Epilepsy after malaria affecting the nervous system — is the burden higher than we thought?

Shaida Nishat[1], Rasesh Joshi[2], Suzanna Mwanza[3], Janet Chilima[3], Joseph Kasolo[3], Clement Lupumaula[3], Angela Masempela[3], Thelma Musakanya[3], Tina Mwale[3], Violet Nambeye[3], Rosemary Nyirongo[3], Ruth A. Tembo[3], Bo Zhang, PhD[4], Maitreyi Mazumdar[2,5], Alexander Rotenberg[2,6], Gretchen L. Birbeck[7,8], Archana A. Patel[2,9]

[1]Massachusetts Institute of Technology, [2]Boston Children's Hospital, [3]Chipata Central Hospital, [4]Harvard Medical School, [5]Harvard T.H. Chan School of Public Health, [6]Beth Israel Deaconess Medical Center, [7]University Teaching Hospitals- Children's Hospital, [8]University of Rochester, [9]University of Zambia School of Medicine

INTRODUCTION

- Cerebral malaria (CM) is considered to be the most severe neurological presentation of *Plasmodium falciparum* infection, with a 15-20% mortality rate and up to 30% risk of neurologic sequelae in survivors, with highest risk for those > 5y (Birbeck, etc)
- In most research studies, **CM is strictly defined as coma and malaria parasitemia**, in absence other coma etiology (WHO)
- More recent data suggests that the **neurological impact of malaria may be broader than even previously known**, with risk of long-term neurobehavioral sequelae even increased in children who present with severe malaria (Bangirana et al)
- Thus, studying the risk of sequelae in children presenting with acute neurological symptoms and severe malaria, even if not meeting criteria for CM, is essential
- Inclusion of this broader definition of CM suggests the number of children affected long-term by severe malaria with neurologic involvement **could be much larger than currently reported**

OBJECTIVES

- Compare baseline characteristics of children enrolled with CM (n=50) compared to CNS malaria (n=96)
- Compare hospitalization characteristics between 2 groups
- Compare 1-month outcomes between 2 groups

METHODS

Inclusion and Exclusion Criteria

- Children aged 6 months to 11 years, enrolled between December 2021- December 2023
- No prior diagnosis of epilepsy
- Meets criteria for
  - 'Cerebral Malaria'- impaired consciousness with Blantyre Coma Score (BCS) of ≤ 2 in children under 2y, or a Glasgow Coma Score (GCS) ≤ 10 in children ≥ 2y, w/o any other explanation for coma
  - 'CNS Malaria', defined as complicated seizures (either prolonged ≥15 minutes, focal or multiple) or impaired consciousness w/o frank coma (i.e., BCS 3-4, GCS 11-14)

Study Procedures

Initial:

- Enrollment and consent
- Baseline characteristics
- Standard 30-minute electroencephalogram
- Hospital course data is recorded upon discharge

Follow-Up:

- Standard 30-minute awake and sleep EEG
- Clinical neurodevelopmental screening is performed (general follow-up information, WHO Epilepsy screen, neuro assessment, executive functioning assessment)

RESULTS

Table 1. Baseline Characteristics	P-value[1]
Sex	0.288
Age (months)	0.016
Ten Questions Development Screen	0.232
HIV Status	0.630

Table 2. Presentation Data and Hospital Course	P-value[1]
Length of illness prior to admission	0.787
Seizures at admission	0.005
HRP2 levels (ng/mL)	0.649
Coma Score (GCS)	<.001
Hypoglycemia	0.052
Maximum temperature during admission (C)	0.084
Length of stay in hospital (days)	0.325
Mortality	0.446

Table 3. 1-Month Follow-Up Outcomes	P-value[1]
Caregiver perception	0.263
Sleep quality	0.170
Epilepsy	N/A
MDAT Gross Motor	0.382
MDAT Fine Motor	0.159
MDAT Language Score	0.161
MDAT Social Score	0.079
BRIEF Score	0.882
BRIEF Score 6+	0.927

Table 4. Visual EEG	Initial[1]	1-Mo[1]
Slowing, n (%)	<.001	0.801
Epileptiform activity, n (%)	0.052	0.213
State change, n (%)	0.031	0.309
Reactivity, n (%)	<.001	N/A
Sleep spindles, n (%)	<.001	0.178

Table 5. EEG Power and Entropy	Initial[1]	1-Mo[1]
Delta power	<0.001	0.4634
Theta power	<0.001	0.0058
Alpha power	<0.001	<0.001
Beta power	<0.001	0.081
Gamma power	<0.001	<0.001
Sample entropy	<0.001	0.0082

CONCLUSIONS

Cerebral malaria has largely been studied in populations that are endemic to outbreaks of this disease. The classification of CM in these studies often encompasses clinical features typical of CM, such as coma, while excluding features that are not as characteristic such as impaired consciousness w/o frank coma. Conducting tests of significance on various metrics of interest have shown that this distinction does not need to be made. On almost all metrics, analyses between CM and CNS malaria showed no significant difference in a one-month clinical follow-up.