ABSTRACT
Malaria is a mosquito-borne infectious disease affecting humans and other animals caused by parasitic protozoans (a group of single-celled microorganisms) belonging to the Plasmodium type like P. vivax, P. falciparum, P. malariae, or P. ovale. If Malaria is neglected or not treated properly, it may further develop into a severe form effecting the brain resulting in Cerebral Malaria. Acute Kidney Injury (AKI) is a known complication of malaria which involves abrupt lose of kidney function. In this present case, a patient came with the complaint of fever associated with chills, rigors, altered sensorium and decreased urine output. He was diagnosed with Complicated malaria (Cerebral Malaria) induced Acute Kidney Injury, Hyperbilirubinemia and Cerebral dysfunction. He was given with appropriate treatment, symptomatically relieved and drug utilization review has been done. Patient was counseled regarding the disease, its complications, prevalence and importance of medication adherence.

KEYWORDS: Sensorium, Hyperbilirubinemia, Cerebral dysfunction, Plasmodium falciparum.

INTRODUCTION

DEFINITIONS:
1. MALARIA: Malaria is a mosquito-borne infectious disease affecting humans and other animals caused by parasitic protozoans belonging to the Plasmodium type like P. vivax, P. falciparum, P. malariae, or P. ovale.[1]
2. CEREBRAL MALARIA:- Malaria will develop a severe form, and in these case it effects brain and diffuse encephalopathy associated with seizures and status epilepticus which can occur in up to one-third of patients with severe malaria, particularly that caused by Plasmodium falciparum\textsuperscript{[2]}

3. ACUTE KIDNEY INJURY:- Acute kidney injury (AKI) is the abrupt loss of kidney function that develops within 7 days. (ARF (serum creatinine level, $\geq 3$ mg/dL or $\geq 265$ μmol/L)).\textsuperscript{[3]}

4. ACUTE TUBULAR NECROSIS (ATN):- This is a medical condition involving the death of tubular epithelial cells that form the renal tubules of the kidneys. ATN presents with acute kidney injury (AKI) and is one of the most common causes of AKI\textsuperscript{[4]}

EPIDEMIOLOGY:- Malaria is a major public health problem in tropical countries. According to the World Malaria Report 2010, there were 225 million cases of malaria and an estimated 781 000 deaths worldwide in 2009.\textsuperscript{[5]} About 500 million people suffer from malaria, leading to death in 1 to 3 million cases. As per World Health Organization criteria, acute renal failure 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.\textsuperscript{[6]} Cerebral malaria (CM) forms part of the spectrum of severe malaria, with a case fatality rate ranging from 15% in adults in southeast Asia.\textsuperscript{[7]} Cerebral malaria is the most severe neurological manifestation of severe malaria. With an incidence of 1,120/100,000/year in the endemic areas of Africa.\textsuperscript{[8]}

CAUSES OF MALARIA: Malaria can occur if a mosquito infected with the Plasmodium parasite bites you. An infected mother can also pass the disease to her baby at birth. This is known as congenital malaria. Malaria is transmitted by blood, so it can also be transmitted through:
- From mother to unborn child
- An organ transplant
- A transfusion
- Use of shared needles or syringes.\textsuperscript{[9]}
- In humans, malaria is caused by P. falciparum, P. malariae, P. ovale, P. vivax and P. knowlesi.\textsuperscript{[10]}
PATHOPHYSIOLOGY OF MALARIA:— Malaria infection develops via two phases: one that involves the liver (exoerythrocytic phase), and one that involves red blood cells Erythrocytic phase. These two phases involves rupturing of RBC and invasion hepatic cells for parasite replication. The rupturing of RBC causes most of the symptoms associated with malaria as it produces toxicv substances, as the host’s immune system responds to the waste products produced by the malaria parasites.\textsuperscript{[12]}

CEREBRAL MALARIA:—The P. falciparum parasite displays adhesive proteins on the surface of the infected blood cells, causing the blood cells to stick to the walls of small blood vessels, thereby sequestering the parasite from passage through the general circulation and the spleen.\textsuperscript{[13]} Sequestered red blood cells can breach the blood–brain barrier and cause cerebral malaria\textsuperscript{[14]}

CLINICAL PRESENTATION

SIGNS AND SYMPTOMS OF MALARIA
Plasmodium vivax, ovale and malariae:— The initial symptoms are often similar to those of influenza:
• an intermittent mild fever
• headache
• muscle aches and chills
• a general feeling of illness (malaise)

Plasmodium falciparum:— Malaria caused by Plasmodium falciparum is the most severe form of malaria. Cerebral malaria is defined as a severe P. falciparum-malaria presenting with neurological symptoms, including coma (with a Glasgow coma scale less than 11, or a Blantyre coma scale greater than 3), or with a coma that lasts longer than 30 minutes after a seizure.\textsuperscript{[15]}

SYMPTOMS OF CEREBRAL MALARIA
Common signs of cerebral malaria include

- mild jaundice
- enlargement of liver and spleen
- KIDNEY FAILURE
- altered state of consciousness
- coma that may last for three days at a stretch
rise in intracranial pressure

delirium and seizures[16]

DIAGNOSIS

Laboratory diagnosis of malaria requires the identification of the parasite or its antigens/products in the patient’s blood.

Current available techniques can be separated in three categories

1. Microscopy
2. Immunological techniques
3. Molecular techniques

1. MICROSCOPY

a) THICK AND THIN BLOOD SMEAR STUDY
i) Thick and thin blood smear study:- It is the gold standard method for malaria diagnosis.

ii) Thick smear:- Thick smears are mainly used to detect infection and to estimate parasitemia.

iii) Thin smear:- Thin smears allow the examiner to identify malaria species, quantify parasitemia, and recognize parasite forms like schizonts and gametocytes.[17]

b) QUANTATIVE BUFFY COAT (QBC) TEST:- QBC test is easier and faster than classic peripheral blood smear microscopy but the equipment required is expensive and species identification and accurate enumeration are impossible.

2. IMMUNOLOGICAL TECHNIQUES

a) ANTIBODY-BASED TECHNIQUES
i) Indirect fluorescent antibody test (IFAT)

ii) Enzyme- linked immunosorbent assay (ELISA):- If the test is positive, the antibody binds the antigen resulting in a visible colour change. When the test is negative, in the absence of antibody, there is no change of colour of the substrate.

b) ANTIGEN-BASED TECHNIQUES
i) Rapid Diagnostic Test (RDT)

RDT is a device that can detect malaria antigen in a small amount of blood (5μl) by immunochromatographic with monoclonal antibodies directed against the parasite antigen.
3. MOLECULAR TECHNIQUES
   a) Polymerase Chain Reaction (PCR):- Using PCR amplification, it is possible to detect all 4 species of malaria parasites with a reportedly 10-fold greater sensitivity than microscopy.[17]

OTHER TESTS
   a) Subjective diagnosis: - Areas that cannot afford laboratory diagnostic tests often use only a history of subjective fever as the indication to treat for malaria.[18]

   b) Differential diagnosis: - In malaria-endemic areas, parasitemia does not ensure a diagnosis of severe malaria, because parasitemia can be incidental to other concurrent disease. Recent investigations suggest that malarial retinopathy is better (collective sensitivity of 95% and specificity of 90%) than any other clinical or laboratory feature in distinguishing malarial from non-malarial coma.[19]

   c) Susceptibility testing: - It is done by testing the DNA of the parasite to detect markers that indicate resistance.

DIAGNOSIS FOR CEREBRAL MALARIA
1. NOVEL INVESTIGATIVE TECHNIQUES FOR THE DIAGNOSIS OF CEREBRAL MALARIA (CM)
   a) Clinical neuroimaging
      Advanced imaging devices have become increasingly accessible in elucidating the etiology of CM[20]

   b) MAGNETIC RESONANCE IMAGING: - This study mainly demonstrates vascular damage attributable to inflammatory processes and allows the analysis of neuronal axon injury during CM[21]

   c) COMPUTED TOMOGRAPHY: - Determination of cerebral volume variation and the detection of infarctions in large vessels[22]

2. INVESTIGATIVE NEURO-IMAGING TOOLS
   a) In vivo bioluminescent imaging
      In vivo bioluminescent imaging is a versatile and sensitive tool that is based on the detection of light emission from cells or tissues[23]
b) $^{18}$f-fluorodeoxyglucose (fdg) positron emission tomography (pet)

FDG-PET is a non-invasive imaging tool used to map cerebral metabolic activity by quantifying the uptake of a glucose analog by brain cells.\[^{24}\]

3. NEW DIAGNOSTIC TOOLS

a) Malarial retinopathy

The sequestration of P. falciparum-infected red blood cells (PRBC) in the cerebral microvasculature is the hallmark of CM.\[^{25}\]

i) Optical Coherence Tomography (OCT):- OCT is an in vivo imaging tool for the detection of retinal changes.\[^{26}\]

4. ELECTROENCEPHALOGRAPHY (EEG) AND MICRO-EEG

a) EEG

This non-invasive technique to record electrical impulses of the brain by measuring voltage fluctuations.\[^{27}\]

5. BIOMARKERS:- Biomarkers include tools and technologies that can facilitate the prediction, cause, diagnosis, progression, regression, or outcome of treatment of disease.\[^{28}\]

MANAGEMENT

Modes of Treatment: Two important concepts in the treatment of malaria are suppressive and radical treatments.

i) SUPPRESSIVE TREATMENT: The symptoms of malaria can be alleviated by suppressing the erythrocytic stage of the parasitic development. Suppressive therapy involves administration of appropriate blood schizonticidal drugs.

ii) RADICAL TREATMENT: Radical treatment is administration of primaquine to all confirmed cases of malaria.

- In P. vivax malaria, 2 weeks’ therapy with primaquine completely cures the infection in the host by its tissue schizonticidal activity and thereby prevents relapses.
- In P. falciparum malaria, a single dose of primaquine destroys the gametocytes, thereby prevents the spread of the infection into the mosquito.\[^{29}\]
- The drugs available to treat malaria include: Chloroquine, Quinine, Hydroxychloroquine (Plaquenil), Artemether and lumefantrine (Coartem), Atovaquone
(Mepron), Proguanil (sold as a generic), Mefloquine, Clindamycin (Cleocin) and Doxycycline.

People with falciparum malaria have the most severe symptoms. People with falciparum malaria may need to be monitored in the intensive care unit of a hospital during the first days of treatment because the disease can cause breathing failure, coma and kidney failure\cite{30}

**TREATMENT FOR SEVERE OR COMPLICATED MALARIA**

i) **ANTIMALARIALS:** All patients with any form of complicated or severe disease should be treated parenterally. The choice of drugs, according to availability and licensing, lies between the cinchona alkaloids, i.e. quinine or quinidine (in the USA), or one of the artemisinin derivatives, preferably intravenous artesunate.\cite{31}

ii) **QUININE:** Since the advent of chloroquine resistance, quinine has been the drug of choice for the parenteral treatment of malaria. Quinine is given by slow intravenous infusion but in an emergency may be given intramuscularly in split doses as has been done in children.\cite{32}

iii) **ARTEMISININ AND ITS DERIVATIVES:** Artemisinin derivatives are increasingly being used in the treatment of malaria of all degrees of severity. Artemisinins, especially artesunate and artemether, result in more rapid parasite clearance (being active on the immature parasite forms).\cite{33}

In children with cerebral malaria and evidence of raised intracranial pressure, mannitol (1 g kg\(^{-1}\) infused over 30 min as a 10 or 20\% solution) has been shown to control intermediate intracranial hypertension, but not when severe (>40 mmHg).\cite{34}

**COMPLICATIONS OF MALARIA**

Life-threatening situations because of malaria infection with P. falciparum may include:

- Severe infection of the brain (cerebral malaria), with seizures, confusion, and increasing tiredness leading to coma and death.
- Fluid in the lungs (pulmonary edema)
- Abnormal liver function
- Low blood sugar (hypoglycemia).
- Altered blood chemistry, including low sodium and lowered pH (lactic acidosis)
• Blackwater fever
• KIDNEY INJURY\textsuperscript{[35]}

**MALARIA INDUCED ACUTE KIDNEY INJURY/ACUTE KIDNEY FAILURE**

This is also indicated as ‘Malarial Nephropathy’. Acute kidney injury (AKI) is a known complication of malaria, and is reported to occur in up to 40\% of adult patients with a severe Plasmodium falciparum infection in endemic regions.\textsuperscript{[36]} Infection with the Plasmodium falciparum produces mainly acute manifestations, ranging from asymptomatic urinary abnormalities and mild electrolyte imbalance to acute renal failure. Renal failure is multifactorial and carries a high mortality and morbidity\textsuperscript{[37]} Over a decade ago, cerebral malaria was the predominant manifestation of severe malaria, where as today the combination of jaundice and renal failure are more common.\textsuperscript{[38]}

**PREVALENCE:**- Prevalence of ARF in malaria all over the world has been reported as 0.57\% to 60\% . In Southeast Asia there is an upsurge in the overall incidence of malarial ARF and has been reported in between 13\% to 17.8\%.\textsuperscript{[39]}

**RISK FACTORS OF OCCURING AKI IN MALARIAL PATIENTS**

- Immuno-compromised patients (Elderly or infants)
- Pathogen/Parasitic overload
- Known case of Renal impairment patient
- Kidney trauma or injury
- Any auto-immune disorders
- If malaria untreated or neglected
- Pregnant women
- Poor people due to lack of effective treatment
- Over use of medicines that are highly burden to the kidneys
- Multi-organ dysfunction.\textsuperscript{[40]}

**PATHOGENESIS:**- The pathogenesis of AKI in falciparum malaria is not clearly known. Several factors; including various chemical mediators, catecholamine release, cytoadherence of parasitized erythrocytes, dehydration, intravascular haemolysis, intravascular coagulation, sepsis hyprebilirubinaemia and hyperparasitaemia have been implicated in the pathogenesis of ARF in malaria.\textsuperscript{[41]} 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.\[^{42}\]

**CYTOADHERENCE**

The pathogenesis of severe P falciparum malaria is attributed in part to the cytoadherence of parasitized red blood cells (PRBCs) to the vascular endothelial cells in different host organs.\[^{43}\] Parasite proteins referred to as variant surface antigens expressed on the PRBC surface mediate the adhesion of infected erythrocytes to host vascular endothelial receptors.\[^{44}\] PRBCs preferentially sequester in the deep vascular beds of vital organs, including the brain, liver, lung, spleen, intestine, and kidney.\[^{45}\] Sequestration of PRBCs in glomerular and tubulointerstitial capillaries has been shown, although at a lesser degree than the cerebral vessels.\[^{46}\] Parasitized erythrocytes initiate the three principal pathogenetic features in plasmodium infections: hemodynamic, immunologic, and metabolic perturbations.\[^{47}\]

Principal pathogenic pathways in severe falciparum malaria was mentioned in the above fig.1.\[^{48}\]

**CYTOKINES, REACTIVE OXYGEN SPECIES, AND NITROGEN SPECIES**

Literature on the influence of cytokine concentrations on renal pathology in malaria is scanty although cytokines, reactive oxygen intermediates, and nitrogen intermediates (ROI and NO) play an important role in both protection against malaria and pathogenesis of severe malaria. Levels of inflammatory cytokines, such as tumor necrosis factor (TNF-\(\alpha\)), interferon- \(\gamma\), and interleukins 1-\(\alpha\), -6, and -8 are increased in malaria.\[^{49}\] Higher blood concentrations of proinflammatory cytokines have been observed in severe complications of malaria.\[^{50}\] Anti–TNF-\(\alpha\) and anti–interferon \(\gamma\)- antibodies are reported to abolish the onset of cerebral
However, in contrast to observations in the murine model, monoclonal antibodies to Malaria and AKI 397 TNF-ameliorate fever but not the manifestations of human cerebral malaria. An early increase in NO stimulates the helper T-cell-1 (Th1) response to control parasitemia similar to natural immunization during malaria infection. Whereas a late increase in NO production in the liver and spleen appear to have pathologic consequences. Regulatory functions of NO are dependent on the presence of various isoforms of the enzyme nitric oxide synthase (NOS). Physiologic function of NO is regulated by low basal concentrations synthesized by constitutive NOS isoforms. A high concentration of NO usually is produced by inducible NOS isoforms (iNOS), which play a crucial role in pathologic consequences. Increased iNOS activity and production of NO have been observed in severe malaria.

RESTRICTED LOCAL BLOOD FLOW IN THE KIDNEYS: This is considered as a major contributor for malarial ARF. Low intake of fluids, loss of fluids because of vomiting and pyrexial sweating may be responsible for dehydration and renal ischemia. Administration of intravenous fluids often worsens the general condition of the patient by inducing pulmonary edema, a situation similar to shock like syndrome. A generalized vasodilatation with an associated decrease in systemic vascular resistance is considered an important contributor for septic shock as well as malarial ARF. Vasodilatation leads to activation of sympathetic nervous system, rennin-angiotensin-aldosterone axis (RAAA), and release of vasopressin for maintaining the falling blood pressure. Unfortunately, these compensatory mechanisms may worsen the renal pathology leading to overt ARF.

LOW INTAKE OF FLUIDS, LOSS OF FLUIDS: Because of vomiting and pyrexial sweating, cytokine and NO mediated arterial vasodilatation specifically organ specific release of NO, resistance to vasoactive hormones, cytopathic hypoxia leading to decreased ATP synthesis, cytoadherence of PRBCs, etc all may contribute singly or in combination towards malarial ARF. Increased fluid administration, oxygen toxicity, and yet unidentified factors may contribute to pulmonary edema, acute respiratory distress syndrome (ARDS), multiorgan failure and death.

CLINICAL PRESENTATION

SIGNS AND SYMPTOMS

- An absolute increase in serum creatinine level of 0.3 mg/dL or more (26.4 mol/L)
- A percentage increase in serum creatinine level of 50% or more (1.5-fold from baseline)
A reduction in urine output (documented oliguria of 0.5 mL/kg/h for 6 hours).\textsuperscript{[58]}

- Swelling in legs, ankles, and around the eyes
- Nausea and vomiting
- Fatigue or tiredness.\textsuperscript{[59]}
- Shortness of breath
- Seizures or coma in severe cases
- Chest pain or pressure
- High blood pressure
- Abdominal pain
- A build-up of fluid in the body
- Fluid imbalances.\textsuperscript{[60]}

**DIAGNOSIS**

The following tests can aid in the diagnosis and assessment of AKI:

- Kidney function studies: Increased levels of blood urea nitrogen (BUN) and creatinine are the hallmarks of renal failure
- Complete blood count
- Peripheral smear
- Serologic tests
- Fractional excretion of sodium and urea
- Bladder pressure: Patients with a bladder pressure above 25 mm Hg should be suspected
- Ultrasonography
- Aortorenal angiography: Can be helpful in establishing the diagnosis of renal vascular diseases, such as renal artery stenosis, renal atheroembolic disease, atherosclerosis with aortorenal occlusion, and certain cases of necrotizing vasculitis (eg, polyarteritis nodosa)
- Renal biopsy: Can be useful in identifying intrarenal causes of AKI.\textsuperscript{[61]}
- Urinalysis
- Creatinine clearance
- Serum creatinine
- Estimated glomerular filtration rate (eGFR)
- AKI can be diagnosed if any one of the following is present:
  - Increase in SCr by $\geq 0.3$ mg/dl ($\geq 26.5$ μmol/l) within 48 hours; or
  - Increase in SCr to $\geq 1.5$ times baseline, which have occurred within the prior 7 days; or
  - Urine volume $< 0.5$ ml/kg/h for 6 hours.\textsuperscript{[62]}
MANAGEMENT
The management of MAKI needs careful and meticulous management of several problems. Early and prompt decisions and institutions are the hallmark of a better prognosis. The outlines of treatment guidelines include the following:
1. institution of appropriate antimalarials
2. maintenance of fluid and electrolyte levels
3. renal replacement therapy as indicated
4. treatment of associated complications and
5. management of infection including pneumonia.

ANTIMALARIA DRUGS:- The preferred antimalarial is artesunate or quinine given parenterally. Intravenous quinine has remained as the time-tested first-line drug. The dose is 10 mg/kg/body weight. If quinine has not been given in the previous 7 days, a loading dose may be given. But it is very difficult to get a definite history, hence it is advisable to start a maintenance dose of 10 mg/kg of body weight every 8 hours. The dose for the initial 48 hours should never be modified, even in the presence of AKI.\textsuperscript{[63,64]} The use of other drugs, namely chloroquine or sulfadoxine pyrimethamine, should be avoided owing to widespread resistance from areas where CM and AKI are common.

FLUID CHALLENGE
Many patients with oligura are dehydrated. They should receive fluid, up to 20 mL/kg of 0.9% saline infused over 60 minutes. To prevent fluid overload, auscultation of the lungs and jugular venous pressure measurements (and, if possible, CVP measurements) should be performed after every 200 mL of fluid. The CVP should always be kept between 0 and ±5. If there is no urine output after fluid replacement, an intravenous diuretic challenge may be given.\textsuperscript{[58]}

DOPAMINE CHALLENGE
The use of dopamine for the prevention and treatment of AKI has not yet been established. Its use is based on the understanding that selective renal vasodilatation will occur when it is infused at a low dose. In a prospective, controlled, cross-over trial in an intensive care unit of an infectious diseases hospital in Vietnam, dopamine at a renal dose (2.5 g/kg/min) was associated with a mean (95% confidence interval) fractional increase in the absolute renal blood flow (RBF) index of 37% (13% to 61%) and in RBF as a fraction of cardiac output of 35% (10%–59%; P = .007 and P = .014, respectively).\textsuperscript{[65]}
VASOPRESSIN THERAPY
As discussed in the pathogenesis, there appears to be a future role for the use of vasopressin in the management of malarial shock as well as MAKI.

ALBUMIN INFUSION
The administration of albumin for volume expansion reduces mortality rates.[66]

DIURETIC CHALLENGE
The loop diuretic (frusemide 40 mg or bumetanide 1 mg) is given initially. If urination does not occur, further diuretic challenge can be tried at every 30-minute intervals with incremental doses (frusemide 100, 200, and 400 mg or bumetanide 2, 4, and 6 mg). If there is still no urine flow, dopamine 2.5 to 5 g/kg/min may be tried[67]

RENA L REPLACEMENT THERAPY:- It should be initiated if any of the following is present
a. Anuria for more than 12 hours;
b. Uraemic symptoms (Encephalopathy or pericarditis)
c. Fluid overload, pulmonary edema, congestive heart failure or Pericardial rub[68]

DIALYSIS:- Dialysis has improved the survival of the AKI cases when instituted early in the course. It can be intermittent haemodialysis (daily or alternate day), or continuous venovenous haemofiltration (CVVH) or arteriovenous haemofiltration (CAVH). Often haemodialysis (HD) is performed in patients with AKI as Peritoneal dialysis (PD) is considered to be less effective in controlling biochemical abnormalities than HD. Thus, whenever RRT is indicated, either PD or HD should be started as early as possible.

FREQUENCY OF DIALYSIS:-
Intermittent HD should be performed daily for better prognosis in acute renal failure. Mortality is reduced in patients receiving six dialyses per week as opposed to those receiving HD every other day.[69,70]

MANAGEMENT OF DIURETIC PHASE:-
Diuretic phase may return gradually or in a few hours. Careful attention needs to be given towards fluid and electrolyte requirements. In addition, repeated estimation of Na, K and bicarbonate is essential.
**NUTRITION:** Suppressing endogenous protein catabolism by providing fat and carbohydrates is recommended. In patients without dialysis, protein restriction is advised, whereas those undergoing daily HD may require additional proteins.\[^{75}\]

**CASE STUDY**
A patient of age 60 years male was admitted in King George Hospital Visakhapatnam, Andhra Pradesh, India, with a complaint of fever since 10 days and altered sensorium since 1 day.

History of present illness: Patient was apparently normal 10 days before. Later he developed fever and yellowish discoloration from 10 days. Fever was found to be high grade, intermittent and associated with chills and rigors, associated with headache. There is decreased output of urine from 4 days. Last day urine output increased. Altered sensorium is observed last day.

Patient experienced cough with expectoration since 5 days and breathlessness since 3 days. On examination patient experienced altered seizures.

There is no history of hematuria/pyuria/dysuria/vomiting/diarrhea/pedal edema/facial puffiness.

Patient didn’t experience any of the above present complaints in the past.

Personal history was found to be alcoholic, smoker and takes mixed diet.

On the day of admission, patient’s blood pressure was found to be 140/50 mm of Hg, Pulse rate 80/min, Respiratory rate 15/min and temperature was afebrile.

On examination by using Glasgow coma scale, measures were done to estimate brain function. Results were found to be $E_2, V_1, M_4$. These scores explain that:

$E_2$ - means eye opening to pain  
$V_1$- means no verbal response  
$M_4$ - means motor response withdraws to pain

On addition of scores of $E, V$ and $M$ we get $2+1+4=7$, it shows that severe brain injury.

\[3-8 \text{ = severe brain injury} \]
\[9-12=\text{moderate brain injury} \]
\[13-15= \text{ mild brain injury} \]

**LABORATORY INVESTIGATIONS**
Hemoglobin-12.8 gm%
RBC- normocytic, hypochromic with mild anisocytes
WBC- count is increased and neutrophilia is seen
Platelets- adequate
Basing on these it was found that normocytic, hypochromic anemia with neutrophilic leukocytosis

Serum creatinine levels: 9.7mg/dl (normal: 0.6-1.4)
Blood urea levels: 199 mg/dl (normal: 14-45)
Serum bilirubin total: 18.4 mg% (0.3 to 1.0 mg%)
SGOT: 74 U/L (Normal: 5-40 U/L)
SGPT: 50 U/L (Normal: 7-56 U/L)
Serum Alkaline Phosphate: 348 U/L (Normal level for 56-60 years: 46-118 U/L)

Patient exhibited sensorium, seizures (E2 V1 M4) and Plasmodium falsiparum positive. So he was diagnosed as CEREBRAL MALARIA and CEREBRAL DYSFUNCTION.
Total Bilirubin levels are abnormal. So the patient was concluded of having HYPERBILIRUBINEMIA.

Serum creatine levels are abnormally high. Previously patient has no complaint of Renal problems. But after getting Malaria, he was tested for serum creatine levels and was concluded that he is having renal impairment so that his serum creatine levels are abnormal.
Basing on this he was diagnosed of having ACUTE KIDNEY INJURY induced by MALARIA.

FINAL DIAGNOSIS
By observing the above diagnostic tests patient was diagnosed as suffering with CEREBRAL MALARIA WITH ACUTE KIDNEY INJURY, HYPERBILIRUBINEMIA, CEREBRAL and DYSFUNCTION

TREATMENT
On the first day of treatment patient was given with Inj.falcigo( artesunate) 120mg IV BD , Inj.clindamycin 600mg IV BD, Inj.pantop(pantoprazole) 40mg IV OD, Tab.paracetamol 500mg QID, IVF( intravenous fluid) 25%dextrose IV TID.
On 2nd day, patient exhibited altered sensorium. Same drugs that are Inj.falcigo( artesunate) 120mg IV BD, Inj.clindamycin 600mg IV BD, Inj.pantop(pantoprazole) 40mg IV OD, Tab. paracetamol 500mg QID, IVF( intravenous fluid) 25%dextrose IV TID were continued.
Dialysis is done by using bicarbonate dialysate.
On 3rd day, BP-160/100mm of Hg, PR-96/min and abdominal examination shows diffuse tenderness. Patient was given with drugs like Tab.Nicardia Retard(nifedipine) 10mg BD, Tab.Falcigo 120mg IV OD, Tab.Clindamycin 600mg IV BD, Inj.Pantop 40 mg IV OD and Tab. B complex OD.

On 4th day, patient is conscious and coherent and found to be afebrile. BP is 140/80 mm of Hg and PR is 92/min. Same drugs continued, that are Tab.Nicardia Retard(nifedipine) 10mg BD, Tab.Falcigo 120mg IV OD, Tab.Clindamycin 600mg IV BD, Inj.Pantop 40 mg IV OD and Tab. B complex OD.

On 5th day, patient is conscious and coherent and found to be afebrile. BP is 140/90 mm of Hg, PR is 72/min and abdomen is soft. Drugs like Tab.Nicardia Retard(nifedipine) 10mg BD, Tab.Falcigo 120mg IV OD, Tab.Clindamycin 600mg IV BD, Inj.Pantop 40 mg IV OD and Tab. B complex OD were given. Patient is given IVF (intra venous fluid) 25% dextrose in 100 ml. dialysis was done using bicarbonate dialysate.

On 6th day, patient is conscious and coherent and found to be afebrile. BP is 140/80 mm of Hg, PR is 74/min and abdomen is soft. Drugs like Tab.Nicardia Retard(nifedipine) 10mg BD, Tab.Falcigo 120mg IV OD, Tab.Clindamycin 600mg IV BD, Inj.Pantop 40 mg IV OD and Tab. B complex OD were given. Patient is given IVF (intra venous fluid) 25% dextrose in 100 ml. dialysis was done using bicarbonate dialysate. Syrup.lactulose 15ml TID and Inj.opitneuron 10 ml in 100 ml normal saline IV OD is given.

On 7th day, patient exhibited fever, BP is 120/80 mm of Hg and PR is 78/min. same drugs were continued. But dialysis is not done.

On 8th day, patient was found to be afebrile, BP is 120/80 mm of Hg and PR is 82/min. same drugs were continued but syrup lactulose is replaced with syrup duphalac 15ml TID.

On 9th day, BP is 120/80 mm of Hg and PR is 90/min. Drugs like Inj.falcigo 120mg IV OD, Inj.clinamycin 600mg IV BD, Inj.pantop 40 mg OD, Tab.Nicardia Retard 20 mg BD, Tab. Bcomplex and Tab. Calcium.

On 10th day, patient was given with Tab. Nicardia Retard 20 mg BD, Tab. B complex OD, Tab. Calcium BD and Tab. IFA (iron folic acid) OD were given.

On 11th day, patient vitals are normal and was given with Tab. Nicardia Retard 20 mg BD, Tab. B complex OD, Tab. Calcium BD and Tab. IFA (iron folic acid) OD were given.

On 12th day, patient was given with Tab. Nicardia Retard 20 mg BD, Tab. B complex OD, Tab. Calcium BD and Tab. IFA (iron folic acid) OD were given.
On 13\textsuperscript{th} day, patient exhibited fever. So Tab. Paracetomol 500mg SOS along with Tab. Nicardia Retard 20 mg BD, Tab. B complex OD, Tab. Calcium BD and Tab. IFA (iron folic acid) OD were given.

On 14\textsuperscript{th} day, patient exhibited fever. BP is 130/90 mm of Hg and PR is 78/min and RR is 20/min. His urine output is >600ml. Blood pressure was controlled so nicardia retard drug has stopped. Tab. B complex OD, Tab. Calcium+ vit D\textsubscript{3} OD, Tab. IFA (iron folic acid) OD, Tab. Pantop 40 mg OD and Tab. Paracetomol 500mg SOS are given. Dialysis was done using bicarbonate dialysate.

On 15\textsuperscript{th} day, patient vitals are normal i.e., BP is 130/80 mm of Hg and PR is 84/min and RR is 18/min. Paracetomol was withdrawn and same drugs are given. But dialysis is not done.

On 16\textsuperscript{th} day, patient vitals are normal and his urine output is 1 liter. Drugs like Tab. B complex OD, Tab. Calcium+ vit D\textsubscript{3} OD, Tab. IFA (iron folic acid) OD, Tab. Pantop 40 mg OD and Tab. Paracetomol 500mg SOS are given.

On 17\textsuperscript{th} day, patient vitals are normal i.e., BP is 120/80 mm of Hg and PR is 82/min and RR is 22/min. His urine output is 1.8 liters. So drugs like Tab. B complex OD, Tab. Calcium+ vit D\textsubscript{3} OD, Tab. IFA (iron folic acid) OD, Tab. Pantop 40 mg OD and Tab. Paracetomol 500mg SOS are given.

On 18\textsuperscript{th} day, patient was prescribed with Tab. B complex OD, Tab.Calcium+ vit D\textsubscript{3} OD, Tab. IFA (iron folic acid) OD, Tab. Pantop 40 mg OD.

On 19\textsuperscript{th} day, patient vitals are normal and his urine output is 1.6 liters. Same drugs were continued.

On 20\textsuperscript{th} day, patient is conscious and coherent and found to be afebrile. BP is 120/70 mm of Hg, PR is 84/min and abdomen is soft. His Urine Output is 1.8 liters. He was prescribed with Tab. B complex OD, Tab.Calcium+ vit D\textsubscript{3} OD, Tab. IFA (iron folic acid) OD, Tab. Pantop 40 mg OD.

On 21\textsuperscript{st} day, patient vitals are normal and his urine output is 1.2 liters. On 22\textsuperscript{nd} day, patient’s Urine output was 2 liters and was given with Tab. Rantac 150mg BD, Cap. IFA (iron folic acid) OD, Tab.Calcium+ vit D\textsubscript{3} OD and Tab. B complex OD.

On 23\textsuperscript{rd} day, patient’s Urine output was 1.8 liters. Drugs like Tab. Rantac 150mg BD, Cap. IFA (iron folic acid) OD, Tab.Calcium+ vit D\textsubscript{3} OD and Tab. B complex OD were given.

On 24\textsuperscript{th} day, patient’s Sr.Cr. levels are 1.7mg/dl and blood urea was 45mg/dl. Patient was generally improved, vitals are stabilized and urine output is also improved. So, he was discharged under stable, general conditions and advised to attend nephrology OPD at regular follow ups.
DISCUSSION: A 60 years old male patient came with a complaint of fever since 10 days and altered sensorium since 1 day. He was diagnosed as suffering with Cerebral Malaria with Acute Kidney Injury, Hyperbilirubinemia and Cerebral dysfunction. So he was given with Inj.Falcigo 120mg IV. Falcigo (Artesunate) is an anti-malarial drug. Artemisinins and cinchona alkaloids are the only classes used to treat severe malaria. So intravenous artesunate was given to treat cerebral malaria. Clindamycin 600mg IV BD was given inorder to treat the Complicated Malaria. Tab. Paracetomol 500mg QID is given as the patient exhibited Fever. Nicardia Retard (Nifedepine) 10mg BD is given in order to treat blood pressure due to Acute Kidney Injury(AKI) which relaxes smooth muscle and produces vasodilation, which in turn improves blood flow and oxygen delivery. Pantop (Pantoprazole) is a proton pump inhibitor that decreases the amount of acid produced in the stomach. Tab B complex, Iron folic acid supplements are mainly given as having chronic kidney disease changes the need for some nutrients, their absorption or their utility and some may lost during dialysis. Optineuron is for relaxing the nerve signals to the brain. Patient was haemodialysed 5 times along with packed cell transfusion. Patient general condition was improved, vitals are stabilized and urine output is improved after 20 days of hospital admission. He was discharged with medications Tab. B complex OD, Tab.Calcium+ vit D3 OD and Tab. IFA (iron folic acid) OD.

1. PATIENT PHOTO
2. HOSPITAL CONSENT FORM

2. TREATMENT CHART

4. SERUM Creatinine Levels
5. CONSENT FORM

CONCLUSION
Malaria is a mosquito-borne infectious disease which is a major public health problem caused by parasitic protozoans belonging to the Plasmodium type like P. vivax, P. falciparum, P. malariae, or P. ovale. If this condition is neglected or untreated it may get complicated and effects brain(Cerebral Malaria). Acute kidney injury (AKI) is the abrupt loss of kidney function which is also a complication of malaria. Present case was apparently normal 10 days before. Later he developed fever, decreased urine output and altered sensorium. He was diagnosed as suffering with Cerebral malaria with acute kidney injury, hyperbilirubinemia and cerebral dysfunction. Given with appropriate treatment, the patient was found to be relieved from symptoms. Patient was explained about the disease condition and its associated complications, importance of medication adherence and discharged with medication. From this case, it is cleared that if Malaria is neglected, it becomes complicated and may be fatal. In every malaria case, serum creatinine levels should be checked compulsorily. If it is correctly treated in right time with right medication, the quality and well being of the patient can be improved.
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