

# Acute pancreatitis due to malaria: A case report of five patients and review of literature

Kundavaram Paul Prabhakar Abhilash<sup>1</sup>, Atif Shaikh Iqbal Ahmed<sup>1</sup>,  
Sowmya Sathyendra<sup>1</sup>, Ooriapadickal Cheria Abraham<sup>1</sup>

<sup>1</sup>Department of General Medicine, Christian Medical College, Vellore, Tamil Nadu, India

## ABSTRACT

Malaria is endemic in large parts of India and can cause multiorgan failure and death. Acute pancreatitis as a complication is rare and is potentially fatal. This case series describes five adult patients between 2005 and 2010 who presented with a short duration febrile illness and diagnosed to have malaria with acute pancreatitis. The mean age of the five patients with acute pancreatitis was 40.4 years and four of them were males. None of them were alcohol consumers and did not have any other risk factor for acute pancreatitis. *Plasmodium falciparum* was responsible for all the cases. Pancreatic enzymes were significantly elevated in all the patients with a mean serum lipase level of 1795 U/L (normal value: <190 U/L) and a mean serum amylase level of 584 U/L (normal value: <100 U/L). Ultrasonography evidence of acute pancreatitis (bulky pancreas) was seen in two patients, and a further two patients had minimal left-sided pleural effusion. Thrombocytopenia (platelet count <100,000/cumm), renal dysfunction (serum creatinine >1.4 mg/dl), and hyperbilirubinemia were seen in all the patients. One patient died due to multiorgan failure. Acute pancreatitis is a very rare complication of malaria, and a high index of suspicion is required in patients presenting with severe malaria and abdominal pain.

**Keywords:** Complication, malaria, pancreatitis

## Introduction

Malaria is a common protozoan disease in tropical countries caused by the genus *Plasmodium* transmitted by the bite of infected anopheles mosquitoes. Severe complicated malaria is most frequently caused by *Plasmodium falciparum* and much less commonly by *Plasmodium vivax* or other *Plasmodium* species. Abdominal pain as a presenting complaint has been reported in 21.4–33.5% of patients with malaria and is usually mild and transient.<sup>[1]</sup> It occasionally can be severe and persistent, especially with complications such as splenic infarction, splenic rupture, splenic torsion, acalculous cholecystitis, and hepatitis. However, acute pancreatitis causing abdominal pain and complicating malaria is very rare and there are only 12 cases reported from

literature till now. We describe five patients who were diagnosed to have malaria complicated by acute pancreatitis.

## Case Report

Five patients admitted in the Christian Medical College, Vellore between 2005 and 2010 with a diagnosis of malaria and acute pancreatitis are described. Malaria was confirmed by demonstration of the characteristic ring forms of either *P. falciparum* or *P. vivax* on a thin blood smear. Acute pancreatitis was diagnosed in the presence of at least two of the following criteria: Acute, persistent, and severe abdominal pain not subsiding with proton pump inhibitors, elevation in serum lipase or amylase to three times greater than the upper limit of normal, and characteristic findings of acute pancreatitis on radiographic imaging. Other causes of pancreatitis such as alcohol, gall stones, and hypercalcemia were ruled out.

**Address for correspondence:** Dr. Kundavaram Paul Prabhakar Abhilash,  
Department of General Medicine, Christian Medical College,  
Vellore - 632 004, Tamil Nadu, India.  
E-mail: kppabhilash@gmail.com

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In addition, a Medline search was performed to identify the cases of malaria with acute pancreatitis reported in the literature using the search terms “malaria,” “*P. falciparum*,” “*P. vivax*”, and “pancreatitis.” Cases were accepted where information regarding the demographics, laboratory tests, and the outcome was provided.

This study was approved by the Institutional Review Board of Christian Medical College, Vellore (IRB Min No. 8327), and patient confidentiality was maintained using unique identifiers.

## Results

The mean age of the patients was 40.4 years, and 4 out of 5 were males. All the patients were healthy before the current illness, and none had prior history of chronic alcohol consumption or cholelithiasis. None of the patients had any prior history of abdominal procedures including endoscopic retrograde cholangiopancreatography. The mean duration of fever before presentation was 7.8 days. All the patients had a history of abdominal pain, which was central and did not improve with proton-pump inhibitors. The pain started 2–9 days after the onset of fever. None of the patients had pain radiating to the back. All of these patients had *P. falciparum* infection with a variable parasitic index, ranging from 0.14 to 32, as demonstrated on a thin film.

Pancreatic enzymes were significantly elevated in all, with a mean serum lipase level of 1795 U/L (normal value: <190 U/L) and a mean serum amylase level of 584 U/L (normal value: <100 U/L). Ultrasonography evidence of acute pancreatitis (bulky pancreas) was seen in two patients, and a further two patients had minimal left-sided pleural effusion. Thrombocytopenia (platelet count <100,000/cumm), renal dysfunction (serum creatinine >1.4 mg/dl) and hyperbilirubinemia were seen in all the patients.

All the patients were treated with an artemisinin-based combination therapy along with doxycycline. Acute pancreatitis was managed conservatively with nil oral intake and opioid pain killers. Gradual feeds were started once the pain reduced. One of the patients (Case 5) required a nasojunal tube placement for pancreatitis. Clinical

characteristics and medications including antibiotics are mentioned in Table 1. Four of the patients required hemodialysis for renal dysfunction. One patient (Case 3) who presented with a parasitic index of 0.5% severe malaria with hepatic, renal, neurological and hematological dysfunction and required invasive ventilator support and multiple sessions of hemodialysis. Despite these aggressive measures, he succumbed to the illness on the 7<sup>th</sup> day of admission. The patient profile, laboratory investigations, and outcome of these five patients are shown in Table 2.

## Discussion

India's expansive geography and tropical environment are ideal for sustaining malaria vectors, and it accounts for 76% of cases from Southeast Asia. Although the overall deaths have reduced since the launch of National Malaria Control Program, it is argued that reports of approximately 1000 deaths per year are grossly underestimated.<sup>[2]</sup> Multiorgan involvement or dysfunction is reported in both *P. falciparum* and *P. vivax* infections. *P. falciparum* contributes to 52% of the total malaria cases in India and is responsible for the majority of deaths.<sup>[2]</sup> Acute pancreatitis as a complication of malarial infection, though rare, has been usually reported with *P. falciparum*. It has been associated with at least four deaths, in the reported 15 cases reported in literature based on our Medline search. Primary care physicians deal mostly with vivax malaria in most parts of India as it is usually the predominant species. In our case series, two patients had pancreatitis due to *P. vivax* malaria. Recent studies have shown that vivax malaria can be as severe as falciparum malaria, a fact consistent with our finding of a severe complications such as pancreatitis due to *P. vivax*.<sup>[3]</sup>

In our case series, one patient died as a result of multiorgan involvement including acute pancreatitis, the causative organism being *P. falciparum*. Only two patients (Case 1 and Case 4) had a high parasitic index. Seshadri *et al.*, Mandal *et al.* and Mohapatra and Gupta have reported pancreatitis with very high parasitic indices.<sup>[4-6]</sup> Hyperparasitemia though a predictor for severe malaria is not the only marker for severity. In patients not previously exposed to malaria poor immunity may result in severe disease even with parasitic index as low as 2%. The pathogenesis of pancreatitis is probably not different from that of other

**Table 1: Clinical characteristics and medications**

	Case 1	Case 2	Case 3	Case 4	Case 5
Severe central abdominal pain, not settling with antacids	Present	Present	Present	Present	Present
Duration of fever	8 days	7 days	10 days	7 days	7 days
Duration of abdominal pain	6 days	1 day	1 day	4 days	1 day
Radiation to back	No	No	No	No	No
Analgesic therapy	Opoids, Diclofenac sodium	Opoids	Opoids	Opoids	Opoids
Naso-jejunal tube	No	No	No	No	Yes
Anti-malarials	Artesunate, Doxycycline	Artesunate, Doxycycline	Artesunate, Doxycycline	Artesunate, Doxycycline	Artesunate, Doxycycline
Antibiotics	Cefotaxime	Piperacillin + Tazobactam	Piperacillin + Tazobactam	Cefotaxime	Cefotaxime

**Table 2: Profile of five cases of malaria with acute pancreatitis**

Number	Age/sex	Species	PI (%)	Lipase (U/L)	Amylase (U/L)	Hemoglobin (g%)	WBC (cells/cumm)	Platelet (cumm)	Serum creatinine (mg%)	Urea (meq/L)	Serum bicarbonate (mEq/L)	Total bilirubin (mg%)	Direct bilirubin (mg%)	Total protein (g%)	Serum albumin (g%)	SGOT (U/L)	SGPT (U/L)	ALP (U/L)	Outcome
Case 1	50/male	Falciparum	0.5	917	348	8.5	11800	77,000	4.6	188	12	29.7	22	5.2	2.5	62	54	136	Alive
Case 2	35/male	Falciparum	12	2809	788	6.6	9700	39,000	6.9	267	11	12.2	9.6	5	2.3	182	38	140	Alive
Case 3	65/male	Falciparum	0.5	935	232	9.9	8700	68,000	8.8	394	7	25.4	16.8	5.4	2.3	59	80	272	Dead
Case 4	21/male	Falciparum	32	1233	609	8.2	6700	14,000	4.3	212	13	10.9	6.9	4.2	2	389	125	55	Alive
Case 5	31/female	Falciparum	0.14	3080	943	3.8	9900	59,000	5.3	11	11	2.5	1.5	5.4	2	53	30	70	Alive

PI: Parasitic index; WBC: White blood cell; SGOT: Serum glutamic oxaloacetic transaminase; SGPT: Serum glutamic pyruvate transaminase; ALP: Alkaline phosphatase

**Table 3: Literature review of patients with malaria and acute pancreatitis**

Case report	Year	Age/sex	Species	PI	Lipase	Amylase	Hemoglobin (g %)	WBC (/cumm)	Platelet	Serum creatinine	Total bilirubin	SGOT (U/L)	SGPT (U/L)	ALP (U/L)	Outcome
Sarma and Kumar <sup>[7]</sup>	1998	17/male	Falciparum	1.5%		2132	9.8	11,800		145	31	84	70		Dead
Desai et al. <sup>[8]</sup>	2001	40/male	Falciparum	0.5%	1329	535	10.6	10,000	48,000	6.3	22.8	91	156	65	Alive
Seshadri et al. <sup>[4]</sup>	2001	58/female	Falciparum	0.5%	1037	133	5.1	10,000	20,000	1.8	14.9	115	35	52	Alive
	2008	21/male	Falciparum and vivax	45%	5217	1712	7.2	9100	31,000	5.8	53.6	197	101	112	Alive
Badhal et al. <sup>[9]</sup>	2009	34/male	Falciparum	1920/ $\mu$ l		1465	3.2	17,700	30,000	4					Dead
Thapa et al. <sup>[10]</sup>	2010	13/male	Falciparum		4562		8	12,500	67,000	4.6	14.5	168	126	94	Alive
Kumar et al. <sup>[11]</sup>	2010	35/male	Falciparum	60%	2460	472	7.6	5800	70,000	Normal	4.7	364	140	71	Alive
Mandal et al. <sup>[5]</sup>	2011	35/male	Falciparum	40%	2255	783	10	7800	94,000	2.9	17.5	49	40	419	Dead
Sharma et al. <sup>[12]</sup>	2011	17/male	Vivax			1234	13.4	12,200	34,000	3.1	4.2	56	68	148	Dead
Mohapatra and Gupta <sup>[6]</sup>	2011	45/male	Falciparum	8000/ $\mu$ l	608	1200	6	12,000	170,000	4.6	3.3	30	42	52	Alive
	2012	28/female	Falciparum	9200/ $\mu$ l	860	2200	10.2	18,000	175,000	1.8	1.8	30	42	52	Alive
	2012	38/male	Falciparum	6200/ $\mu$ l	960	2050	8	16,000	220,000	1.6	1.4	30	41	62	Alive
Sundriyal et al. <sup>[13]</sup>	2013	35/male	Vivax		414	756									Alive
Ghosh et al. <sup>[14]</sup>	2014	40/male	Falciparum		250	525	10.2	15,100	275,000	1.2	4.4				Alive
Singh et al. <sup>[15]</sup>	2014	24/male	Falciparum	60%	1200	2800	13	11,600	160,000	1.1	0.3	39	23	40	Alive

PI: Parasitic index; WBC: White blood cell; SGOT: Serum glutamic oxaloacetic transaminase; SGPT: Serum glutamic pyruvate transaminase; ALP: Alkaline phosphatase

organ involvement in malaria and includes cytoadherence of infected red blood cells (RBCs) to the vascular endothelium, sequestration of RBCs, and rosetting. This is especially true in falciparum malaria. However, sequestration occurring in other organs including pancreas is not known as of now.

In our literature search, we found only 15 cases of malaria complicated by pancreatitis and their profile is summarized in Table 3.<sup>[4-15]</sup>

In our country, malaria continues to be a major public health problem in India, accounting for sizeable morbidity and mortality. The burden of falciparum malaria is very high in places such as Orissa and the Northeastern states where the mortality rate due to malaria is even higher. Fever and abdominal pains are very common presentations to the emergency department and pancreatitis accounts for about 11% of those cases.<sup>[16]</sup> Primary care physicians' deal with these common problems in their daily practice and their etiology quite often remains a diagnostic dilemma. Greater awareness of the rare complications of a common infection such as malaria is essential to recognize it early and to initiate early management or early referral to a higher center.

## Conclusion

Physicians may be familiar with the various complications of falciparum malaria but less so with acute pancreatitis. The ability to properly diagnose and to manage acute pancreatitis due to malaria is particularly important in malaria-endemic areas such as India. Maintaining a high index of suspicion for acute pancreatitis in patients with malaria presenting with abdominal pain can be important in the early diagnosis and prevention of pancreatic complications.

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## Conflicts of interest

There are no conflicts of interest.

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