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Cerebral Malaria in Adults: A Retrospective Descriptive Analysis of 80 Cases in a Tertiary Hospital in The Gambia, 2020–2023

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Keywords: adolescent | adult | cerebral malaria | critical care | in hospital mortality

ABSTRACT

Background and Aim: Cerebral malaria in Gambian children has been studied but there is limited information on CM in adults. The study assesses the clinical features and outcome of CM in adult patients admitted at the Edward Francis Small Teaching Hospital.

Method: This was a retrospective review of all adult patients with malaria admitted to the internal medicine department from October 18, 2020 to February 2, 2022.

Results: A total number of 319 adults were admitted with malaria. Eighty (25%) patients met the criteria for CM. The median age of the CM patients was 19 years. CM patients were younger ($p < 0.001$), more likely to be of the adolescent age group ($p < 0.001$), more likely to be referred from a lower-level health facility ($p < 0.001$), and more likely to be admitted in intensive care $p < 0.001$) as compared to NSCM or UM patients. The total in-hospital mortality of CM patients was 23.8%. Ten (52.6%) out of the 19 patients died within the first 24 h of admission. In multivariate analysis, CM patients with acute kidney injury at presentation was an independent predictor of mortality in this study.

Conclusion: CM seems to affect the adolescent age group more than the older adults in The Gambia. The clinicians should be able to identify these high-risk patient group and institute prompt critical care interventions and/or treatment. The findings in this study also identify the need to expand access of critical care interventions and hemodialysis to help improve the prognosis of adult CM patients in The Gambia.

Abbreviations: BF, thick blood film; CM, cerebral malaria; EFSTH, Edward Francis small teaching Hospital; GCS, Glasgow coma score; NCSM, non-cerebral severe malaria; RDT, rapid diagnostic test; UM, uncomplicated malaria; WHO, World health organisation.

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1 | Introduction

Malaria continues to be a major cause of illness and death in the world. Globally in 2021, there were approximately 619,000 deaths and 247 million cases [1]. In 2022, estimated malaria deaths declined to 608,000 [2]. In sub-Saharan Africa, *Plasmodium falciparum* malaria continues to be a major cause of disease and death and in The Gambia young adults are significantly affected [3–5]. In Gabon, children aged 0–5 years were the most affected by severe malaria and adolescents over 15 years of age were the least affected (Gabon) [6]. In Nigeria, the prevalence of malaria in the adolescent age group was 71% [7, 8].

The clinical features of severe *P. falciparum* infection varies, with cerebral malaria (CM) resulting in high mortality [9]. CM, the most frequent severe neurological complication is characterized by impaired consciousness and coma is the most severe manifestation. CM survivors can remain with life-long complications which can affect their quality of life [10]. The presentation of CM in children differs from adults. The mortality in children with CM is reportedly lower than in adults and children with CM also have higher proportion of convulsions and post-CM neurological deficits [9].

In The Gambia, CM in children has been extensively studied but there is relatively little knowledge of CM in adults. The aim of this study is to describe and compare the clinical features and in-hospital mortality of CM, non-cerebral severe malaria (NCSM) and uncomplicated malaria (UM) in adult patients admitted at the internal medicine department of the only tertiary Hospital in The Gambia. The results from this study will help the prompt identification of CM patients who are more likely to benefit from preventive measures and treatment and also identify those who are at risk of dying.

2 | Methods

2.1 | Study Hospital and Design

This retrospective descriptive hospital-based study reviewed records from October 18, 2020, to February 2, 2022, at the Edward Francis small teaching hospital (EFSTH) in Banjul, The Gambia. EFSTH has a 627-bed capacity and receives patients from across the country. It is a tertiary hospital and provides specialized clinical services in the majority of the medical field in addition to having a critical care unit and an accident and emergency unit. Additionally, it serves as a training and research hub for resident physicians, house and medical officers, and medical students.

2.2 | Study Population

In this study, adult patients with CM hospitalized in EFSTH, Banjul, The Gambia were evaluated. The World Health Organization (WHO) defined CM as patients having a Glasgow coma score (GCS) of less than 11 with Plasmodium falciparum present in thick blood film (BF) and/or positive rapid diagnostic test (RDT) [1]. Older adult was defined as age above 24 years and 15 to 24 years as youth (including adolescent 15–19 years) [11]. The study included all patients who were at least 15 years old with confirmed malaria by RDT and/or BF who were hospitalized to the EFSTH internal medicine department. Data from the patient's records, such as the referral facility, demographic information, symptoms, signs, laboratory tests, treatment, and clinical outcome (in-hospital mortality) were extracted using a standardized questionnaire. Patients with underlying severe chronic heart [2], kidney [1], or liver disorders [3], hyperglycaemic emergencies [3] as well as those with acquired immunodeficiency syndrome/human immunodeficiency virus [2], or cerebrovascular disease [11], which may affect the evolution of malaria, as well as one with incomplete data were not included in the analysis.

2.3 | Investigations

RDT test (paraHIT -f Ver1.0, Arkray, Gujarat, India) using capillary blood and/or BF stained with Giemsa, and viewed under x100 oil immersion microscopy was used to diagnose malaria. A HemoCue hemoglobinometer (HemoCue 301, Angelhom, Sweden) was used to estimate hemoglobin concentrations. All patients had their blood glucose levels checked at the time of presentation using the Accu-Chek active bedside equipment (Roche Diagnostics, Mannheim, Germany).

2.4 | Management

Severe malaria patients or non-severe malaria cases who could not take oral medication were put on parenteral artesunate 2.4 mg/kg at 0, 12, and 24 h, and then once every 24 h until the patient could take oral antimalarial therapy (artemether-lumefantrine) as instructed by the WHO [1]. Intravenous medication was changed to a 3-day oral artemether-lumefantrine combination treatment when the patients were able to take oral medicines. In accordance with WHO guidelines [1], patients also received resuscitation and supportive care, which included intravenous diazepam for convulsion termination, 50% glucose for those presenting with hypoglycemia, blood transfusions for patients with severe anemia (hemoglobin < 7 g/dL), and hemodialysis for acute kidney injury patients.

2.5 | Data Analysis

A Microsoft Excel sheet was used for data entry. The data sheet was imported into STATA/SE 14.2 (Statacorp, TX, USA) and analyzed. For discrete variables, a simple proportion was calculated. ANOVA and Mann-Whitney U-test were used for continuous data with skew distribution. Chi-squared test were used for discrete variables. A multivariate logistic regression model was used to identify prognostic factors for CM patients. P value less than 0.05 was considered statistically significant.

3 | Results

3.1 | Demographic2 Features of the Cerebral Malaria Patients

There were 319 adults admitted with malaria into the internal medicine department during the period reviewed. Of these cases, 80 (25%) patients were diagnosed with CM.

TABLE 1 | Clinical characteristics and in hospital mortality of patients with cerebral malaria in EFSTH.

Variable	Cerebral malaria: $n = 80$(%)	Non-cerebral severe malaria: $n = 71$ (%)	Uncomplicated malaria n = 169 (%)	p value
Age: mean (y)	22.3	27.1	31	< 0.001
Age groups (y)				
15–19	44 (55)	20 (28.2)	51 (30.2)	< 0.001
20–24	22 (27.5)	24 (33)	28 (16.6)	
> 24 (Adult)	14 (17.5)	27 (38)	90 (53.3)	
Sex (M:F)	56 (70):24 (30)	41(57.8): 30 (42.3)	102 (60.4):67 (39.6)	0.23
Type of referral Self-referral: Health facility	11 (13.8):69(86.3)	19 (26.8): 52(73.2)	82 (48.5):87(51.5)	< 0.001
Symptoms at presentation				
Fever	76 (95)	64 (90.1)	158 (93.5)	0.48
Headache	72 (90)	60 (84.5)	153 (90.5)	0.38
Vomiting	59 (73.8)	54 (76)	138 (81.7)	0.32
Malaise	21 (26.3)	21 (29.6)	91 (24.3)	0.69
Convulsion	24 (30)	3 (4.2)	16 (9.5)	< 0.001
Duration of admission (hrs): Median (range)	96 (6–648)	120 (4–562)	96 (4–864)	0.003
Intensive care unit admissions	28 (35)	5 (7)	9 (5.3)	< 0.001
In hospital mortality	19 (23.8)	8 (11.3)	4 (2.4)	< 0.001

The total severe malaria cases in this study was 169 and 80 (47.3%) of them had CM based on the criteria defined by WHO. The median age of the CM patients was 19 years, range (15–72) and most of them were within the youth age group 66 (82.5%) with 44 (55%) within the 15–19 age group (Table 1). The majority of the patients with CM were also male 56 (70%). Sixty-nine of the CM patients (86.3%) were referred from lower-level health facilities. The most common symptoms of the CM patients at presentation were fever 76 (95%) and headache 72 (90%) and the most common signs at presentation were pallor 31 (38.8%) and jaundice30 (37.5%). The median duration of admission was 96 h (range, 6–648 h) (Table 1).

3.2 | Cerebral Malaria With Associated Features

CM patients were younger ($p < 0.001$), more likely to be referred from a lower level health facility ($p < 0.001$) and more likely to present with convulsion ($p < 0.001$) as compared to patients with NCSM or UM. CM patients were also more likely to be within the adolescent age group ($p < 0.001$) and more likely to be admitted in intensive care unit ($p < 0.001$) as compared to the NCSM OR UM patients (Table 1). Proportion of CM patients also decreased with age ($p < 0.001$ (Table 1).

3.3 | In Hospital Mortality

Overall, 19 (23.8%) out of the 80 patients with cerebral malaria died during admission (Table 1). Ten (52.6%) out of the 19 patients died within the first 24 h of admission. It was more likely for CM patients to die as compared to those without CM ($p < 0.001$) (Table 1). Multivariate analysis showed that CM patient with acute kidney injury at presentation was an independent predictor of mortality in this study (OR = 22.9, 95% CI2.3–224.5: p:0.007) (Table 2).

4 | Discussion

This study describes the clinical features and outcome of CM in adults admitted in EFSTH, The Gambia. CM was very common among the adult cases with *p. Falciparum* malaria admitted during the study period (25% of all cases). In an Indian study, 17.5% of all malaria cases had CM [12] and 16.5% in Sudan [13]. This was different from a study done in Malawi where no cases of CM were diagnosed in adults with malaria [14]. This study also found 47.3% of the severe malaria cases having CM. This was 54% in an Asian study [15] and 69% of severe malaria cases in Senegal [16]. These findings suggest that CM is a significant clinical feature of severe malaria among adults and thus requires urgent attention by clinicians. It was also more likely for patients with CM to be referred from a lower-level health facility. As already known, referred patients are more likely to develop severe malaria due to delay in diagnosis and late effective treatment [17], especially among patients who self-treat themselves [18]. As EFSTH is the only tertiary hospital in The Gambia, this confirms the fact that the majority of critically ill malaria cases are referred to this hospital and the milder or uncomplicated malaria cases are managed in the lower-level health facilities.

TABLE 2 | The characteristics associated with in hospital mortality in adult patients with cerebral malaria.

Variable	Univariate (unaOR)	95% CI	*P* value	Multivariate (aOR)	95% CI	*p* value
Age: Adolescent (15–19 y)	1.17	0.29–4.7	0.822			
Female sex	3.73	1.26–10.9	0.017	1.3	0.212–8.23	0.77
Patients with						
Jaundice	1.71	0.60–4.8	0.312			
Severe anemia	1.24	0.29–5.2	0.768			
Convulsions	0.78	0.25–2.5	0.689			
Acute kidney injury	24.9	2.7–229.6	0.005	22.9	2.3–224.5	0.007

The median age of the patients with CM was 19 years and most of the patients were within the youth age group. Amongst the CM patients within the youth age group, majority were adolescent. Patients with CM were also younger and more likely to be adolescent. This confirms the fact that majority of the patients admitted in the internal medicine department with CM were adolescent. These findings are different from that found in Gabon where children aged 0–5 years were the most affected by severe malaria and adolescents over 15 years of age were the least affected [6]. The reason for having more adolescent having CM could be due to several factors: first, the declining of anti-malarial immunity following reduced exposure to parasites [19, 20]. Second, the successful implementation of control interventions in under-five children and pregnant women could have also contributed to the shift in the burden of malaria in this age group [21]. Apart from the declining malaria immunity and the lack of targeted control interventions in the youths and adolescent other factors of CM in this age group remain unclear and need further investigation. Further analysis in this study also suggested a decrease in CM as age increases. As already known, in countries where conditions of long-term exposure to malaria exist, adults develop antiparasite immunity more quickly as compared to children and younger adults [22]. In Kenya, prevalence of malaria steadily decreased to very low levels from the age of 30 years to older ages, suggesting a continued acquisition of immunity to infection throughout adulthood [23]. This possibly contributes to the decrease in the number of CM in older adults in The Gambia.

The majority of the patients with CM were also male with a male-to-female ratio of 2.3:1. This finding is similar to other studies [24]. The most common symptom at presentation was fever which is a characteristic feature of *p. falciparum malaria* [5]. In contrast, a significant proportion of patients may be afebrile at the time of presentation due to self-medication with antimalarial/antipyretic medication before presentation [18, 24]. As majority of our CM patients are referred from lower-level health facilities, clinicians in the tertiary hospitals should also be aware that antimalarial/antipyretic medication can similarly be given at these facilities and thus patients with CM from these facilities may also be afebrile at the time of presentation. It was more likely for patients with CM to present with convulsion in this study. Convulsion at the time of presentation was documented in 30% of the CM patients which is similar to that found in India [9]. Studies have also found a decrease in the incidence of convulsion with increasing age [25] and convulsions were higher in children with CM as compared to adults with CM [24]. Even though convulsion is a more common symptom in children with CM, a significant proportion of adults may still present with it. These findings suggest that CM should be considered as a differential diagnosis in youths presenting with convulsion.

The total in-hospital mortality of CM patients in our study was 23.8%. Mortality of CM varies from 8%–33% (8% in Zambia, 13.9% in Thailand, 32.7% in Bangladesh, and 23%–33% in India) [12]. Majority (52.6%) of the CM patients died within the first 24 h of admission. There may be several factors responsible for this (1) delay in referring CM patients from the lower level facilities (2) delay in the presentation of these patients to the lower level facilities due to poor transportation or the visiting of herbalist or pharmacies first and (3) Inadequate intensive care capacity in the tertiary facility which is important in the management of these patients. The CM patients were also more likely to die if they were female patients or had acute kidney injury at presentation. A study in India showed that male CM patients and those with acute kidney failure were more likely to die [12]. CM mortality also increases when associated with acute kidney injury and metabolic acidosis and is also dependent on the availability of intensive care facilities [26]. In this study, patients with CM are more likely to be admitted in the intensive care unit as compared to non-CM patients. However, in EFSTH there are limited intensive care beds and equipments for monitoring [27] and limited access to dialysis which all could have an effect on the prognosis of CM patients [4]. There is therefore need to expand access of critical care interventions and hemodialysis in EFSTH to help improve the prognosis of CM patients in The Gambia.

There are limitations in this study: (1) it is a retrospective study from a single center, which may not be generalizable; and (2) severe malaria features, like hyperparasitaemia and acidosis, could not be investigated because of the limited access to laboratory studies. Nonetheless, the study offers insight into the clinical characteristics and in-hospital mortality of adults with CM in The Gambia.

5 | Conclusion

CM seems to disproportionately affect adolescent amongst the adults in The Gambia and prognosis is very poor. There is a

need to identify these patients urgently and institute prompt critical care interventions and/or treatment. The findings in this study also identify the need to expand the access of critical care interventions and hemodialysis to help improve the prognosis of adult CM patients in The Gambia.

Author Contributions

Sheikh Omar Bittaye: conceptualization, methodology, writing–original draft, writing–review & editing, formal analysis, project administration, data curation, supervision, resources. **Abubacarr Jagne:** writing–original draft, writing–review & editing, methodology, conceptualization, project administration, supervision, resources. **Lamin E S Jaiteh:** writing–original draft, writing–review & editing, methodology. **Alfred Amambua-Ngwa:** conceptualization, writing–original draft, writing–review & editing, methodology, funding acquisition. **Abdul Karim Sesay:** conceptualization, writing–original draft, writing–review & editing, methodology. **Williams Estrada Ramirez:** writing–original draft, writing–review & editing. **Asmell Ramos:** writing–original draft, writing–review & editing. **Emmanuel Effa:** writing–original draft, writing–review & editing. **Ousman Nyan:** writing–original draft, writing–review & editing. **Ramou Njie:** writing–original draft, writing–review & editing, supervision.

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Ethics Statement

This study was approved by the Institutional Review Board of Edward Francis small teaching hospital (EFSTH-REC-017).

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request. The dataset for this publication is available on reasonable request from the corresponding author.

Transparency Statement

The lead author Sheikh Omar Bittaye affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

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