.
- [4]. Idro R, Jenkin e N, Newton RJC Charles, 2005. Pathogenesis, clinical features, and neurological outcome of cerebral malaria.
- [5]. Lewallen S, Taylor E Terrie, Molyneux E. Malcom, Wills A Bridget, Courtright P, 1993. Ocular Fundus findings in Malawian children with cerebral Malaria.
- [6]. Newton RC, Peshu N, Kendall B, Kirkham, Sowunmi A, Waruiru C, Mwangi I, Murphy AS and Marsh K, 1994. Branin swelling and ischaemia in Kenyans with cerebral malaria.
- [7]. Newton, CRJC, Winstanley PA, Peshu.N, Marsh, RRCP, Kirkham. F.J Pasvol. G and Warrel DA., 1991. Intracranial pressure in African children with cerebral malaria
- [8]. MacPherson GG, Warrell MJ, White NJ, Looareesuwan S, Warrell DA. Human cerebral malaria: a quantitative ultrastructural analysis of parasitized erythrocyte sequestration. Am J Pathol 1985;119: 385-401.
- [9]. Murphy CS and Breman GJ, 2001. Gaps in the childhood malaria burden in Africa: cerebral Malaria, Neurological sequelae, Anemia, Respiratory Distress, hypoglycaemia and complications of pregnancy.
- [10].Potchen MJ, Kampondeni SD, Seydel KB, et al. Acute brain MRI findings in 120 Malawian children with cerebral malaria: new insights into an ancient disease. AJNR Am J Neuroradiol 2012;33:1740-6.

DOI: 10.21522/TIJAR.2014.SE.19.01.Art006

ISSN: 2520-3088

[11]. Taylor TE, Fu WJ, Carr RA, et al. Differentiating the pathologies of cerebral malaria by postmortem parasite counts. *Nat Med* 2004;10:143-5.

[12]. Waller D, Crawley J, Noster. F, Chapman D, Krishna S, Craddock C, Brewster D and White JN, 1990. Intracranial pressure in childhood cerebral malaria.

[13]. Wassmer CS, Combes V and Grau EG, 2003 Pathophysiology of cerebral malaria.

[14]. World malaria report. Geneva: World Health Organization, 2014 (http://www.who.int/malaria/publications/world_malaria_report/en).