

“Outcomes And Predictors of Outcome In Malaria AKI: A Single Centre Experience”

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I. Need for study

Malaria has protean clinical manifestations and acute kidney injury (AKI) is one of its serious and life threatening complications. The overall prevalence of AKI in falciparum malaria varies between <1 and 60%, with the mortality rate as high as 45%. None of the studies on malaria and AKI have classified AKI on AKIN criteria. We plan to look at outcomes of Malaria AKI based on severity of AKI and organ dysfunction. Outcomes are need for HD and mortality.

II. Review Of Literature

Malaria is a major public health problem in tropical countries. About 500 million people suffer from malaria, leading to death in 1 to 3 million cases. Acute kidney injury (AKI) is one of the most dreaded complications of severe malaria. As per World Health Organization criteria, acute renal failure (serum creatinine level, > or =3 mg/dL or > or =265 micromol/L) occurs as a complication of Plasmodium falciparum malaria in less than 1% of cases, but the mortality rate in these cases may be up to 45%. It is more common in adults than children. Renal involvement varies from mild proteinuria to severe azotemia associated with metabolic acidosis. It may be oliguric or nonoliguric. AKI may be present as a component of multi-organ dysfunction or as a lone complication. The prognosis in the latter is generally better. Several pathogenic mechanisms interplay for the clinical manifestation. The predominant lesions are acute tubular necrosis and mild proliferative glomerulonephropathy.

The pathogenesis of AKI in falciparum malaria is not clearly known. Malarial complications possibly are caused by the interaction of the parasite with the host, resulting in mechanical, immunologic, and humoral responses. These responses, while attempting to eliminate the parasites, may also injure the host tissues. Different hypotheses proposed for MAKI include mechanical obstruction by infected erythrocytes, exaggerated host immune response mediated through cytokines and reactive oxygen and nitrogen species, immune complex deposi-

tion, hypovolemia, disturbances in the renal microcirculation, and so forth. No explanation, however, is available for the consistent increase in the incidence of MAKI in some areas.

In September 2004, the Acute Kidney Injury Network (AKIN) was formed. AKIN advised that the term acute kidney injury (AKI) be used to represent the full spectrum of renal injury, from mild to severe, with the latter having increased likelihood for unfavorable outcomes (eg, loss of function and end-stage renal disease [ESRD]).

A report by the AKIN proposed the following criteria for AKI :

- Abrupt (within 48 h) reduction in kidney function currently defined as an absolute increase in serum creatinine of 0.3 mg/dL or more ($\geq 26.4 \mu\text{mol/L}$) **or**
- A percentage increase in serum creatinine of 50% or more (1.5-fold from baseline) **or**
- A reduction in urine output (documented oliguria of < 0.5 mL/kg/h for >6 h).

According to a study it was seen that GCS <11 had poor outcome. Similarly AKI ARDS also had poor outcome. According to a study done in Varanasi low Haemoglobin, raised AST and ALT and elevated LDH were considered to be important marker of mortality. Cerebral Malaria was an important determinant of mortality. Similar study done by Kute abd et al it was found that APACHE II ≥ 20 , SOFA and MODS scores ≥ 12 were associated with higher mortality .

Objective of study

Aims: To determine factors, if any, which predict need for dialysis and mortality.

Source of data :

Patients with Malaria and AKI admitted in Father Muller Medical College Hospital

Sample Size : 100

Study design : Prospective hospital based observational study.

Sampling technique and methodology :

100 patients with malaria-associated AKI seen at our center in 2014 will be included in the study. This will be a prospective observational study. The patient management will be done by the primary treating physician.

The diagnosis of malaria will be confirmed by direct visualization of the parasite in Giemsa-stained peripheral blood smears. In addition, once a diagnosis has been established and treatment has been initiated, serial examinations to monitor parasitological response will be noted. Clinical history and assessment will be recorded in all the study patients and all other relevant investigations to exclude known etiological causes of fever and jaundice will be noted. All the patients records will be reviewed for investigations like complete hemogram, Urine routine and microscopy examinations, Serum sodium, potassium, alkaline phosphatase, alanine aminotransaminase, bilirubin. Serological tests for Human Immunodeficiency Virus and hepatitis B and C. Estimation of blood sugar, coagulation profile for disseminated intravascular coagulation (DIC), and arterial blood gas analysis will be noted. Chest x-ray and ultrasonography (USG) of abdomen will be recorded in all the patients.

AKI will be defined by AKIN criteria. Jaundice was defined as icteric sclera and/ or total bilirubin levels >3 mg/dl. The severity of illness will be assessed using SOFA scores. The patients management data like anti malarial drugs, fluid replacement, and RRT will be noted.

When RRT is initiated indications for the same will be noted. (fluid overload, hyperkalemia, clinical evidence of uremia, metabolic acidosis, rapidly increasing SCr level, blood urea nitrogen (BUN)>100 mg/dl, and SCr >4 to 5 mg/dl).

The HD prescription will be noted like use polysulfone membrane dialyzer, surface area of dialyser, blood flow rate, dialysate flow rate, Heparin use and use of temporary femoral/ jugular catheter.

Definition of recovery: In oliguric patients, the increase in urine output will be noted as recovery. In patients who were nonoliguric, recovery of kidney function defined as a progressive decline in SCr concentration after initial attainment of stable values (assessed predialysis in patients managed with intermittent HD), despite a constant dose of renal support. Patients with severe malaria with clinically significant DIC who receive fresh whole blood transfusions, vitamin K, and fresh frozen plasma will be noted

Inclusion Criteria :

Patients with malaria and AKI admitted in Father muller medical college hospital.

Exclusion Criteria :

- Patients <18years
- Not willing to consent for the study.
- AFI and jaundice with other causes

III. Statistical Analysis

Data entry and statistical analysis will be performed using the SPSS 12.0 software. The continuous variables will be presented as mean ± standard deviation and assessed by analysis of Mann–Whitney U-test to identify the differences between groups, with statistical significance set at P < 0.05. Univariate and multivariate analysis will be performed using SPSS version-12. Multivariate analysis of variance (MANOVA) will be performed using SPSS version-12.

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Subject’s Initials: _____ **Subject’s Name:** _____

Date of Birth / Age: _____

Subject : Voluntary Consent to participate in study for medical research.

(i) I confirm that I have read and understood the information sheet dated ____ for the above study and have had the opportunity to ask questions.

(ii) I understand that my participation in the study is voluntary and that I am free to withdraw at any time, without giving any reason, without my legal rights being affected.

(iii) I understand that the Sponsor of the study, others working on the Sponsor's behalf, the Ethics Committee and the regulatory authorities, publishers will not need my permission to look at my participation both in respect of the current study and any further research that may be conducted in relation to it, even if I withdraw from the study. I agree to this access the data.

However, I understand that my identity will not be revealed in any information released to third parties or published.

(iv) I myself as a legally acceptable representative agree not to restrict the use of any data or results that arise from this study provided such a use is only for scientific purpose(s)

(v) I agree to take part in the above study.

Signature (or Thumb impression) of the Subject: _____

Date: ____/____/____

Signatory's Name: _____

Signature of the Investigator: _____ Date: ____/____/____

Study Investigator's Name: _____

Signature of the Witness _____ Date: ____/____/____

Name of the Witness: _____

IV. Patient Information Sheet

- *This is observational study .*
- *You will not be put on any new medicines/will not be asked to get any investigations /will not be asked to undergo any interventional procedures.*
- *Personal information of patient and guardians will be kept confidential throughout the study.*
- *All your queries related to research will be answered to best of our knowledge.*
- *You will be given complete liberty to reject participation or withdraw from the participation at any point of time , without any reason.*
- *If you wish to know the results of the study, the results will be made available at the end of the study.*

Information will be collected from many patients and results will be generated to know the predictor of outcome in Malaria AKI. Your participation can help us to know more regarding the disease, so that it helps in adding knowledge to medical fraternity and helps to improve treatment protocols for patients like you.

Thank you

Regards,

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