

# OUTCOME OF CEREBRAL MALARIA IN CHILDREN ADMITTED IN PEDIATRIC WARD CIVIL HOSPITAL SUKKUR

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#### DOI: https://doi.org/10.5281/zenodo.15305248

Keywords Cerebral Malaria, Outcome, Children, Mortality, Neurological Deficits

Article History

Received on 13 March 2025 Accepted on 13 April 2025 Published on 29 April 2025

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## Abstract

*Objective*: To determine the outcome of cerebral malaria in children admitted in pediatric ward GMC Sukkur.

**Methods:** A cross-sectional study was conducted in the Department of Pediatric Medicine at GMC Sukkur from 1<sup>st</sup> April to 30<sup>th</sup> September 2024, using nonprobability consecutive sampling. Children aged 2 to 12 years, diagnosed with cerebral malaria, were included, while those with impaired consciousness due to other causes, sickle-cell disease, glucose-6-phosphate dehydrogenase deficiency, trauma, or operated hydrocephalus were excluded. Detailed history, physical examination, and neurological assessments, including Blantyre's coma scale, were performed. Blood samples for tests such as random blood sugar, complete blood count, blood film for malaria parasites, and serum electrolytes were collected. Cerebrospinal fluid was also analyzed. Blood films were monitored daily for parasite species. All patients received intravenous artesunate as per WHO guidelines and supportive therapies. Outcomes were assessed based on length of hospital stay, neurological deficits at discharge, and mortality. Data recorded in a pre-designed proforma.

**Results:** A total of 115 children aged 2 to 12 years with cerebral malaria were admitted, with 61 males (53%) and 54 females (47%). The mean age was 6.07  $\pm$  2.73 years, and the average weight and height were 20.20  $\pm$  5.93 kg and 109.98 ± 15.39 cm, respectively. The mortality rate was 32.2%, and 41.7% of survivors (48 patients) were discharged with neurological deficits. The mean length of hospital stay was  $5.17 \pm 1.52$  days. Gender and place of residence showed no significant association (p = 0.750), but a significant link was found between gender and mortality (p = 0.032), with more male deaths. Similarly, 33 male and 15 female patients discharged with neurological deficits (p = 0.004), indicating males were more likely to experience long-term complications. Rural residency was significantly associated with neurological deficits (p = 0.014), with rural children at higher risk, possibly due to healthcare access or delays. The length of stay was slightly higher for males, but not significantly (p = 0.305). There was no significant difference in family monthly income between males and females (p =0.246). The findings highlight gender and rural-urban disparities in health outcomes.

Conclusion: This study supports existing literature on the increased vulnerability



### ISSN: (e) 3007-1607 (p) 3007-1593

of male children to mortality and neurological sequelae in cerebral malaria. It also highlights rural-urban disparities in health outcomes, emphasizing the need for improved healthcare access in rural areas. While parental education and family income showed no significant association, social and healthcare factors remain crucial in addressing pediatric malaria outcomes.

## INTRODUCTION

Malaria is one of the most serious infectious diseases affecting children worldwide, with an especially high impact in sub-Saharan Africa and Asia. Malaria is a major public health problem and is still a cause of considerable morbidity and mortality to vulnerable populations, the most affected being children (1). As one of the most serious complications in their disease, cerebral malaria (CM) or neurological impairment in malaria, has long-term sequelae and can even be fatal. This condition, although preventable and treatable, poses significant challenges to healthcare systems, particularly in countries with high malaria burdens. Pakistan is one of those nations among such nations which have been severely affected by Malaria and particularly in its rural areas (2).

Pakistan has endemic malaria, and most affected cases are in rural and semi-urban areas. Pakistan is a country with a great malaria burden in the South Asia region, as per the World Health Organization (WHO). All these factors play a role in increasing the malaria burden in Pakistan, including climatic conditions, poor healthcare facilities in the rural areas, and the presence of Plasmodium falciparum, the most virulent type of malaria parasite (3). According to WHO, in 2020, there were approximately 2.7 million reported cases of malaria in Pakistan, with about 2,000 deaths due to the disease. Malaria prevalence has declined over the years through extensive efforts (distribution of insecticide-treated nets and indoor residual spraying), but the disease continues to cause annual deaths, which are mainly children under the age of 5 (4).

In particular, their immature immune systems make under-12-year-old children, especially those between the two and five-year age group, highly vulnerable to the most severe form of malaria, including cerebral malaria (5). In Pakistan, children are mostly infected with the disease during monsoon when there is stagnant water providing strategic Anopheles mosquitoes, the vectors to transmit the malaria parasite. Not only does the direct impact of malaria exert a great burden on the health system, in particular with high demand for medical resources, hospital admissions, and treatment, making other health problem-solving in the population very difficult (6).

Cerebral malaria in children is particularly worrying as it carries substantial neurological impairment, long-term disabilities, and high mortality rates. Malaria cerebral is due to the brain contamination of the parasite of malaria parasite that causes encephalopathy and neurological manifestations like altered consciousness, seizures, and coma (7). Cerebral malaria accounts for a fairly small fraction of all cases of malaria, but its consequences on pediatric health are enormous. Cerebral malaria affects 10- 15% of the malaria cases in Pakistan, especially in rural areas where the facilities for early diagnosis and treatment are limited. Recent treatment options, including intravenous artesunate have been developed into treatment options for cerebral malaria in children, but the mortality rate has been reported to be high in between 15%- 30%, in different parts of Ghana (8).

In areas with very limited access to the healthcare infrastructure, there is a major concern for the mortality rate of cerebral malaria in children. Cerebral malaria in a child is a serious illness where he is at risk of rapid deterioration and death if he does not get early and effective treatment (5). Mortality from cerebral malaria in Pakistan is high due to a lack of early diagnosis, insufficient access to health care, and delay in seeking treatment. Administering antimalarial drugs, including intravenous artesunate or quinine, which are essential in treating severe malaria, delays can result in irreversible brain damage and, many times, death (9).

Additionally, there are long-term neurological defects in cerebral malaria survivors. Their deficits may range from mild cognitive impairment to gross

motor dysfunction, epilepsy, and persistent vegetative states. Studies on the issue in Pakistan and other malaria-endemic areas have shown that a large majority of those who survive cerebral malaria go on to develop some neurological sequelae (10). Up to 30-40% of children who survive cerebral malaria in low-resource settings will have long-term disabilities, including the development of impairments in cognitive, motor, and speech functions. All of these constitute a considerable burden on the affected children and their families, but also on the healthcare system, as lifelong care and rehabilitation are usually required (11).

Several factors contribute to result in cerebral malaria in children. The early diagnosis and treatment are imperative to prevent severe complications and to decrease the mortality rates. Unfortunately, children from many areas of Pakistan are brought to the healthcare facilities when the disease is far advanced, with severe neurological symptoms. The higher mortality and morbidity with cerebral malaria in rural areas are largely due to delays in seeking medical care due to socioeconomic factors, lack of awareness, as well as geographical barriers (12).

#### Methodology:

A cross-sectional study was carried out in the Department of Pediatric Medicine, GMC Sukkur, from 1<sup>st</sup> April 2024 to 30<sup>th</sup> September 2024, and a non-probability consecutive sampling technique was applied for the selection of participants. The study evaluated the outcomes of cerebral malaria in children aged 2 to 12 years, admitted to the Department of Pediatric Medicine,GMC Sukkur, following approval from the CPSP and the ethical review committee. Children meeting the inclusion criteria (age 2-12 years, any gender, with cerebral malaria) were included, while those with impaired



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consciousness due to causes other than cerebral sickle-cell disease, glucose-6-phosphate malaria, dehydrogenase deficiency, trauma, or operated hydrocephalus were excluded to avoid bias. A detailed history and general physical examination were conducted, recording patient ID, sex, weight, and length (measured by stadiometer). Neurological assessment, including fundoscopy and Blantyre's coma scale, was performed. Blood samples were taken for tests including random blood sugar, complete blood count, blood film for malaria parasites, serum electrolytes, urea, and creatinine. Cerebrospinal fluid (CSF) was collected for analysis. Blood films were monitored daily for parasite species and density. Additional tests, like blood cultures and urinalysis, were carried out as needed. All patients received intravenous artesunate treatment in line with WHO guidelines, along with supportive therapies. Outcomes were assessed based on length of hospital stay, neurological deficits at discharge, and mortality, with all data recorded in a predesigned proforma.

## RESULTS

There were 115 children aged 2 to 12 years admitted with complaints of cerebral malaria admitted in the department. Out of them, 61 were males and 54 were females, which constitutes about 53% and 47% respectively. The mean age of the children was 6.07  $\pm$  2.73 years, while the mean weight and height were found to be 20.20  $\pm$  5.93 kg and 109.98  $\pm$  15.39 cm (Table-1).

In our study, the outcomes of cerebral malaria were evaluated based on mortality, length of hospital stay (LOS), and neurological deficits at discharge. The mortality rate was found to be 32.2%, while 41.7% of the survivors (48 patients) were discharged with neurological deficits. Additionally, the mean length of hospital stay was  $5.17 \pm 1.52$  days (Table-1).

Table-1: Demographic, Anthropometric, and Clinical Outcome Profile of (	Children with AFP
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Demographic information	N (%) Total=115		
Gender			
Male	61 (53%)		
Female	54 (47%)		
Anthropometric measurements (Mean ± SD)			
Age	6.07 ± 2.73 years		
Weight	20.20 ± 5.93 kg		



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Height	109.98 ± 15.39 cm
Outcomes [n(%)]	
Mortality rate	32.2%
Neurological deficits at discharge	48 patients (41.7%)
Mean length of hospital stay (LOS) (in days)	5.17 ± 1.52 days

(n = 115)

An analysis was conducted to explore the relationship between gender and place of residence among the 115 pediatric patients included in the study. The results showed no statistically significant association between these two variables (p = 0.750), indicating that the distribution of male and female patients was similar across urban and rural areas. Specifically, 11 males and 11 females were from urban settings, while 50 males and 43 females came from rural areas (Table-2).

In contrast, a significant association was found between gender and mortality. Among the patients who died during hospitalization due to cerebral malaria, 25 were male and 12 were female, indicating a higher number of deaths among males. The difference was statistically significant (p = 0.032), suggesting that male children may be at greater risk of dying from cerebral malaria compared to females (Table-2).

A similar trend was observed about neurological deficits at discharge, where gender again showed a significant association with outcomes. Of the 48 patients discharged with neurological deficits, 33 were male and 15 were female. This difference was also statistically significant (p = 0.004), indicating that male patients were more likely to suffer from long-term neurological complications following cerebral malaria. (Table-2).

Similarly, the association between parental level of education and gender showed no significant relationship (p = 0.808). The distribution of male and female patients across various levels of parental education was relatively balanced (Table-2).

Variable	Male (n = 61)	<b>Female</b> (n = 54)	P-Value
Place of Residence			
Urban	11 (18.0%)	11 (20.4%)	0.750
Rural	50 (82.0%)	43 (79.6%)	
Mortality		(1)	
Yes	25 (41.0%)	12 (22.2%)	0.032*
No	36 (59.0%)	42 (77.8%)	
Neurological Deficit			
Yes	33 (54.1%)	15 (27.8%)	0.004*
No	28 (45.9%)	39 (72.2%)	

Table-2: Association Between Gender and Clinical Outcomes in Children with AFP (N = 115)

A more nuanced association was found when looking at the place of residence and neurological deficits at discharge. The analysis indicated that the place of residence has a significant impact on the likelihood of developing neurological deficits. For patients in rural areas, the pearson chi-square test showed a significant association (p = 0.014), with 29 males and 14 females in rural areas developing neurological deficits. On the other hand, for patients in urban areas, there was no significant association (p = 0.127). This suggests that children from rural areas are at a higher risk of neurological complications compared to those from urban areas, which could be related to differences in access to healthcare, delays in seeking treatment, or other socio-economic factors. Overall, the total analysis of all patients showed a significant relationship between place of residence and neurological deficits (p = 0.004), emphasizing the rural-urban disparities in health outcomes.

The mean length of hospital stay was found to be slightly higher for male patients  $(5.31 \pm 1.57 \text{ days})$ compared to female patients  $(5.02 \pm 1.47 \text{ days})$ . However, the t-test for equality of means revealed no significant difference between the two groups (p = 0.305), indicating that gender did not significantly influence the duration of hospitalization in this study.

The mean family monthly income was  $81,763.35 \pm 30,619.01$  PKR. The statistical analysis demonstrates that there is no significant difference in the family's monthly income between males and females (p = 0.246).

## DISCUSSION

The purpose of our study was to determine the outcome of cerebral malaria in children aged 2-12 years and the effect of gender, place of residence, death, neurological deficit, and length of hospital stay. The results reveal higher mortality (32.2%) and gender differences, with increased likelihood of mortality and neurological deficits at discharge for the male children. This concurs with several studies showing that male children are particularly vulnerable to severe outcomes in cerebral malaria (5). As an example, Mseza B et al. (2024) observed that male sex was associated with increased risks of mortality in pediatric cerebral malaria cases (12); also, we found that male children had statistically higher death rates (p = 0.032). Oluwayemi IO et al (2013) additionally reported that male children are more predisposed to develop severe neurological sequelae (13), as we observed that of the 48 children discharged with neurological deficits, 33 were male (p = 0.004).

Therefore, biological factors such as sex differences in immune response may have contributed to gender differences in mortality and neurological outcomes. Males may have a weaker immune response to Plasmodium falciparum infection and thus be susceptible to a more severe form of cerebral malaria (14). In addition to this, there may also be differences in healthcare-seeking behavior, access to healthcare, or even socioeconomic factors due to gender as well.

Finally, in terms of place of residence, our study observed a significant association between rural residency and neurological deficits (p = 0.004), as rural children were found to be at higher risk. This is consistent with other research, which has shown rural-urban disparities in health outcomes in lowresource settings such as urbanization in South Africa (15). Lack of access to healthcare professionals, poorer healthcare infrastructure, and delays in



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diagnoses, treatment may contribute to the poorer outcomes seen in rural children. Moreover, the significance of timely healthcare access in reducing the risk of long-term neurological complications is highlighted by the fact that we did not observe a similar association in urban areas (p = 0.127).

We also study the association between parental education and gender effects, and do not find a statistically significant one (p = 0.808). That is in contrast to some studies that have found a higher level of parental education tends to be related to better health outcomes for children, even regarding the case of malaria (16). However, a non-significant finding in our study may be explained by socio socioeconomic context of the region studied, where other factors such as healthcare infrastructure and early treatment access might be more important determinants of outcomes than the level of parenthood education.

We compared the mean length of hospital stay between genders, in which male patients, on average, stayed slightly longer  $(5.31 \pm 1.57)$  in comparison to female patients  $(5.02 \pm 1.47)$ ; however, this difference was not statistically significant (p = 0.305). These results support findings of other studies, who have observed that differences in length of hospital stay were minor (or did not reach statistical significance when there were differences) (17). Although variation in hospital stay between males and females could be changes in the severity of disease, comorbidities, or the course of treatment, it does not seem to be a major determinant of outcome in our cohort.

On the other hand, mean family monthly income was found to be  $81,763.35 \pm 30,619.01$  PKR, had no significant differences among male and female patients (p = 0.246). The evidence is consistent with the finding of a study by McDonald CR et al. (2022) that income differentials did not necessarily relate to differences in sex in clinical outcomes resulting from malaria (18). Nevertheless, socioeconomic status in general has been demonstrated to be a determinant of health care access and outcomes among the treatment for malaria in pediatric patients, and lower-income families tend to encounter delays in seeking care (19).

### Conclusion

The results from our study strengthen many of the main aspects of the current pediatric cerebral malaria literature, such as the greater susceptibility of both mortality and neurological sequelae in male children. Furthermore, it reveals that the rural-urban disparities in health outcomes, such as cerebral malaria, underscore the need to enhance access to healthcare in rural regions to minimize the burden of cerebral malaria. Parental education and family income did not relate to malaria in our study, and there is a need to consider multiple social and healthcare variables in addressing the broader influences on the health outcomes of pediatric malaria patients.

**Conflict of interest:** - The authors declare no conflict of interest.

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