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Co-occurrence and Co-infection of COVID-19 and dengue: A serious public health issue

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Abstract

The prevailing COVID-19 pandemic has created havoc all around the world taking the lives of more than one million people. While the entire world is struggling hard to combat this pandemic; unfortunately, the burden has been further intensified by another fatal mosquito vector borne disease-dengue, particularly in dengue-endemic nations. The shared clinical features like fever, aches, respiratory ailments and so on by both the viral disease has led to the difficulty in their diagnosis and also to distinguish one from the other. In this regard, cases of misdiagnosis due to false positive test result has also been reported in some places. Hence the co-occurrence and co-infection of COVID-19 and dengue is indeed a great threat to public health in dengue endemic nations. This article aims to provide an overview of epidemiology, transmission and shared clinical features of COVID-19 and dengue besides highlighting the issue of misdiagnosis of both under clinical setting. Scientific evidence proving the fact that mosquitoes do not transmit SARS-CoV-2 pathogen has also been discussed. The present scenario of dengue outbreak in India amidst the prevailing COVID-19 pandemic has also been highlighted.

Keywords: COVID-19, pandemic, SARS-CoV-2, dengue, disease

1. Introduction

Viruses are non-cellular, nucleoprotein particles whose genetic material is capable of causing infection ^[1]. They are obligate parasites. Outside the living cell, they remain as an inert crystalline structure. Viruses entirely depends upon the host cell for replication. After infesting the host cell, they take control of the host cell machinery in order to replicate. However, each type of virus has developed a unique approach at each phase of replication- starting from entering into the host cell till the release of virion progeny ^[2]. Structurally, a typical virus consist of a protein coat which protects the viral genetic material i.e. either DNA or RNA, but never both ^[1]. Viruses can infect both plants and animals as well as bacteria. Viruses causes a wide array of diseases in humans like influenza, small pox, mumps, herpes, corona virus, AIDS and many more. Recent corona virus outbreak has created a burden to public health all around the globe.

Corona virus disease (COVID-19) is caused by a virus belonging to the family Coronaviridae called severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) ^[3]. The World Health Organization (WHO) announced SARS-COV-2 outbreak as Public Health Emergency of International Concern (PHEIC) on 30 January 2020 ^[4]. Considering the fatality and massive transmission of this deadly virus, the WHO has declared COVID-19 as global pandemic outbreak ^[5, 6]. This deadly virus causing havoc has spread across 213 nations across the globe ^[7]. As of 30 September, 2020, total confirmed cases of COVID-19 recorded were 33,249,563 while 1,000,040 deaths were recorded around the world ^[8].

While the entire world is battling to combat COVID-19, this burden has been further aggravated by the outbreak of mosquito vector borne disease-dengue, particularly in dengue-endemic countries around the world ^[7]. Presently, there is co-existence of both COVID-19 and dengue virus in dengue-endemic nations. Similar clinical symptoms such as fever, aches and respiratory ailments shared by both the viral diseases have raised serious concerns in dengue endemic countries having scarce resources. Therefore, co-infection pose great challenge for correct diagnosis and treatment where symptoms are overlapping. Many a times, the shared clinical features by both the diseases ends up in misdiagnosis ^[9].

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Besides mentioning the dengue-endemic regions and nations of the world, this article also aims to provide in a nutshell, the epidemiology, transmission and shared clinical features of both COVID-19 and dengue, provide evidence of misdiagnosis of both the diseases due to shared clinical symptoms and the probable immunological reasons behind this, remove the speculation that mosquitoes transmit SARS-CoV-2 pathogen, and provide an overview of dengue outbreak amidst COVID-19 pandemic in India.

2. Epidemiology and Transmission of COVID-19

People of all age group are susceptible to COVID-19 infection [10]. The pathogen is transmitted via large droplets produced during sneezing and coughing by an infected person bearing symptoms of the disease. However, the virus can also be transmitted from asymptomatic persons as well, even before signs of any symptoms is seen [11]. Those viral contaminated droplets can spread to a distance between 1-2 m. A healthy person acquires this infection either by inhaling infected droplets or by touching eyes, mouth and nose with hands contaminated by such droplets. This happens by inoculation of the virus to the mucous membranes of nose, eyes or mouth [4, 12]. Apart from droplets, the SARS-CoV-2 has also been reported in faeces and sewage, thereby providing a provision for faecal-oral transmission [13, 14]. Further research have revealed the fact that the load of virus is higher in the nasal cavity than the throat of an infected individual, whereby the viral potential is same in both symptomatic and asymptomatic individual [15].

2.1 Clinical Symptoms

COVID-19 infection shows a diverse clinical feature which varies from being asymptomatic to septic shock, acute respiratory distress syndrome and multi-organ dysfunction [10]. On the basis of severity of occurrence, this disease has been categorized into mild, moderate, severe and critical [16]. General symptoms like fever was observed in 98.6% infected individuals, fatigue or weakness in 69.6% patients, other symptoms include loose bowels and dry cough [17].

2.2 Diagnosis

As per WHO guidelines, samples may be collected from both upper and lower respiratory tract. The collected samples are tested for viral RNA through polymerase chain reaction. If the result is found positive, the test process should be repeated for further verification [18].

3. Mosquito Vector Borne Disease – Dengue

Mosquitoes are the vectors of various diseases like malaria, dengue, Japanese Encephalitis, chikungunya, lymphatic filariasis posing serious threats to public health in the tropical countries [19]. Among these diseases, dengue hemorrhagic fever along with dengue is the fastest growing mosquito vector borne disease in the world [20].

3.1 Epidemiology and Transmission of Dengue Virus

Dengue is a mosquito borne arboviral disease caused by a virus – Dengue virus (DENV) which occurs in four stereotypes namely DENV1, 2, 3 and 4. The mosquito vector which transmits dengue virus is mainly female mosquitoes of *Aedes aegypti* and *Aedes albopictus*. *Aedes aegypti* is the major vector species of dengue which has high adaptability to both natural and man-made environments [21]. Currently,

dengue is endemic to more than 100 countries around the globe, where Asia alone accounts for nearly 70% of global dengue burden. The highest confirmed cases of dengue globally were recorded in the year 2019 [22].

3.2 Diagnosis

Diagnosis of dengue virus is carried out by means of ELISA technique and available commercial kits wherein presence of IgM antibodies or NS-1 antigen in the blood of patient is detected [23]. In recent times, the use of Reverse Transcriptase PCR (RT-PCR) technique in the diagnosis of dengue is also widely used [24].

3.3 Distribution and global burden of dengue

In the last two decades, the number of reported dengue cases to WHO has increased over 8 fold times. Severe dengue as epidemic was reported only in 9 nations around the globe before 1970. Today dengue is endemic in more than 100 nations around the world and includes regions of South-East Asia, the Western Pacific, areas of Africa, the Eastern Mediterranean and the America [22]. However, Asia records around 70 % of the global dengue cases. The outbreak of dengue has spread in mainland Portugal and 10 other European nations as well [22].

Presently, the South American nations like Brazil, Olivia, Argentina, Paraguay, Mexico, Columbia, and countries of South-East Asia like Philippines, Singapore, Malaysia, Thailand, Vietnam, Indonesia, Pakistan, India, Nepal and Bangladesh are suffering from serious dengue outbreak this year [7, 22].

4. Overlapping symptoms between dengue and COVID-19

It is very difficult to differentiate between COVID-19 and dengue fever since both the diseases share common laboratory and clinical features [25]. Common clinical symptoms like fever, headache and cough were seen in most patients confirmed with COVID-19 infection [26]. Similarly, fever, rash in skin are also symptoms of dengue [27]. Clinical symptoms in the very beginning like fever, myalgia and headache are generally seen in both COVID-19 and dengue infected patients. However symptoms pertaining to respiration like sore throat, cough, loss of smell or taste may encourage to proceed for COVID-19 test [28].

Therefore, coinfection of dengue and COVID-19 is a big challenge for correct and precise diagnosis of these viral diseases where both share similar clinical features [7].

5. Misdiagnosis of the two diseases due to shared clinical features

Few common clinical symptoms shared by both COVID-19 and other endemic arboviral infections in Asia like dengue often leads to misdiagnosis [29, 30]. This may ultimately lead to wrong treatment. Although diagnosis and detection of dengue is mainly depended on serological tests by means of ELISA techniques, the use of point-of-care card tests for rapid result is also gaining popularity [28]. The reliability of such card test kits is in question after the first ever false positive result of dengue was reported in Singapore, wherein two patients were preliminarily confirmed with dengue through rapid IgM and IgG serology test, but were later confirmed to be COVID-19 positive through RT-PCR testing [9].

Similar clinical traits of dengue and COVID-19 leading to wrong diagnosis may be the result of serological cross

reactivity between the two viruses DENV and SARS-CoV-2 [6]. A hypothesis was drawn that individuals who were earlier exposed to DENV developed anti DENV antibodies in blood which works as cross-reactive agents with SARS-CoV-2 antigens [29]. On the other hand, there may also be similarities between antigens of SARS-CoV-2 and DENV, such that the memory B cells are activated to produce anti-DENV antibodies in response to SARS-CoV-2 infection [29].

According to a recent report, a person coinfecting with Covid-19 and dengue died in Thailand. Similar was the case with another patient in India and two patients from Bangladesh where one of them died [7].

6. Incapability of SARS-CoV-2 to replicate in mosquitoes

There was a speculation among people that mosquitoes might get infected by SARS-CoV-2 and those mosquitoes in turn transmit the virus. In response to this public speculation, the WHO stated that the virus cannot be transmitted by mosquitoes [3]. This statement of WHO was experimentally proven by a recent study conducted on three widely distributed mosquito species-*Aedes aegypti*, *Aedes albopictus* and *Aedes quinquefasciatus* [31]. Through intrathoracic inoculation of SARS-CoV-2 in these three species of mosquitoes, their susceptibility to the virus was studied. The results have shown the absence of infectious virus in either of the 277 test samples collected at different intervals after 24 hours post-inoculation. From this experiment, a hypothesis was drawn that even after intrathoracic inoculation of SARS-CoV-2 in mosquitoes, if the virus failed to replicate, then the virus cannot be transmitted to people even if a mosquito feed upon the blood of a viremic host [31]. Therefore, lack of viral replication would check the biological transmission of SARS-CoV-2 through mosquito vector. Moreover, for arthropods to transmit viruses mechanically, there is need of very high viremia [32]. Therefore, the mouthparts of mosquitoes remain free from contamination even if there is interruption during feeding on a SARS-CoV-2 infected host.

7. Recent outbreak of Dengue in India amidst COVID-19 pandemic

India being a dengue-endemic nation faces adversity every year due to massive outbreak of dengue. Dengue outbreak in the ongoing COVID-19 pandemic is a serious threat to public health in this populous country. As of 15 September 2020, the total dengue positive cases in the National Capital of India-Delhi reached 131, where around 35 positive cases were recorded in a single week [33]. As of May 16, a total of 14 dengue positive cases have been reported in Assam in the present year as per the statement obtained from the National Health Mission, Assam [34]. Amidst the devastating floods in many districts and COVID-19 outbreak, mosquito vector borne disease is on the rise in Assam. 220 confirmed malaria cases, 19 cases of dengue and 199 cases of Japanese Encephalitis cases have been reported till 25 July, 2020 [35]. Finally, dengue cases reached to 24 in the state as on September 23 this year [36]. Mainly urban areas of the state of Assam are affected with dengue, whereas a number of municipal wards in the city of Guwahati are identified as hot spots of dengue outbreak. Besides the rampant spread of COVID-19 in the metro city of Kolkata, few patients have tested positive for dual infection- both COVID-19 and dengue, thereby raising the concern of health workers [37]. Amidst the battle to combat COVID-19, the city of Chennai

too is facing a rise in dengue cases. The Public Health department have identified as many as 30 hotspots where stagnation of sewage and rainwaters occurs [38]. The state of Odisha is also not an exception to dengue outbreak amidst COVID-19. As per the department of health, 49 samples of blood out of 139 samples were found to be positive for dengue from Rayogada district of the state where dengue have started to emerge [39].

8. Conclusion and Discussion

There is no doubt that co-occurrence and co-infection of dengue and COVID-19 have created a great burden on the medical and public health in dengue-endemic nations around the world [40]. It has also raised concern in those nations with limited resources and where the health care infrastructure is not up to the mark. Above all, co-infection is a challenge for correct laboratory diagnosis because of shared clinical symptoms shown by infected individuals being infected with either or both the viruses. Moreover, in many cases health workers and researchers are deceived by false positive results which is also a matter of concern [9].

Moreover, serological cross reactivity between antibodies against SARS-CoV-2 and DENV have also been reported in recent research [6]. Therefore, an affordable and rapid test that can distinguish between DENV and SARS-CoV-2 with high precision is the need of the hour.

However, it is experimentally proven that SARS-CoV-2 is incapable to infect or replicate in mosquitoes [31], else the present miserable situation would have worsen.

With regards to India, it has been observed that cases of co-occurrence of these two viruses is increasing gradually. Therefore, considering the current rise in COVID-19 and dengue cases, hospitals should develop sufficient infrastructure to treat patients with dual infection.

It is also suggested that in tropical countries where there is co-occurrence of both COVID-19 and arbovirus infection, patients should be diagnosed for both the viruses since clinical diagnosis is not easy due to overlapping symptoms [27].

The number of COVID-19 positive cases and death is also increasing around the world. Researchers all around the globe are engaged in search of remedy to overcome this pandemic and develop vaccine against this fatal disease. The world has witnessed many epidemic and pandemic outbreak since ages. Hence, even if mankind gains victory over this pandemic outbreak, the world should be prepared for such health emergencies that may arise in future through implementation of advanced disease control and management strategies, improved health care infrastructure and investing more time and funds in health care research.

It can finally be assumed that co-infection of COVID-19 and dengue may take a peak in the season of monsoon and retreating monsoon in dengue-endemic nations. Hence, these nations should adopt strong measures like effective mosquito vector control strategies which is as important as maintaining hygiene and social distancing norm in today's world.

Conflict of interest: The authors declare that they have no competing interests.

Author Contributions: All the authors have equal contribution in this paper. All the authors conceived the study, conceptualized the paper, prepared, critically read and revised the manuscript, and gave final approval for publication

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