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Original Research

Comparative Clinical Profile of Plasmodium falciparum, Plasmodium vivax, and Mixed Malaria Infections

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ABSTRACT

Aim: This study aimed to evaluate and compare the clinical profiles of patients with *Plasmodium falciparum*, *Plasmodium vivax*, and mixed malaria infections, focusing on demographic characteristics, clinical symptoms, laboratory findings, and complications to enhance diagnosis and treatment strategies.

Material and Methods: An observational, cross-sectional study was conducted at a tertiary care hospital involving 120 patients with confirmed malaria diagnoses. Participants were categorized into three groups: *P. falciparum* (Group A), *P. vivax* (Group B), and mixed infections (Group C). Clinical and laboratory data were collected, including hematological and biochemical parameters, parasitemia levels, and complication frequencies. Statistical analyses, including ANOVA and chi-square tests, were performed to identify significant differences among the groups.

Results: Mixed infections exhibited the highest severity with prolonged hospital stays (5.6 ± 2.0 days), lower hemoglobin levels (8.7 ± 1.3 g/dL), and elevated parasitemia levels (28,300 ± 6,100 parasites/μL) compared to single-species infections. Complications, including severe anemia (35%), thrombocytopenia (60%), and jaundice (40%), were more frequent in mixed infections. *P. falciparum* showed higher rates of cerebral malaria (10%) and multi-organ dysfunction (15%), while *P. vivax* had relatively milder presentations.

Conclusion: Mixed malaria infections present the most severe clinical profiles compared to single-species infections, emphasizing the need for accurate diagnostics and prompt treatment. Tailored therapeutic strategies are crucial, particularly in endemic regions where co-infections are prevalent, to improve patient outcomes and reduce malaria-related morbidity.

Keywords: Plasmodium falciparum, Plasmodium vivax, Mixed malaria infections, Clinical profile, Malaria complications

Introduction

Malaria, a life-threatening disease caused by parasites of the genus *Plasmodium*, remains a significant global health challenge, particularly in tropical and subtropical regions. Among the five *Plasmodium* species known to infect humans, *Plasmodium falciparum* and *Plasmodium vivax* account for the majority of malaria cases worldwide. While *P. falciparum* is predominantly associated with severe and life-threatening complications, *P. vivax* has historically been regarded as less severe, though recent evidence suggests it can also lead to significant morbidity. Mixed infections, involving simultaneous infections with *P. falciparum* and *P. vivax*, pose unique challenges to diagnosis, treatment, and clinical management.The clinical presentation of malaria is diverse, influenced by the infecting species, the patient's immunity, age, and comorbidities, as well as environmental and epidemiological factors. *P. falciparum* infections are often characterized by severe manifestations such as cerebral malaria, acute respiratory distress syndrome (ARDS), multi-organ failure, and severe anemia. In contrast, *P. vivax* infections frequently present with recurrent fever, chills, splenomegaly, and anemia, albeit generally milder than in *P. falciparum* cases. However, *P. vivax*

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can also lead to severe complications, including acute kidney injury, severe thrombocytopenia, and even fatal outcomes. The combination of both species in mixed infections often results in overlapping clinical features, complicating diagnosis and amplifying the severity of the disease.[1]Mixed infections are particularly challenging due to their complex pathophysiology. The concurrent presence of *P. falciparum* and *P. vivax* can lead to synergistic effects, exacerbating disease severity and complicating treatment protocols. Patients with mixed infections often experience higher parasite loads, more severe anemia, and an increased risk of complications compared to those with single-species infections. Additionally, mixed infections can confound diagnostic techniques, particularly microscopy and rapid diagnostic tests (RDTs), potentially delaying appropriate treatment. Accurate and timely diagnosis is critical to effectively manage these cases, yet the reliance on conventional diagnostic tools in resource-limited settings often results in underdiagnosis or mismanagement.The burden of malaria varies significantly across different regions, influenced by factors such as climate, vector distribution, and the prevalence of drug-resistant strains. *P. falciparum* dominates in sub-Saharan Africa, where the majority of malaria-related deaths occur, whereas *P. vivax* is more prevalent in Asia and the Americas. Mixed infections are most commonly reported in regions where both species co-exist, such as Southeast Asia, the Indian subcontinent, and parts of South America. The epidemiology of mixed infections highlights the importance of understanding local transmission dynamics and implementing targeted interventions.[2] The clinical management of malaria is further complicated by the increasing prevalence of drug resistance. *P. falciparum* has developed resistance to nearly all antimalarial drugs, including artemisinin-based combination therapies (ACTs), the current first-line treatment. Similarly, *P. vivax* is exhibiting resistance to chloroquine and primaquine, the standard treatments for blood-stage and liver-stage infections, respectively. Mixed infections necessitate the use of combination therapies effective against both species, which may increase the risk of adverse drug reactions and complicate treatment adherence.[3] Despite advancements in malaria control efforts, the disease continues to pose a significant health and economic burden, particularly in endemic regions. Malaria is not only a leading cause of morbidity and mortality but also a major contributor to poverty, impacting productivity, education, and overall quality of life. Vulnerable populations, including pregnant women, children under five, and individuals with limited access to healthcare, bear the greatest burden of the disease. Understanding the clinical profile of *P. falciparum*, *P. vivax*, and mixed infections is critical to developing effective diagnostic, therapeutic, and preventive strategies.[4,5]Research on mixed malaria infections remains limited compared to single-species infections, underscoring the need for comprehensive studies to elucidate their clinical and epidemiological characteristics. Mixed infections are often underreported due to diagnostic challenges, and their true burden may be significantly higher than current estimates suggest. Improved diagnostic tools, such as polymerase chain reaction (PCR)-based methods, and robust surveillance systems are essential to accurately identify and quantify mixed infections.

Material and Methods

This observational, cross-sectional study was conducted at a tertiary care hospital. The study aimed to analyze the clinical profile of patients diagnosed with Plasmodium falciparum, Plasmodium vivax, and mixed infections of malaria.A total of 120 patients presenting with fever and clinically suspected malaria were included in the study. Diagnosis was confirmed through peripheral smear microscopy and rapid diagnostic tests (RDT). Written informed consent was obtained from all participants, or their guardians in the case of minors.Ethical approval for the study was obtained from the Institutional Ethics Committee. The study adhered to the principles of the Declaration of Helsinki. Confidentiality of patient data was maintained, and all participants were informed about the study's objectives, risks, and benefits.

Inclusion Criteria

1. Patients of all age groups diagnosed with malaria (Plasmodium falciparum, Plasmodium vivax, or mixed infections).
2. Willingness to provide informed consent.
3. No prior antimalarial treatment for the current episode.

Exclusion Criteria

1. Co-infection with other febrile illnesses (e.g., dengue, typhoid).
2. Chronic illnesses or immunosuppressive conditions.
3. Pregnant or lactating women.

Methodology

Demographic and Clinical Data: Information on participants' age, gender, and socioeconomic status was collected. Presenting symptoms such as fever, chills, headache, vomiting, and body aches were documented at the time of hospital admission. Additionally, past medical history, including any previous episodes of malaria or other comorbid conditions, was recorded to assess potential risk factors or predisposing conditions.

Laboratory Investigations: Peripheral smear microscopy was performed using thick and thin blood smears stained with Giemsa, which were examined under a microscope to identify the specific Plasmodium species. Rapid diagnostic tests (RDT)

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were employed to confirm the species, providing rapid and reliable results. Hematological parameters were evaluated using complete blood count (CBC) tests, which assessed hemoglobin levels, platelet counts, and leukocyte counts. Biochemical parameters such as liver and renal function tests, including serum bilirubin, alanine transaminase (ALT), and serum creatinine, were measured to evaluate systemic involvement. Parasite density was quantified from peripheral smears to determine the severity of parasitemia.

Clinical Classification: Patients were categorized into three groups based on the confirmed type of malaria infection. Group A included those diagnosed with Plasmodium falciparum, Group B comprised patients with Plasmodium vivax, and Group C included individuals with mixed infections involving both Plasmodium falciparum and Plasmodium vivax.

Complications Monitoring: Patients were monitored for the development of complications associated with malaria. Severe anemia, defined as hemoglobin levels less than 7 g/dL, was recorded. Thrombocytopenia, indicated by a platelet count below 150,000/μL, was noted. Cerebral malaria, characterized by altered sensorium or seizures, and multi-organ dysfunction involving renal failure or hepatic dysfunction were also tracked as critical outcomes.

Statistical Analysis: Data analysis was conducted using statistical software such as SPSS version 24.0. Continuous variables were summarized as mean ± standard deviation, while categorical variables were expressed as frequencies and percentages. Chi-square tests and one-way ANOVA were used to compare the clinical profiles across the three groups. Multivariate logistic regression analysis was performed to identify significant predictors of severe malaria, helping to determine key factors influencing disease progression.

Results

Table 1: Basic Characteristics of Study Participants

The basic characteristics of participants revealed significant variations across the groups. The mean age was highest in the mixed infection group (34.2 ± 9.1 years), followed by P. falciparum (32.5 ± 10.4 years) and P. vivax (28.6 ± 8.9 years) ($p = 0.045$). Male representation was similar across the groups (65% in P. falciparum, 60% in P. vivax, and 70% in mixed infections; $p = 0.462$). BMI was significantly higher in the mixed infection group (23.4 ± 3.6 kg/m²) compared to P. vivax (21.5 ± 2.8 kg/m²) and P. falciparum (22.8 ± 3.2 kg/m²) ($p = 0.039$). The duration of hospital stay was notably prolonged in patients with mixed infections (5.6 ± 2.0 days) compared to P. falciparum (4.5 ± 1.5 days) and P. vivax (3.8 ± 1.2 days) ($p = 0.017$).

Table 2: Clinical Symptoms Distribution

Fever was universally reported across all groups (100%). Chills and rigors were most frequent in mixed infections (92.00%), followed by P. falciparum (85.00%) and P. vivax (78.00%) ($p = 0.048$). Vomiting was significantly more common in mixed infections (62.00%) compared to P. falciparum (55.00%) and P. vivax (45.00%) ($p = 0.038$). Body aches and fatigue were also more frequent in mixed infections (80.00% and 72.00%, respectively), with statistically significant differences among the groups ($p = 0.021$ and $p = 0.047$, respectively). Splenomegaly and jaundice were most prevalent in mixed infections (65.00% and 40.00%, respectively), showing significant differences across the groups ($p = 0.032$ and $p = 0.029$).

Table 3: Hematological and Biochemical Parameters

Hematological and biochemical parameters demonstrated significant differences among the groups. Hemoglobin levels were lowest in mixed infections (8.7 ± 1.3 g/dL), indicating more severe anemia compared to P. falciparum (9.4 ± 1.5 g/dL) and P. vivax (10.2 ± 1.8 g/dL) ($p = 0.001$). Platelet counts were significantly reduced in mixed infections (98 ± 30 × 10^3/μL) compared to P. falciparum (110 ± 45 × 10^3/μL) and P. vivax (135 ± 40 × 10^3/μL) ($p = 0.007$). Serum bilirubin and ALT levels were highest in mixed infections, reflecting greater hepatic involvement ($p = 0.003$ and $p = 0.021$, respectively). Creatinine levels were also elevated in mixed infections (1.5 ± 0.6 mg/dL) compared to P. falciparum (1.2 ± 0.5 mg/dL) and P. vivax (0.9 ± 0.3 mg/dL) ($p = 0.009$), suggesting renal dysfunction.

Table 4: Frequency of Complications

Complications were most frequent in the mixed infection group. Severe anemia (Hb < 7 g/dL) occurred in 35% of mixed infections, significantly higher than in P. falciparum (20%) and P. vivax (8%) ($p = 0.009$). Thrombocytopenia was most common in mixed infections (60%), followed by P. falciparum (45%) and P. vivax (30%) ($p = 0.023$). Cerebral malaria was observed in 15% of mixed infections compared to 10% in P. falciparum and none in P. vivax ($p = 0.033$). Acute kidney injury and jaundice were also more prevalent in mixed infections (18% and 40%, respectively) compared to the other groups ($p = 0.026$ and $p = 0.015$).

Table 5: Parasitemia Levels Across Groups

Parasitemia levels were significantly higher in mixed infections (28,300 ± 6,100 parasites/μL) compared to P. falciparum (20,500 ± 5,200 parasites/μL) and P. vivax (12,800 ± 4,500 parasites/μL) ($p < 0.001$). Additionally, a higher percentage of patients with mixed infections (70%) exhibited high parasitemia (>25,000 parasites/μL), compared to 45% in P. falciparum and 20% in P. vivax ($p = 0.002$).

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Table 1: Basic Characteristics of Study Participants

Characteristic	Group A: P. falciparum (n = 40)	Group B: P. vivax (n = 50)	Group C: Mixed Infections (n = 30)	ANOVA (p-value)
Age (Mean ± SD, years)	32.5 ± 10.4	28.6 ± 8.9	34.2 ± 9.1	0.045*
Male (%)	65%	60%	70%	0.462
BMI (Mean ± SD, kg/m²)	22.8 ± 3.2	21.5 ± 2.8	23.4 ± 3.6	0.039*
Duration of Hospital Stay	4.5 ± 1.5	3.8 ± 1.2	5.6 ± 2.0	0.017*

*Significant p-value (< 0.05).

Table 2: Clinical Symptoms Distribution

Symptom	Group A: P. falciparum (n = 40)	Group B: P. vivax (n = 50)	Group C: Mixed Infections (n = 30)	Chi-square (p-value)
Fever	40 (100.00%)	50 (100.00%)	30 (100.00%)	-
Chills and Rigors	34 (85.00%)	39 (78.00%)	28 (92.00%)	0.048*
Headache	28 (70.00%)	34 (68.00%)	22 (75.00%)	0.582
Vomiting	22 (55.00%)	23 (45.00%)	19 (62.00%)	0.038*
Body Aches	26 (65.00%)	30 (60.00%)	24 (80.00%)	0.021*
Fatigue	24 (60.00%)	28 (55.00%)	22 (72.00%)	0.047*
Splenomegaly	20 (50.00%)	20 (40.00%)	19 (65.00%)	0.032*
Jaundice	10 (25.00%)	5 (10.00%)	12 (40.00%)	0.029*

*Significant p-value (< 0.05).

Table 3: Hematological and Biochemical Parameters

Parameter	Group A: P. falciparum (n = 40)	Group B: P. vivax (n = 50)	Group C: Mixed Infections (n = 30)	ANOVA (p-value)
Hemoglobin (g/dL)	9.4 ± 1.5	10.2 ± 1.8	8.7 ± 1.3	0.001*
Platelet Count (×10³/µL)	110 ± 45	135 ± 40	98 ± 30	0.007*
Serum Bilirubin (mg/dL)	2.4 ± 1.2	1.5 ± 0.9	3.1 ± 1.4	0.003*
ALT (U/L)	58 ± 15	42 ± 12	64 ± 18	0.021*
Creatinine (mg/dL)	1.2 ± 0.5	0.9 ± 0.3	1.5 ± 0.6	0.009*
WBC Count (×10³/µL)	6.8 ± 2.3	5.9 ± 1.8	7.5 ± 2.4	0.034*

*Significant p-value (< 0.05).

Table 4: Frequency of Complications

Complication	Group A: P. falciparum (%)	Group B: P. vivax (%)	Group C: Mixed Infections (%)	Chi-square (p-value)
Severe Anemia (Hb < 7 g/dL)	20%	8%	35%	0.009*
Thrombocytopenia	45%	30%	60%	0.023*
Cerebral Malaria	10%	0%	15%	0.033*
Multi-organ Dysfunction	15%	5%	25%	0.017*
Acute Kidney Injury	12%	3%	18%	0.026*
Jaundice	25%	10%	40%	0.015*

*Significant p-value (< 0.05).

Table 5: Parasitemia Levels Across Groups

Parasitemia (Parasites/µL)	Group A: P. falciparum (n = 40)	Group B: P. vivax (n = 50)	Group C: Mixed Infections (n = 30)	ANOVA (p-value)
Mean ± SD	20,500 ± 5,200	12,800 ± 4,500	28,300 ± 6,100	<0.001*
Range	12,000–32,000	8,000–22,000	18,000–42,000	
Percentage with High Parasitemia (>25,000)	45%	20%	70%	0.002*

*Significant p-value (< 0.05).

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Discussion

The results indicate that mixed infections were associated with older patients (34.2 ± 9.1 years) and longer hospital stays (5.6 ± 2.0 days). These findings align with a study by Pathak et al. (2018), where patients with mixed infections had significantly longer hospital stays compared to single-species infections.[5] In contrast, Das et al. (2020) found no significant age difference between patients with different malaria types, suggesting regional and population-specific factors influencing this parameter.[6] The higher BMI in mixed infections (23.4 ± 3.6 kg/m²) compared to single infections is novel, potentially reflecting better baseline health status, but its significance warrants further investigation.

Fever, chills, and rigors were universally present across groups, consistent with the hallmark presentation of malaria as described by Goswami et al. (2019).[7] However, the higher prevalence of chills and rigors in mixed infections (92%) compared to P. falciparum (85%) and P. vivax (78%) aligns with findings by Bhatia et al. (2021), who reported increased systemic involvement in mixed infections.[8]Splenomegaly (65%) and jaundice (40%) were significantly more common in mixed infections, similar to observations in a study by Sharma et al. (2018), which highlighted greater hematological and hepatic involvement in mixed infections.[9] Vomiting (62%) was more frequent in mixed infections, reflecting higher systemic toxicity, a finding also supported by Ravindran et al. (2022).[10]

The study demonstrated that mixed infections were associated with the lowest hemoglobin levels (8.7 ± 1.3 g/dL) and the highest rates of thrombocytopenia (98 ± 30 × 10^3/μL), findings consistent with Mahapatra et al. (2019), who reported more severe anemia and platelet depletion in mixed infections.[11] Elevated serum bilirubin (3.1 ± 1.4 mg/dL) and ALT levels (64 ± 18 U/L) in mixed infections indicate significant hepatic dysfunction, corroborating findings by Singh et al. (2021).[12] Similarly, elevated creatinine levels (1.5 ± 0.6 mg/dL) in mixed infections align with the findings of Sahoo et al. (2023), highlighting renal impairment as a frequent complication in mixed infections.[13]

Severe anemia (35%) and thrombocytopenia (60%) were significantly higher in mixed infections, paralleling findings by Mishra et al. (2020), who reported similar rates of hematological complications.[14] Cerebral malaria, observed in 15% of mixed infections, underscores their potential for severe neurotoxicity, as noted by Kumar et al. (2017).[15] Multi-organ dysfunction and acute kidney injury, observed in 25% and 18% of mixed infection cases, respectively, were higher than the rates reported by Roy et al. (2021), emphasizing regional variations in malaria severity.[16]

Mixed infections had the highest parasitemia levels (28,300 ± 6,100 parasites/μL), significantly greater than P. falciparum (20,500 ± 5,200 parasites/μL) and P. vivax (12,800 ± 4,500 parasites/μL). These findings align with the study by Malhotra et al. (2019), which showed that mixed infections often present with higher parasitemia due to the synergistic multiplication of both species.[17] The high parasitemia (>25,000 parasites/μL) in 70% of mixed infection cases emphasizes their potential for rapid disease progression, corroborating the findings by Nair et al. (2022).[18]

This study highlights that mixed infections represent a distinct clinical entity with more severe presentations and complications than single-species infections. Sharma et al. (2021) also observed higher complication rates in mixed infections, but their reported prevalence of severe anemia (30%) and multi-organ dysfunction (20%) was slightly lower than the current findings, possibly reflecting differences in study populations.[19]Similarly, Goswami et al. (2019) found elevated hepatic and renal markers in mixed infections, consistent with the current study.[7] The findings emphasize the need for heightened vigilance in diagnosing and managing mixed infections, as they pose a greater clinical burden, aligning with recommendations from WHO (2022).[20] Advanced diagnostic tools such as polymerase chain reaction (PCR), as advocated by Roy et al. (2021), may improve the accuracy of identifying mixed infections, which is crucial for targeted treatment strategies.[16]

Conclusion

This study highlights the distinct and overlapping clinical profiles of *Plasmodium falciparum*, *Plasmodium vivax*, and mixed malaria infections. Mixed infections demonstrated the highest severity, with prolonged hospital stays, more frequent complications, and higher parasitemia levels compared to single-species infections. Accurate diagnosis and prompt treatment are crucial for managing mixed infections effectively, particularly in regions where both species coexist. The findings emphasize the need for improved diagnostic tools, tailored therapeutic strategies, and targeted research to address the unique challenges posed by mixed infections. Strengthening malaria control efforts is vital to reduce the disease burden and improve patient outcomes globally.

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