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Research Report

## AN APPROPRIATE DIAGNOSIS OF DENGUE VIRUS INFECTION IN SOME CASES WHO HAD AND WERE BEING TREATED IN SOERYA HOSPITAL SEPANJANG – INDONESIA

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### ABSTRACT

Since January 2014, Soerya Hospital has found many cases with positive result of NS<sub>1</sub> or IgM and IgG Dengue. The clinical manifestations mostly were high fever with headache, vomiting and also malaise convulsion and unconsciousness. Aim of the study is to find out an appropriate diagnosis of Dengue Virus Infection. Observasional study had been done since January–April 2014 with 50 cases of dengue Virus Infection. The diagnostic procedure was made based on the WHO 2011 criteria. Result Many cases had come with fever within couple days, some of them showed convulsions. Therefore, it should be made a differential diagnosis with other disease, such as acute tonsilopharyngitis, etc. The patient also had to be tested with NS<sub>1</sub> if the patient come in the first, second and third day of fever and followed by IgM/IgG dengue on the fourth, fifth or sixth days of fever. The diagnosis of Dengue Virus Infection was made based on the WHO criteria 2011. This study showed that not all cases showed positive result of NS<sub>1</sub> or IgM/IgG dengue on the first or second test. For the negative result, we should not think that the case is not a case of Dengue Virus Infection, especially if it happens at *Aedes aegypti* breeding season, the patient should be observed and performed the test again to get a proper diagnosis for Dengue Virus Infection. Monitoring clinical manifestation should always be done, to predict the appropriate diagnosis of Dengue Virus Infection.

**Key words:** Dengue Virus, Diagnosis Dengue Virus NS<sub>1</sub>, IgM test, IgG test, WHO criteria

### ABSTRAK

Sejak Januari 2014, Rumah Sakit Soerya telah menemukan banyak kasus dengan hasil positif dari NS<sub>1</sub> atau IgM dan IgG Dengue. Manifestasi klinis sebagian besar adalah demam tinggi dengan sakit kepala, muntah dan juga kejang, lemas. Tujuan penelitian untuk mengetahui diagnosis yang tepat Dengue Virus Infeksi. Materi dan metode penelitian Observasional telah dilakukan sejak Januari–April 2014 dengan 50 kasus Infeksi Virus dengue. Prosedur diagnostik dibuat berdasarkan kriteria WHO 2011. Hasil yang ditemukan diantaranya demam dalam beberapa hari, beberapa dari mereka menunjukkan kejang. Oleh karena itu, harus dibuat diagnosis diferensial dengan penyakit lain, seperti tonsilofaringitis akut, dll. Pasien juga harus diuji dengan NS<sub>1</sub> jika pasien datang pertama, kedua dan ketiga hari demam dan diikuti oleh IgM/IgG dengue pada hari keempat, kelima atau keenam demam. Diagnosis Virus Dengue Infeksi dibuat berdasarkan kriteria WHO 2011. Studi ini menunjukkan bahwa tidak semua kasus menunjukkan hasil positif dari test NS<sub>1</sub> atau IgM/IgG dengue pada pertama atau kedua menunjukkan hasil negatif, kita tidak harus berpikir bahwa kasus ini bukan kasus Dengue Virus Infeksi, terutama jika hal itu terjadi pada musim nyamuk *Aedes aegypti*, pasien harus diamati dan dilakukan tes lagi untuk mendapatkan diagnosa yang tepat untuk Dengue Infection. Kesimpulannya Pemantauan virus berdasarkan manifestasi klinis harus selalu dilakukan, untuk memprediksi diagnosis yang tepat Dengue Virus Infeksi.

**Kata kunci:** Dengue Virus, Diagnosis Virus Dengue NS<sub>1</sub>, tes IgM, tes IgG, kriteria WHO

## INTRODUCTION

Dengue fever and severe dengue infection an important causes of morbidity in tropical and sub tropical region. Most half world population live in area at risk infection.<sup>1,2</sup> One step Dengue NS1 antigen test is a highly conserved glycoprotein that seems to be essential for virus viability, but has no established biological activity, This NS1 antigen is present, at high concentration in the sera of dengue virus infection patients during the early clinical phase of the disease so it could be used as a suitable marker of dengue virus infection.<sup>3,4,5</sup>

Since January 2014, Soerya Hospital has found many cases with positive result of NS<sub>1</sub> or IgM and IgG Dengue. The clinical manifestations mostly were high fever with headache, vomiting and also malaise convulsion and unconsciousness.

Pathogenesis of DHF and DSS is still controversial. Two theories, which are not mutual exclusive-were frequently invited to explain the pathogenetic changes; secondary infection or immune enhancement hypothesis, viral virulence theory. Both theory is supported by epidemiologic and laboratory evidence, are most probably valid.

Risk factor reported for DHF; virus strain, pre-existing anti-dengue antibody: previous infection, maternal antibodies in infant, host genetics, age, Higher risk in secondary infections, higher risk in locations with two or more serotypes circulating simultaneously at high levels (hyperendemic transmission).

Diagnosis dengue NSI Ag as Rapid test is an in vitro immunochromatographic, one step assay designed to detect Dengue virus NS1 antigen human serum, plasma or whole blood.<sup>11,12,13</sup> Diagnosis early acute dengue infection to detect NSI antigen. Dengue NSI Ag can be detected from day 1 after on set of fever.<sup>14</sup> Sensitivity-92.8%, Spesificity-98.4%. The Speciment: Serum, plasma an wholeblood (100 µl).<sup>9,10</sup> Test result: 15–20 minutes. The introduction of few device model: fully covered device.

Diagnosis Dengue IgG/IgM test is a solid phase in vitro immunochromatographic test for the qualitative and differential detection of IgG and IgM antibodies to dengue virus serotype DEN-1,2,3 and 4. Differential detection of IgG and IgM antibodies. Serum, plasma, and Whole blood. Test result: 3-lines (IgG, IgM, control). Highest accuracy in low titer specimen.<sup>15</sup>

Presumptive differentiation between primary and secondary dengue infection have good correlation with Haemagglutination-Inhibition (HI) test.<sup>11</sup>

## MATERIAL AND METHODS

To make a diagnosis a cases, the doctor showed ask to family who brought the patient to the hospital for getting history why the patient suffer for illness. What is the reason?

Based on his answer or her history: the doctor in charge should make a plan the laboratory examination with can support the diagnosis. What kind laboratory should be done?

Laboratory examination was done based on clinical manifestation that had been found. For doing laboratory examination the doctor in charge should know the clinical manifestation of cases based on answer of the question. Therefore the doctor incharge had found a sign an symptoms of Dengue Virus Infection (DVI).

Observasional study had been done since January–April 2014. There were 50 cases of Dengue Virus Infection had been studied. The diagnostic procedure was made based on the WHO 2011 criteria.

Sample collection and diagnosis of Dengue. The patient came early had to be tested with NS<sub>1</sub> if the patient come in the first, second and third day of fever and followed by IgM/IgG dengue on the fourth, fifth or sixth days of fever. The diagnosis of Dengue Virus Infection was made based on the WHO 2011 criteria. The patient came late (4, 5, 6 dengue of fiver) should be test IgM IgG dengue.

## RESULT AND DISCUSSION

10 cases who came early (1, 2, 3 dengue of fiver) showed positip NS1 test and the other 7 cases also came early but showed negatif NS1 test. See table 1.

And then 7 cases who had a negatif result NS1, were followed IgM IgG test on the fourth until sixth day fever.

**Table 1.** NS1 Test as Early Diagnosis in Suspected DVI who had come earlier in Soerya Hospital Sepanjang

Day of Fever	Ns1 Test examination		Total Cases
	+	-	
First day		1	1
Second day	5	3	8
Third day	5	3	8
Total Cases	10	7	17

**Table 2.** IgM/IgG/IgM & IgG rapid test Followed negatif test Ns1 that had been done in earlier cases Dengue Virus Infection

Day of Fever	Dengue test examination		Total Cases
	IgM (+)	IgM & IgG(+)	
Fourth Day	1	2	3
Fifth Day	3		3
Sixth Day	1		1
Total Cases	5	2	7

**Table 3.** IgM/IgG/IgM & IgG rapid test for Identification Dengue Virus Infection in who had came late to the Hospital

Day of Fever	Dengue test examination			Total
	IgM	IgG	IgM & IgG	
Fourth	8	2	6	16
Fifth	6		3	9
Sixth	2		2	4
Seven	3		1	4
Total Cases	9	2	12	33

The result there were 5 cases showed an IgM (+), 2 cases showed IgM IgG positif. See table 2.

There were 33 cases suspected Dengue Virus Infection came late: all of them had been identified IgM IgG Dengue test. The result 9 cases should IgM (+), 2 cases IgG (+), 12 cases IgM IgG Dengue (+). See table 3.

Buy doing faster test of IgM IgG an all suspected dengue cases with day of fever 4, 5, 6,7 could be identified as a true cases of dengue virus infection.

Dengue virus NS1 antigen was detected in 199 of 213 acute serum samples from patients with laboratory confirmation of acute dengue virus infection. The dengue NS1 antigen – capture ELISA Sensitivity of 93.4%, Specificity of 100%. The sensitivity was significant higher in acute primary dengue (97.3%) than in acute secondary dengue (70.0%). The positive predictive value the dengue NS1 antigen –capture ELISA 100%. Negative predictive value was 97.3%. Virus isolation gave on overall positive isolation rate 68.1% with a. Positive isolation rate 73.9 for acute primary dengue and 31.0% acute secondary dengue. Molecular detection of dengue RNA by RT-PCR gave on overall positive detection rate 66.7%. Detection rate of 65.2 for acute primary dengue and 75.9% for acute secondary dengue.<sup>14</sup>

We have found that NS1 serotype-specific immunoglobulin G (IgG) enzyme linked immunosorbent assay (ELISA) can be used differentiate primary and secondary dengue virus infection.<sup>4,6</sup> This is due to the fact that the NS1 specific IgG antibody cannot be detected before day 6 of illness for primary infection. So the NS1-specific IgG antibody measure in acute phase serum some of them as previous infection. Comparison of NS1 specific IgG ELISA with envelope-and membrane-specific capture IgM and IgG elisa in the differentiation of primary and secondary dengue virus infection showed correlation (95,90% agreement). Most important we have found that the serotype of the dengue virus from the majority of patients with primary infection could be correctly identified when convalescent-phase or postinfection sera were analyzed by NS1 serotype-specific IgG ELISA. These findings suggested the NS1 serotype-specific IgG ELISA could be

reliably applied for serodiagnosis and seroepidemiological study of dengue virus infection.<sup>7,8,15</sup>

50 cases of suspected Dengue Virus Infection who had been admitted in Soerya Hospital Sepanjang Sidoarjo and had been collected since January 1–April 30, 2014 had been studied. They had come with clinical manifestation of fever, vomiting, convulsion, head ache and gastric pain. And than two groups of cases suspected Dengue Virus Infection had been made, as: 1. first) who had come on the first, second and third of fever and 2. second) who had come on the fourth, fifth and sixth of fever. NS1 test had been done in the first group cases of Dengue Virus Infection and the result showed on table 1.

There were five cases who had shown a clinical manifestation on the second days of fever and had been identified as a positive result of NS1 test. These event were also found on the following five cases that had a clinical manifestation on the third days of fever. The result showed that there were 10 cases who came early had shown as a positive result of NS 1 test but the others 7 cases who came early had shown as a negative result of NS 1 test. It mean that all cases of suspected Dengue Virus Infection who had early come in hospital had been test by NS 1, not always shown totally had a positive result but only 58,8% showed positive result. These negative result cases should be observed and followed on the next day for getting IgM, IgG and IgM & IgG test, the result had been showed on table 2. All of them were positive. This experience give an idea that: if we found some cases which have been identified as the true a suspected clinical manifestation of Dengue Virus Infection, we should try to follow the clinical manifestation and try to do the other test Dengue related with occurring antibody. For some cases who came late more than 3 days of fever we should test IgM & IgG dengue. The result were showed on table 3.

There were 19 cases positive only IgM, it mean that all cases has been suffered from primary infection of dengue virus. All of them showed a mild clinical manifestation and didn't show plasma leakage and shock. 2 cases showed a positive IgG and 12 cases showed a positive IgM & IgG; it mean that all cases had been suffered from secondary infection dengue; these cases showed severity of clinical manifestation of Dengue Hemorrhage Fever. It was due to enhancement Ag Ab reaction that promoting increasing plasma leakage and shock. In some cases this event occurred and showed a clinical manifestation of plasma leakage and promoting shock and need a special treatment.

## CONCLUSION

Monitoring clinical manifestation should always be done, to predict the appropriate diagnosis of Dengue Virus Infection for making a good management of DF or DHF and DSS.

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