Research Article

SEROPREVALENCE OF DENGUE VIRAL INFECTION IN PATIENTS ATTENDING TO TERTIARY CARE HOSPITAL DURING COVID-19 PANDEMIC

Kiranjeet Kaur and Aditi Goyal

College / Institute / University / Adesh Medical College

ABSTRACT

Introduction: Co-infection and co-occurrence of Covid-19 and dengue have introduced a significant burden on healthcare systems in dengue-endemic regions[10]. The complexity of diverse disease severities, prolonged infectious periods, and shared clinical manifestations and pathogenesishave made their diagnosis, treatment, and resource allocation challenging, particularly in developing countries in Asia with high prevalence of dengue and other arboviruses. **Aim:** To assess seroprevalence of dengue viral infection in patients attending to tertiary care hospital during covid-19 pandemic. **Material and methods**: All blood samples tested collected from clinically suspected dengue were tested by rapid qualitative immunochromatographic assay for differential detection of Dengue Virus (DENV) NS1 antigen, DENV specific IgM and IgG antibodies and the rapid detection of Dengue infection was performed by commercially available kits. **Results:** During the study period of one year, a total 703 samples from suspected dengue patients were tested for dengue NS1, IgM and IgG serology of which 151(21.5%) samples were positive. Primary dengue infection seen among 141(93.4%), secondary dengue infection among 6(4.0%) and old dengue infection was seen among 4(2.6%). Co-infection of dengue was reported among 4(2.6%) patients who were Covid positive. **Conclusion:** This pandemic has further exacerbated the burden in tropical and subtropical regions of the world, where dengue fever is already endemic to the population. Similar clinical manifestations shared by COVID 19 have raised concerns especially in dengue endemic countries with limited resources leading to diagnostic challenges.

INTRODUCTION

Dengue is a major public health problem throughout tropical and sub-tropical regions. This disease is caused by any of the foursero types of dengue virus (DENV), transmitted by mosquitoes, primarily the Aedesaegypti species and the development of vaccine still remains a challenging task[1,2,3]. Clinical manifestations of dengue virus infection range from asymptomatic, mild flu-like symptoms, to severe life-threatening dengue complications such as dengue shock syndrome (DSS) and dengue hemorrhagic fever (DHF)[4]. DHF/DSS cases are associated with a secondary-type dengue antibody response, which makes the second dengue infection worse than the first due to "antibody-dependent enhancement of infection"[4].

Dengue virus has antigenically four distinct serotypes which are called DEN-1, DEN-2, DEN-3, DEN-4. Each serotype of virus produces a specific, life-long immunity but only a short term cross-immunity[5]. Dengue virus infection presents with a diverse clinical picture that ranges from asymptomatic illness to DF to the severe illness of dengue hemorrhagic fever/dengue shock syndrome (DHF/DSS)[6]. Patients may present like pain abdomen, bleeding diathisis like rash, hematuria, respiratory symptoms. Four main characteristic manifestations of dengue illness are (i) continuous high fever lasting 2-7 days; (ii) haemorrhagic tendency as shown by a positive tourniquet test, petechiae or epistaxis; (iii) thrombocytopoenia (platelet count <100×109/l); and (iv) evidence of plasma leakage manifested by haemoconcentration (an increase in haematocrit 20% above average for age, sex and population), pleural effusion and ascites, etc[7].

Dengue virus infection exhibit varied clinical presentation, hence, accurate diagnosis is difficult and relies on laboratory confirmation. The condition is usually self-limiting and antiviral therapy is not currently available. Supportive care with analgesics, hydration with fluid replacement, and sufficient bed rest forms the preferred management strategy. DHS and DHF are fatal complications which are often associated with infection by second serotype. Novel coronavirus disease 2019 (COVID-19) is a respiratory illness caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was first reported as an outbreak in Wuhan, China, and spread worldwide, causing a pandemic disease.

The first epidemic of clinical dengue like illness was recorded in Chennai. In past dengue has assumed pan India proportions. In fact dengue case fatality rate has been above 1% over last 10 years[8]. This is due to unplanned urbanization and migration of population from rural to urban areas with lack of proper

---

Corresponding author: **Aditi Goyal**
College / Institute / University / Adesh Medical College

sanitation facilities, are important factors which have resulted in an increased burden of dengue in recent times[9].

Co-infection and co-occurrence of Covid-19 and dengue have introduceda significant burden on healthcare systems in dengue-endemicregions[10]. The complexity of diverse disease severities, prolonged infectious periods, and shared clinical manifestations and pathogenesis have made their diagnosis, treatment, and resource allocation challenging, particularly in developing countries in Asia with high prevalence of dengue and other arboviruses. Clinical symptoms of Covid-19 include cough, muscle aches, fatigue, skin rash, and petechiae, making it challenging to differentiateCovid-19 from other endemic viral infections in the region, such as dengue[11], and thus potentially leading to misdiagnosis[12].Beyond the similar clinical manifestations of Covid-19 and dengue, misdiagnosis may be due to serological cross-reactivity betweenSARS-CoV-2 and DENV. It was hypothesized that patients with previous exposure to DENV possess anti-DENV antibodies that are cross reactive with SARS-CoV-2 antigens[11].

Co-epidemics can create a burden on healthcare systems in the affected areas. The world, at present, is facing the pandemic of coronavirus disease. Nonetheless, many areas worldwide suffer from endemics that are not of less danger than the current pandemic. During the pandemic, vector control measures might have decreased in the community and dengue prevention programs might have been paused in some countries. Therefore, countries that are experiencing or have high risk for dengue outbreak should maintain the vector control measures during the pandemic. A good laboratory-based disease surveillance is essential for early detection of outbreaks and also for estimating the disease burden due to dengue.

Aims & Objectives

To study the seroprevalence of dengue viral infection in patients attending to a tertiary care hospital during COVID- 19 pandemic.

MATERIAL AND METHODS

The study was conducted in Virology section of Microbiology Laboratory, A desh Hospital after clearance from research and ethics committee. All blood samples tested collected from clinically suspected dengue were tested by rapid qualitative immunochromatographic assay for differential detection of Dengue Virus (DENV) NS1 antigen, DENV specific IgM and IgG antibodies and the rapid detection of Dengue infection was performed by commercially available kits. The kit provides two windows, one detection of NS1 antigen and other for dengue specific IgM and IgG antibodies. All tests in this study were carried out in accordance with the manufacturer's instructions and results were examined and interpreted accordingly; the blood sample of individuals containing IgM or/and NS1 were considered as primary/acute dengue infection, i.e. they were infected by DENV for the first time[13]. The tests indicating IgG + IgM/NS1 were considered as secondary infection, i.e. such patient was already infected by dengue in past. If the individual was detected positive for IgG but negative for other tests (IgM and NS1), were considered as past infection or secondary DENV infection with symptoms. The presence color line (control) in each result window indicates a negative result. All positive serum was sent for confirmation by ELISA method to sentinel surveillance hospital and followed up for confirmatory results. Clinical data of patient was collected from the patients record files and compiled.

RESULTS

During the study period of one year, a total 703 samples from suspected dengue patients were tested for dengue NS1, IgM and IgG serology of which 151(21.5%) samples were positive. A total 461(65.6%) samples were collected from male patients and 242(34.4%) from female patients. 436(62%) samples were collected from opd patients and 267(38%) from indoor patients. Age wise distribution was as shown in Table 1 showing maximum samples were collected from 40-59(23.7%) age group followed by 20-39(22.2%) years and similar pattern of positivity. Serological marker distribution was as shown in Table 2. Primary dengue infection seen among 141(93.4%), secondary dengue infection among 6(4.0%) and old dengue infection was seen among 4(2.6%). Co-infection of dengue was reported among 4(2.6%) patients who were Covid positive.

Table 1 Age wise distribution of patients

Age in years	No. of samples tested	No. of samples positive	Percentage
0-9	59	8	13.5%
10-19	46	10	21.7%
20-39	198	44	22.2%
40-59	232	55	23.7%
>60 Above	168	34	20.4%
Total	703	151	21.5%

Table 2 Serological marker distribution of primary and secondary dengue infection

Type of dengue serology	Number	Percentage
Primary dengue infection with only IGM Positive	61	40.4%
Primary dengue infection with only NS1 positive	48	31.8%
Primary dengue infection with both NS1 and IGM Positive	32	21.2%
Number of secondary dengue infection(IgG positive with IgM/NS1 or both positive	6	4.0%
No. of old infection (only IgG positive	4	2.6%
Total dengue positive	151	21.5%

DISCUSSION

Dengue has been known to be endemic in India for over two centuries. It is an important emerging disease of the tropical and subtropical regions today. This study was conducted to analyze the seroprevalence of dengue specific antibodies from patients with clinically suspected dengue fever.

Laboratory diagnosis of dengue infection is crucial as the broad spectrum of clinical presentations can make accurate diagnosis difficult. Seroconversion of IgM or IgG antibodies is the standard for serologically confirming a dengue infection[14.] Dengue virus specific IgM antibodies tend to appear as early as 3 days after infection and remains in circulation for 30 to 60 days. IgG antibodies arise at about 7 days, they reach peak at 2-3 weeks and persist for life. Detection of dengue specific IgM antibodies allows a provisional diagnosis to be made from a single serum sample[15].

In this study, 21.5% patients had serologically confirmed dengue infection. In conformation to our findings Garg et al reported the seroprevalence of dengue infection at a teaching hospital in northern india to be 19.7%[6]. A recent study was conducted in government hospital in delhi, where

seroprevalence was 19.6%[16]. However another study was done on suspected dengue cases ehereseroprevalence was 44.56%[17]. A study from central India reported 31.3% patients to be serologically positive for dengue infection[18].

A higher prevalence of dengue infection was seen in males than in females. The male to female ratio in this study was 1.9:1. This may be representation of those who visited the hospital to seek care rather than truly infected population.

The age group which was most commonly affected in this study was 40-59(23.7%)years age group. Our findings were contrary to those of some Indian studies which had reported the vulnerability of children to dengue infection[6]. However a few hospital based studies have similarly reported increasing infection rate among adults[19].

On the basis of data which was collected, the population of this study could be categorized into several distinct groups: among the 703 patients who were screened 21.5% (151) were dengue positive. 78.5%(552) were dengue non sufferers. 40.4% were primary dengue cases with only IgM antibodies, 31.8% with NS1 antigen positive. These included 2.6% old dengue cases with both IgG antibodies and 4% true secondary dengue cases with both IgG and IgM antibodies.

A month wise analysis of dengue infections revealed that dengue cases increased in number gradually from july onwards and that it peaked in the month of October each year. This seasonality of transmission of dengue, with an increased activity post monsoon, was in accordance with reported patterns of dengue transmission. The presence of stagnating water after rainfall favours breeding of mosquito vector, resulting in an increase in dengue cases. Hence it is recommended that preventive measures should be implemented during monsoon and post monsoon months.

CONCLUSION

This pandemic has further exacerbated the burden in tropical and subtropical regions of the world, where dengue fever is already endemic to the population. Similar clinical manifestations shared by COVID 19 have raised concerns especially in dengue endemic countries with limited resources leading to diagnostic challenges.

Acknowledgement

References

1. Wilder-Smith A, Ooi EE, Horstick O, Wills B. Dengue. Lancet. 2019; 393:350-363.
2. Redoni M, Yacoub S, Rivino L, et al. Dengue: status of current and under-development vaccines. Rev Med Virol. 2020; 30:e2101.
3. Wilder-Smith A. Dengue vaccine development: status and future. Bundesgesundheitsblatt Gesundheits for schung Gesundheits schutz. 2020; 63:40-44. 21.
4. Pang X, Zhang R, Cheng G. Progress towards understanding the pathogenesis of dengue hemorrhagic fever. Virol Sin. 2017; 32:16–22. 4.
5. Abrol A, Dewan A, Agarwal N, Galhotra A, Goel NK, et al. A clinic-epidemiological profile of dengue fever cases in a peri-urban area of Chandigarh. The internet J of Epidemiology. 2007; 5 (7).
6. Garg A, Garg J, Rao YK, Upadhyay GC, Sakhuja S. Prevalence of dengue among clinically suspected febrile episodes at a teaching hospital in North India. J Infect Dis and Immun. 2011; 3(5):85-89.
7. Lal M, Aggarwal A, Oberoi A. Dengue fever-An emerging viral fever in Ludhiana, North India. Ind J Pub Health. 2007; 51(3):198-99.
8. Kennedy RS. Some notes on an epidemic of Dengue form fever among Indian troops, Calcutta. Ind Med Gaz 1912; 17: 42.
9. http://www.apiindia.org/pdf/medicine_update_2010/infectious_disease_01.pdf.
10. Saavedra-Velasco M, Chiara-Chilet C, Pichardo-Rodriguez R, Grandez-Urbina A, Inga-Berrospi F. Coinfection between dengue and covid-19: need for approach in endemic zones. Revista de la Facultad de CienciasMedicas (Cordoba, Argentina). 2020; 77:52-54.
11. Biswas S, Sukla S. COVID-19 virus infection and transmission are observably less in highly dengue-endemic countries: Can dengue vaccines be "repurposed" to prevent COVID-19? OSF Preprints. 2020.
12. Joob B, Wiwanitkit V. COVID-19 can present with a rash and be mistaken for dengue. J Am AcadDermatol. 2020; 82:e177. 34. Yan GL, Kiat C, Lam LTM, et al. Convert COVID 19 and false - positive dengue serology in Singapore. Lancet Infect Dis. 2020; 20:536.
13. 13.http://panbiodengue.com/product/dengue-duo-cassette accessed on July 21st, 2012. [14] Ghosh SN, Pavri KM,
14. Guzman MC, Halstead SB, Artsob H, Buchy P, Farrar J, et al. Dengue: a continuing global threat. Nature Reviews 2010; S8-16.
15. Vijaykumar TS, Chandy S, Satish N, Abraham M, Abraham P, et al. Is dengue an emerging as a major public health problem? Ind J Med Res. 2005; 121:100-07.
16. Sharma Y, Kaur M, Singh S, Pant L, Kudesia M, et al. Seroprevalence and trend of dengue cases admitted to a government hospital, Delhi -5-year study (2006- 2010): a look into the age shift. Int J Prev Med. 2012; 3(8):537-43.
17. Gupta E, Dar L, Kapoor G, Broor S. The changing epidemiology of dengue in Delhi, India. Virology Journal. 2006; 3:92.
18. Ukey PM, Bondade SA, Paunipagar PV, Powar RM, Akulwar SL. Study of Seroprevalence of Dengue Fever in Central India. Ind J Community Med. 2010; 35(4): 517-19.
19. Kumar A, Rao CR, Pandit V, Shetty S, Bammigatti C, et al. Clinical manifestations and trend of dengue cases admitted in a tertiary care hospital Udupi district, Karnataka. Ind J Community Med. 2010; 35(3):386-90.

****