Malaria-Related Acute Kidney Injury in Adolescents and Young Adults in a Tertiary Hospital in the Gambia

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ABSTRACT

Background: Malaria is still an important public health problem in The Gambia, particularly in the adolescent and young adults (AYA). This study therefore assesses the clinical characteristics and outcome of malaria related AKI in AYA in The Gambia.

Method: This is a cross sectional retrospective descriptive study that reviewed records of admitted malaria patients in the Department of Internal Medicine, EFSTH, from October 18th2020 to February 2nd, 2022. A specific designed form was used to extract patients' biodata, clinical features, referral facility, laboratory investigations, treatment, and outcome. STATA/SE 14.2 software was used for data analysis.

Results: The study included 163 malaria patients. Fifty patients (30.7%) had AKI. The mean age of patients with AKI was 26.5 years and majority were AYA 35 (70%). Most of the malaria patients with AKI were also male 31 (62%). The most common symptom in these patients was fever 47 (94%) and the most common sign was jaundice 26 (52%). Malaria patients with AKI had a lower haemoglobin level 9.7 (4.8-14) vs 11 (4.1-18.3), p value=0.001 compared to those without AKI. 14 (28%) AKI patients had haemodialysis. Male patients with AKI were more likely to have haemodialysis as compared to female patients 13 (92.9%):1 (7.2%) vs 18 (50%):18 (50%), p value=0.004. The total mortality amongst the patients with malaria-related AKI were 10 (20%). Patients with malaria related AKI were more likely to die as compared to malaria patients without AKI 10 (20%) vs 5(4.4%), p value=0.002.

Conclusion: This study has showed that malaria-related AKI is a significant problem in AYA in The Gambia and mortality is high. There is therefore a need for targeted interventions in this age group to help reduce morbidity and mortality related to malaria in The Gambia.

Keywords: Malaria, acute kidney injury, adolescent and young adults, Gambia

INTRODUCTION

Malaria is still an important cause of morbidity and mortality, globally (1) and in particular sub- Saharan Africa(2).However, recent findings has also shown a significant reduction of the burden of malaria worldwide(3). The World Health Organization's (WHO) African region, in 2022 had an estimated 233 million malaria cases(1).

There are four common species of plasmodium and plasmodium falciparum has the greatest morbidity and mortality(4). Complications related to p.falciparum in The Gambia include cerebral malaria, hypoglycaemia, anaemia and acute kidney injury (AKI)(5)(6).

Acute kidney injury is an important complication of malaria which can also result in chronic kidney disease and poor outcome (7). KDIGO (Kidney Disease Improving Kidney Outcome) has defined AKI as changes in kidney function, including serum creatinine (SCr) changes and urine output within 48 hours or 7 days(8). In a study done in a Rwandan district hospital, 16.3% of the adult malaria patients had AKI with 15% mortality and 30% referred for haemodialysis(9). Studies have also shown a high mortality rate of AKI patients in sub-Saharan Africa, 34% in children and 32% in adults with AKI. These mortality rates rose to 73% in children and 86% in adults when no dialysis was done(10).

Malaria related acute kidney disease has been a significant problem in children in The Gambia. In studies done in The Gambia 17 (0.6%) of the malaria patients had AKI and mortality was 9 (52.9%)(11).In a multi-centre study, severe malaria children with uraemia on admission were more likely to present with coma, jaundice and hypoglycaemia(12).There is limited study on malaria related acute kidney injury in AYA In The Gambia. The study therefore assesses the clinical characteristics and outcome of malaria-related AKI in AYA in The Gambia. This study will thus help to identify AYA with malaria who are at high risk of developing AKI and thus initiate prompt intervention to prevent mortality.

METHODS

Study place and design

This is a cross sectional retrospective descriptive study that reviewed patient's records from October 18, 2020, to February 2, 2022, at the Edward Francis Small teaching hospital (EFSTH) in Banjul, The Gambia. EFSTH is a tertiary hospital and has a 627-bed capacity. It receives patients from across the country and provides specialized clinical services. It also has a critical care unit and an accident and emergency unit. It also provides training for nurses, resident physicians, house and medical officers, and medical students.

Study population

In this study, all patients with malaria admitted into the Internal Medicine department, EFSTH were evaluated and included into the study. The World Health Organization (WHO) defined AKI as patients having creatinine level of 265 µmol/l with Plasmodium falciparum present in thick blood film (BF) and/ or positive rapid diagnostic test (RDT)(1). AYA was defined as age group 10-24 years.

A questionnaire was used to extract patient's biodata, clinical features, referral facility, laboratory investigations, treatment, and outcome.

Investigations

Using capillary blood, RDT test (paraHIT® -f Ver1.0, Arkray, Gujarat, India) and/or Thick Blood Film stained with Giemsa and viewed under x100 oil immersion microscopy was used to diagnose malaria. Haemoglobin was estimated using HemoCue hemoglobinometer (HemoCue 301, Angelhom, Sweden). Renal function test analysis was done using the automated clinical chemistry analyzer. HS600, Human Diagnostic. Germany

Management

Patients with malaria were treated with parenteral artesunate 2.4 mg/kg at 0 h, 12 h, and 24 h, and then once every 24hrs until the patient could take oral antimalarial therapy (artemether-lumefantrine) as recommended by the WHO (1). A three-day oral artemether-lumefantrine combination treatment was started once the patients were able to take oral medication(1). Additional supportive care in the form of diazepam for those presenting with convulsion, 50% glucose for patients with hypoglycemia, blood transfusions for those with severe anemia (hemoglobin < 7 g/dl) and hemodialysis for acute kidney injury patients with indication(1).

Data analysis

Data was entered into Microsoft excel spread sheet, imported and analyzed using STATA/SE software 14.2. Simple proportion was calculated for discrete variables and chi square test or Fisher's exact test to compare

groups. ANOVA and Mann-Whitney U-test were used for continuous data with skew distribution. Statistical significance was determined by p value ≤0.05).

RESULTS

Three hundred and nineteen patients were admitted during the study period but only 163 patients had kidney function test requested and done and were included in this study.

Table 1: Characteristics of malaria patients who had kidney function requested and done

Variable	Malaria patients with kidney function results: n=163 (51%)	Malaria patients without kidney function results: n=156 (49%)	P value
Age (mean, yrs)	27.2	28.9	0.303
Age groups (yrs)			
10-24 (AYA)	104 (55.9%)	82 (44.1%)	0.042
>24 (OA)	59 (44.4%)	74 (55.6%)	
S**ex (M:F)**	107(53.8):56(46.7)	92(46.2):64(53.3)	0.219
Type of referral			
Self vs Health Facility	44 (26.9):119 (73)	68 (43.6):88(56.4)	0.002
Symptoms at presentation			
Fever	153(93.9)	144 (92.3)	0.583
Headache	146 (89.6)	138 (88.5)	0.751
Vomiting	137 (84.1)	113 (72.4)	0.012
Malaise	43 (26.4)	39(25)	0.778
Convulsion	28 (17.2)	15 (9.6)	0.048
Signs			
Pallor	75 (46.0)	67 (42.9)	0.582
Jaundice	75 (46.0)	53 (33.9)	0.028
Glasgow coma score at presentation	14(3-15)	15 (4-15)	0.015
Duration of admission (hrs)	120 (24-864)	72(4-360)	<0.001
Outcome	15 (9.2)	16(10.3)	0.751

Clinical characteristics of malaria patients with acute kidney injury

The study included 163 malaria patients that had kidney function test requested and done. Number of patients who had AKI were 50 (30.7%). The mean age of patients with AKI was 26.5 years and majority were adolescent and young adults 35 (70%). Only 3 (6%) of the patients were 60 years and above. Most of the malaria patients with AKI were also male 31 (62%). The most common symptom in these patients was fever 47 (94%) and the most common sign was jaundice 26 (52%). Malaria patients with AKI had a lower haemoglobin level 9.7 (4.8-14) vs 11 (4.1-18.3), p value=0.001 compared to those without AKI. The mean duration of admission was 168 +/- 114 hrs. The median duration of admission was also longer in patients with AKI when compared to patients without AKI 144 (24-553hrs) vs 120 (24-864hrs), p=0.014 (Table 2).

Table 2: Clinical characteristics of malaria patients with acute kidney injury

Variable	Acute kidney injury: n=50(31%)	Non-acute kidney injury: n=113(69%)	P value
Age (mean, yrs)	26.5	27.5	0.352
Sex (M:F)	31(62):19(38)	76(67):37(32.7)	0.515
Type of referral			
Self vs Health Facility	12 (24):38 (76)	30 (28.3):81(71.7)	0.567
Symptoms at presentation			
Fever	47(94)	106 (93.8)	0.962
Headache	44 (88)	102 (90.3)	0.663
Vomiting	41 (82)	96 (84.9)	0.635
Malaise	12 (24)	31(27.4)	0.646
Convulsion	6 (12)	22 (19.5)	0.244
Signs			
Pallor	22 (44)	53 (46.9)	0.732
Jaundice	26 (52)	49 (43.4)	0.308
Glasgow coma score at presentation	13 (3-15)	14 (3-15)	0.082
Haemoglobin (g/dl)	9.7 *(4.8-14)	11$^{\#}$(4.1-18.3)	0.001

Duration of symptoms (days)	3.5 (1-21)	3 (1-14)	0.198
Duration of admission (hrs)	144 (24-552)	120(24-864)	0.014
Outcome (Dead)	10 (20)	5(4.4)	0.002

*Ranges of patient's haemoglobin, Duration of symptoms, duration of admission, and composite end point for those AKI

Ranges of patient's haemoglobin, Duration of symptoms, duration of admission, and composite end point for those without AKI

Malaria related AKI patients who underwent haemodialysis

Out of the 50 patients that had AKI, 14 (28%) had haemodialysis. Male patients with AKI were more likely to have haemodialysis as compared to female patients 13 (92.9%):1 (7.2%) vs 18 (50%):18 (50%), p value=0.004.The duration of admission was also longer in AKI patients who had haemodialysis as compared to AKI patients who did not have haemodialysis 264 (120-552hrs) vs 120(24-264hrs), p value=0.001. The average number of dialysis sessions for the AKI patients on haemodialysis was 5.7(Table 3).

Table 3: Characteristics of malaria related AKI patients who had haemodialysis

Variable	AKI with haemodialysis: n=14(%)	AKI with no haemodialysis: n=36(%)	P value
Age (mean, yrs)	24.1	27.4	0.255
Sex (M:F)	13(92.9):1(7.1)	18(50):18(50)	0.004
Type of referral			
Self vs Health Facility	4 (28.6):10 (71.4)	8 (22.2):28(77.8)	0.448
Symptoms at presentation			
Fever	14(100)	33 (91.7)	0.364
Headache	41 (78.6)	33 (91.7)	0.208
Vomiting	10 (71.4)	31 (86.1)	0.207
Malaise	5 (35.7)	7(19.4)	0.198
Convulsion	2 (14.3)	4 (11.1)	0.545
Signs			

Pallor	7 (50)	15 (41.7)	0.413
Jaundice	9 (64.3)	47 (47.2)	0.222
Haemoglobin (g/dl)	7.4 (4.8-12.8)	10.1 (4.9-14)	0.066
Creatinine (µmol/l)	768.7 (388.4-2967)	582.3(208.8-2062.6)	0.076
Duration of symptoms (days)	3.5 (1-21)	3.5 (1-7)	0.850
Duration of admission (hrs)	264 (120-552)	120(24-264)	<0.001
Outcome (Dead)	1 (7.1)	9 (25)	0.153

Outcome of malaria patients with AKI

The total mortality amongst the patients with malaria related AKI was 10 (20%). Patients with malaria related AKI were more likely to die when compared to malaria patients without AKI 10 (20%) vs 5(4.4%), p value=0.002 (Table 2). Only one patient (7.1%) died amongst the patients with malaria related AKI who had haemodialysis. All patient with AKI that met the criteria for haemodialysis had the dialysis. However, there was no difference in mortality between malaria related AKI patients who underwent haemodialysis as compared to AKI patients who didn't have haemodialysis 1 (7.1%) vs 9 (25%), p value=0.153 (Table 3).

DISCUSSION

This study presents the clinical characteristics and outcome of malaria related AKI in AYA in The Gambia. These findings suggest that AYA with malaria were disproportionately affected with AKI and its related mortality is high in The Gambia. However, providing affordable and accessible dialysis machines can help improve outcome of malaria related AKI in AYA in The Gambia.

In this study, 30.7% of malaria patients had AKI. The prevalence of AKI amongst children with malaria ranges from 24-59%(14)(15)(16)(17). Prevalence of AKI in imported plasmodium falciparum patients was 38%(7). In Senegal, the prevalence of AKI in adults with malaria was 49.2%(18). This variation in prevalence could be due to different factors such as the presence of co-morbidities in the different studies, the age group studied, the use of different definition of AKI and difference in lifestyle and socioeconomic status of the different study groups.

The mean age in this study was 26.5 years, and the majority were adolescent and young adults representing 70% of the patients. In Senegal, the mean age of their patients was 36.3 years. There were much older adults in the Senegalese study as compared to this study (15). This shows that malaria related AKI is a significant problem in AYA in The Gambia. Most of the malaria patients with AKI in this study were males with no significant difference in sex between patients with malaria related AKI and those without AKI. In a study done in Ethiopia, there was significant association of AKI with male malaria patients(17). The most common symptom in these patients was fever, and the most common sign was jaundice. This is different from other studies that has found vomiting as a common symptom in these patients(9)(19).

Malaria patients with AKI had a lower haemoglobin level compared to those without AKI. Due to increased oxidative stress, inflammation, endothelial dysfunction and reduced nitric oxide results in haemolysis which mediates AKI in severe malaria patients(20)(19)(21). Anaemia may also contribute to hypoxia and circulatory failure which can also worsen AKI in malaria patients(17).

In this study, 28% of the AKI patients who met the criteria for haemodialysis were dialyzed. In Sub Saharan Africa, about 66% of children and 70% of adults with AKI needed dialysis(10). Other studies from Africa show the incidence of malarial related AKI requiring dialysis to be 30%, 12% and 1.9% in Rwanda, Senegal and Ethiopia (9)(18)(17) respectively. Haemodialysis is a lifesaving intervention which can help improve survival in patients with AKI. However, its availability in resource limited countries is limited(22). The average number of dialysis session for the AKI patients on haemodialysis was 5.7 sessions and in Senegal 1.89 session(18). Male patients with AKI were more likely to have haemodialysis as compared to female patients in this study. In Ethiopia, male sex is associated with AKI(17).This suggest a significant burden of malaria associated AKI in the male sex.

The mean duration of admission of malaria patients with AKI was 168 hrs which was shorter than a study done in India(23).There was also a significant longer duration of admission in patients with AKI as compared to patients without AKI. The duration of admission was also longer in AKI patients who underwent haemodialysis as compared to AKI patients who didn't have haemodialysis. This is understood as malaria patients with AKI may need further specialised interventions, such as haemodialysis which will make them stay longer in hospital before discharge.

The total mortality amongst the patient with malaria related AKI were 10 (20%).Malaria related AKI deaths in adults were 20%, 15% and 0% in Senegal, Rwanda and Ethiopia(9)(17)(18). Patients with malaria related AKI were more likely to die as compared to malaria patients without AKI. This is confirmed by other studies in adult and children(14) (18)(19). Only one patient died amongst the patients with malaria related AKI who had haemodialysis and there was no significant difference between AKI patients with or without dialysis. This therefore confirms the fact that providing affordable and accessible dialysis to malaria patients can help improve the outcome of malaria related AKI in AYA.

There are limitations in this study: 1. It is a hospital-based study and may not reflect what happens at the community or primary health care facilities 2. It is a retrospective study and may not be able to capture all the relevant and important information regarding the Patients with AKI. 3. There were also limited laboratory investigations in this study and kidney function test results were available in only 163 patients out of 319 patients.

Notwithstanding, this is the first study that is looking at malaria related AKI in AYA in The Gambia. This study will therefore form the basis of any future study on malaria related AKI in AYA in The Gambia.

Conclusion: This study has shown that one third of our patients with malaria had malaria-related AKI which constitute a significant public health problem among AYA in The Gambia. Mortality rate of 20% was recorded, which was high. Hence, the need for aggressive public health campaign and health education on malaria prevention and its complications general population with AYA target population. This form of interventions in this age group will help reduce morbidity and mortality related to malaria in The Gambia.

List of abbreviations

AYA; Adolescent and Young Adult

EFSTH; Edward Francis Small Teaching Hospital

AKI; Acute Kidney Injury

WHO; World Health Organization

KDIGO; Kidney Disease Improving Kidney Outcome

BF; Blood Film

RDT; Rapid Diagnostic Test

Declarations

Ethics approval and consent to participate

Ethics approval for this study was granted by the EFSTH Institutional Review Board. Informed consent was not needed in this study.

Consent for publication: Not applicable

Availability of data and materials

The dataset for this publication is available on reasonable request from the corresponding author.

Competing interest: The authors declare no conflicting interests.

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Author's contributions: SOB was involved in all stages of the study. OSM, KB, RB participated in the design of the study and data collection. SOB performed the data analysis and interpretation. All authors contributed to the writing of the manuscript. All authors read and approved the final manuscript.

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