DOI: 10.7860/JCDR/2023/63628.18195

Original Article

Internal Medicine Section

Renal Complications of Benign Tertian Malaria: A Case-control Study from South Delhi, India

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ABSTRACT

Introduction: *Plasmodium vivax* (*P. vivax*) malaria is a major public health problem worldwide, particularly in the tropical and subtropical regions. Although *P. vivax* malaria is generally considered less severe than *Plasmodium falciparum* (*P. falciparum*) malaria, it can still cause severe illness, including severe anaemia, respiratory distress, and cerebral malaria, which can be fatal. Additionally, due to its relapsing nature it can further complicate treatment. Despite being a significant cause of morbidity and mortality, *P. vivax* malaria has received relatively less attention than *P. falciparum* malaria. Therefore, present study was designed to evaluate renal complications.

Aim: To study the prevalence of renal involvement and its associations with clinical manifestations, laboratory parameters, and other complications in monoinfection of *P. vivax* malaria.

Materials and Methods: This was a retrospective case-control study done over three years duration between April 2017 to March 2020. A total of 380 patients data were taken from hospital records of Hakeem Abdul Hameed Centenary (HAHC) Hospital, New Delhi, India admitted with a diagnosis of *P. vivax* infection. Renal complications were assessed in all patients admitted with the diagnosis of *P. vivax*. Renal involvement was defined as per Acute Kidney Injury Network (AKIN) criteria for Acute Kidney Injury (AKI). For statistical calculations, data was analysed into two groups i.e., AKI and non AKI. Clinical, laboratory and other complications were assessed for statistical significance by t-test/Mann-Whitney test and for correlation between AKI and these variables univariate analysis was done initially followed by multivariate analysis.

Results: Male to female ratio in present study was 1.8:1. The prevalence of AKI was 22.59% with a male: female=2.1:1. Mean age in the AKI group was 35.89±14.69 years as compared to the non AKI group was 29.40±12.44 years (p-value=0.019). Renal involvement was significantly associated with rising hepatic transaminases (p-value=0.02, 0.018 for each variable). Leukopenia was protective for AKI; however rising leukocyte count was associated with increasing odds of renal involvement with Odd Ratio (OR) of 7.486 (p-value=0.001). AKI was strongly associated with increasing age, leukocytosis, and hyperbilirubinaemia. Whereas hepatic transaminases, hyponatraemia, cerebral malaria, acute respiratory distress syndrome, and thrombocytopaenia were weakly associated with AKI.

Conclusion: *P. vivax* is not benign malaria anymore; complications should be anticipated and treated at an early stage.

Keywords: Acute kidney injury, Renal insufficiency, Severe manifestations

INTRODUCTION

Malaria is caused by the transmission of any of the five strains of the *Plasmodium* species to humans, most commonly by the bite of a female anopheles mosquito. Despite the advancements in public health measures, insecticidal agents, and antimalarial drug therapy, malaria continues to be a major causative agent of acute febrile illness in the tropics. In the year 2021, there was an estimated 247 million malaria cases globally, and 4.9 million of these were due to *P. vivax* [1]. While *P. falciparum* is the predominant strain worldwide and is also considered the most fatal [2]. However, some recent studies have highlighted the morbidity and mortality, of the potential of infections with *P. vivax* [3-6]. India has the highest case burden of malaria (79%) in the Southeast Asia region and accounts for 83% of mortality associated with malaria in this region [1]. As per the world malaria report 2022, 39.7% of malaria cases in the Southeast Asia region can be attributed to *P. vivax* which is much higher than its global contribution of 2% [1].

The National Vector Borne Disease Control Programme management guidelines for malaria warrant the use of light microscopy, wherever available or atleast bivalent rapid diagnostic tests in remote settings to distinguish the *Plasmodium* species [7,8]. Since *P. vivax* has been historically considered a benign variant of the disease, it can lead to delay in diagnosing a complicated case [9]. Cerebral malaria, pulmonary oedema, AKI, sepsis, jaundice, severe haemolysis, thrombocytopaenia, and shock are some of the recognised complications of malaria infection [10]. Even though these complications have most commonly been associated with the *P. falciparum* they can occur nevertheless with *P. vivax* as well [10]. AKI is a common complication in patients seeking acute critical care. AKI can further complicate the disease by adding to the acid base abnormalities and electrolyte abnormalities and causing fluid overload. AKI can be diagnosed in patients based on oliguria, or a rising trend in serum creatinine or urea levels [11]. Since, a complicated malarial illness is a medical emergency, physicians should have a high index of suspicion for the same irrespective of the malarial species [10,12,13].

A few case reports in recent years have reported AKI in *P. vivax* infection but the data available is limited in number. *P. vivax* has a propensity to cause AKI due to intravascular haemolysis and due to it's a relapsing nature it may further complicate the disease. It has much higher morbidity as estimated previously warranting an extensive study to be carried out [13-15]. Hence, present study was planned to study the AKI in *P. vivax* and its correlation with clinical parameters, laboratory parameters and with respect to other complications in *P. vivax* malaria.

MATERIALS AND METHODS

The present study was a retrospective case-control study done by extracting the data of patients admitted to HAHC Hospital, which is

a tertiary healthcare centre in New Delhi, India. Due clearance from the hospital's ethics committee (IEC number HIMSR/IEC/48/2017) was obtained before the data collection.

Inclusion criteria: In present study patients which were admitted to this hospital between April 2017 and March 2020 with a final diagnosis of *P. vivax* Malaria were included in the study. The diagnosis of *P. vivax* was confirmed by either Giemsa-stained peripheral blood smear examination of thin or thick smear, and/or by *P. vivax* specific lactate dehydrogenase rapid antigen test.

Exclusion criteria: All patients with a co-infection of any documented viral, bacterial, or mixed malarial infections. Patients who had chronic kidney disease, or were on immunosuppressants and pregnant females were excluded from the study.

Study Procedure

The study included a total of 380 patients diagnosed with *P. vivax* malaria, out of which 17 were excluded as per exclusion criteria. A total of 363 patients were included for data analysis, 82 were included in the AKI group (cases) and the remaining 281 formed the non AKI group (controls). Detailed data regarding the history, findings of physical examination, treatment advised along with disease progression and the daily laboratory analysis were recorded as per fixed performa in Microsoft excel sheet from the hospital records. Haematological tests were performed using the Sysmex haematological analyser, biochemical investigations were performed using the Siemens Xp and biochemistry autoanalyser. All the relevant information was compiled in a spreadsheet.

The AKIN criteria is a more accurate reflection of the development of AKI and require concurrent measurements of serum creatinine and urine output. To label a patient with the development of AKI there should be an acute rise in serum creatinine of ≥0.3 mg/dL or a decrease in urine output to <0.5 mL/kg/hr for >6 hours with normal sized kidneys confirmed with ultrasonography [11]. As the maximum upper limit of the standard value of creatinine of 1.2 mg/dL, hence, by applying AKIN criteria, any patient with a serum creatinine of ≥1.5 mg/dL were labelled as AKI and hence such patients formed the case group, and patients with serum creatinine <1.5 mg/dL were labelled as non AKI group and formed the control group.

STATISTICAL ANALYSIS

All the analysis was performed in International Business Machines (IBM) Statistical Package for the Social Sciences (SPSS) version 26.0. Categorical data were represented in percentage form and continuous data was represented in Mean±SD format. In categorical data, Z test of proportion was applied to compare two groups and for Normal distributed data Independent t-test was applied while in non normal distributed data the Mann-Whitney test was used. To know the association of risk factors in AKI vs non AKI patient's univariate and multivariate analysis was done at 95% confidence interval. The p-values <0.05 were considered statistically significant.

RESULTS

As per present study, 363 patients were enrolled in the study and out of which as per AKIN criteria 82 were diagnosed as AKI secondary to *P. vivax* infection, hence a 22.59% incidence was obtained. *P. vivax* infection distribution as per gender was 232 (63.91%) males and 131 (36.09%) females i.e., male to female ratio of 1.8:1. Despite the high rate of infection of *P. vivax* in the male gender, the rate of AKI development was slightly higher in the male population 68.29% vs 31.7% in females i.e., male to female ratio of 2.1:1, which was statistically non significant.

In the evaluation of age, the mean age was 30.8 in total patients, 35.89 in the case group, and 29.4 in the control group. However, there was no significant statistical difference between the age in the case and the control group. None of the individual co-morbidity played a significant role in the development of AKI among *P. vivax* patients. Amongst the history and physical examination variations between the two groups, breathlessness, cough, and cerebral malaria were statistically significant and were higher in the AKI group [Table/Fig-1]. Other history and examination details such as fever, chills, vomiting, bodyache, and abdominal pain had approximately similar incidences in both groups. The present study also showed a difference in the incidence of bleeding in the two groups i.e., 15.85% vs 8.89% in cases vs control group, but the difference was clinically insignificant.

Variables	AKI group (N1=82)	Non AKI group (N2=281)	Total patients (N=363)	p-value
Males	56 (68.29%)	176 (62.63%)	232 (63.91%)	0.347
Females	26 (31.71%)	105 (37.37%)	131 (36.09%)	0.418
Mean age (years)	35.89±14.69	29.40±12.44	30.84±13.25	0.0001
Hypertension	2 (2.44%)	11 (3.91%)	13 (3.58%)	0.588
Diabetes	3 (3.65%)	9 (3.20%)	12 (3.30%)	0.388
Hypothyroidism	2 (2.44%)	5 (1.77%)	7 (1.92%)	0.684
Fever	73 (89.02%)	254 (90.39%)	327 (90.08%)	0.877
Chills	69 (84.14%)	238 (84.69%)	307 (84.57%)	0.984
Vomiting	30 (36.58%)	108 (38.43%)	138 (38.01%)	0.768
Bodyache	43 (52.43%)	152 (54.09%)	195 (53.71%)	0.889
Headache	45 (54.87%)	161 (57.29%)	206 (56.74%)	0.762
Abdominal pain	20 (24.39%)	66 (23.48%)	86 (23.69%)	0.983
Bleeding	13 (15.85%)	25 (8.89%)	38 (10.46%)	0.070
Breathlessness	15 (18.29%)	25 (8.89%)	40 (11.01%)	0.020
Cough	22 (26.83%)	45 (16.01%)	67 (18.46%)	0.036

[Table/Fig-1]: Comparison of demographic details and clinical features between the AKI (case) and non AKI group (control).
Data are expressed as numbers and percentage of patients in respective category and mean data in case of age. The p-value was calculated using Z-score of two proportion between the AKI and non AKI group using the unpaired t-test. The p-value <0.05 is considered as statistically significant difference. (SD: Standard deviation at 95% confidence interval)

Further, various laboratory and imaging results were also compared between the two groups to establish any correlation or for early predication of development of AKI in acute *P. vivax* infection. The differences between the case and the control group were statistically significant for leukopenia, or leukocytosis, severe thrombocytopaenia, hyperbilirubinaemia, and a rise in hepatic transaminases. However, development of shock and mortality were approximately similar in both groups. Radiological findings were also approximately similar in both groups but non significant [Table/Fig-2].

Variables	AKI group (N1=82)	Non AKI group (N2=281)	Total patients (n=363)	p-value
Haemoglobin <7 g/dL	10 (12.19%)	33 (11.74%)	43 (11.84%)	0.987
TLC <4000 cells/mm^3	25 (30.48%)	122 (43.41%)	147 (40.49%)	0.049
TLC 4000-10000/mm^3	49 (59.75%)	155 (55.16%)	204 (56.19%)	0.541
TLC >10000/mm^3	8 (9.75%)	4 (1.42%)	12 (3.305%)	0.002
Platelet count <50 1000/µL	49 (59.75%)	122 (42.41%)	171 (47.10%)	0.002
ARDS	9 (10.97%)	14 (4.98%)	23 (6.33%)	0.498
Potassium <3.5 mEq/L	21 (25.60%)	72 (25.62%)	93 (25.61%)	0.999
Bilirubin >3 mg/dL	29 (35.36%)	45 (16.01%)	74 (20.38%)	0.001
AST >135 U/L	13 (15.85%)	21 (7.47%)	34 (9.36%)	0.022
ALT >135 U/L	20 (24.39%)	38 (13.52%)	58 (15.97%)	0.018
Bleeding	13 (15.85%)	25 (8.89%)	38 (10.46%)	0.070
Cerebral malaria	8 (9.75%)	8 (2.84%)	16 (4.4%)	0.007

Mortality	1 (1.21%)	4 (1.42%)	5 (1.37%)	0.888
Shock	7 (8.53%)	16 (5.69%)	23 (6.33%)	0.352
Radiology				
Pleural effusion	3 (3.65%)	8 (2.84%)	11 (3.03%)	0.703
Hepatosplenomegaly	37 (45.12%)	108 (38.43%)	145 (39.94%)	0.275

[Table/Fig-2]: Comparison of laboratory findings and complications between AKI and non AKI groups.
Data are expressed as number and percentage. The p-value was calculated using Z-score of two proportion between the AKI and non AKI group using the unpaired t-test. The p-value <0.05 is considered as statistically significant. (Where, K: Thousand; TLC: Total leukocyte count; Plat.: Platelet; AST: Aspartate aminotransferase; ALT: Alanine aminotransferase; ARDS: Acute respiratory distress syndrome)

To establish the correlation and causal relationship between the variables and AKI, univariate analysis was performed for all possible variables for the risk of developing AKI. As per univariate analysis, it was found that age more than 60 years, hyponatraemia, cerebral malaria, raised bilirubin, Aspartate Aminotransferase (AST), Alanine Aminotransferase (ALT), Alkaline Phosphatase (ALP), thrombocytopaenia (platelet count <50,000 cells/uL), and a rising Total Leukocyte Count (TLC) i.e., >4000/uL were all found to be significantly correlated with the development of AKI, for these significant variables, further multivariate analysis was done to identify most significant risk factor or variable for the development of AKI [Table/Fig-3]. In elderly patients increased age i.e., >60 years, leukocytosis (TLC >10,000) and an increased level of serum bilirubin were found to be the most significant factors associated with the development of AKI by multivariate analysis [Table/Fig-4].

Variables	Odd's ratio	Std. Error	Z	p>I Z I	95% Confidence interval
Age	3.653	2.009	2.35	0.019	1.242-10.739
Sex	0.778	0.208	0.94	0.348	0.460-1.314
Bleeding	1.929	0.709	1.79	0.074	0.938-3.967
ARDS	2.351	1.051	1.91	0.056	0.978-5.648
CNS	3.689	1.906	2.53	0.012	1.339-10.160
Shock	1.545	0.729	0.92	0.356	0.613-3.896
Hepatosplenomegaly	1.383	0.350	1.28	0.200	0.842-2.272
Sodium (mEq/L)	2.066	0.529	2.83	0.005	1.249-3.415
Potassium (mEq/L)	0.999	0.287	0.00	0.998	0.568-1.755
T.Bil (mg/dL)	2.869	0.810	3.73	<0.001	1.649-4.992
AST (U/L)	2.332	0.881	2.24	0.025	1.111-4.893
ALT (U/L)	2.062	0.641	2.33	0.020	1.121-3.792
ALP (U/L)	1.773	0.454	2.24	0.025	1.073-2.931
Haemoglobin (g/dL)	1.043	0.401	0.11	0.911	0.490-2.219
TLC >4000/mm^3	1.749	0.469	2.08	0.037	1.033-2.960
TLC >10000/mm^3	7.486	4.688	3.21	0.001	2.194-25.544
Platelet count (1000/µL)	1.935	0.494	2.59	0.010	1.173-3.192

[Table/Fig-3]: Calculation of odd's risk and p-value of different variables in AKI Group vs. non AKI group by univariate linear, logistic regression analysis and calculation of the p-value.
The p-value was calculated by using the OR. The p-value <0.05 is considered as statistically significant difference. (Z: Standard normal deviate; CNS: Neurological symptoms; T.Bil: Total Bilirubin; TLC: Total leucocyte count; ARDS: Acute respiratory distress syndrome; AST: Aspartate aminotransferase; ALT: Alanine transaminase; ALP: Alkaline phosphatase)

Variables	Odd's ratio	Std. Error	Z	p>I Z I	95% Confidence interval
Age	3.449	2.079	2.05	0.040	1.058-11.243
ARDS	1.154	0.596	0.28	0.781	0.419-3.178
CNS	2.649	1.558	1.66	0.098	0.836-8.389
Sodium (mEq/L)	1.694	0.470	1.90	0.057	0.983-2.919
T. Bil (mg/dL)	2.538	0.801	2.95	0.003	1.366-4.712
AST (U/L)	0.718	0.356	0.67	0.506	0.271-1.900
ALT (U/L)	1.768	0.667	1.51	0.131	0.844-3.704
ALP (U/L)	1.475	0.423	1.36	0.175	0.840-2.589
TLC >4000 cells/mm^3	1.634	0.483	1.66	0.097	0.915-2.919
TLC>10000 cells/mm^3	4.515	3.194	2.13	0.033	1.128-18.067
Platelet count (1000/µL)	1.522	0.465	1.38	0.169	0.836-2.772

[Table/Fig-4]: Calculation of Odds Ratio (OR) and p-value of different variables in AKI Group vs. non AKI group by further assessment of significant variables in univariate analysis by applying multivariate logistic regression analysis.
The p-value was calculated by calculating the OR. The p-value <0.05 is considered as statistically significant difference. Z: Standard normal deviate; ARDS: Acute respiratory distress syndrome; T.Bil: Total bilirubin; CNS: Neurological symptoms; TLC: Total leucocyte count; AST: Aspartate aminotransferase; ALT: Alanine transaminase; ALP: Alkaline phosphatase

DISCUSSION

As most cases of complicated malaria are historically considered to be due to the less common *P. falciparum* malaria, studies linking the clinical and laboratory parameters in complicated *P. vivax* infection have been sparse and limited. The incidence of AKI was 22.59% amongst diagnosed *P. vivax* malaria cases and previous studies had estimated the prevalence of AKI in *P. vivax* cases ranging from 6-40% [4,16,17]. Hence, the present study had almost the same frequency of AKI as documented previously in other studies [4,12].

The mean age for the AKI group was approximately 35 years of age and in the non AKI group was 29 years of age, however a definite correlation between age and development of AKI could not be established, but in patients developing AKI, patients more than 60 years of age or elderly people with *P. vivax* infection were more prone for developing AKI than the patients with younger age, and younger age were more prone than children. Risk of AKI increase with increasing age which was confirmed to be a significant parameter on univariate, in which age was found to be significant with a p-value=0.040 even in multivariate regression, similar risk of AKI with increasing age had been described in many studies [4,5,18,19]. Hence, elderly patients should have close monitoring of laboratory parameters as well as clinical parameters and should be monitored more frequently than the younger population. The most probable postulated reasons for developing AKI in these patients could be due to compromised renal function due to age-related fall in glomerular filtration rate, due to multiple co-morbidities or patients already on polypharmacy which may play a role in AKI or due to some unknown pathology or immune dysfunction which need further elaborate studies.

Distribution of patients as per gender for male; female was in a ratio of approximately 1.8:1 in the total population, which was slightly higher in patients in the AKI group i.e., 2.1:1 but there was no statistical significance, similar male predilection had been documented in various studies, however no definite cause had been detected and it is non significant statistically in previous studies too [4,19]. Even though the distributions of common clinical symptoms such as fever, chills, vomiting, body aches, and abdominal pain were not significantly different in the two groups. These clinical symptoms had been found significant in few studies whereas other studies label these as non significant, abdominal pain and vomiting had been found closely associated in few studies with AKI [6,20], it was noted that breathlessness and cough had a higher prevalence in the AKI group in present study and similar association was seen in another study where ARDS was also correlating with AKI [17]. Hence, clinical symptoms cannot be used as a guide to predict the development of AKI. But patients having cough and breathlessness should definitely be monitored for renal dysfunction. These symptoms may also be attributed to AKI and volume overload. However, these symptoms do predict ARDS, but ARDS was not found to be significantly associated with AKI in present study. Hence, these two symptoms should be visualised de novo for the development of ARDS or AKI. Definitive evidence of this can only be known by the temporal development of these symptoms, as in a previous published research, these symptoms were significant but AKI was associated with ARDS [17].

The pathogenesis of AKI because of malaria has not been well understood. It is believed that renal microcirculation obstruction, haemodynamic factors, and hypovolemia along with activation of the immune system and endothelial damage with the accompanying release of inflammatory mediators have a role to play in the development of AKI in patients infected with *P. vivax* [12-14,18,19]. Previous studies have also shown hepatic dysfunction and increased bilirubin and liver enzymes to be closely associated with the development of AKI in malaria patients [4,14,16]. This along with the other laboratory derangements has the potential to serve as an early indicator for the development of AKI in *P. vivax* infections. As also seen in present study AKI patients had raised total bilirubin [4,6,14,17,21] and transaminase level three times the upper normal limit and the variations in the level of these were statistically significant in AKI vs non AKI group. Multiple studies published from across the globe shows similar association of AKI with total bilirubin and transaminases, among all available literature, approximately all studies agrees on association of AKI with total bilirubin [5,14,16,21]. Similarly, presence of encephalopathy was also significant in AKI patients [6,20]. Hence, it can be postulated that some strains of *P. vivax* malaria have a predilection for capillary microcirculation in the liver, kidney, and brain vessels, hence the presence of one of these should alert the physician for prediction of presence of the other two variables [5,15,16,20]. Hence, few patients have these complications together, while few have other complications like bleeding, ARDS, hypoglycaemia, anaemia etc., which may be due to variations in strains of *P. vivax* [15].

In haematological parameters, haemoglobin variations were not found to be significant implying, there was no severe haemolysis in AKI patients [18]. Therefore, haemoglobinuria causing AKI cannot be postulated as a major cause of AKI. In evaluation of leukocytes, leukopenia was protective for development of complications, while leukocytosis was significantly correlated with development of AKI, which may be due to rising inflammation, and inflammatory mediators leading to AKI. This was a unique association noted in this study that as TLC rises, so the chances of AKI also rise and vice versa, there are very few studies which had correlated leukocytosis with AKI and had similar outcome [14,18]. Thrombocytopaenia was also significant in AKI patients, which may be due to severe acute inflammation leading to platelet adhesions and thrombocytopaenia [18,22,23]. Hypovolemia or shock and mortality both were insignificant in AKI patients, implying that shock doesn't predispose to AKI. However, there were wide variations in shock, mortality and acidosis in *P. vivax* patients few had significant correlations, while others negate any correlation. As per present study due to absence of shock in AKI patients, cause of AKI being prerenal was unlikely, which was well established in various other studies, even proven with kidney biopsy [12,13,20]. So overall, after evaluation of laboratory parameters, it can be derived that, the cause of AKI was not tubular or prerenal. Hence, most likely cause being interstitial intrinsic AKI due to inflammation caused by some strains of *P. vivax* malaria [14,18]. However, even the presence of AKI doesn't increase chances of mortality in these patients. So malarial strains causing AKI, increase morbidity, hospital stay, and treatment cost, but mortality was not raised because of these strains [4-6].

So as discussed above there were multiple variables that were significant and hence there was a confusion of actual variables associated with AKI pathogenesis. Hence, to remove confounding variables and to isolate the most strongly associated variables/factors associated with AKI, regression equations were applied to all possible parameters causing AKI. In univariate analysis, findings were exactly similar as written above with extra additional findings of significant hyponatraemia in AKI patients [20], which may be attributed to volume overload causing hypervolemic hyponatraemia, which is very well studied in AKI [20]. Another additional finding was the TLC counts, that signifies leukopenia is protective, however even a normal leukocyte count is a risk factor for AKI but leukocytosis is definitely a grave sign with p-value of 0.001 suggesting inflammation to be the main role for the pathogenesis of AKI [17].

To correlate the variables multivariate regression analysis was done only on the variables which were found significant on univariate analysis. Postmultivariate analysis, only clinical parameter found to be significant was age [4,18,19], while for laboratory parameters total bilirubin levels [4,6,14,17,21], leucocytosis [5,17] were highly significant, hyponatraemia [6,20,23] was borderline significant with a p-value of 0.057. Hence, hepatopathy with or without transaminitis and AKI with hyponatraemia were most closely correlated [4,6,19]. Pathogenesis of this AKI can be postulated by the absence of severe haemolysis or shock in this group hence ruling out intrinsic tubular or prerenal causes respectively. So, after ruling out these causes, intrinsic AKI due to interstitial nephritis was the most probable cause for AKI [12,13,18]. This pathogenesis of interstitial nephritis was either linked to severe inflammation caused by malarial *P. vivax* infection, as correlated by leukocytosis, thrombocytopaenia, and mild transaminitis or this may also be attributed to predilection of some strains to specific microvasculature, hence causing AKI and hepatopathy [4,14,16] in few while ARDS, encephalopathy, bleeding, metabolic acidosis, etc., in others. So, inflammation theory may explain AKI, but can't explain why different patients have different complications and why some of them occur together more commonly than others.

In general, clinicians should not consider malaria caused by *P. vivax* to be benign and have a high degree of suspicion for the development of AKI, especially in older patients or the ones with derangements in bilirubin or high leukocyte count [4,6,13]. Early diagnosis and recognition of AKI can lead to early referral/administration of the renal replacement therapy along with other aggressive treatment administration which can considerably reduce the morbidity [4-6].

Limitation(s)

The present study had multiple limitations which had led to underestimation of AKI such as AKIN criteria for urine output was not taken into account for all patients as this was retrospective analysis. Secondly, a fixed criteria for diagnosis of AKI was used i.e., creatinine >1.5 mg/dL, however as per AKIN criteria, a patient whose baseline creatinine maybe 0.6 mg/dL, even a creatinine value of 1.0 mg/dL should be considered AKI. Hence, if a baseline creatinine would have been available then AKI would have been diagnosed more accurately.

CONCLUSION(S)

The AKI is a common complication of *P. vivax* malaria and correlates with the morbidity of the disease. Incidence of AKI was higher in elderly patients, those with raised bilirubin, or with a raised leukocyte count. Hence, patients with the above mentioned characteristics should warrant for a stringent monitoring schedule. Such patients should be maintained on a positive fluid balance. Patients who develop AKI should be under close monitoring for hepatic dysfunction. Further studies are needed to evaluate the cause effect relationships and the temporal association of AKI and hepatic dysfunction caused by *P. vivax*.

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PLAGIARISM CHECKING METHODS: [Jain H et al.]
- Plagiarism X-checker: Feb 28, 2023
- Manual Googling: Apr 13, 2023
- iThenticate Software: May 12, 2023 (8%)

ETYMOLOGY: Author Origin

EMENDATIONS: 5

AUTHOR DECLARATION:
- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? Yes
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. NA

Date of Submission: **Feb 22, 2023**
Date of Peer Review: **Mar 29, 2023**
Date of Acceptance: **Jun 17, 2023**
Date of Publishing: **Jul 01, 2023**