Case Report

Rare Occurrence of Novel Covid-19 Infection in a patient of Dengue Fever being Treated With Phytochemicals In A Herbal Extract (Kahwa) of Camellia Sinensis in a Developing Country

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[1,2,3] *Conception of study*
[5] *Experimentation/Study conduction*
[1,2,3,4] *Analysis/Interpretation/Discussion*
[1,2,3] *Manuscript Writing*
[6] *Critical Review*
[4,6] *Facilitation and Material analysis*

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Article Processing
Received: 08/12/2021
Accepted: 02/09/2022

Cite this Article: *Bashir MN, Bhutta M, Adil ML, Mannan MS, Shabbir H, Gondal SS. Rare Occurrence of Novel Covid-19 Infection in a patient of Dengue Fever being Treated With Phytochemicals In A Herbal Extract (Kahwa) of Camellia Sinensis in a Developing Country. Student Supplement of Journal of Rawalpindi Medical College (SJRMC). 2023;27(1).*

Conflict of Interest: *Nil*
Funding Source: *Nil*

Access Online:

Abstract

Introduction: The concurrence of an epidemic and a pandemic is a harsh reality in numerous developing countries around the world. As the entire world suffers from the novel coronavirus (SARS COV-2) pandemic, many areas of the world have had the added burden of endemics that are equally burdensome as the current pandemic.

Case Presentation: In our report, we presented a case in Pakistan of a 28-year-old patient suffering from Dengue fever who also contracted COVID-19 and was subsequently treated conservatively along with oral intake of polyphenols present in the traditional herbal extract from Camellia sinensis plant & inhalational steam following which he tested negative. To date, such cases have only been reported extremely rarely even in Pakistan. Our study highlights the plausible effect of the herbal extracts of Camellia species in treating the Covid-19 infection and halting its progression.

Discussion: This case study highlights the significance of extracting, purifying and pharmacologically testing those specific phytochemical compounds in the Camellia herbs that have the potential therapeutic properties effective against respiratory viral illnesses, in particular, COVID-19, and can prove to be effective treatment modalities in the future. Polyphenols are active substances against various types of viral infections. Researchers have characterized methods of how to isolate polyphenols without losing their potential to formulate pharmaceutical products. Researchers have also described mechanisms against common viral infections (i.e., influenza, herpes, hepatitis, rotavirus, coronavirus).

Our work also paves the way for future interventional research to elucidate the plausible interactions between the pathophysiology of these two viral illnesses and the resultant effects on their prognosis. Since both Flavivirus and SARS-COV-2 are enveloped, single, positive-stranded RNA viruses, there is a significant possibility of interaction between their pathogenesis at the molecular level, which can translate into a wide range of clinical outcomes, when these infections concur. Particularly our case study reflects upon the alleviation of Covid-19 symptoms in the concurrent setting of dengue. This case report emphasizes the importance of rigorous clinical testing of polyphenol extracts of all Camellia species for possible novel Anti-viral drugs. Moreover, our study also depicts the alarming situation of two epidemics happening simultaneously which imposes an exponential burden on an already overburdened healthcare system in the third world and draws attention towards medical legislation by health ministries & pre-emptive readiness of infectious disease specialists in case of an emergency outbreak.

Keywords: COVID-19, SARS-COV2, Dengue fever, Camellia sinensis, Thrombocytopenia, Flavonoids.

Introduction

Green tea is derived from the plant Camellia sinensis. The buds and leaves of this plant undergo oxidation and withering procedures to create black and oolong teas. Although green tea originated in China, it is now cultivated and produced in various eastern Asian nations. Green tea contains numerous polyphenolic compounds, such as flavandiols, flavonols, flavonoids, and phenolic acids, which can make up over 30% of its dry weight. Among these compounds, catechins, a type of flavonol, are the most abundant polyphenols found in green tea.[1]

Tea polyphenols have antiviral properties, mediated through a variety of mechanisms, which is essential during a pandemic situation, as researchers are racing to find treatments against coronavirus disease 2019 (COVID-19). The potential of polyphenols was underlined during the SARS-CoV-2 pandemic because they present multiple defense mechanisms against coronaviruses. The effect of polyphenols on coronavirus infections is complex. First of all, selected polyphenols—e.g., luteolin—show a high affinity with the S protein of the virus, thus preventing its entry into human cells. Epigallocatechin gallate (EGCG) attaches to the viral hemagglutinin, preventing the virus from binding to the cell's target receptor, which prevents the virus from spreading.[2]

Coronavirus disease 2019 (COVID-19), is a respiratory illness caused by a virus called severe acute respiratory syndrome coronavirus 2 (SARS COV-2) which was first introduced to the world after an outbreak in Wuhan City, China. On December 31, 2019, it was reported to World Health Organization (WHO) and was declared a global health emergency on January 30, 2020.[3] According to WHO, symptoms of Covid-19 infected individuals include fever, cough, malaise, sore throat, conjunctivitis, ageusia, and anosmia etc.[4] The first case of Covid-19 in Pakistan was detected on 26 February 2020, and the number of cases has increased exponentially ever since, with a death toll of 28,830 to date (12/12/2021).[5]

Dengue is an acute febrile illness caused by a single-stranded RNA virus with 4 serotypes: DEN-1, DEN-2, DEN-3, and DEN-4.[6] is Aedes aegypti the most important mosquito vector of

the disease, due to being highly anthropophilic and preference for habitats in proximity to humans.[7] Dengue virus infection continues to rise as one of the world's emerging infections, with approximately 50 million cases being reported annually.[8] Pakistan, being the fifth most populous country and having an annual growth rate of 2%, with rapid urbanization, makes the environment favorable for vector breeding.[9] From 1995 to 2019, there were around 147,200 cases of dengue infection and over 800 deaths.[10]

The symptoms of Dengue virus infection include high-grade fever, typically accompanied by any of the following: chills, retro-orbicular pain, photophobia, backache, severe muscle & joint ache, nausea, vomiting, and abdominal pain.[11]

We present a case of a 28-year-old male who was diagnosed with COVID-19-Dengue virus coinfection.

Case Presentation

A 28-year-old male, a medical lab technician by profession, with no significant past medical history presented to the OPD with a low-grade fever, chills, pain in nostrils, shortness of breath, and loss of appetite for 4 days. Upon presentation, his vital signs showed fever that fluctuated between 102-degree Fahrenheit to 104-degree Fahrenheit, B.P of 120/80 mmHg, heart rate of 100 beats per minute, respiratory rate of 12-14 breaths per minute, and O2 saturation of 92 % while breathing ambient air. Cardiac auscultation was normal and lung auscultation revealed bilateral fine basal crepitations. Being a medical lab worker, he had a significant history of close contact with suspected Covid-19 patients as he collected NP swabs throughout this time.

A complete blood count revealed mild Thrombocytopenia with platelet count decreasing from 230 x 10^9/liter (day1) to 139 x 10^9/l (day 4), a decreasing leukocyte count from 5.6 x 10^9/l (day 1) to 4.3 x 10^9/l (day 4) with a raised monocyte count of 13 % (N= 2%-10%), and a neutrophil count of 56%. There was also a Decrease in hemoglobin level from 14.6 g/dl (day 1) to 12.6 g/dl (day 4), with an insignificant decline in total RBCs from 4.8 x 10^12/l to 4.5 x 10^12/l. ESR was elevated - 34mm/1st hour, CRP levels were raised - 1.27 mg/dl (N= < 0.5 mg/dl), and serum ferritin levels were 252.89 ng/ml (N= 20-250 ng/ml). [Table 1].

His liver and renal profiles were in normal ranges, but his coagulation profile showed an INR of 1.2 (N <1.1). His chest X-rays showed ground-glass haze with alveolar opacities in the lower zones of both lung fields (more marked on the right side) [Fig 1]. Dengue serology came back positive with raised Non- Structural Antigen (NS-1 = 2.1; R.R = < 0.9). Additionally, as a part of the hospital's protocol to screen all patients for COVID-19, the SARS COV-2 was detected through a nasopharyngeal swab.

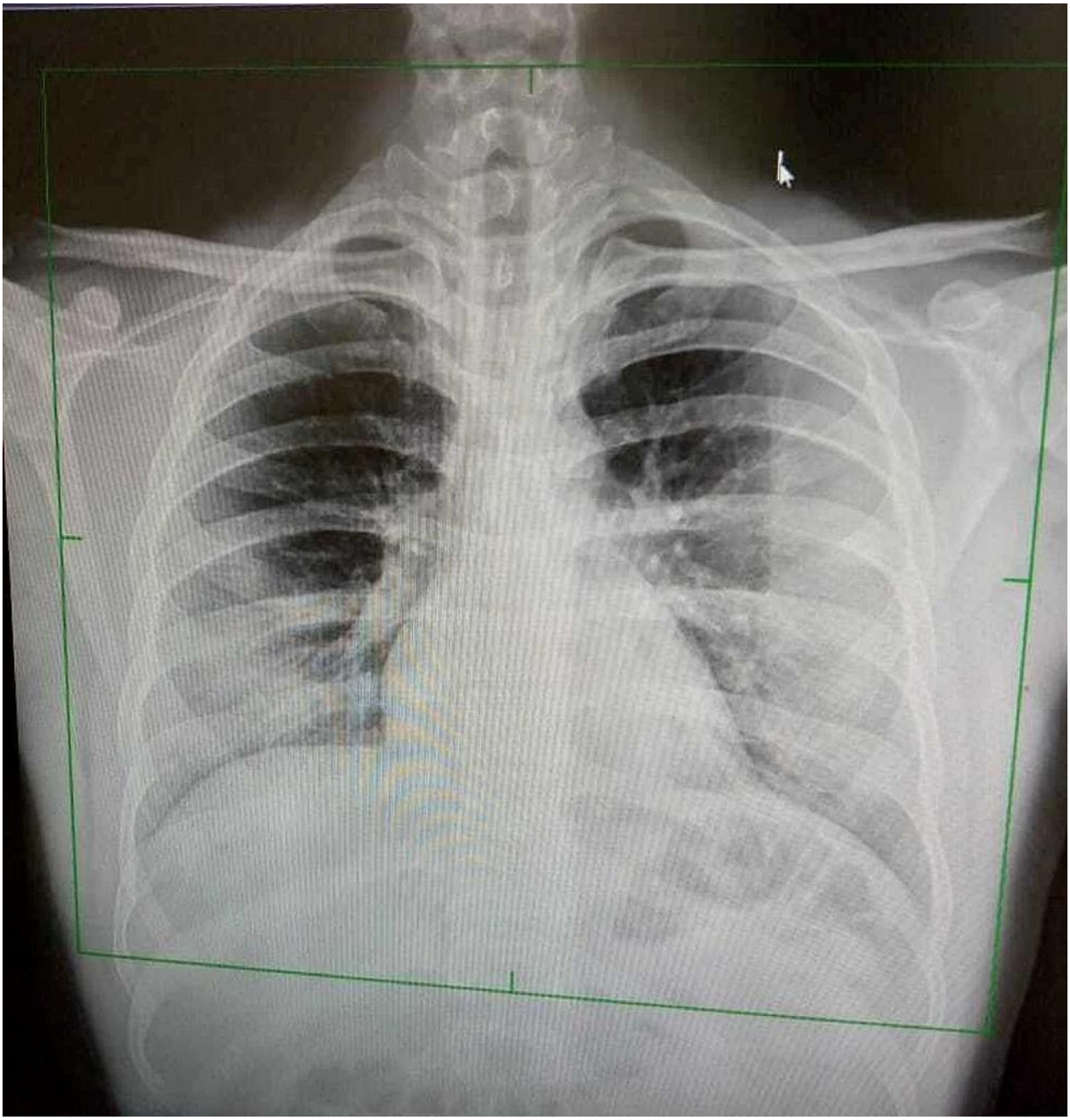

Figure 1: Chest X-ray showing ground glass haze at the lung base

The patient took a herbal extract of Camellia sinensis traditionally known as Kashmiri kahwa three times a day for two weeks along with steam inhalation just before sleep. The steam mixture also contained the green leaves of Camellia sinensis. In addition the patient was treated on an outpatient basis with Acetaminophen (500 mg TDS) for 14 days, Azithromycin (500mg OD) for 7 days, tablet Surbex (500mg), Zinc (22.5 mg OD), Calcium

Carbonate (1250mg OD), and Vitamin D3 supplements (125IU OD), as per standard treatment guidelines for COVID-19 being followed in tertiary care hospitals in Pakistan. Instructions to monitor Oxygen saturation and to look out for the warning signs of dengue (including but not limited to epistaxis, petechiae, and hematuria) were given to the patient. He had an uneventful recovery. After 14 days, a follow-up RT-PCR for COVID-19 was repeated using nasopharyngeal swab specimen, performed through Zybio SARS COV-2 nucleic acid detection kit real-time PCR assay. The PCR turned out negative and the patient was discharged afterwards from the hospital

Hemoglobin	14.6 g/dl	12.6 g/dl
RBC count	4.8 x 10^12/l	4.5 x 10^12/l

Table-1 Laboratory findings on Day 1 and Day 4

Parameter	Day 1	Day 4
Leucocyte count	5.6 x 10^9/l	4.3 x 10^9/l
Platelet count	230 x 10^9/liter	139 x 10^9/l
ESR	34mm/1st hour	Not repeated
CRP	1.27 mg/dl	Not repeated
Serum Ferritin	252.89 ng/ml	Not repeated

Discussion

After a cluster of respiratory tract infections was identified in Wuhan district, China, in December 2019, Chinese authorities identified the culprit as a novel coronavirus on 7 January 2020 and temporarily named it "2019-nCoV".[12] WHO declared it as a pandemic on 11 March 2020.[13] Pakistan, like every other country, has had to face this incredible disease burden. Being ranked 152th out of 189 countries with a Human Development Index value of 0.560, the country's healthcare system is severely overburdened by the patient load amidst this pandemic.[14] On 23 April 2020, Pakistan was warned by WHO about the impending danger to the country by COVID-19 and was advised to take measures to prevent it from happening.

There is a significant overlap in symptoms of COVID-19 infection and Dengue Viral Illness (DVI).[15] This has posed a diagnostic dilemma for countries where Dengue virus remains an endemic disease. Multiple patients have been reported with coinfection with both these diseases all around the world.[16-18]

Amidst a pandemic, with the saturation of limited health resources being directed to handle the COVID-19 burden, there seems to be the imminent threat of a worsening epidemiological profile of dengue in the country. This poses as an incredible problem while dealing with the diagnosis and management of other diseases, like dengue.

WHO has emphasized the need to sustain efforts to prevent, detect, and treat vector-borne diseases, such as malaria, during this pandemic.[19]

Another challenge faced in the diagnosis of coinfection seems to be the significant overlap in symptoms of the two diseases. The diagnostic complexity proves to be a challenge for doctors due to the resembling nonspecific symptoms of both diseases like fever, body aches, headache, malaise etc. This overlap has even led to an under diagnosis of dengue during the COVID-19 pandemic. A similar situation has occurred with other diseases with similar presentation to COVID-19, like Typhoid fever being underreported in Pakistan.[20]

Patient in our study presented with constitutive symptoms including fever, loss of appetite, and pain in the nostrils. On labs he had a positive Dengue NS-1 antigen test, mild thrombocytopenia, decreasing leukocyte count, decrease in Hemoglobin, elevated INR, serum Ferritin and elevated ESR. These symptoms correspond to the findings reported for both COVID-19 and DVI in literature published locally and internationally.[11]

As per the screening protocol, the patient was tested for COVID and he presented with similar findings as in Covid Patients but was not diagnosed initially because his symptoms overlapped with that of dengue fever illness (DVI). The patient had similar findings in chest X-Rays showing bilateral infiltrates and deranged labs including a decrease in leucocyte count and mild thrombocytopenia, but overall had a good prognosis.

The patient was subsequently treated symptomatically for fever, along with prophylactic Azithromycin to prevent any superadded bacterial infection. The patient was treated in an Outpatient setting and was managed in OPD exclusively. The patient regularly consumed an extract of Camellia sinensis (Kashmiri kehwa) thrice daily for two weeks along with steam inhalation just before sleep. The steam mixture also contained the green leaves of Camellia sinensis.

The antiviral activity of polyphenols has long been known to the scientific community. As this patient's symptoms of COVID-19 and Dengue fever got better through the use of herbal extract of Camellian sinensis, therefore, we recommend that the polyphenol compounds like flavanols, flavonoids, luteolin, phenolic acids, etc, be isolated and purified from the herbal extract of Camellia leaves and subsequently tested for their particular efficacy against SARS-COV-2 and Flaviviruses.

We also recommend that in areas with a high prevalence of dengue fever, as now in Punjab, Pakistan, serological screening of dengue should also be made part of the COVID investigation, especially if symptoms correspond. During the COVID-19 pandemic, precautionary isolation of patients presenting with Acute Febrile Illness should be considered to prevent the spread of infection. A multi-sectoral approach should be

taken and proper prevention for both diseases should be integrated to solve this problem.

To prevent this co-epidemic from further burdening a resource-limited healthcare system, proper care should be taken to prevent Dengue Virus Illness from spreading and reaching an unmanageable scale. These would include proper mosquito control measures, regular spraying of breeding sites of larvae with insecticide formulations, educating the general population regarding the prevention and control of the vector, engaging the general population in vector control strategies, and prompt diagnosis, treatment, and isolation of patients infected with Dengue virus. Special precautions of social distancing should be made by the vector control team as well as the public to prevent the further spread of either disease.

Conclusion

In this case report, we have analyzed and reported the simultaneous infection of SARS COV-2 and Dengue virus (flavivirus) for the first time at a government healthcare facility in a dengue-endemic region of Pakistan. This case report accomplishes the following objectives:

i. Our work enlightens the antiviral activity of polyphenol compounds like Catechins and Flavonoids in the herbal extract of Camellian sinensis as a possible remedy against COVID-19 and warrants the need for intense biochemical testing of various polyphenols compounds from the extracts of Camellia leaves in order to discover potential therapeutic agents for treating Covid-19.

ii. This report opens room for interventional biochemical research to look for a plausible interaction between the pathophysiology of these two RNA viruses at a molecular level. A possible overlap between the pathophysiological mechanisms of two viruses can open new horizons in our understanding of these two viruses in detail and provide a foundation for the development, as well as, testing of novel antiviral therapeutics that could target both infections.

iii. In this case report, we have analyzed and reported the simultaneous infection of SARS-COV-2 and dengue fever virus (flavivirus) for the first time at a government healthcare facility in a dengue endemic region like Pakistan. Both Covid-19 and dengue fever can lead to potentially fatal outcomess, especially in patients with underlying co-morbidities, therefore overlapping infections may increase the need for immediate medical intervention as well as the number of intensive care unit facilities especially in the third world regions.

iv. In a nutshell, our case report has brought to light the concurrence of two deadly RNA viral infections, their subsequent prognosis in an otherwise healthy adult, the addition of Camellia sinensis leaves as part of the treatment plan in addition to the typical medications given in tertiary care hospitals of Pakistan. This report warrants the healthcare authorities, particularly in developing countries, to promote mosquito control programs, raise awareness regarding social hygiene, and closely monitor the prognosis of these two viral infections if they co-occur.

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