



## Glasgow Coma Score as a Predictor for Development of Retinopathy in Children's with Cerebral Malaria

Authors

**Dr Puneet Agrawal<sup>1</sup>, Dr Jyoti Singh<sup>2</sup>, Dr Sujata Lakhtakia<sup>3</sup>**

<sup>1</sup>Senior Resident, Department of Pediatrics, S.S. Medical College, Rewa

<sup>2</sup>Professor and Head, Department of Pediatrics, S.S. Medical College, Rewa

<sup>3</sup>Assistant Professor, Department of Ophthalmology, S.S. Medical College, Rewa

Corresponding Author

**Dr Puneet Agrawal**

Room no.8, PG Boys Hostel, S.S. Medical College, Rewa (M.P.), Pin – 486001 India

Phone: 9425721482, Email: [dr.puneetagrwal@gmail.com](mailto:dr.puneetagrwal@gmail.com)

### Abstract

**Objectives:** To assess the relationship of retinopathy with Glasgow coma Scoring in cerebral malaria.

**Design:** Prospective, observational, cohort study. Cohort study comprising of all malaria positive patients.

**Setting:** Study was carried out in Department of Paediatrics, S.S.M.C and associated G.M. Hospital Rewa, Madhya Pradesh during the period of 1<sup>st</sup> August 2015 to 31<sup>st</sup> July 2016.

**Participants:** 100 consecutive patients with cerebral malaria evaluated by ophthalmologist for changes of retinopathy were included in the study. All 100 cases were malaria positive.

**Main Outcome Measure(s):**

**Results:** Retinopathy was present in 41% of children in cerebral malaria (malaria positive with encephalopathy). In Cerebral malaria on the basis of GCS we found that 79% patients with Glasgow score less than or equal to 6 had retinopathy, while only 35% who had Glasgow score more than 6 had retinopathy.

**Conclusions:** A positive association of patients having Glasgow coma score less or equal to 6 had proportionally high incidence of retinopathy. This shows that the incidence of retinopathy increases as the Glasgow coma score decreases and retinopathy is significantly associated with low GCS. Retinopathy and low GCS together in turn is related to high mortality in cerebral malaria.

**Keywords:** Cerebral Malaria, Retinopathy, GCS.

### Introduction

Cerebral malaria appears to be one of the most common non-traumatic encephalopathy in the world<sup>[1]</sup>. Cerebral malaria can be fatal in the absence of prompt recognition of the disease and its complication, and in the absence of active appropriate management of patients, especially in

the high risk groups like pregnant women and young children. By this study we aim to recognize such cases early and limit mortality and morbidity related to malaria.

The pathogenesis of coma in cerebral malaria remains poorly understood. Obstruction of the brain microvasculature because of sequestration of

parasitized red blood cells is one of the mechanism that could contribute to coma. Sequestration occurs to a variable degree throughout the microvasculature, and previous quantitative light and electron microscopic studies have confirmed a quantitative association between sequestration and coma, with higher levels of sequestration seen in the cerebral microvasculature in patients dying of Cerebral malaria [2-6]. The retina provides a unique opportunity to observe the central nervous system vasculature and therefore to study cerebral vasculature directly i.e. eye being regarded as an extension of the brain. The detection of malarial retinopathy can be a good diagnostic tool for cerebral malaria.

### Objective

Objective of the present study is to assess the relationship of retinopathy with Glasgow coma scoring in cerebral malaria.

### Methodology

The study was carried out in the Department of Pediatrics, SS Medical College and associated GM Hospital, Rewa, Madhya Pradesh during the period of 1<sup>st</sup> August 2015 to 31<sup>st</sup> July 2016, after clearance from the Institutional Ethics Committee.

The study design is observational cohort study.

This area of Madhya Pradesh is classified under hyper endemic zone for malaria [7, 8].

The study group comprised of 100 consecutive children with cerebral malaria between age 1 month to 18 years presenting with acute febrile encephalopathy and either peripheral smear or Rapid diagnostic test positive for malaria with Glasgow Coma Scale  $\leq 10$  with or without seizures. All cases were malaria positive. Children were managed as per standard guidelines for treatment of cerebral and non-cerebral malaria. All cases were evaluated by ophthalmologist for any changes of retinopathy.

A detailed clinical evaluation including history and examination was carried out for all study participants at the time of admission. A base line evaluation in the form of blood sugar estimation

(glucose strip), complete blood counts, and blood culture were done at the time of admission in all children. By using aseptic precautions, finger prick sample of blood was collected to prepare thick and thin smears of blood on glass slides, and evaluated for presence of any malaria parasite under oil immersion, as per standard procedures.

Rapid diagnostic test kits were also used for the diagnosis of malaria. (SD BIOLINE Malaria Ag Pf./Pan kit manufactured by Standard Diagnostics (Alere) limited, Korea.)

Fundus examination was performed by ophthalmologist in all patients, after pupils were fully dilated using mydriatic eye drops. Presence of papilledema, retinal haemorrhages and vessel changes, peripheral whitening, and blurring of disc margins were noted and recorded separately, in addition to any other ophthalmologic abnormality.

Subsequently, all investigations required for clinical management were done.

In unconscious patients, vitals, Glasgow Coma Score and blood sugar were recorded until they became conscious or till demise. Initially, it was done every 6 hours for first 24 hours then every 12 hours until they became conscious.

### Statistical Analysis

The data of the study were entered and analysed using the software Microsoft Excel 2013 for windows. Appropriate univariate and bivariate analysis were carried out using the Student t test for the continuous variable / proportion test (z test/ t test) and two-tailed Fisher exact test or chi-square ( $\chi^2$ ) test for categorical variables. The critical levels of significance of the results were considered at 5% i.e.  $P < 0.05$  was considered significant.

### Results

In our study in the cerebral malaria group (malaria positive with encephalopathy), 59% were males and 41% were female patients. (Table no. 1)

Retinopathy was present in 41% of the children in cerebral malaria group. (Table no 2)

In CM group mortality was observed in 39% of patients who had retinopathy, compared to 15% who did not have retinopathy. The difference found is statistically significant i.e. those patients who had retinopathy were at a higher risk of dying. (Table no 2)

On the basis of GCS we found that 79% patients

with Glasgow score less than or equal to 6 had retinopathy, while only 35% who had Glasgow score more than 6 had retinopathy.(Table No.3) We found p value of 0.0053 suggesting statistical association that Glasgow scores of <6 is a risk factor for developing retinopathy.

**Table I**

Sex	Cerebral malaria(CM) (n=100)
Male (M)	59(59%)
Female(F)	41(41%)
Total	100(100%)
Age	
<6 month	5(5%)
6 month – 5 years	27(27%)
6 years – 12 years	47(47%)
13 years – 18 years	21(21%)

**Table II** Retinopathy in relation to Outcome

Fundus	Cerebral malaria (CM) (n=100)		
	Total	Mortality	Survived
Normal	59	9(15%)	50
Retinopathy	41	16(39%)	25
Total	100	25 (25%)	75
P value	0.0097		

**Table III** Retinopathy in relation to Glasgow coma Scoring

EVM Glasgow score	Cerebral malaria (CM) (n=100)			Statistical Analysis
	Retinopathy Present	Retinopathy Absent	Total	
≤ 6	11(79%)	3(21%)	14(100%)	P=0.0053
> 6	30(35%)	56(65%)	86 (100%)	
Total	41	59	100	

## Discussion

In our study we found that in the CM group (malaria positive with encephalopathy) 59% patients had normal fundus and 41% patients had retinopathy. In CM group mortality was observed in 39% of patients who had retinopathy, compared to 15% who did not have retinopathy. This difference found was statistically significant (p=0.0097) in CM group i.e. those patients who developed retinopathy were at an increased risk of dying.

Beare, et al. (2004)<sup>[9]</sup> reported 61% while Birbeck, et al. (2010)<sup>[10]</sup> reported 79% incidence of retinopathy in their studies of cerebral malaria. Mortality reported by various authors in patient having any fundal abnormality was 21% in children (Beare, et al. 2004)<sup>[9]</sup> and 24% in adults

(Kochar & Shubhakaran, et al. 1998)<sup>[11]</sup>. In CM group on the basis of GCS we found that 79% patients with Glasgow score less than or equal to 6 had retinopathy, while only 35% who had Glasgow score more than 6 had retinopathy.

On statistical analysis, this difference was found to be significant (p= 0.0053) indicating a positive association that patients having Glasgow coma score less or equal to 6 had proportionally high incidence of retinopathy. This shows that the incidence of retinopathy increases as the Glasgow coma score decreases.

Mark J. Ponsford et al<sup>[12]</sup> found both sequestration and congestion were inversely associated with time to death after admission to hospital . The level of consciousness, as measured by the GCS, was also inversely correlated with both parameters

Schemann et al 2002<sup>[13]</sup> reported depth of coma as significant risk factor for death in cerebral malaria.

### Conclusions

Malarial retinopathy is significantly associated with mortality in children with cerebral malaria. A positive association of patients having Glasgow coma score less than or equal to 6 had proportionally high incidence of retinopathy. This shows that the incidence of retinopathy increases as the Glasgow coma score decreases and retinopathy is significantly associated with low GCS. Retinopathy and low GCS together inturn is related to high mortality in cerebral malaria.

### References

1. Snow RW, Newton CRJC, Craig MH & Steketee RW. The public health burden of plasmodium falciparum malaria in Africa: deriving the numbers. Disease Control Priorities Project Working 2003, Paper No. 11. Bethesda, Md.
2. 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.
3. Pongponratn E, Riganti M, Punpoowong B, Aikawa M. Microvascular sequestration of parasitized erythrocytes in human falciparum malaria: a pathological study. Am J Trop Med Hyg 1991; 44:168–75.
4. Silamut K, Phu NH, Whitty C, et al. A quantitative analysis of the microvascular sequestration of malaria parasites in the human brain. Am J Pathol 1999; 155:395–403.
5. Pongponratn E, Turner GD, Day NP, et al. An ultrastructural study of the brain in fatal Plasmodium falciparum malaria. Am J Trop Med Hyg 2003; 69:345–59.
6. Taylor TE, Fu WJ, Carr RA, et al. Differentiating the pathologies of cerebral malaria by postmortem parasite counts. Nat Med 2004; 10: 143–5
7. Jain V, Avinash C, Pradeep K, Manmohan S, Mrigendra P, Rasik B, et al. Burden of cerebral malaria in Central India (2004–2007). Am J Trop Med Hyg. 2008;79:63642.
8. Singh J, Soni D, Mishra D, Singh HP, Bijesh S. Placental and neonatal outcome in maternal malaria: A prospective cohort study from Central India. Indian Pediatr. 2014;51:2858
9. Beare NAV, Southern C, Kayira K, Taylor TE, Harding SP. Visual outcomes in children in Malawi following retinopathy of severe malaria. Br J Ophthalmol 2004 88 321-324.
10. Birbeck G, Beare N, Lewallen S, Glover SJ, Molyneux ME, Kaplan PW & Taylor TE. Identification of malaria retinopathy improves the specificity of the clinical diagnosis of cerebral malaria: findings from cohort study. 2010a, Am J Trop Med Hyg, 2010 82. 231-4.
11. Kochar & Shubhakaran, et al. Ophthalmologic abnormalities in adults with plasmodium falciparum malaria; Q J Med. 1998., 91:845-852.
12. Mark J. Ponsford, Isabelle M. Medana, Panote Prapansilp et al. Sequestration and Microvascular Congestion Are Associated With Coma in Human Cerebral Malaria The Journal of Infectious Diseases 2012;205:663–71
13. Schemann JF, Doumbo O, Malvy D, Traore L, Kone A, Sidibe T, Keita M. Ocular lesions associated with malaria in children in Mali. Am J Trop Med Hyg 2002 67 61-63.