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Clinical Profile, Complications and Outcomes of Patients Having Malaria

KEYWORDS: Malaria, mixed species, clinical features, complications

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ABSTRACT ***Background:*** *Malaria, one of the oldest diseases known to mankind, can have a variety of clinical pictures, from acute to chronic, and from simple fever to life threatening multiple organ failure. The clinical picture dif fers with the species of parasite involved.*
Objective: *To study the different clinical features and complications following malaria due to different parasites.*
Methodology: *A hospital based cross sectional study was conducted among 213 patients admitted with malaria, between April 2014and March 2016 in the medicine wards of a tertiary care hospital of eastern India. In all cases a detailed clinical history and repeated thorough physical examination were carried out which was followed by blood smear (thick and thin) and subsequently required routine and special investigations as dictated by the condition and presentation of the patient.*
Results: *Among the study population, 94 had confirmed Plasmodium vivax, 89 had infection with Plasmodium falciparum and the rest (30) had dual infection with both Plasmodium vivax and Plasmodium falciparum. The proportion of nausea/ vomiting and headache was significantly higher among patients with confirmed Pl.falciparum alone. Severe anaemia and hypoglycaemia were significantly higher in patients with mixed species infection*
Conclusion *The present study has revealed that mixed species malaria with multi organ involvement is potentially fatal dis ease with a very high mortality. However, larger studies will be needed to judge the extent of complications.*

Introduction

Malaria is one of the oldest diseases known to mankind that has had intense bearing on our history. But for malar-ia, the conclusions of many a wars and fortunes of many a kings would have been different. For eras it prevented any economic development in vast regions of the earth. It con-tinues to be an enormous social, economical and health problem, particularly in the tropical countries.[1]

Malaria is the one of the most wide spread disease of the planet.[2] The World Health Organization estimates about 3.2 billion people – almost half of the world's population – are at risk of malaria, with 90% of this burden being in Africa. In the Southeastern Asian Region of WHO, 1.2-bil lion are exposed to the risk of malaria, most of who live in India. However, Southeast Asia contributed to 2.5-mil lion cases to the global burden of malaria.[3,4] Of this, India alone contributes to 61 percent of malaria cases and 41 per cent of malaria deaths. [5]

Malaria is endemic in all of India except at elevations above 1800 meters and in some coastal areas. In most parts of the country, periodic epidemics of malaria occur every five to seven years.[6]Although the total number of cases of malaria in India has stabilized somewhat over the past ten years, there has been an increase in the number of P. falciparum cases. 65% of malaria infections in India are caused by P. vivax and 35% are caused by P. falcipa rum.[3]

In India, the epidemiology of malaria is complex because of geo-ecological diversity, multi-ethnicity, and wide distri bution of nine anopheline vectors transmitting three Plas modial species: P. falciparum, P. vivax, and P. malariae. Anopheles culicifacies is widely distributed and is the prin cipal vector of rural malaria, An. stephensi is the primary urban vector, An. fluviatilis is a vector in the hills and foot hills, and An. minimus, An. nivipes, An. philippinensis, and An. dirus are vectors in the northeast and An. sundaicus is restricted to Andaman and Car Nicobar islands.[7]

In India, the burden is generally higher in men than women in all age groups.[8] Children in the states of-As sam, Arunachal Pradesh and Rajasthan had a higher-inci dence of malaria than adults, whereas in the indo-Gangetic plains, the situation was reversed.[9]

In India, reports suggested that mortality in complicated P. falciparum malaria in Vellore in the southern state of-Ta mil Nadu was 7.9%, whereas in Jabalpur (Madhya Pradesh) and Rourkela (Orissa), it was 25.6% and 30%, respectively. A general shift in the clinical profile in patients with com plicated malaria has been observed, and multiple organ dysfunction/failure is becoming a common feature.[11,12]

Malaria has a variety of clinical pictures, from acute to chronic, and from simple fever to life threatening multiple organ failure. The clinical picture differs with the species of parasite involved, but also with the immune status of the patient. P. falciparum is by far the most dangerous, with the most dramatic symptoms and signs.[13]

Clinical syndromes like black water fever, cerebral ma laria, hyperreactive malarial splenomegaly are recognized as distinct entities. In recent years minor, atypical malaria syndromes have been recognized. The boundary between malaria "infection" and malaria "disease" is not clear. [14]

The classic malarial paroxysms, in which fever spikes, chills, and rigors occur at regular intervals, are relatively unusual and suggest infection with P. vivax or P. ovale. Although childhood febrile convulsions may occur with any of the malarias, generalized seizures are specifically associated with falciparum malaria and may herald the development of cerebral disease.[15]

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Many clinical abnormalities have been described in acute malaria, but most patients with uncomplicated infections have few abnormal physical findings other than fever, malaise, mild anemia, and (in some cases) a palpable spleen. Anemia is common among young children living in areas with stable transmission, particularly where resistance has compromised the efficacy of antimalarial drugs. Mild jaundice is common among adults; it may develop in patients with otherwise uncomplicated falciparum malaria and usually resolves over 1–3 weeks.[16]

In this context, the present study was planned to study the different clinical features and complications following malaria due to different parasites.

Methodology
A hospital based cross sectional study was conducted among patients admitted with malaria, between April 2014and March 2016 in the medicine wards of a tertiary care hospital of eastern India.

Study participants were defined as all patients more than 12 years with malaria, selected on the basis of clinical presentation and subsequent peripheral blood smear (thick and thin films) examination with Leishman's stain showing the presence of malaria parasites. Only patients with peripheral blood smear positive for malaria parasites were included. In clinically suspected but slide negative cases, Rapid Diagnostic Test for malaria –Parachek test was employed to confirm the diagnosis.

However, patients having malaria associated with rheumatic fever, pneumonia, presence of any other active infection or sepsis, present or past tuberculosis, enteric fever were excluded.

Prior to conduction of the study, permission was taken from the Institutional Ethics Committee Written, informed consent was obtained from all subjects and the study was performed in accordance with the tenets of the Declaration of Helsinki 2013.

Data was collected from the patients and/or their relatives with the help of a brief structured questionnaire concerning signs and symptoms of malaria The questionnaire was interviewer – administered and done by a single investigator. In all cases a detailed clinical history and repeated thorough physical examination were carried out which was followed by blood smear (thick and thin) and subsequently required routine and special investigations as dictated by the condition and presentation of the patient. Severe falciparum malaria was diagnosed on the basis of the features in the presence of asexual parasitemia.[17]

Statistical analysis:
The data collected were entered in Microsoft Excel data sheet after checking for completeness and consistency. Data are presented with the principles of descriptive statistics. Categorical data were analysed using Chi-square test and t-test was used for continuous variables. SPSS 20 was used as the data analysis software.

Results:
The final analysis included 213 patients ; of which 94 had confirmed Plasmodium vivax, 89 had infection with plasmodium falciparum and the rest (30) had mixed species infection. The mean age of the study participants was 32.2 ± 14.3 years; the age of presentation was significantly high among patients suffering from Pl.falciparum. Theproportion of males were significantly higher for all the species than the female participants. The length of hospital stay was significantly higher among patients suffering from malaria due to both Pl. vivax and Pl. falciparum. (p=0.01)

Table 1 shows the proportion of different presenting-features among the patients suffering from different types of malaria. It can be seen that the proportion of nausea/vomiting and headache was significantly higher among patients with confirmed Pl.falciparum alone.

It can be seen from table 2 that the presenting features of malaria due to different species were myriad and quite different from each other. The mean values of serum sodium, potassium and albumin were significantly higher in patients with Pl. vivax. However, the pulse rate was significantly higher among patients with confirmed Pl.falciparum alone. The platelet count was significantly reduced in patients with mixed species infection.

There may be various complications among patients of malaria. Table 3 shows that severe anaemia and hypoglycaemia were significantly higher in patients with mixed species infection compared to the counterparts. More importantly, death rate was also significantly higher among patients with mixed species infection.

Discussion:
Being a common cause of huge morbidity and a number of case fatalities in every year, malaria is well recognized for its varied presentation. In 2015, the estimated annual mortality attributed to malaria ranges from 2,36,000 to 6,35, 000globally.[3] Falciparum malaria is a potentially fatal disease causing multi-organ dysfunction in the form of cerebral malaria, acute renal failure, hepatopathy, adult respiratory distress syndrome, coagulation failure, anemia, shock, hypoglycemia etc.[16]

Ali et al in his study with 76 patients found a mean age of presentation was 32 years with a standard deviation of 13.84 years and most of the patients in his series were young.[18]Similarly, Soni et al carried out a study with 144 malaria patients in which the median age of the patients was 25 years. So, the present study compares well with the above mentioned studies.[19]

Male preponderance, as was evident in the present study, has been well documented by othe authors. Ali et al[18] reported incidence in male's as78.9%. Similarly many previous studies including Dash et al[20], Mahmood et al[21], Mishra G et al[22] reported the incidence of malaria in males as 68%, 68.5%, 60% respectively.Frequent travel history, more outdoor activities and less clothing in males compared to females could be the reason for high incidence in males.[22,23]

In the present study, 156 patients (73.2%) presented with nausea and/or vomiting. Faiz M et al found vomiting in 80% of cases.[24]The increases frequency of nausea can be due to that most of the patients already received one or more medications including empirical Chloroquine therapy given by the peripheral heath workers, which is highly emetogenic.

In the present study, 59.6% of the patients had associated headache. Among the cases of falciparum malaria, 65.2% had headache which was significantly higher. Getahun et al mentioned headache in 65% of his series.[25]Chowta et al found headache in 52% of his series.[26]

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In the present study, out of 89 cases of falciparum malaria, 42 (47.7%)patients presented with jaundice. The incidence of jaundice in falciparum malaria varies in different studies from 10% to 58%.[22,27]

In this study, 90 patients presented with altered sensorium (44.9% out of 89 cases of falciparum malaria) out of which 25 cases were diagnosed as cerebral malaria. The 18 other cases with altered sensorium had dyselectrolytemia, or multiple other causes.Ali et al found the incidence of altered sensorium and cerebral malaria in falciparum malaria as 46% and 22.36% respectively. Mahmood et al found cerebral malaria in 20% of his 108 falciparum cases.[21]Getahun et al in his work with 408 patients of falciparum malaria observed 28.7% cases having cerebral malaria.[25]

In the present study, 78 cases of malaria presented with oliguria, out of which 47 patients (31%) were later diagnosed as ARF.The higher incidence of ARF in the present study may be due to multi-system involvement and long pre-hospital phase in many of these cases, leading delayed treatment.Ali et al found ARF in 40% cases.[18] Mishra et al found ARF in 37% of his patients.[22]Getahun et al in his work with 408 patients of falciparum malaria observed 3.7% cases having ARF.[25]

The complications were more pronounced in cases of mixed species infection with both Plasmodium vivax and falciparum. A study in Orissa reveals 66.6% of patients with mixed species infection had single complication and 33.3% cases had multiple complication. This may be due to higher burden of parasites. [28]

In the present study 23.5% cases had severe anemia as a complication. Mishra SK et al found anemia in 9.7% of cases. Whereas, Ali et al and Getahun et al found anemia in 72.4%, and27% of their cases respectively.[18,25]The lower incidence of anemia in the present series may be due to previous blood transfusions which the patients received during their stay in the peripheral heath care facilities before being referred to this institute for development of other more life threatening complications.

In this study, only 5.6% of patients of falciparum malaria presented with h/o Spontaneous bleeding. Out of these 5 patients, 3 patients had bleeding from gums along with sub-conjunctival hemorrhage, 1 patient had upper gastrointestinal bleed and 1 patient had epistaxis along with sub-conjunctival hemorrhage. In all of these patients, the platelet count was found to be low. Kochar et al reported 9.9% and 25.52% incidence of spontaneous bleeding, in 1994 and 2001 respectively.[27]Getahun et al found 2.2% of spontaneous bleeding in his study with 408 cases of falciparum malaria.[25]

Out of 213 cases of malaria ,23 cases representing 25% of all falciparum patients presented with Respiratory difficulty, out of which 16 (7.5%) developed ARDS.Mishra et al found ARDS in 6% of his patients[29] and Getahun et al in his work with 408 patients of falciparum malaria observed 7.4% cases having ARDS.[25] Krishnan et al reported ARDS in 26% patients of severe falciparum malaria.[30] Therefore the result in the present study is consistent with the above mentioned studies.

In this study, out of 107 patients presented with jaundice, 99 had malarial hepatitis. 77% had predominantly conjugated type of hyperbilirubinemia and in them the mean AST/ALT level was 208/189 IU/l. Most of these cases had AST/ALT value <100 IU/L. Majumdar R et al found mean AST level 98IU/L and mean ALT level 151 IU/L.[31] Manan et al recorded mean AST level 128 IU/L and mean ALT level 321 IU/L.[32]Ali et al found malarial hepatitis in 47.36% of cases.[18]Getahun et al found malarial hepatitis in 21% of cases.[25]

In the present study of 213 cases of malaria including 89 cases of falciparum malaria, 24 (11.3%) patients expired, indicating 30% mortality rate among mixed species infection cases.The highest mortality rate was found recorded in patients with ARDS (100%), followed by cerebral malaria (40%), renal failure (28%), malarial hepatitis (22%) and severe anemia (20%).Mortality was very high (50%) in patients who presented with three or more complications of malaria.

Similarly, Ali et al studied 76 cases of smear positive falciparum malaria and found an overall mortality of 28.95%.[18]Getahun et al found an overall mortality of 28.4%. The increased frequency of complication in mixed species infection may be due to the higher parasite load in these patients.

CONCLUSION

The present study has revealed that mixed species malaria with multi organ involvement is potentially fatal disease with a very high mortality. Cerebral malaria, malarial hepatitis and acute renal failure are some of the common complications observed. Prognostic studies will be needed to judge the extent of complications.

FIGURES AND TABLES

Fig.1: Gender distribution of the study population n=213

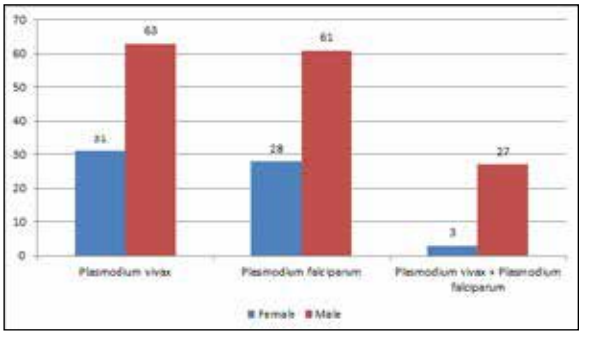

Table 1: Clinical features of malaria among the study population N=213

	Pl. vivax	Pl. falcipa-rum	Pl.vivax + Pl. falcipa-rum	Total	Pearson Chi-Square, p value
Nausea/ vomiting	71 (75.5)	70 (78.7)	15 (50.0)	156 (73.2)	9.849, .007
Pain abdo-men	17 (18.1)	18 (20.2)	5 (16.7)	40 (18.8)	.239, .887
Oliguria	34 (36.2)	32 (36.0)	12 (40.0)	78 (36.6)	.173, .917
Altered sensorium	39 (41.5)	40 (44.9)	11 (36.7)	90 (42.3)	.670, .715
Headache	57 (60.6)	58 (65.2)	12 (40.0)	127 (59.6)	5.976, .049
Convulsion	7 (7.4)	9 (10.1)	2 (6.7)	18 (8.5)	.564, .754
Haematuria	11 (11.7)	3 (3.4)	4 (13.3)	18 (8.5)	5.178, .075

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Pallor	52 (55.3)	46 (51.7)	10 (33.3)	108 (50.7)	4.457, .108
Jaundice	46 (48.9)	42 (47.7)	19 (63.3)	107 (50.5)	2.34, .311
Hepato-megaly	69 (73.4)	66 (74.2)	20 (66.7)	155 (72.8)	.669, .716
Spleno-megaly	64 (68.1)	67 (75.3)	16 (53.3)	147 (69.0)	5.122,.077

Table 2: Presenting features and laboratory findings of malaria among study population
n=213

	Pl. vivax		Pl. falciparum		Pl.vivax + Pl. falciparum		Statistics	
	Mean	SD	Mean	SD	Mean	SD	F	Sig.
Tem-perature	102.1	1.6	101.8	1.5	101.5	1.3	2.2	.113
Pulse/ min	95.5	9.0	104.2	14.6	99.9	11.4	12.3	.000
SBP	112.9	10.6	111.6	12.0	106.5	12.5	3.5	.031
DBP	72.1	10.7	71.4	10.9	67.3	11.6	2.2	.116
TLC	7930.9	2608.2	7633.7	2745.1	6689.7	2080.2	2.6	.078
ESR mm	48.1	28.1	42.8	27.3	37.8	27.7	1.8	.165
Plate-lets	1277 76.6	6250 9.6	10995 5.1	6036 1.2	86733 .3	6183 1.2	5.5	.005
RBS mg/dl	115.8	50.6	103.9	42.3	112.2	56.6	1.4	.244
Creati-nine	2.8	3.2	2.9	3.3	2.8	3.4	0.0	.995
Total bilirubin	4.1	5.5	3.3	3.0	4.5	5.1	1.0	.353
AST U/L	129.7	199.4	112.0	195.4	94.6	94.7	0.5	.629
ALT U/L	118.0	270.5	103.4	276.8	73.4	62.8	0.4	.702
ALP U/L	111.0	67.9	124.2	69.9	124.4	70.6	1.0	.384
Total pro-tein	6.6	0.8	6.3	0.8	6.4	0.8	2.2	.117
Albu-min	3.2	0.6	3.1	0.7	2.6	0.6	9.6	.000
Na+	137.0	6.8	136.0	6.5	133.5	7.9	3.1	.047
K+	4.2	0.6	3.9	0.6	3.8	0.7	9.9	.000

Table 3: Complications of malaria among the study pop ulation
n=213

Complica-tions	Pl. vivax	Pl. falcipa-rum	Pl.vivax + Pl. falci-parum	Total	Pearson Chi-Square, p value
Malarial Hepatitis	47 (50.0)	37 (41.6)	15 (50.0)	99 (46.5)	1.479, .477
ARF	21 (22.3)	20 (22.5)	6 (20.0)	47 (22.1)	0.087, .957
Severe anemia	17 (18.1)	20 (22.5)	13 (43.3)	50 (23.5)	8.156, .017
Spontaneous bleeding	8 (8.5)	5 (5.6)	2 (6.7)	15 (7.0)	.592,.744
Hypoglyce-mia	18 (19.1)	26 (29.2)	10 (33.3)	54 (25.4)	6.686, .035
Acidosis	7 (7.4)	9 (10.1)	2 (6.7)	18 (8.5)	.564, .754
Shock	12 (12.8)	9 (10.1)	3 (10.0)	24 (11.3)	.378, .828
ARDS	12 (12.8)	3 (3.4)	1 (3.3)	16 (7.5)	3.622, .163
Death	0 (0.0)	15 (16.9)	9 (30.0)	24 (11.3)	25.244, .000

REFERENCES

1. Carter R, Mendis KN. Evolutionary and Historical Aspects of the Burden of Malaria. Clinical Microbiology Reviews. 2002;15(4):564-594. doi:10.1128/CMR.15.4.564-594.2002.
2. Hay SI, Cox J, Rogers DJ, Randolph SE, Stern DI, Shanks GD, Myers MF, Snow RW. Climate change and the resurgence of malaria in the East African highlands. Nature. 2002 Feb 21;415(6874):905-9.
3. World Health Organization. World malaria report 2015. Geneva: World Health Organization; 2015.
4. World Health Organization. Global technical strategy for malaria 2016–2030. Geneva: World Health Organization; 2015.
5. Sharma RK, Thakor HG, Saha KB, Sonal GS, Dhariwal AC, Singh N.Malaria situation in india with special reference to tribal areas. Indian J Med Res 141, May 2015, pp 537-545
6. Sharma VP. Re-emergence of malaria in India. Indian J Med Res. 1996 Jan;103:26-45.
7. Kumar A, Chery L, Biswas C, et al. Malaria in South Asia: Prevalence and control. Actatropica.2012;121(3):10.1016/j.actatropica.2012.01.004.
8. Medical Certification of Cause of Death—1998. New Delhi: Ministry of Home Affairs; 2002.
9. Das NG, Gopalakrishnan R, Talukdar PK, Baruah I. Diversity and seasonal densities of vector anophelines in relation to forest fringe malaria in district Sonitpur, Assam (India). Journal of Parasitic Diseases: Official Organ of the Indian Society for Parasitology. 2011;35(2):123-128. doi:10.1007/s12639-011-0053-4.
10. Dev V, Sangma BM, Dash AP. Persistent transmission of malaria in Garo hills of Meghalaya bordering Bangladesh, North-east India. Malar J. 2010;9:263. doi: 10.1186/1475-2875-9-263.
11. Kumar A, Valecha N, Jain T, et al. Burden of Malaria in India: Retrospective and Prospective View. In: Breman JG, Alilio MS, White NJ, editors. Defining and Defeating the Intolerable Burden of Malaria III: Progress and Perspectives: Supplement to Volume 77(6) of American Journal of Tropical Medicine and Hygiene. Northbrook (IL): American Society of Tropical Medicine and Hygiene; 2007 Dec. Available from: http://www.ncbi.nlm.nih.gov/books/NBK1720/
12. Shukla MM, Singh N, Singh MP, et al. Cerebral malaria in Jabalpur. Indian J Malariol. 1995;32:70–5.
13. Trampuz A, Jereb M, Muzlovic I, Prabhu RM. Clinical review: Severe malaria.Critical Care. 2003;7(4):315-323.
14. Crutcher JM, Hoffman SL. Malaria. In: Baron S, editor. Medical Microbiology. 4th edition. Galveston (TX): University of Texas Medical Branch at Galveston; 1996. Chapter 83. Available from: http://www.ncbi.nlm.nih.gov/books/NBK8584/
15. Patel DN, Pradeep P, Surti MM, Agarwal SB. Clinical Manifestations of Complicated Malaria – An Overview. JIACM 2003; 4(4): 323-31
16. White NJ, Breman JG. Harrisons Principles of Internal Medicine, 19th ed, Kasper D, Fauci A, Hauser S, et al (Eds), McGraw Hill, New York 2015
17. Severe falciparum malaria. World Health Organization, Communicable Diseases Cluster.Trans R Soc Trop Med Hyg. 2000 Apr; 94 Suppl 1:S1-90.
18. Ali H, Ahsan T, Mahmood T, Bakht SF, Farooq MU, Ahmed N. Parasite density and the spectrum of clinical illness in falciparum malaria. J Coll Physicians Surg Pak. 2008 Jun 1;18(6):362-8..
19. Soni S, Dhawan S, Rosen KM, Chafel M, Chishti AH, Hanspal M. Characterization of events preceding the release of malaria parasite from the host red blood cell. Blood Cells Mol Dis.2005;35:201–211.
20. Dash AP, Adak T, Raghavendra K, Singh OP. The biology and control of malaria vectors in India. Current Science. 2007;92:1571–1578.
21. Mahmood A, Yasir M. Thrombocytopenia: A predictor of Malaria among febrile patients in Liberia. Infect Dis J 2005; 14:41–4.
22. Mishra SK, Mohapatra S, Mohanty S. Jaundice in falciparum malaria.-Jl ACM. 2003;4(1):12-3.

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23. Park K. Park's Textbook of Preventive and Social Medicine. 22 nd ed. Jabalpur, India: M/s Banarsidas Bhanot Publishers; 2013. p. 209-25
24. Faiz MA, Rahman MR, Hossain MA, Rashid HA, 1998. Cerebral malaria—a study of 104 cases. Bangladesh Med Res Counc Bull 24: 35–42
25. Getahun A, Deribe K, Deribew A. Determinants of delay in malaria treatment-seeking behaviour for under-five children in south-west Ethiopia: a case control study. Malaria Journal. 2010 Nov 11;9(1):1.
26. Chowta MN, Chowta N. Study of Clinical Profile of Malaria at KMC Hospital, Attavar. Journal of Clinical and Diagnostic Research. 2007;1(3):110-5.
27. Kochar DK, Saxena V, Singh N, Kochar SK, Kumar SV, Das A. Plasmodium vivax malaria. Emerg Infect Dis. 2005 Jan 1;11(1):132-4.
28. Mohapatra MK, Dash LK, Bariha PK, Karua PC. Profile of mixed species (Plasmodium vivax and falciparum) malaria in adults. J Assoc Physicians India. 2012 Oct;60:20-4.
29. Mishra SK, Mohanty S, Mohanty A, Das BS. Management of severe and complicated malaria. Journal of postgraduate medicine. 2006 Oct 1;52(4):281.
30. Krishnan A; Karnad DR. Severe falciparum malaria: An important cause of multiple organ failure in Indian intensive care unit patients. Critical Care Medicine 2003; 31 (9): 2278-84
31. Mazumdar S. Prevalence, risk factors and treatment-seeking behaviour for malaria: the results of a case study from the Terai region of West Bengal, India. Annals of Tropical Medicine & Parasitology. 2011 Apr 1;105(3):197-208.
32. Manan JA, Ali H, Lal M. Acute renal failure associated with malaria. J Ayub Med Coll Abbottabad. 2006;18(4).