Seizures in adult cases of cerebral malaria in rural based teaching hospital – A Review of literature

Umesh Babu¹, Nishant T², Venkateshwarlu Nandyala^{3*}, Sripada Muvvagopal⁴

Professor, Department of Medicine, SVS Medical College, Mahabubnagar, Telangana, INDIA. **Email:** <u>umeshdoc@rediffmail.com</u>, <u>nishanttrao@yahoo.com</u>, <u>venkatatreya@gmail.com</u>, <u>muvvagopal@gmail.com</u>

Abstract Background: In adults the incidence of seizure in cerebral malaria varies grossly from around one or two per cent cases of cerebral malaria 80 % in the literature. The study was planned and executed at semi-urban hospital. **Materials and Methods:** A total of confirmed 1219 cases of malaria admitted in the Department of Internal Medicine, 954patients satisfied the World Health Organization (WHO) criteria of severe malaria guidelines 2010¹¹ with cerebral malaria and admitted in Medical Intensive Care Unit of SVS Medical College Hospital. Detailed history of symptoms and signs and necessary investigations including CT scan or MRI scan and EEG **Observations and Results:** Out of 1219 cases of malaria admitted in the Department of Internal Medicine, 954patients satisfied the World Health Organization (WHO) criteria of severe malaria guidelines 2010¹ with cerebral malaria in 64 [8.25%] cases had convulsions. Extensive search was done in the literature to know the incidence and outcome of convulsions in severe malaria. **Discussion:** Malaria is common disease in India. Severe malaria and cerebral malaria are also common in these parts of the country. Though not common feature, convulsions are ominous symptoms of this disease in adults

Key Words: Cerebral malaria, CT/ MRI Brain, EEG, Seizure activity.

*Address for Correspondence:

Dr. Venkateshwarlu Nandyala, Professor and HOD, Department of Medicine, SVS Medical College, Telangana, INDIA.

Email: <u>venkatatreya@gmail.com</u>

Received Date: 04/07/2018 Revised Date: 30/07/2018 Accepted Date: 20/08/2018 DOI: <u>https://doi.org/10.26611/1021729</u>



INTRODUCTION

Seizure is one of the important problem of emergency admission. One to 5% of epilepsies were presumed to be due to central nervous system infections in countries like the United States, Norway and Israel¹. This incidence may be higher in developing countries. Malaria affects 5% of the world population at any one time and causes more than a million deaths worldwide annually. In adults the incidence of seizure in cerebral malaria varies. In the

1980's 50% of cerebral malaria patients in Thailand and Vietnam was reported to have generalized tonic-clonic seizures². Seizure activity had been noted in around 80 % of South African children and around 20-40 % of South Asian adult cases of Cerebral Malaria [Idro et al]. In the 1990's the same countries reported an incidence of 20% or less³. In 1989, Kochar et al reported a 23% incidence of seizures in Rajasthan, India⁴. Most of the seizures in adults were generalized. In children about 30% of all malarial patients had seizures^{5,6} while 60% to 85% of cerebral malarial patients had seizures⁶⁻⁹. More than 75% of seizure occurred in uncomplicated malaria and more than 70% of cerebral malarial patients had more than one seizure. In endemic and hyperendemic areas in Africa the commonest seizure is partial, which accounts for 52-84% of all seizures; 34% is generalizes and another 14% partial with secondary generalized^{5,7}. In Papua New Guinea, on the other hand, generalized seizure accounts for 85% of seizures, and 53% of cerebral malarial patients have status epilepticus⁶. 217 million were affected with

How to cite this article: Umesh Babu, Nishant T, Venkateshwarlu Nandyala, Sripada Muvvagopal. Seizures in adult cases of cerebral malaria in rural based teaching hospital – A Review of literature. *MedPulse International Journal of Medicine*. August 2018; 7(2): 72-76. https://www.medpulse.in/Medicine/

malaria annually in 2015, 21 % reduction in incidence and a reduction of 29 % reduction in mortality¹⁰.

MATERIALS AND METHODS

The present study was conducted in SVS Hospital, Mahabubnagar, a tertiary care teaching hospital. This was a hospital based clinico-epidemiological study. Cerebral malaria (CM) was defined as a clinical syndrome of coma (inability to localize a painful stimulus) at least an hour after termination of a seizure or correction of hypoglycemia, detection of asexual forms of malarial parasite on peripheral blood smear and exclusion of other causes of encephalopathy¹¹.Cases of confirmed malaria patients admitted between January 2007 to December 2016 were collected in a preformed proforma. Out of 1219 cases of malaria admitted in the Department of Internal Medicine, 954patients satisfied the World Health Organization (WHO) criteria of severe malaria guidelines 2010^{11} with cerebral malaria and admitted in Medical Intensive Care Unit. We further studied the clinical profile, treatment and outcome of these patients. Data was collected in a preformed proforma and analysed by SPSS 20.0 software. Values are expressed in number and percentage (%).

OBSERVATIONS AND RESULTS

Table 1 shows the details of cases admitted to SVS Medical College Hospital from 1-1-2007 till 31-12-2016.

Table 1: Total cases of Malaria with respect to species
encountered in SVS Hospital during study period of 10 years (1-1-
2007 to 31 12 2016

	2007 10 31-1	2-2010)
Description	Number	Percentage %
Total number of positive	1210	100
Malaria cases	1217	100
Total number of severe	054	79.26
Malaria cases	754	78.20
Total number of Cerebral	660	54 14
Malaria	000	54.14
Total cases presented with		13.45 [of total Malarial case]
seizure activity	164	24.85 [of cerebral Malarial
seizure activity		cases]
Known cases of Epilepsy	11	-
Lost to follow up	13	-
Total number of cases included in this study		12.30 [of total malaria cases]
	150	22.73 [of cerebral malarial
		cases]

CT [Computed Tomography] scan or MRI [Magnetic Resonance Imaging] scan done in 240 cases of cerebral malaria cases and EEG [Electro-encephalography] done in 120 cases. The findings are tabulated in following tables.

Table 2: Showing CT Br	ain abno	rmalities i	in 308
CT finding	Numbe	r Perc	entage
Normal	198	6	4.29
Cerebral edema	92	2	9.87
Periventricular infarct	10		3.24
Cerebellar infarct	8	4	2.59
Table 3: Showing MRI Brain abnormalities in 265 cases			
MRI finding	N	lumber	Percentage
Normal		92	34.71
Cerebral edema		140	52.83
Cerebral infarct		12	4.53
Periventricular hemorrhagic infarct		11	4.15
Myelin changes		10	3.77

Table 4: Various abnormalities in this study		
Report of EEG	Number of cases	Percentage
Normal	34	28.33
Diffuse spike waves	38	31.67
Focal seizure activity	36	30
Slow waves in occipital region	12	10
Total	120	100

Of 86 abnormal EEG cases only 42 patients had repeat EEG done at 6 weeks only 3 had showed residual abnormality. These three patients were treated like epilepsy. Patients were followed for at least a period of 2 years. Last case of malaria with convulsions included in this study was admitted on 20th October 2015. In 10 years of the present study 660 cases of cerebral malaria SVS admitted to Medical College Hospital, Mahabubnagar, Telangana State. 164 patients had seizure activity. Fortunately, we had only 16 cases of cerebral malaria expired. Of these 14 patients presented with status epilepticus.

DISCUSSION

Cerebral malaria is a medical emergency demanding urgent clinical assessment and treatment. The diagnosis requires presence of neurologic symptoms and asexual forms of the parasite on peripheral blood smears. Every effort was taken, and necessary investigations were done to exclude other causes of coma. Seizure activity was noticed more in children up to 80% while 20% of adults had convulsions. [Idro *et al* 2007] An extensive search was done from the literature. The table V shows the detailed summary of incidence of seizures in various earlier studies. The table explains mainly study population and incidence of seizure activity. Image studies EEG and other investigations mainly were more of nonspecific and mainly to exclude other causes.

Serial Number	Study	Comments
1 2	Schutzhard E and Gerstenbrand F 1984 ¹³ White NJ <i>et al</i> 1988 ⁵	Study of Tanzanian children; two-thirds had convulsions Study of Thai adults; one third cases had convulsions
3	Kochar <i>et al</i> 1989 ⁴	Reporting from Bikaner, Rajasthan India, Kochar <i>et al</i> reported 23% incidence of seizures.6
4	Brewster DR, Kwiatkowski D, White NJ. 1990 ¹⁴	Study of 65 children; Sixty-two percent of patients had seizures following admission, of whom half had an episode of status epilepticus. Fifty-two percent of seizures were partial motor, 34% generalized tonicclonic, and 14% partial with secondary generalization
5	Bondi 1992 ¹⁵	Of 78 children with cerebral malaria from Ibadan, Nigeria, between March 1987 and October 1988, 16 (20.5%) died and 62 (79.5%) survived. 11[17.7%] had neurological problems like severe recurrent convulsions. Study of 487 children: 42% patients presented with topic clonic. 16% had
6	Akpede G, Sykes R, Abiodun F 1993 ¹⁶	focal convulsions becoming generalized while 21% presented both generalized and focal fits.Twenty-six percent of the active epilepsy group
7	Asindi <i>et al</i> 1993 ¹⁷	134 children febrile convulsions 55% are cerebral malaria
8	Molyneux ME et al 1995 ⁸	131 Malawian children admitted with cerebral malaria; 12 patients [9%] had neurological sequelae like convulsions
9	Lallo <i>et al</i> 1996 ¹⁸	17% children presented with convulsions at the start of presentation to hospital.
10	Waruiru CM, Newton CR, Forster D, <i>et al</i> . 1996 ⁷	1324 children admitted in the pediatric ward of the Kilifi District hospital in Kenya, over a year period and found seizures in 15.8% of children as part of their illness, with malaria accounting for 69% of the causes of seizures. Most seizures occurred between the ages of 6 months and 5 years and 64.3% of malaria-associated seizures occurred greater than two years old. 65 patients (38 female) admitted to Kilifi
11	Crawley J, Smith S, and Kirkham F <i>et al</i> 1996 ⁹	Hospital in 1994.Fifty-two percent of seizures were partial motor, 34% generalized tonic clonic, and 14% partial with secondary generalization
12	Bajia, Kochar <i>et al</i> 1997 ¹⁹	40 (21.62%) patients had convulsions at the time of presentation. 17 (42.5%)
13	Crawley J, Smith S, Muthinji P, Marsh K and Kirkham F <i>et al</i> 2001 ²⁰	Fifty-two percent of cerebral malaria in children had partial motor seizures, 34% generalized tonicclonic, and 14% partial with secondary generalization.
14	Kochar <i>et al</i> 2002 ²¹	In an Indian study from Bikaner, Rajasthan on 441 patients of strictly defined cerebral malaria, 21.31% had convulsion
15	Carter JA, Neville BGR, White S, <i>et al.</i> 2004 ²²	487 children (aged 6-9 years). 9.2 % of cerebral malaria had seizures. The most commonly reported seizure types were tonic-clonic (42%), focal becoming secondarily generalized (16%), and both (21%). Twenty-six percent of the active epilepsy group initially had EEG abnormalities.
16	ldro <i>et al</i> 2007 ¹²	Of 19,560malaria children, 9,313 were cerebral malaria; 6,563 had seizures.
17	Genton <i>et al</i> 2008 ²³	Out of 9,537 (55%) had a confirmed Plasmodium parasitaemia, 2.5% of Pf had convulsions and 1.1% cases of Pv had repeated convulsions.
18	Sarkar and Bhattacharya 2008 ²⁴	3 adult male cases cerebral malaria with convulsions
19	Jain <i>et al</i> 2008 ²⁵	Plasmodium falciparum and 18 cases of P vivax, 119 were cerebral malaria; seizures were noted in 40% cases.
20	Tanwar <i>et al</i> 2011 ²⁶	11 children out 13 cases of cerebral malaria had convulsions
21	Mohapatra MK et al 2012 ²⁷	Convulsion noted in 110(14.3%) of P falciparum cases.
22	Jagjit Singh <i>et al</i> 2013 ²⁸	110 patients – 3 had cerebral malaria convulsions
23	S Nandwani et al ²⁹	Out of 160 patients, 110 (68.75 %) had P. vivax, 30 (18.75 %) had P. falciparum and 20 (12.5 %) had co-infection due to P. vivax and P. falciparum 2 cases of p f had GTCS
24	Kumar <i>et al</i> 2014 ³⁰	Observational study of cerebral malaria. 2/27 p v [7.40%], 1/26 pf [3.84%],
25	Islam <i>et al</i> 2016 ³¹	Of 187 cases from Bangladesh, 29 patients (15.5%) had convulsion before or

Table 5: Summary of the earlier studies with the present study

		after admission.
		This was a prospective observational study in 170 patients with a clinical
26	Veer Bahadur Singh <i>et al</i> 2016 ³²	diagnosis of malaria admitted in of PBM Hospital, Bikaner during epidemic
	-	of malaria. 5 [4.55%] had convulsions.
27	Jelia <i>et al</i> 2016 ³³	Four out of 32 cases [12.5%] of falciparum malaria had convulsions
28 Present study 2018	Procent study 2010	660 cases of cerebral malaria admitted to SVS Medical College Hospital,
	Present study 2018	Mahabubnagar, Telangana State. 164 [8.25%] patients had seizure activity.

Of the 16 patients fourteen presented with status epilepticus. This fact conforms with earlier studies.

CONCLUSION

This is a prospective study spread over 10 years executed at a semi-urban tertiary Hospital attached to SVS Medical College. A total 1219 positive malaria cases were recorded in various wards of SVS Hospital;660 adult cases were of cerebral malaria. 164 patients had seizure activity. Of 16 deaths 14 cases presented with status epilepticus. An adult patient presenting with convulsions and fever a diagnosis of cerebral malaria should strongly be considered in tropical countries like ours and intense search for the diagnosis of malaria even if smear for malaria parasite is negative once, a repeated search in the presence of temperature and chills or PCR or antigen detection in RDT. Status Epilepsy in cerebral malaria may be an ominous sign for prognosis though statistically not significant. Further studies are needed for the confirmation.

Limitations: This was a prospective observational study without comparing control group, which was the main limitation of this study.

REFERENCES

- Annegers JF, Hauser WA, Beghi E, Nicolosi A, Kurland LT. (1988); The risk of unprovoked seizures after encephalitis and meningitis. Neurology 38: 1407-10
- White NJ, Looareesuwan S, Phillips RE, Chanthavanich P and Warrel DA. (1988) Single dose phenobarbitone prevents convulsions in cerebral malaria. Lancet 2: 64-6
- 3. Tong HT (2004); Seizures and epilepsies secondary to central nervous system Infection (2004) Neurology Asia 9 (Supplement 1): 20 23
- Kochar DL, Shubhakaran, Kumawat BL, Kochar SK. (1996) Seizures in cerebral malaria. (letter) Q J Med 89: 591-7.
- 5. Waruiru CM, Newton CR, Forster D, et al. (1996); Epileptic seizures and malaria in Kenyan children. Transac R Soc Trop Med Hyg; 90: 152-5.
- Allen SJ, O'Donnell A, Aller NDE and Clegg JB. (1996); Severe malaria in children in Papua New Guinae. Q J Med 89: 779-88
- Crawley J, Smith S, Kirkham F et al. (1996); Seizures and status epilepticus in childhood cerebral malaria. Q J Med 89: 591-7
- Molyneux ME, Taylor TE, Wirima JJ and Borgstein A. (1989); Clinical features and prognostic indicators in paediatric cerebral malaria: A study of 131 comatose Malawian children. Q J Med; 265: 441-59.

- 9. Waller D, Krishna S, Crawley J, et al. (1995): Clinical features and outcome of severe malaria in Gambian children. ClinInfDis 21: 577-87.
- WHO. Global Technical Strategy for Malaria 2016–2030. Geneva: World Health Organization (WHO); 2015 (http://www.who.int/malaria/areas/global_technical_ strategy/en, accessed 16 November 2016).
- World Health Organization. Severe falciparum malaria. World Health Organization, communicable diseases cluster. Trans R Soc Trop Med Hyg. 2000; 94: S1–90. [PubMed: 11103309]
- Idro R, Ndiritu M, Ogutu B, et al (2007): Burden, features and outcome of neurological involvement in acute falciparum malaria in Kenyan children JAMA, 2007; 297 (20): 2232 – 40
- Schmutzhard E, Gerstenbrand F. Cerebral malaria in Tanzania. Its epidemiology, clinical symptoms and longterm sequelae in the light of 66 cases. Trans R Soc Trop Med Hyg 1984; 78: 351-3
- Brewster D, Kwiatowski D, White N. Neurological sequelae of cerebral malaria in children. Lancet 1990; 336:1030–43.
- Bondi F. The incidence and outcome of neurological abnormalities in childhood cerebral malaria: a long term follow up of 62 survivors. Trans Roy Soc Trop Med Hyg 1992; 84:17–19.
- Akpede G, Sykes R, Abiodun F. Convulsion with malaria

 febrile or indicative of cerebral involvement? J Trop Pediatr 1993; 39: 350 –5
- Asindi A, Ekanem E, Ibia E, Nwangwa M. Upsurge of malaria-related convulsions in resistant Plasmodium falciparum infection. Trop Geogr Med 1993; 45: 110-3.
- Laloo DG, Trevett AJ, Paul M, Korinhona A, Laurenson IF, Mapao J, et al. Severe and complicated falciparum malaria in Melanesian adult in Papua New Guinea. American J Trop Med Hyg. 1996; 55:119-24.
- Bajiya HN, Kochar DK. Incidence and neurological sequelae in survivors of cerebral malaria. JAPI 1996; 44: 679-81.
- Crawley J, Smith S, Muthinji P, Marsh K and Kirkham F. Electroencephalographic and clinical features of cerebral malaria. Arch Dis Child (2001); 84: 247-53.
- Kochar DK, Shubhakaran, Kumawat BL et al (2002); Cerebral malaria in Indian adults: a prospective study of 441 patients from Bikaner, north-west India. J Assoc Physicians India 50: 234–241.
- 22. Carter JA, Neville BG and White S et al (2004) Increased prevalence of epilepsy associated with severe falciparum malaria in children. Epilepsia. 2004 Aug; 45(8): 978-81.
- 23. Genton B, D'Acremont V, Rare L, Baea K, Reeder JC, Alpers MP, et al. (2008) Plasmodium vivax and Mixed Infections Are Associated with Severe Malaria in

Children: A Prospective Cohort Study from Papua New Guinea. PLoS Med 5(6): e127. https://doi.org/10.1371/journal.pmed.0050127

- 24. S Sarkar and P Bhattacharya Cerebral malaria caused by Plasmodium vivax in adult subjects Indian J Crit Care Med. 2008 Oct-Dec; 12(4): 204–205.
- Jain V, Nagpal AC, and Joel M et al (2008): Burden of Cerebral Malaria in Central India (2004-2007) Am. J. Trop Med Hyg 2008 79(4): 636-642
- Tanwar GS et al Clinical profiles of 13 children with Plasmodium vivax cerebral malaria: Annals of Tropical Paediatrics (2011) 31, 351–356
- 27. Jagjit Singh, Bhargav Purohit, Anupama Desai, et al (2013); Clinical Manifestations, Treatment, and Outcome of Hospitalized Patients with Plasmodium vivax Malaria in Two Indian States: A Retrospective Study Malaria Research and Treatment2013(6):341862 · December 2013
- 28. MK Mohapatra, LK Dash, PK Bariha, PC Karua Profile of Mixed Species (Plasmodium vivax and falciparum)

Malaria in Adults JAPI • October 2012 • VOL. 60 20 – 24

- 29. S Nandwani, A Pande and M Saluja 2012 Clinical profile of severe malaria: study from a tertiary care center in north India J Parasit Dis (Jan-Mar 2014) 38(1):11–15
- Kumar R, Agarwal D, Kumar P. Severe Plasmodium vivax Malaria in Children: An emerging threat. Journal of Pediatric Sciences. 2014; 6: e210
- Islam AT, Rahman M, Islam RT(2016); Falciparum malaria with neurological manifestations a study among tribal community in Bangladesh International Journal of Applied Research 2016; 2(2): 210-213
- 32. Veer Bahadur Singh, Harish Kumar, Babu Lal Meena, Subhash Chandra, Jatin Agrawal, Naresh Kanogiya (2016); Neuropsychiatric Profile in Malaria; Journal of Clinical and Diagnostic Research. 2016 Jul, Vol-10(7): OC24-OC28
- 33. Jelia S, Meena S, Meena SR, Arif Md., Jain P, Ajmera D et al. A study of clinical profile and complication of malaria in a tertiary care centre in South-eastern region of Rajasthan, India. Int J Adv Med 2016; 3:614-20.

Source of Support: None Declared Conflict of Interest: None Declared