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Thrombotic Microangiopathy and acute kidney injury with malaria: One-year experience at SIUT

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Abstract:

Introduction: Acute Kidney Injury (AKI) has been widely reported with malarial infection, both falciparum and vivax species. AKI, anemia, jaundice and thrombocytopenia are documented associated findings with malarial AKI. Thrombotic Microangiopathy (TMA) in relation with malarial AKI is less reported subject. During last year we have seen more such patients and aim to report this series.

Patients and Methods: Between January 2023 to December 2023, patients with diagnosis of malaria and developing AKI (according to KDOQI guidelines definition), who were brought to Sindh Institute of Urology and Transplantation (SIUT), showing some clinical and basic laboratory features of TMA or shown delayed recovery were subjected to renal biopsy. Only those where histological diagnosis of TMA was confirmed were included in present study.

Results: During last calendar year 17 adult patients fulfilled criteria of malaria, AKI and TMA, of these 15 (88%) were female. Malaria was caused by vivax species in 15 (88%), falciparum in one and one patient who arrived late here had report of malarial parasite seen in private laboratory, species was not mentioned. All had febrile illness, associated symptoms were oligo-anuria in 15(88%), vomiting 13 (76%), body aches 12(70%), and jaundice in 6 (35%). The mean age was 26.58±8.9 years, hemoglobin 7.84±1.78, urea 162.70±67.94, creatinine 8.06±4.69 and LDH 1434.05±925.36. Hemodialysis was required in 16 (94%) patients. After getting biopsy results plasma exchanges done in 15 (88%) patients. Complete recovery of renal function seen in 6 (35%), CKD in 7 (41%).

Conclusion: TMA in association with malarial AKI is less reported in literature. Vivax malaria has shown devastating complications with this previously labelled "benign" species of plasmodium.

Key Words: Thrombotic Micro Angiopathy (TMA), Acute Kidney Injury (AKI), Malaria, Plasmodium vivax, Plasmodium falciparum.

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Introduction: Acute Kidney Injury (AKI) has been widely reported with malarial infection, both falciparum and vivax species contribute to this.[1,2,3] AKI, anemia, jaundice and thrombocytopenia are documented associated findings with malarial AKI. Thrombotic Microangiopathy (TMA) in relation with malarial AKI is less reported subject.[4,5] Contributing factors to pathogenesis here could be volume depletion resulting from high grade fever and associated vomiting and/or diarrhea, hemolysis resulting from injury to red blood cells caused by malaria, disseminated intravascular coagulation and sepsis.[6] During last year we have seen more such patients and aim to report this series.

Patients and Methods:

Between January 2023 to December 2023, patients with diagnosis of malaria and developing AKI (according to KDIGO definition), who were brought to Sindh Institute of Urology and Transplantation (SIUT), showing some clinical and basic laboratory features of TMA (thrombocytopenia, raised lactate dehydrogenase levels and presence of schistocytes on peripheral blood film) or the patients who show delayed recovery were subjected to renal biopsy. Only those where histological diagnosis of TMA was confirmed were included in present study.

Results:

During one calendar year 17 adult patients fulfilled criteria of malaria, AKI and TMA, of these 15 (88%) were female. Malaria was caused by P.vivax species in 15 (88%), P.falciparum in one and one patient who arrived late here had report of 'malarial parasite seen' in private laboratory, species was not mentioned. Clinical symptoms, laboratory parameters at time of hospital admission, treatment prior to coming to this hospital or provided here all given in Table 1.

Table 1: Demographics of study population (n=17)

Malaria species:	
P. Vivax	15 (88)
P. Falciparum	1 (6)
Not specified	1 (6)
Gender:	
Female	15 (88)
Male	2 (12)
Age (years) ±std	26.58±8.9
Days of insult at presentation	15.23±8.73
Presenting symptoms:	
Fever	17 (100)
Decline in urine output	15 (88)
Vomiting	13 (76)
Yellow discoloration of sclera	6 (35)
Diarrhea	5 (29)
Laboratory parameters:	
Hemoglobin (g/dl)	7.84±1.78
WCC (/mm^3)	11.06±5.21
Platelets (/mm^3)	117.94±114.21
Urea (mg/dl)	162.70±67.94
Creatinine (mg/dl)	8.06±4.69
LDH (U/L)	1434.05±925.36
Total Bilirubin (mg/dl)	2.39±2.4
Direct Bilirubin	1.25±1.6
SGOT (U/L)	96.76±87.90
SGPT (U/L)	135±158.57
Hyponatremia (Na ≤129)	4 (24)
Hyperkalemia (K≥5.3)	3 (18)
Acidosis (HCO3 ≤19)	11 (65)
Anti-malarial:	
Artemether	6 (35)
Gen M	6 (35)
Chloroquine	3 (18)
Primaquin	1 (6)
Not known	1 (6)
Renal Replacement (HD)	16 (94)
Plasma Exchange	15 (88)

*(%) in parenthesis

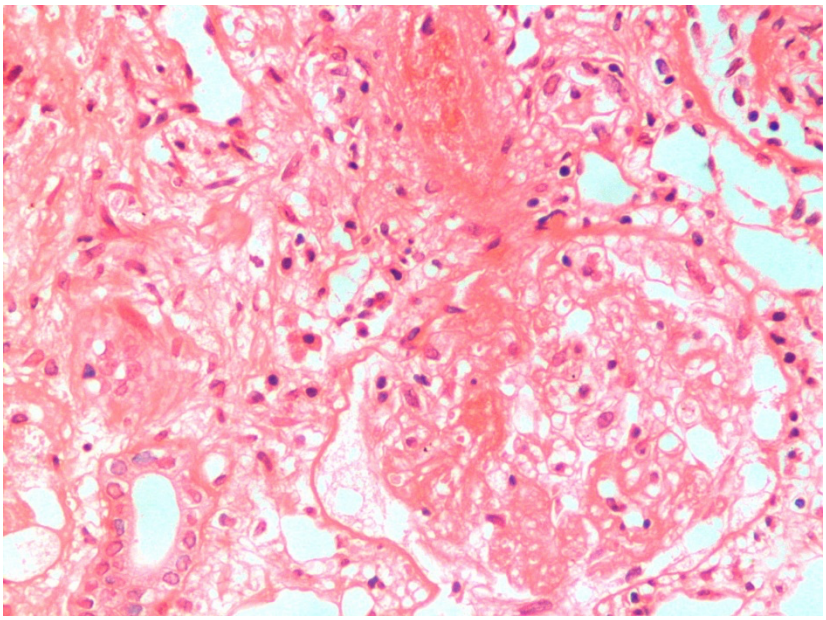

Figure 1: High power view showing a partially infarcted glomerulus with an arteriole in the upper part of the field. The latter is showing fibrin thrombus in the lumen with luminal occlusion (Hand E x400). Photo courtesy: Histopathology Department SIUT, Karachi, Pakistan

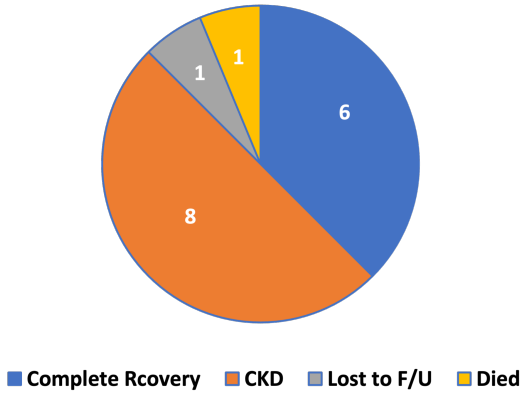

Figure 2: Outcome of patients with Malaria developing AKI and TTP.

Complete recovery of renal function seen in 6 (35%), CKD in 8 (47%), lost follow up 1(6%), died 1 (6%), one has not yet completed 90 days, Figure 2.

Discussion:

According to World Health Organization fact sheet uploaded on 4th December' 2023, during year 2022, estimated cases of malaria were 249 million reported from 85 countries, among them 608000 died with infection.[7] While AKI widely reported with malarial infection from different countries, TMA in association with malarial AKI is less reported in literature, often found are single case reports.[4,5] Most recently series of three patients reported from India having TMA and acute cortical necrosis after vivax malaria.[8] Hemolytic uremic syndrome (HUS) is type of TMA which is distinguished from TTP by presence of renal failure along with common features of thrombocytopenia and microangiopathic hemolytic anemia. HUS could be typical with shiga toxin diarrhea related or atypical with autoimmune

(like SLE, scleroderma), pregnancy related, malignancies, drug related or infection related. aHUS in about 50% of cases involve complement regulatory genes like factor H, factor I, factor B or membrane co-factor protein (MCP/ CD46).[9] However, the triggering or precipitating factor is necessary to cause endothelial damage which evolves to TMA. Other than viruses some parasitic (plasmodia) infections can also cause TMA. The previously considered or labelled as "benign" species of plasmodium that is vivax, has been reported to lead to some devastating complications.[2,3,10] Autoimmune hemolytic anemia has also been reported with vivax malaria.[11] In present case series we report 17 cases of malaria causing HUS over a span of one calendar year, majority (88%) of these were from vivax malaria.

Conclusion: Malaria is life threatening parasitic infection in human over centuries. There are various complications reported with this infection. The species (p. vivax) once considered 'benign' is no more benign and can give rise irreversible renal failure in considerable number of cases. TMA is one of the cause contributing to CKD in malarial AKI.

Conflict of Interest: None Declared

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