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Comparison of Immunochromatographic test with ELISA for detection of Dengue in a Tertiary Care Hospitalat Jalna.

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Abstract*: Dengue infection ,caused by a flavivirus is a major cause of mortality and morbidity in India.The infection ranges from self-limited,undifferentiated fever (dengue fever) to more severe form dengue haemorrhagic fever (DHF) to dengue shock syndrome(DSS).Early diagnosis will help in foreseeing the complications at an early stage and help in reduction of mortality and morbidity.*
Aims and objectives*: To compare the rapid immunochromatographic test for detection of NS1 antigen and IgM withEnzyme Linked Immunosorbant Assay(ELISA) in suspected dengue patients.*
Materials and methods*: This cross sectiontal study was carried out in the Department of Microbiology at IISMR,Warudi, Jalna over a period of six months. All the samples in dengue suspected patients were subjected to rapid diagnostic tests and then cross verified by ELISA .*
Results*: The rapid immunochromatographic tests had a sensitivity of 95% and specificity of 93% for NSI antigen when compared with ELISA and sensitivity of 90.9% and specificity of 98.9% for IgM antibody as compared to ELISA.*
Conclusion*: Considering their high sensitivity and specificity,these rapid immunochromatographic tests can be used as an early predictor of dengue infections in resource poor settings, and in peripheral health care centres,*
Key words: *Rapid immunochromatographic test,ELISA.*

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I. Introduction:

Dengue virus infection in humans is an acute mosquito-borne flaviviral transmitted mainly by *Aedesaegypti* mosquito and*Aedesalbopictus*(1,2).It manifests as aspectrum of illness ranging from inapparent or mildfever to severe and fatal haemorrhagic disease [3,4].Classic dengue fever is marked by a rapid onset ofhigh grade fever, headache, retro-orbital pain, diffusemyalgia, weakness, vomiting, sore throat, an alteredtaste sensation, and a centrifugal maculopapular rash[5]. DHF and DHS are potentially fatalcomplications which are often associated with aninfection by a second serotype [6].These complications can lead to plasma leaking, fluid accumulation, respiratory distress, severe bleeding, or organ impairment.(7)

Currently the three basic methods used by most laboratories for the diagnosis of dengue virus infection are viral isolation, detection of the viral genomic sequence by a nucleic acid amplification technology assay (Reverse transcription polymerase chain reaction(RT-PCR)), and detection of Dengue specific IgM antibodies and antigen by the IgM –Capture enzyme linked immunosorbent assay (MAC-ELISA) and /or the rapid dengue immunochromatographic test (ICT)(8).Virus isolation and RTPCR tests for Dengue diagnosis arelaborious ,require specialized laboratory facilities and as the antibodies become detectable,the level of the circulating virus wanes and so these procedures are successful only when done within a few days of the onset of illness(9).Serological tests like ELISA and Rapid Immunochromatographic tests are more commonly used nowadays to diagnose dengue infections because of their ease of use compared to the above techniques .

Early and accurate diagnosisis is not only essential in foreseeing the complications thereby reducing the morbidity and mortality due DHF and DHS but it is also essential for the effective surveillance and control of disease outbreaks. Thus, there is a need for specific, inexpensive dengue diagnostic tests that can be used for

clinical management, surveillance and outbreak investigations and would permit early intervention to treat patients and prevent or control epidemics.(10,11,12)

With this intention, we undertook a study in which the suspected dengue patients were initially screened using the rapid diagnostic tests and further confirmed with ELISA. The efficacy of the rapid test was then compared with ELISA.

II. Materials and Methods:

This was prospective observational study conducted in the Department of Microbiology**,**IIMSRWarudi ,Badnapur - a tertiary care hospital from July 2021 to December 2021after receiving permission from the institutional ethical committee.A total of 750 serum samples collected from clinically suspected cases of dengue –like illness attending the outpatients departments and admitted in inpatient departments and sent for serological diagnosis of Dengue infection were included in this study.

Samples were tested by a rapid qualitative immunochromatographic assay (J.MitraandCoPvt Ltd, Dengue Day 1 test) for differential detection of dengue specific IgM and IgG antibodies and NS1 antigen.

The samples which were found positive and with a strong clinical history suggestive of Dengue were cross checked on ELISA using two different kits each for NS1 antigen(Qualisa Dengue NS1) and IgM antibody(QualisaDenIgM) supplied by QualproDiagnostics.An absorbance ratio of 2.1 or more than that with respect to negative controls was considered as positive while less than that was considered as negative.Statictical analysis was done using the software---

III. Results:

Of the 750 samples that were collected,205 were found to be positive with either Immunochromatographic test or ELISA.

When NS1 antigen was considered ,out of 144 samples which were positive by the Rapid immunochromatographic test ,140 were confirmed to be positive by ELISA while 7 samples which were found negative by Rapid immunochromatographic test were found positive on ELISA.This showed that sensitivity of Rapid immunochromatographic test was found to be 95% in comparison with ELISA while its specificity was found to be 93%.(table 1 and 2)

Table 1: Comparison of NS1 antigen between ELISA and Immunochromatographic (RDT-Rapid Diagnostic Test)test.

	ELISA +ve	ELISA -ve	Total
RDT +ve	140	4	144
RDT -ve	7	54	61
Total	147	58	205

Table 2: Accurary indices of rapid immunochromatographic test for NS1 antigen with ELISA .

Statistic	**Value**	**95% CI**
Sensitivity	95.24%	90.43% to 98.06%
Specificity	93.10%	83.27% to 98.09%
Positive Likelihood Ratio	13.81	5.36 to 35.58
Negative Likelihood Ratio	0.05	0.02 to 0.11
Disease prevalence (*)	71.71%	65.01% to 77.76%
Positive Predictive Value (*)	97.22%	93.14% to 98.90%
Negative Predictive Value (*)	88.52%	78.86% to 94.10%
Accuracy (*)	94.63%	90.60% to 97.29%

(*) These values are dependent on disease prevalence.

Similarly,ForIgMantibody,of the 22 samples which were positive for Rapid immunochromatographic test,20 were positive with ELISA while 2 samples found positive on ELISA were detected as negative on Rapid immunochromatographictest.The sensitivity and specificity of Rapid immunochromatographic test for IgM antibody was thus 90.9% and 98.9% respectively.(table 3 &4)

Table 3: Comparison of IgM antibody between ELISA and Immunochromatographic(RDT-Rapid Diagnostic Test) test.

	ELISA +ve	ELISA -ve	Total
RDT +ve	20	2	22
RDT -ve	2	181	183
Total	22	183	205

Table 4: Accurary indices of rapid immunochromatographic test for IgM antibody with ELISA .

Statistic	Value	95% CI
Sensitivity	90.91%	70.84% to 98.88%
Specificity	98.91%	96.11% to 99.87%
Positive Likelihood Ratio	83.18	20.83 to 332.18
Negative Likelihood Ratio	0.09	0.02 to 0.34
Disease prevalence (*)	10.73%	6.85% to 15.80%
Positive Predictive Value (*)	90.91%	71.46% to 97.56%
Negative Predictive Value (*)	98.91%	96.02% to 99.71%
Accuracy (*)	98.05%	95.08% to 99.47%

(*) These values are dependent on disease prevalence

IV. Discussion:

As per Indian national guidelines, a dengue patient is labelled as a "probable case" if he satisfies the clinical criteria during dengue outbreak or positive non ELISA based immuno-chromatography tests (ICT) such as NS1 antigen (Ag) ICT / IgM ICT.11.A case is labelled as 'confirmed' when NS1 Ag / Ig M is positive by ELISA or detection of viral nucleic acids PCR or by culture and isolation of Dengue virus.(13)

An ideal diagnostic test should be sensitive, regardless of the stage of infection [14]and diagnose a dengue infection roughly from the onset of fever to 10 days post-infection;

Acute Infections can be diagnosed by detection of specific IgM by ELISA .However, it has variousdisadvantages,firstly , antibodies appear only from 5-10 days after the onset of illness in case ofprimary dengue virus infection and 4-5 days after the onset of illness in secondary infections [8].Secondly, dengue antibodies are cross reactive withother flavivirus such as West Nile virus (WNV), St. Louis encephalitis virus (SLE), Japanese encephalitis virus (JEV),and yellow fever virus (YFV).Also hosts humoral immune response will considerably change the IgM antibody response .[15,16].

In our study,the sensitivity and specificity of RDT for detection of IgM antibody as compared to ELISA was found to be 90.9% and 98.9% respectively.This corresponded to the study done by Sarah Et al who found their sensitivity and specitivity to be 90% and 100% respectively.However Moorthy et al and Pattanayak et al have found IgM antibody detection by RDTas less sensitive and specific as compared to ELISA.This shows that IgM with its limitations can still be used as a useful tool for the diagnosis of acute Dengue infection in resource poor settings.(17,7)

NS1 is a highly conserved nonstructural glycoprotein secreted by virus infected cells during the acute phase of dengue,and it is essential for virus viability [18].Detection of NS1 has been a promising test to diagnose dengue in its early febrile stage due to its long half-life in blood. It correlates with the development of DHF. There is no cross-reaction of the dengue NS1 protein with those of other related *flaviviruses*.[(8)]

Circulating NS1 can be detected from the first day to the early convalescent phase after onset of disease.(18) RDT being used for detecting DEN NS1 has many advantages like rapidity, convenience and cost-effectiveness.

When RDT were used for the diagnosis of NS1 antigen in our study,they revealed a high sensitivity (95%)and specificity (93%) as compared to ELISA. Similar findings have been found by Kumar et all and Sarah et al.(19,20) Because NS1 can be diagnose even in the early stages of disease,even before the IgM appears in blood, NS1 Antigen detection by RDT provides the earliest diagnosis of dengue and also gives an indication of impending complications if they are bound to occur.

Hence we observed that RDT can be used in peripheral laboratories due to the advantages they have that is they were easy to perform,were less expensive, gave reliable results in a short period of time(30 min) and no expensive equipment was required. However they had certain limitations that is variations observed with different manufactures which was obvious in the above findings and to some interobserver variations. Therefore

the validation of these kits with national agencies is required and confirmation of the doubtful cases with ELISA must be done .

V. Conclusion:

We found RDT as good diagnostic tool in the diagnosis of acute Dengue infections with the results in accordance with ELISA.Consideringthe mortality and morbidity attached with Dengue virus infections Rapid Immunochromatographic tests for the early diagnosis of infection can serve as a useful tool in resource poor setting .

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