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**Dr. Nimish Kumar Singh**  
Junior Resident, RIO,  
Rajendra Institute of Medical  
Sciences, Ranchi, Jharkhand,  
India

**Dr. Sunil Kumar**  
Associate Professor, RIO,  
Rajendra Institute of Medical  
Sciences, Ranchi, Jharkhand,  
India

**Dr. VB Sinha**  
Professor & H.O.D., RIO,  
Rajendra Institute of Medical  
Sciences, Ranchi, Jharkhand,  
India

**Corresponding Author:**  
**Dr. Nimish Kumar Singh**  
Junior Resident, RIO,  
Rajendra Institute of Medical  
Sciences, Ranchi, Jharkhand,  
India

## Prevalence and prognostic significance of retinal findings in pediatric cerebral malaria cases at a Tertiary Care Centre in eastern India

**Dr. Nimish Kumar Singh, Dr. Sunil Kumar and Dr. VB Sinha**

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### Abstract

**Objective:** To find out the prevalence of retinal findings in pediatric cerebral malaria cases and their correlation, if any, with the final disease outcome.

**Material and method:** The fundi of all pediatric cerebral malaria cases admitted at a tertiary care center in east India over a period of 15 months were examined by direct and indirect ophthalmoscopy for the presence of retinal signs of cerebral malaria, which include retinal hemorrhage, papilledema, vessel discoloration and retinal whitening. The patients were treated for malaria and final disease outcome was documented

**Result:** Almost half of the cases of pediatric cerebral malaria had the presence of retinal signs. These were associated with poorer disease outcome and increased mortality. Among specific signs retinal hemorrhage had maximum association with increased mortality while retinal whitening didn't have any significant association with mortality

**Conclusion:** The presence of retinal signs in cerebral malaria is a significant predictor of prolonged coma and death. Thus the physician can decide which cases demand more aggressive treatment just by looking at their fundus.

**Keywords:** Malaria, cerebral malaria, pediatric cerebral malaria, fundus examination, retinal signs, disease outcome

### Introduction

Malaria is an endemic disease in east India causing a significant morbidity and mortality in the general population as well as the pediatric age group. It is caused by Plasmodium spp. Cerebral Malaria (CM) is one of the dreaded complications of malaria, caused by Plasmodium falciparum and carrying a substantial mortality and associated with various neurological sequelae [1]. The classical definition of cerebral malaria defines it to be a peripheral parasitemia with coma, not attributed to any other cause such as hypoglycemia or coma. However this definition misclassifies cerebral malaria in upto 25% cases as determined by histopathological examination. The retinal signs associated with cerebral malaria, collectively known as malarial retinopathy, include retinal whitening, vessel discoloration, retinal hemorrhages and papilledema [2]. Malarial retinopathy helps distinguish between histopathologically confirmed CM and cases that meet the broad clinical definition of CM but actually have another cause of death. The presence of signs of malarial retinopathy has been associated with poorer prognosis [3, 4]. This study aims to find out the prevalence of these signs among pediatric cerebral malaria cases and determine their correlation, if any, with the final outcome of the disease.

### Material and Method

All the cases of cerebral malaria, admitted in the Department of Pediatrics of Rajendra Institute of Medical Sciences (RIMS), Ranchi, India from June 2016 to September 2017 were included in the study. The diagnosis of cerebral malaria was made on the basis of acute febrile encephalopathy and either peripheral smear or rapid diagnostic test positive for malaria. These patients were pharmacologically dilated with Tropicamide (0.5%) eye drops and a detailed fundus examination was done using direct and indirect ophthalmoscope. The retinal signs of cerebral malaria if present were documented. These patients were then treated for malaria and a meticulous follow-up was done to determine the final disease outcome which was also documented. The outcomes were categorized as recovery, recovery with neurological sequelae and death. A correlation of presence of retinal signs with these

outcomes was determined. Any change in the retinal signs over a period of time was also documented during follow-up.

**Statistical Analysis:** The data were entered into MS Excel sheets and analysed using SPSS software for Windows. Appropriate univariate and bivariate analyses 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 test for categorical variables. P value of less than 0.05 was considered significant.

## Results

A total of 100 patients were included in the study. Out of these 48 (48%) were boys and 52 (52%) were girls. The mean age of patients was  $8.4 \pm 2.7$  years. The average interval of fundus examination from admission was 4.64 hours. 48 patients (48%) showed any of the retinal signs of cerebral malaria, out of which 18 (18%) had white-centered hemorrhages (Figure 1 and 2), 23 (23%) had papilledema, 21 (21%) showed vessel changes while 2 (2%) had peripheral whitening of the retina (Table 1). A total of 74 (74%) patients survived and 26 (26%) died during their

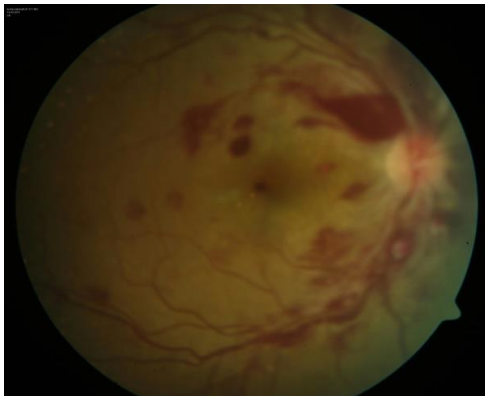
treatment. Out of the survivors 64 recovered fully while 10 had some neurological sequelae. Amongst those who died 20 had malarial retinopathy while 6 had normal fundus. Presence of 'any retinopathy' and either of papilledema, hemorrhages or vessel changes were associated with increased risk of death (Table 2). Multivariate logistic regression analysis showed that papilledema, hemorrhage, and vessel changes were significantly associated in predicting the mortality, while peripheral whitening was insignificant. The signs of retinopathy resolved completely after discharge in all the survivors during subsequent follow-up visits.

**Table 1:** No. (%) of patients with cerebral malaria

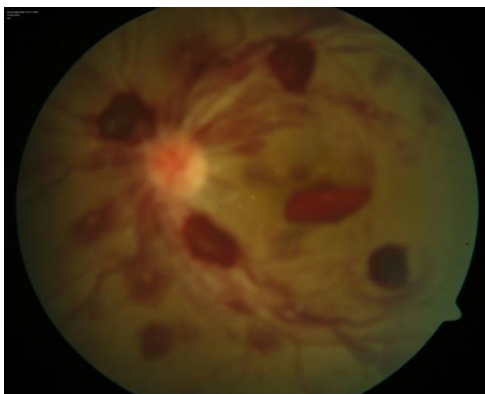
Retinal signs	No. (%) of patients with cerebral malaria
Normal fundi	52 (52)
Any retinopathy	48 (48)
Hemorrhages	18 (18)
Papilledema	23 (23)
Vessel changes	21 (21)
Peripheral whitening	2 (2)

**Table 2:** Values for Deaths/No. of case, P value and Odds' ratio (95% CI) of death in relation to Retinal signs

Retinal signs	Deaths/No. of cases (%)	P value	Odds' ratio (95% CI) of death
Any retinopathy	20/48 (41.7)	0.00006	5.5 (1.3, 23.4)
Papilledema	12/23 (52.2)	0.0011	5.5 (1.3, 23.2)
Hemorrhages	12/18 (66.7)	0.000014	9.7 (1.9, 48)
Vessel changes	13/21 (61.9)	0.000024	7.1 (1.6, 31.9)
Peripheral whitening	1/2 (50)	0.434	9.0 (0.3, 235.4)



**Fig 1:** Fundus photograph of one of the patients showing white centered hemorrhages



**Fig 2:** Fundus photograph of another patient showing multiple white centred hemorrhages and sub hyaloid hemorrhages

## Discussion

This study has shown that retinal changes in CM are significantly associated with poor outcome. It has also shown that retinal signs are present in almost half of the cases of pediatric CM, which is lower than that reported in literature (61-79%). The mortality rates associated with malarial retinopathy has been shown to be higher than those in previous studies. (Kochar A *et al*, Beare NA *et al*.)<sup>[5, 6]</sup>. The mortality in children with retinal hemorrhages in our study (66.7%) is much higher than previous studies (37.5%) although similar to a study by Singh J *et al*.<sup>[3]</sup>

Sample size and absence of a comparator group maybe the possible lacunae of our study. Presence of retinopathy, particularly retinal whitening in non-cerebral forms of severe malaria may prove to be a deterrent in finding a correlation between retinal findings and mortality in cerebral malaria cases in children<sup>6</sup>.

## Conclusion

Ocular examination by indirect and direct ophthalmoscopy in patients with CM is of immense importance. The presence and severity of retinal signs are significant predictors of prolonged coma and death. The findings of our study are consistent with the hypothesis that retinal changes in CM relate to cerebral pathophysiological processes<sup>7</sup>. Retinal features are an integral part of the clinical picture, and ophthalmic observations can contribute to continuing studies of pathophysiological processes and therapeutic interventions. It will be important to assess the extent to which general practitioners in malarial areas can identify some or all of the changes described.

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