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EVALUATION OF CONCURRENT MALARIA AND DENGUE CO-INFECTIONS AMONG FEBRILE PATIENTS VISITING A TERTIARY CARE HOSPITAL: A CROSS-SECTIONAL OBSERVATIONAL STUDY

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ABSTRACT

Background

Malaria and dengue are mosquito-borne diseases found in Bihar, West Bengal, Uttar Pradesh, Punjab, Haryana, Delhi, Gujarat, Kerala, Karnataka, and Tamil Nadu. High mortality and morbidity rates make these diseases a major public health issue in these places. The underreporting and misdiagnosis of dengue and malaria concomitant infection is common.

Aim and Objective

To assess the incidence of co-infections with dengue and malaria and to evaluate and compare the severity of these co-infections with that of mono-infections of either disease, based on clinical and laboratory parameters.

Material and Method

A cross-sectional observational study was conducted involving patients who presented with fever and symptoms indicative of malaria and/or dengue. A total of 497 serum samples were collected from these clinically suspected cases. All samples were tested for dengue NS1 antigen and IgM/IgG antibodies using ELISA and immunochromatographic (ICT) tests. Diagnosis of malaria was confirmed via rapid malaria antigen test kits and the identification of Plasmodium spp. through peripheral blood smear microscopy (both thick and thin films).

Results

Among the febrile patients, 155 (31.19%) tested positive for dengue infection, while 342 (68.81%) tested positive for malaria parasites. Notably, 15 (3.02%) cases exhibited co-infections with both dengue and malaria parasites, predominantly *Plasmodium falciparum*. Haemoglobin <12g/dl 100%, thrombocytopenia, haemorrhagic symptoms (26.67%), renal failure (13.33%), and hepatomegaly (46.67%). 93.33% prevalent in co-infections, more with *Plasmodium falciparum*.

Conclusion

Co-infections are not uncommon, and failing to identify either condition in cases of concurrent infections can lead to severe complications and potentially disastrous outcomes. Patients from endemic regions must be thoroughly examined, as early diagnosis is critical for effective treatment and can be lifesaving.

Recommendation

It is essential for all febrile patients exhibiting suggestive symptoms to undergo comprehensive testing for both dengue and malaria infections.

Keywords: *Dengue, Malaria, Co-infections*
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INTRODUCTION

Malaria and Dengue are two vector-borne diseases that cause high mortality and morbidity and represent a major worldwide public health burden [1]. Malaria is caused by protozoan Plasmodium species in the form of sporozoites, present in infected female Anopheles mosquitoes transmitted to people via bite, which is preventable and curable. Dengue is an arthropod-borne viral disease caused by ssRNA viruses belonging to the family Flaviviridae and is transmitted in humans by Aedes aegypti mosquitoes [2].

In endemic tropical countries like India, where both vectors co-exist, the simultaneous occurrence of Malaria and Dengue in an individual, which is rare but not uncommon, cannot be exceptional [3,4,20]. As dengue and malaria have overlapping clinical features, it becomes difficult to distinguish between them. Hence, accurate species identification and exact laboratory investigations are

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required to differentiate between the two of them, or else it gives poor outcomes [5-7].

There are scarce published reports of concurrent Malaria and Dengue co-infections from this region. Therefore, the present study aimed to find out the incidence of dengue and malaria co-infections as well as to ascertain and compare the severity of such co-infections with Dengue or Malaria mono-infection based on clinical and laboratory parameters.

MATERIALS AND METHODS

Study design

Tertiary care hospital based cross-sectional observational study.

Study setting

Department of Medicine, Bhagwan Mahavir Institute of Medical Sciences in Pawapuri, Nalanda, Bihar. Our institute is ideally located near Rajgir, a hotspot area for mosquito-borne diseases. This study was conducted from July 2023 to December 2023.

Study population

Patients with acute febrile illnesses, who presented with symptoms suggestive of dengue and/or malaria, including headache, myalgia, nausea, vomiting, and generalized rashes.

Sample size

We included a total of 497 patients, seeking treatment for acute febrile illnesses from outpatient and inpatient units of Department of Medicine.

Inclusion criteria

All febrile patients with suggestive symptomatology irrespective of age and sex.

Exclusion criteria

We excluded patients who were critically ill patients and cases with alternative diagnosis for acute febrile illness.

Procedure

We collected 4 ml blood samples from each patient in both plain and ethylenediaminetetraacetic acid (EDTA) vials through venipuncture. For malaria diagnosis, we employed microscopy of peripheral blood smears, using both thin and thick films stained with Leishman's Stain for the accurate identification of Plasmodium species. In parallel, we conducted a rapid immunoassay Malaria card test to detect malarial antigens in human whole blood, confirming infections caused by Plasmodium falciparum and other species.

Dengue screening was performed utilizing a rapid immunochromatographic test that detects NS1 antigen alongside IgM/IgG antibodies in human serum or plasma. All samples were further assessed using the ELISA method. We diligently followed the manufacturer's instructions [8] for all serological tests. Additionally, we gathered and analyzed clinical, haematological, and other laboratory parameters and made comparisons with our findings to enhance the outcomes of the study.

Statistical analysis

Data was analyzed using SPSS 23.0. Categorical variables were frequencies and percentages whereas continuous variable was mean.

Ethical considerations

The study was carried out with the approval of the ethical committee of our institute and written informed consent was taken from all study participants.

Figure 1: Rapid immunochromatographic test used for Malaria and Dengue

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RESULTS

Total of 497 blood samples collected from patients suffering from acute febrile illness were screened for Dengue & Malaria infections. Out of the 497 samples studied, 155 were seropositive by rapid immunochromatographic test for dengue, while dengue ELISA test showed positive results in 148 patients only (Table1).

Table 1: Incidence of Malaria, Dengue mono-infection and co-infections cases

Total number of cases	Malaria mono-infection		Dengue mono-infection		Co-infections
N= 497	342		155		15
	PBS	ICT	ELISA	ICT	
	340	342	148	155	

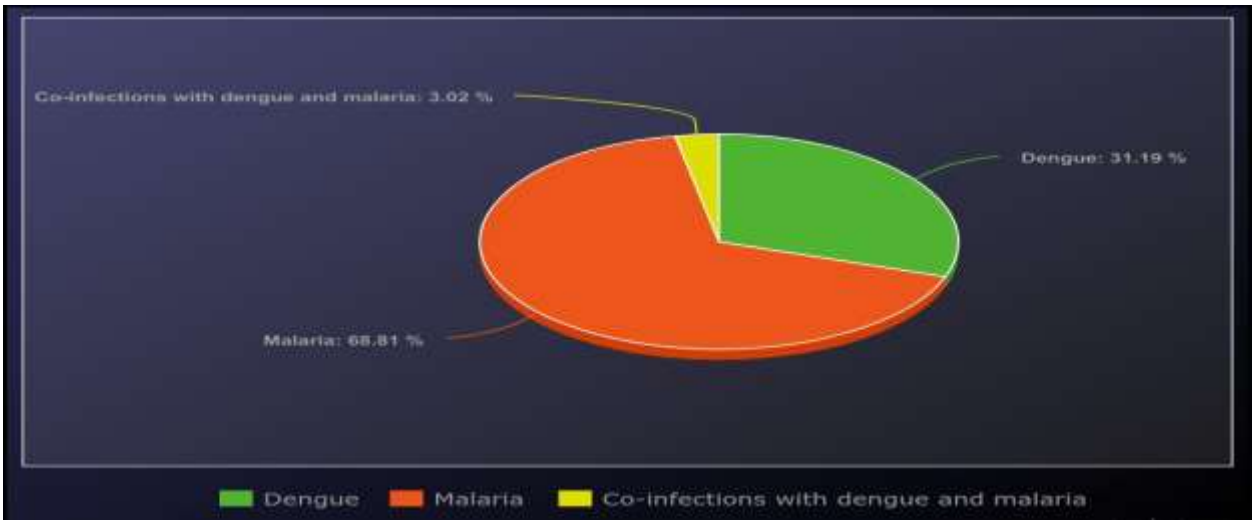

Table 2: Comparative evaluation of peripheral blood smear for serologically (by card test) diagnosed malaria cases

Total number of Malaria positive cases	Plasmodium vivax		Plasmodium falciparum	
N=342	PBS	ICT	PBS	ICT
	214	215	126	127

Table 3: Species distribution of Malaria in co-infections cases

Number of Dengue cases with co-infections	Plasmodium vivax	Plasmodium falciparum	Both vivax & falciparum
N=15	6(40%)	8(53.33%)	1(6.67%)

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Out of 497 samples, malaria parasite was found in 342 patients through immunochromatographic test. Among them 215 cases were infected with *Plasmodium vivax* while 127 cases were due to *Plasmodium falciparum* infection. The result for pheripheral blood smear suggested only 340 malaria cases, among them 214 positives for *Plasmodium vivax* and 126 positives for *Plasmodium falciparum* (Table 2).

Dengue malaria co-infections were present in 15(3.02%) patients among which *Plasmodium falciparum* was predominant (Table 3)

Table 4: Incidence of complications in co-infections cases

Complications	Number of co-infections cases
Hepatomegaly & Jaundice	7(46.67%)
Hemorrhagic manifestations	4(26.67%)
Acute kidney injury	2(13.33%)
Anemia	15(100%)
Thrombocytopenia	14(93.33%)

Complications such as hepatomegaly and jaundice 46.67%(7cases), haemorrhagic manifestations 26.67%(4), kidney failure 13.33%(2), haemoglobin<12g/dl 100%(15) and thrombocytopenia (platelet count <150,000/cmm) 93.33%(14) were common in co-infections group and were much more common with Plasmodium falciparum infection (Table 4, Figure 2).

DISCUSSION

Dengue and malaria are both curable and preventable vector-borne diseases that pose significant public health challenges, particularly in tropical countries where they are endemic. The frequent coexistence of these diseases can lead to misdiagnosis or misinterpretation as a mono-infection due to their similar clinical presentations. In our comprehensive study, we identified that 155 samples (31.19%) from febrile patients tested positive for dengue infection. As a re-emerging disease, dengue continues to threaten public health with annual outbreaks and an increase in both incidence and severity. Currently, treatment options are limited to supportive management, while a vaccine is actively under development [9].

In our research 342 samples (68.81%) tested positive for malaria. This disease is particularly prevalent during the rainy season, from July to September, contributing to a rise in incidence in this region and neighboring areas. The presence of numerous large water bodies and stagnant water in agricultural fields after rainfall creates ideal breeding sites for malaria vectors, facilitating transmission. Furthermore, these breeding sites can be influenced by geographical and climatic changes, as well as socioeconomic factors affecting patients and their understanding of healthcare and public health practices [10,11].

In our study, we observed a co-infection incidence of 3.02% for dengue and malaria. Other studies have reported varying prevalence rates for concurrent infections: 6% in India, 0.99% in French Guiana, and 27% in Pakistan [12-15]. A notable study by Abrahamsen SK et al. from Karnataka

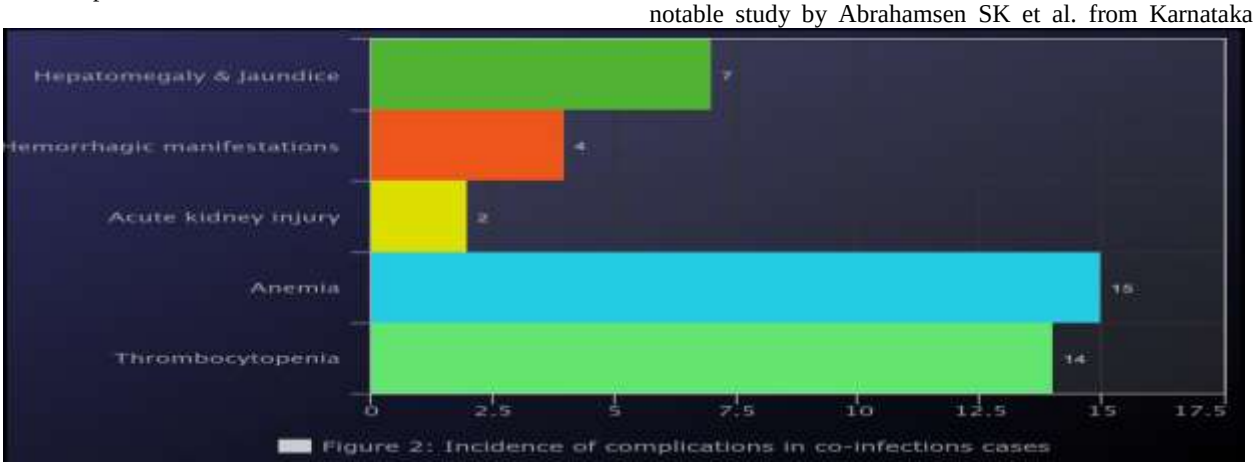

Figure 2: Incidence of complications in co-infections cases

diagnosed 100 patients with acute febrile illness, revealing that 25% had dengue, 8% had malaria, and 14% had enteric fever [16]. Additionally, the first documented case of concurrent dengue and Plasmodium falciparum infection was reported by Charrel et al. in 2005, which detailed a patient returning to France after an 18-day journey to Guinea, Senegal, and Sierra Leone [17].

The accuracy of serological tests for diagnosing patients with dengue and malaria has been subject to scrutiny, particularly due to the nonspecific reactivity seen in certain rapid serological assays. However, the ELISA serological test has demonstrated more than 90% specificity for dengue [18]. For malaria, peripheral blood smear microscopy and malarial antigen card tests are utilized. Notably, research by Bharti et al. has shown that the rapid diagnostic card test for Plasmodium falciparum and Plasmodium vivax achieves 93% sensitivity and 85% specificity, with a positive predictive value (PPV) of 79% and a negative predictive value (NPV) of 95% [19].

Considering that both infections are endemic in our region, co-infection with dengue and malaria is quite common. Nevertheless, published evidence on this topic remains limited despite the co-endemic nature of these diseases in South Asia [20]. Concurrent infections can present with indistinguishable clinical features, creating significant diagnostic challenges for clinicians. It is essential to recognize that the treatment approaches for these diseases differ considerably; therefore, delays in administering appropriate therapy can be life-threatening. Our study has shown that the clinical presentation of co-infection often resembles that of dengue mono-infection.

CONCLUSION

The findings of this study indicate that all febrile patients with clinical suspicions of dengue and/or malaria, must be tested for both the infections as co-infection is not uncommon. If any one missed to diagnose in case of concurrent infections, can lead to severe complications and disastrous outcomes. Patients from endemic areas must be thoroughly evaluated because both the infections present overlapping clinical features and pose diagnostic challenges clinically. Hence high index of clinical suspicion and prompt laboratory evaluations may result in early diagnosis and can be lifesaving. If any one of the infections is confirmed first, then it should not perclude the possibility of co-infection.

LIMITATIONS

The limitations of the present study includes small sample size, antigenic cross-reactivity among serology of Dengue and Malaria and lack of molecular diagnostics facilities at our institution.

RECOMMENDATION

It is crucial for clinicians to maintain a heightened awareness of the possibility of concurrent infections in such clinical scenarios, as mixed infections are likely more frequent than the current literatures indicate. Consequently, proactive screening for both conditions should be conducted following thorough clinical and haematological evaluations.

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LIST OF ABBREVIATIONS

ELISA: Enzyme Linked Immunosorbent Assay

ICT: Immunochromatographic Test

NS1: Non-Structural protein 1

SSPS: Statistical Package for the Social Sciences

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No funding was received for this study.

CONFLICT OF INTEREST

We declare no conflict of interest

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