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ORIGINAL RESEARCH

A retrospective study of co-infection of COVID-19 with tropical fevers – Impact on hematology and clinical outcome

[1]Dr. Jyoti Jindal, [2]Dr. Vikas Garg, [3]Dr. Veenu Gupta, [4]Dr. Manisha Aggarwal

[1]Assistant Professor, [2]Professor, Department of Medicine, DMCH, Ludhiana, Punjab, India
[3]Professor & Head, [4]Assistant Professor, Department of Microbiology, DMCH, Ludhiana, Punjab, India

Corresponding author
Dr. Jyoti Jindal
Assistant Professor, Department of Medicine, DMCH, Ludhiana, Punjab, India
Email: jyoti_jindal@yahoo.co.in

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ABSTRACT

Background: Tropical fevers are defined as infections that are prevalent to tropical or subtropicalregions. DuringCovid-19 pandemic, risk of other tropical fevers was increased. Mostpeople with these co-infections had mild illness. However, both tropical fevers and COVID-19can cause severe illness that can result in death.Due to clinical similarities to COVID-19, tthis retrospective study was conducted to investigate the role of co-infection on the clinical andhematology profile and outcome of COVID-19 patients. **Material & method**: For this purposea retrospective study has been conducted in Dayanand Medical college andHospital, Ludhianaenrolled patients admitted during from June 15 to October15, 2022.A totalof confirmed 20 patients of co-infections. Out of total suspected Covid patients admitted to theEmergency of thehospital wereenrolled.Data of Throat swab, nasopharyngeal swab andblood sample from suspected patients werecollected. All swab samples were tested fortheconfirmation of SARS-CoV-2.Based upon hematologychanges, further sample for serologytesting of tropical infections were sent. **Results:** Out of all suspected patients admitted in emergency, SARS COVID 19 was found to be positive in 523 patients and co-infection with tropical fever was seen in 20 patients.Co-infection withDenguewas seen in 20 cases, Leptospira in 2 cases and scrub typhus in 1case. Fever was present in all 20 cases. Thrombocytopenia was present in all 20 cases. Out of20 cases 17 got discharged and 3 got expired. **Conclusion:** A detailed analysis of disease onset, symptoms, signs, warning signs and lab values will help us to diagnose co-infections early and it will significantly affect our choice of treatment and improve the outcome.

Key words: co-infection, covid-19, dengue, tropical, clinical, hematology

INTRODUCTION

Tropical fevers are defined as infections that are prevalent to tropical orSubtropical regions. During Covid-19 pandemic, risk of other tropical fevers have beenincreased. The WHO has declared corona virus disease-2019 (COVID-19) outbreak as a globalpandemic[1]. The COVID-19 pandemic in dengue-endemic areas is a public health concern because of the overlapping clinical and laboratory features of these diseases. In dengue-endemic countries people areat the high risk of possible co-infection. [2] This causes challenges in the correct diagnosis and management of both diseases.[3] Among these tropical fevers maximum number of dengue cases have beenincreased. The countries in South America are at high risk of dengue outbreak. [3,4,5]Due to clinical similarities to COVID-19, the present study was conducted to investigate the roleof tropical fever co-infection on the clinical profile and outcome of COVID-19 patients.Despite similarities in signs and symptoms (like fever, headache and body pain), and laboratory characteristics (like thrombocytopenia and leukopenia) of these two diseases, the management of these diseases are completely different[6,7]. Hence, specific tests using real-time reverse transcription polymerase chain reaction (RT-PCR) or enzyme-linked immunosorbent assay (ELISA) are necessary to confirm the diagnosis of these diseases. Further, infection with the dengue virus has been reported in SARS-CoV-2 infected patients during the pandemic[8,9]. Co-infection with these diseases has been associated with higher morbidity than single infections.[10,11] Delayed diagnosis of co-infection can result in serious patient complications with poor outcomes.So the aim of this study was to find out the

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incidence of co-infection between COVID-19 and tropical fevers and its clinical outcome.

MATERIAL AND METHODS

This is a retrospective studyconducted in tertiary care hospital over a period of four months from 15th June to 15th Oct 2022. Allsuspected COVID patients more than 18 years admitted in the emergency ward were included. Patients with Age less than 17 years, malignancy, immunocompromisedStatus and on chemotherapy were excluded from the study. Nasopharyngeal swab and throat swab were collectedin a viral transport mediaand transported to Department of Microbiology in a triple packagingas per ICMR guidelines.Viral RNA was extracted fromthe specimen according to the manufacturer's protocol and confirmation of SARS-CoV-2done by reversetranscription-PCRmethod. Based upon hematological findings, samples were sent for serological testing of tropical infections like Dengue, Scrub typhus,Leptospirosis and malaria.For detection of Scrub typhus and Leptospira specific IgM, ELISA was performed. For Dengue, NS1antigen and/or specific IgM antibodies were detected by MAC ELISA. For Malaria, rapid immune-chromatography test was done. The impact of co-infection on clinical profile, hematology and outcome of patient was further evaluated.

RESULTS

Out of all suspected patients admitted in emergency, SARS COVID 19 was found to be positive in 523 patients in four months period. Out of 523 COVID 19 confirmed patients, co-infection with tropical fever was seen in 20 patients. Our findings showed that out of total 20 patients 10 patients were between of age 50-70 years and 10 patients were in the age group of 25-50 years. Out of total 20 patients 7 were femalesand 13 were males. (Table 1) Co-morbidities such as cardiovascular diseases, strokeand diabetesmellitus were also seen in 8 cases.Fever was present in all 20 cases.Cough andbreathlessness was seen in 6cases. Rash was seen in 6 cases out of 20 patients. Headache waspresent in 4 cases. (Figure: 1)This study showed that there is strong association of decreased white bloodcell, neutrophils, lymphocytes and platelets count, with SARS CoV-2 and dengueco infection.Leucopenia and thrombocytopeniawasseen in 15 out of 20Cases. Thrombocytopenia was present in all patients.Mild transaminitiswas also seen inmajorityofcases with co-infection.Dengue NS1 antigen was positive in 7 cases and dengue serology(IgM by ELISA) was positive in 13 cases. Dengue serology was positive between 5-7 days afterdate of admission in majority of cases. Leptospiraserology (IgM by ELISA) was positive in 2patients and scrubtyphusIgM was positive in 1 patientalong with Dengue. (Figure 2).

Out of 20 patients 3 patients got expired. All three expired patients were more than 50 yearsof age and with co-morbidities.Rest all of the 17 patients with COVID-19 and co-infectionsrecovered completely and discharged from the hospital.This report highlights theimportance todiagnosethe COVID- 19 and co-infection mainly inendemic countries as boththe diseases has entirely different treatmentstrategies especially in severe disease and it hassignificant impact on mortality.

Table -1Demographic & Hematological profile of patients with Co Infection

Demographic Characteristics	COVID-19 and Tropical fever co-infection n=20 patients
Age Distribution (Years)	
25-50	10
50 -75	10
Sex Distribution	
Male	13
Female	7
Hematological Parameters	
Thrombocytopenia	20
Leucopenia	16
Increased ALT	16

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Figure 1: Distribution of symptoms among Co infection patients

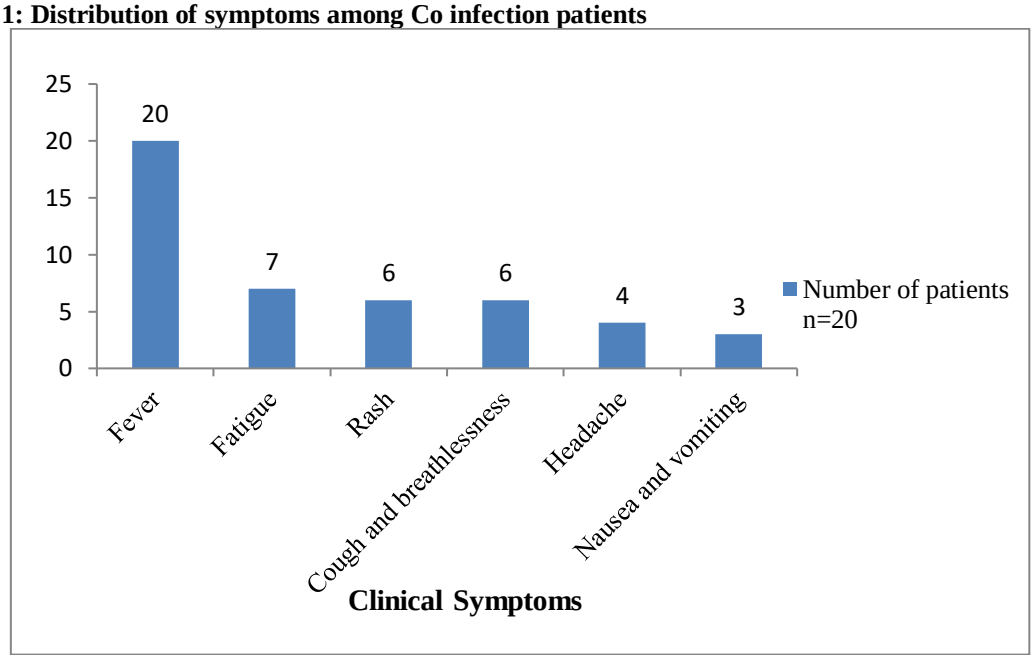
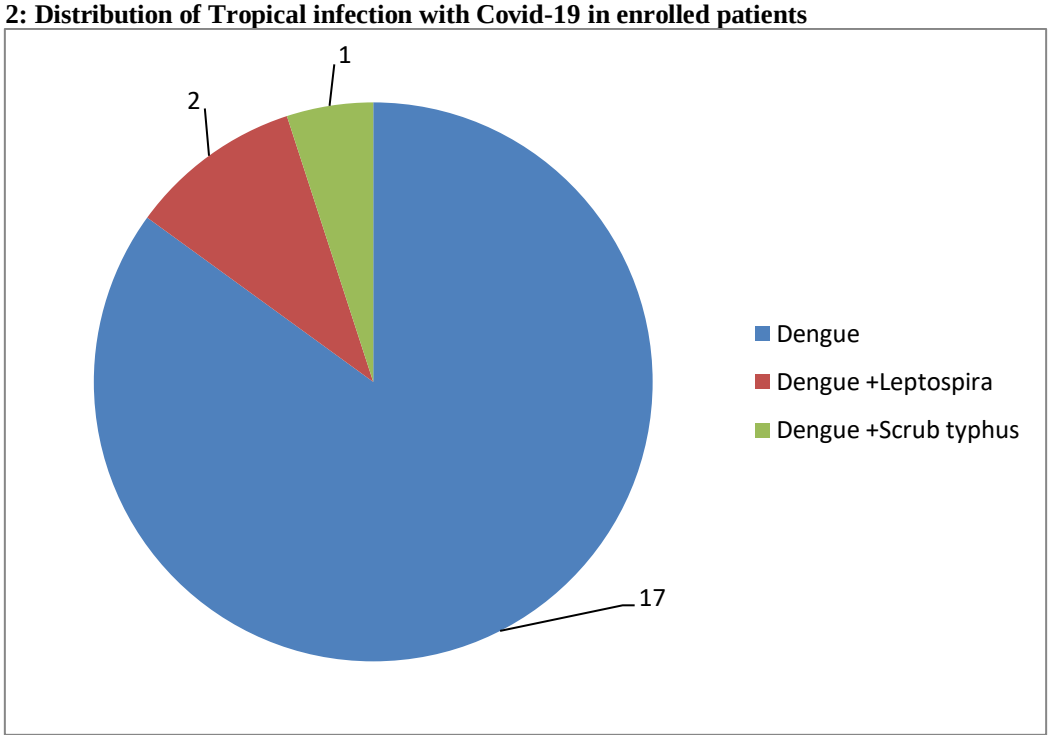


Figure 2: Distribution of Tropical infection with Covid-19 in enrolled patients



DISCUSSION

The endemicity of tropical diseases posed the emergence of an epidemiological scenario marked by overlaps with the progressive circulation of the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) and its Coronavirus Disease 2019 (COVID-19). With the spreading of SARS-CoV-2 in areas endemic to tropical pathogens during regional epidemics, the occurrence and detection of multiple types of coinfections are therefore anticipated. The chances of Co infection of COVID 19 with dengue has been increased in prevalent areas. Due to clinical similarity between these two infections, dengue patients remain under diagnosed during pandemic. In our study, out of 523 confirmed cases of SARS COVID-19 patientscoinfection with tropical fevers was found in 20 patients. So the incidence of coinfection in our study was 3.82%. Our results were comparable with the study done by Rodrigues *et al*who assessed Brazil's Dengue Virus (DENV) and SARS-CoV-2 co-circulation. He described a cohort of 57 COVID-19 patients with 5 DENV (8.8%) coinfections enrolled at the Hospitals Rede Casa.[12]

Most people with these tropical fevers andCOVID-19 has mild illness and can recover at home. However, severe form of both tropicalfevers and COVID-19 can

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cause severe illness that can result in death Severe dengue is aLeading cause of serious illness[13]. In Singapore, a patient with COVID-19 produced false-positive dengue results in rapid serological test.[14] It is very important to diagnose co-infection foraccurate diagnosis and treatment, as clinical presentation is similar and treatment is entirelydifferent for severe cases of COVID-19 and co-infection. In fact, the symptoms of these viral diseases begin with fever. Besides, patient with COVID-19 could present with a rash that can be mistaken for dengue.[15] Guan et al[16] in their recent study reported that fever, cough, and headache wereobserved as the most common symptoms for patients with COVID-19 whereas fever,headache and skin rash were observed in patients with dengue.

This is similar to our study as fever and rash was found to be the common symptoms inpatients with co-infection of COVID-19 and Dengue. The clinical and laboratory features of bothDengue and COVID-19 are quite identical, and therefore, it is difficult to distinguish. The clinical,hematological and biochemical findings associated with a SARS-CoV-2 and co-infection withtropical fevers are consistent with the known clinical characteristics of COVID-19.[17,18]

Our findings showed a strong association of decreased white blood cell, neutrophils, andlymphocytes and platelets count, with SARS CoV-2 and dengue confection. Thrombocytopeniaand elevated liver enzymes are also reported in both diseases. But there are not many studieson this lab parameters to differentiate between the two co-infection and Covid-19.Thus,confection and co epidemics trigger alert, especially in the endemic countries where theepidemics of tropical fever especially dengue fever occurred repeatedly. For facingthe upcoming dengue epidemic, special measures should be taken in these countries and therefore, an effective mosquito control program is strongly recommended.

CONCLUSION

If there is a co-infection, then apart from the febrile illness there may beconstellation of signs and symptoms that may lead to difficulty in diagnosis. A detailed analysisof disease onset, symptoms, signs, warning signs and lab values will help us to diagnose co-infections early and it will significantly affect our choice of treatment and improve the outcome.

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