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"SEROPOSITIVITY OF DENGUE AMONG PATIENTS ATTENDING INTEGRAL INSTITUTE OF MEDICAL SCIENCES & RESEARCH HOSPITAL, LUCKNOW"

Microbiology

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ABSTRACT

Objective: To Compare the dengue specific parameters (NS1, IgM and IgG) among the suspected dengue Patients and to Study the Socio-demographic profile of study Population.

Methods: Blood samples were collected from 314 Patients with clinical suspension of dengue infection were further screened for Dengue NS1 Antigen and dengue specific antibodies IgM & IgG by rapid immuno-chromatographic test (ICT) Dengue day 1 test kit (J. MITRA. Co. Pvt. Ltd.)

Results: Out of the 314 cases tested, 117 cases (37.2%) were tested positive for one or more of three markers. Among the 117 positive Dengue cases, 89 (77%) were positive for NS1 Ag, 28 (23%) were positive for IgM antibodies and very less account of Patients showed IgG positivity (1.1%). Males 65 (56.6%) outnumbered females 52(44.4%) during this study. Adults between the ages 21-40 years were found to be the most vulnerable group as 104 (53%)positive cases belong to this group. Fifty-nine percent of positive cases were found in the month of July, thus indicating that the monsoon period was affected the most.

Conclusion: From the present study it can be concluded that, dengue cases are on rise and this underlines the need for continuous surveillance and rapid implementation of dengue control programme.

KEYWORDS

Dengue Virus, Dengue fever, NS1 antigen, IgM , IgG, Immunochromatograghic test, WHO

INTRODUCTION

Dengue was once a periodic disease that caused long-interval epidemics but today it is considered as one of the most important mosquito-borne viral disease in the World **(WHO et al.,2015).** Dengue infect approximately 50 to 100 million people worldwide a year with half a million life-threatening infections requiring hospitalization, resulting in approximately 2.5% deaths **(WHO et al., 2012).** Among mosquito-borne viral infections. Dengue is serious disease affecting tropical and subtropical counties like India. Dengue in India has been endemic for over two centuries with mostly benign and self-limited course. India is one of the seven identified countries that is reporting regularly incidence of dengue fever & dengue hemorrhagic fever outbreak & may soon transform into a major niche for dengue infection **(Kumara A et al., 2010).**

DEN is a single stranded positive polarity RNA viruses of the family Flaviviridae and are the most common cause of Arboviral disease in the World **(Gubler et al., 1998)**. Dengue infection is caused by any one of the serotypes of dengue virus (DEN-1, DEN-2, DEN-3, DEN-4) **(WHO et al., 2014).** In 2013 a fifth variant DEN5 has been isolated from Bangkok **(Mustafa et al., 2015).** The viruses are transmitted from human to human by the bite of female mosquito *Aedes aegypti, Aededs albopictus & Aedes polynesiensis* **(Sharma et al., 2010).** Many other factors that contribute to the viral transmission includes: temperature, rainfall, rural-urban migration, population growth, stored water, and increased solid waste, which provides larval habitat for the vectors **(Kraemer M., et al2015).**

The incubation period of dengue infection varies from 5 to 10 days of illness **(Pervin et al., 2004)**. The clinical manifestation includes asymptomatic infection, mild dengue fever (DF), dengue hemorrhagic fever (DHF) or dengue shock. syndrome (DSS) **(San Martin JL et al.,2010).**

Severe dengue usually occurs among patients that have been infected previously with a dengue virus (i.e. secondary infection) **(Hause et al. 2016).** The uptake of virus by cells that express Fc receptors, is enhanced by the non-neutralizing antibodies, thus allowing for antibody dependent enhancement (ADE) in DHF **(Gubler DJ et al 1995)**.

The Degree of morbidity and mortality of dengue infection necessitates the early diagnosis, by demonstrating dengue specific immunoglobulin (IgM and IgG) or detection of viral antigen in clinical sample. **(Blackshell SD et al 2008)**.

IgM antibodies are detected from seventh day onwards while IgG antibody appears after 14 days and persists for life in case of primary dengue infection and rise within 1-2 days after onset of symptoms in secondary infection **(Kumarswamy V et al 2007)**.

Non-structural protein 1 (NS1) antigen is a highly conserved glycoprotein which is very essential for the viral replication. NS1 antigen begins to appear in blood from Day1 of infection **(Mackenzie JM et al 1996).** It is recognized as a major antigen in dengue infection as it possesses both group and type specific determinants. It can be detected during acute phase of the infection in patients experiencing primary & secondary infection. Thus targeting NS1 antigen detection should be approach for early diagnosis & timely management **(Shrivastava A et al 2011)**.

MATERIAL AND METHODS

The Present study was conducted at the Department of Medical Microbiology, Integral Institute of Medical Sciences and research, Integral University Lucknow, India.

Blood samples were collected from 314 Patients with clinical suspension of dengue infection were further tested for Dengue NS1 Antigen and dengue specific IgM & IgG antibodies by rapid immuno chromatographic test (ICT) Dengue day 1 test kit (J. MITRA. Co. Pvt. Ltd.)

The study protocol was approved by the Institutional ethical committee at IIMS&R, Integral University, Lucknow.

Figure 1. Dengue Reactive Test

Inclusion Criteria -

All the outdoor and the indoor patients attending at Integral Institute of Medical Sciences and Research, Hospital Lucknow, whose blood samples were received at the Microbiology department for Dengue Screening of (NS1 Ag, IgM & IgG by ICT).

Exclusion Criteria -

Samples which were mislabeled & were not collected properly was excluded.

Procedure For NS1 Antigen

2 drops (70µl) of sample (serum) was added using dengue antigen test sample dropper to the sample well of Antigen device then the reaction was allowed to occur for 20 minutes. Further the results were interpreted.

Procedure For Dengue IgM/IgG

10ul of sample (serum) was added using micropipette to the sample well marked with "S" of the device. 2 drops (70µl) of dengue antibody assay buffer was added to the buffer well marked with "B" of the device then the reaction was allowed to occur for 20 minutes. Further the results were interpreted.

Interpretation Of Dengue Test Results

A) Dengue NS1 Antigen Device:

The appearance of two bands in test and control region indicated that the sample was reactive for dengue NS1 antigen. If only one band appears in control region indicate that the sample was non-reactive for dengue NS1 antigen. When no line appeared in control and test region the test was treated as invalid.

B) Dengue IgM & IgG Antibodies Test:

If red color line appeared in control and test region of (IgM and IgG region) indicates that the sample was reactive for both IgM and IgG antibodies. The presence of red color line in control and test region of (IgM region 'M') indicated that the sample was reactive for IgM antibodies. & similarly if red color line appeared in control and test region of (IgG region 'G') indicated that the sample was reactive for IgG antibodies.

RESULTS

In this study, out of total 314 suspected Patients who attended the Integral Hospital, 117 (37.2%) Patients were found to be positive for dengue and 197 (62.7%) cases were found to be negative by using dengue day 1 Test. The Seropositivity of dengue cases in the present study was 37.2%.

Table No. - 1.1 Seropositivity

TOTAL NO.OF CASE	POSITIVE CASES	NEGATIVE CASES	SEROPOSITIVITY
314	117	197	37.2%

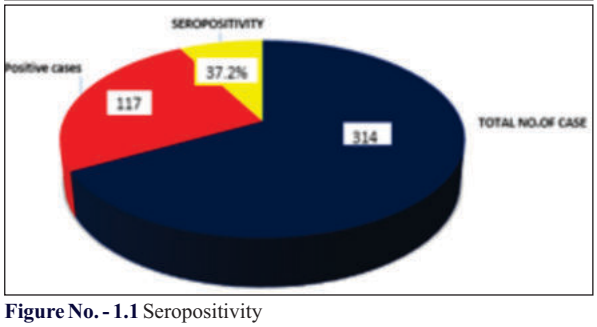

Figure No. - 1.1 Seropositivity

Table No.1.2- Age Distribution In Dengue Cases

Age group	Reactivity	Non-reactivity	Positive	p value
0-20	39	67	34%	
21-40	62	104	53%	0.018
>40	16	26	13%	
Total	117	197	100%	

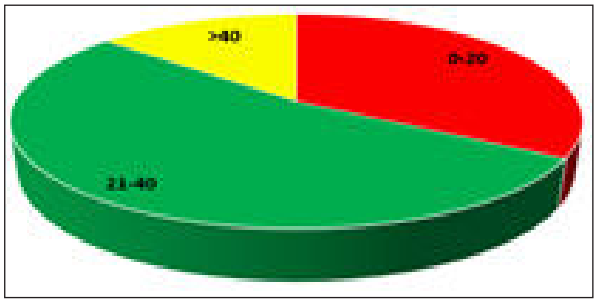

Figure No.1.2 - Age Distribution In Dengue Cases

Table No. -1.3. Sex Distribution Of Dengue Cases

Male/female	Reactive	Non-reactive	Percent	p-value
Male	65	110	56.00%	
Female	52	87	44.40%	1.000
Total =314	117	197	100%	

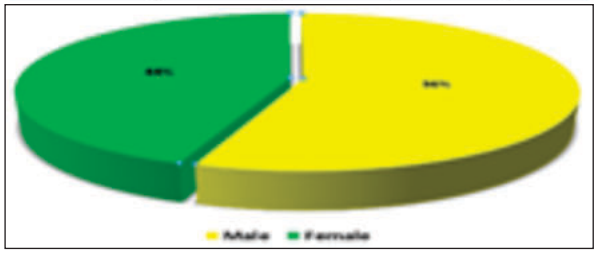

Figure No.-1.3. Sex Distribution Of Dengue Cases

Table No.1.4. - Clinical Presentation Of Dengue

Clinical representation	No. of Patients	Percentage
Fever	117	100%
Arthralgia/myalgia	83	71.%
Headache	56	48%
Rash	32	27%

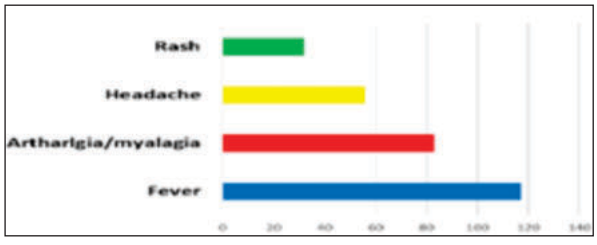

Figure 1.4: Clinical Presentation of Dengue

Table No.1.5- Serodiagnosis

DIAGNOSIS	Reactive	Non-reactive	Percentage	p -value
NS1	89	152	77%	
IgM	28	45	23%	0.8903
TOTAL	117	197	100%	

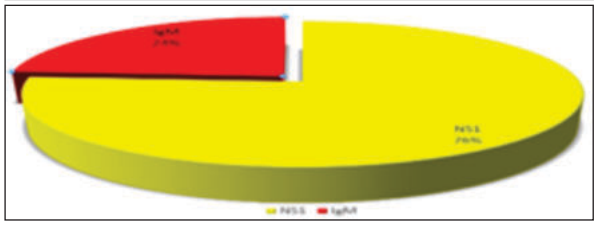

Figure No. -1.5.– Serodiagnosis

Table No. 1.6- Seasonal Distribution Of Dengue Cases

Month	Total no. of suspected cases	Total no. of positive cases	Percentage
February	45	07	15.5%
March	17	01	5.88%
April	24	03	12.5%
May	51	17	33.3%
June	72	27	37.5%

July	105	62	59.0%
Total	314	117	

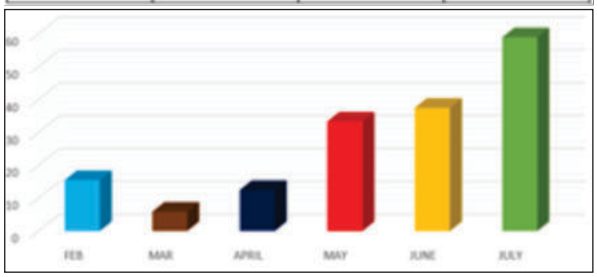

Figure No.1.6- Seasonal Distribution Of Dengue Cases

DISCUSSION

In the present study, out of 314 samples collected,117 were positive with a positivity of 37.2% (Table no.1.1). in the studies done by Santosh S.T et al., have positivity rates of 25.46%-39.41% respectively **(Kulkarni, R. D et al., (2011).** Sharma et al., in their study in 1998. Reported 64% cases with recent infection, which was higher than our report this was due to the limitation of our study that we only took sample from Integral Hospital whereas they had cases from all over Delhi, or it suggested that there was reduction of cases with current infection.

Dengue affects humans of all age groups worldwide. In several parts of the world, dengue infection predominantly affects a childhood disease; however, it affects adult population primarily during first few years of its emergence. In India where the most affected population range lies between 15-30 years (29.27%) **(P.M. Ukey et al.,2010)**. Similar, result was found in our study we found a high burden of dengue in (20-40;) age group (Table no.1.2) which is in correlation with other studies by Mehta et al., (16-30 yrs; 49%). Quader A.J et al., (20-30 yrs;42%), Pm Ukey et al., (15-30 yrs; 31.71%), Ravichitra et al., (17-30 yrs; 34.4%).

In the present study, male (55.5%) outnumbered females (44.4%). The male to female ratio in present study was 1.3 showing male predominance as reported by several authors **(Neeraja M, Laxmi etal.,2006, Chakravarti A, et al.,2012).**

The most common symptoms in the present study (Table-1.4) were fever (100%), myalgia/ arthralgia (71.1%), headache (48.88%), Rash (27.77%). In the study published by Min-Shen Lee et al in 2005, a year study involving 1551 patients in Taiwan, fever was the most common symptom (96.1%), followed by myalgia (68.5%), headache (55.4%), skin rash (53.7%) and retro-orbital pain (15.8%), which correlated well with the present study **(Mas P et al.,1997).** In a study of Shahid Ahamed et al in 2008, involving 5200 fever cases, they showed that fever was the commonest symptom (100%), followed by, myalgia (67%), headache (54%) and rash (28%) **(Nadeem Sajjad Raja et al.,2006).**

Out of the 117 cases positive for Dengue Fever, majority were positive for NS1 Ag 89 (77%) which is similar to the findings in studies by Bhaswati Bandyopadhyay et al. (61.29%) **(Bandyopadhyay et al., 2013).** IgM reported for 28 (23%) of the total positive cases.

Combination of the NS1 antigen and antibody tests increases the diagnostic efficiency for early diagnosis of dengue infection which has been earlier reported **(Blackshell SD et al., 2008).**

The incidence of dengue is higher during the monsoon and the post monsoon period. True to this, in the present study, a clear cut increase in incidence of dengue cases was seen 59% in the month of July which receives a heavy rainfall.

CONCLUSION

The present study concluded that, a Dengue virus infection is one of the causes of acute undifferentiated fever among febrile patients attending at Integral Institute of Medical Sciences and Research, Hospital. As It is a complex disease whose symptoms are difficult to distinguish from other common febrile illnesses and can progress from a mild, non-specific viral disease to irreversible shock and death within a few hours.

The study aimed at determining the seropositivity of DENV infection. Out of the 314 cases tested for Dengue NS1 Antigen, IgM and IgG antibodies by Immunochromatography (ICT) method, 117 cases (37.2%) tested positive for Dengue fever indicating high prevalence of Dengue in this area. The present study thus commends that Clinicians/physicians should consider the possibility of dengue cases while examining for febrile patient so that early serological diagnosis and management of dengue cases can thereby minimize the mortality.

Male predominance (55.6%) in dengue cases and age group of 21-40 years (53%) would have been masked when collapsing the data over all age group. Therefore, the present study finding indicates the importance of reporting age and gender stratified data dengue surveilleillance to help in targeting specific preventive measures.

Among the 117 positive Dengue cases, 89 (77%) were positive for NS1 Ag, 28 (23%) were positive for IgM only. Combination of antigen and antibody assays on a single serum sample, ease and time taken by ICT test make it preferable test of choice for making a reliable diagnosis. Serodiagnostic test dengue specific NS1 positive and IgM and IgG antibodies when conducted simultaneously would be able to diagnose confirmed dengue cases categorizing primary and secondary dengue along with the duration of the disease, whether early or prolonged.

In the present study, fifty-nine percent of positive serum samples were collected which shows a clear cut increase in incidence of dengue cases in the month of July indicating that the monsoon period was the most affected. Therefore, a seasonal trend observed, stresses the importance of initiation of preventive and control measures prior to monsoon to prevent outbreaks. Prompt diagnosis of index cases can facilitate vector control activities in the community so as to mitigate further transmission.

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