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Original Research Article

The Relationship of Fever Duration with NS1 Examination Results, IgM and IgG in Dengue Hemorrhagic Fever Patients

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Abstract

Duration of fever is the average number of days of fever from the onset of fever to the time of IgM and IgG examination. Determination of the duration of fever when performing this serological examination cam play a role in optimizing the results of the examinations In November 2021 there has been an increase in cases of Dengue Hemorrhagic Fever at the Karawang Health Center, Sukabumi. The purpose of this study was to determine the relationship between duration of fever and the results of dengue antigen and antibody examination. The design used in this study was descriptive analysis with a cross sectional approach and obtained a sample of 50. Analysis of the data used in the form of Chi Square test. The conclusion of this study is that there is a relationship between the duration of fever and the results of the NS1 and IgG Dengue examinations shown with p-value = 0.000 while there is no relationship between the duration and the results of the IgM Dengue examination shown with p-value = 0.695. We found NS1 and IgG dengue examination to be significantly related to days of fever. NS1 were detected mostly in the first three days of fever while IgG were reactive in more than five days of fever. This showed importance of timing to perform the tests and its interpretation.

Keywords: Dengue hemorraghic fever, Duration of fever, NS1, IgM Dengue, IgG Dengue

EFEKTIFITAS AROMATERAPI LAVENDER DAN CHAMOMILE TERHADAP KUALITAS TIDUR IBU HAMIL TRIMESTER KETIGA

Abstrak

Lama demam adalah rata-rata jumlah hari demam dari mulai demam sampai saat pemeriksaan NS1, IgM dan IgG. Penentuan lama demam saat melakukan pemeriksaan serologi ini dapat berperan dalam mengoptimalkan hasil pemeriksaan. Pada November 2021 telah terjadi peningkatan kasus Demam Berdarah Dengue di Puskesmas Karawang. Tujuan dari penelitian ini adalah untuk mengetahui hubungan antara lama demam dengan hasil pemeriksaan antigen dan

antibodi dengue. Desain yang digunakan dalam penelitian ini bersifat deskriptif analisis dengan pendekatan cross sectional dan diperoleh sampel sebanyak 50. Analisis data yang digunakan berupa uji chi square. Terdapat hubungan antara lama demam dengan hasil pemeriksaan NS1 dan IgG Dengue ditunjukkan dengan p-value = 0.0001 sedangkan tidak terdapat hubungan antara lama demam dengan hasil pemeriksaan IgM Dengue ditunjukkan dengan p-value = 0.695. Deteksi pemeriksaan NS1 dan IgG dengue terbukti berkaitan dengan onset demam. NS1 terdeteksi pada pemeriksaan dasar (hari 1-3), sedangkan IgG dengue terdeteksi pada hari ke lebih dari 5. Hal ini membuktikan memperhatikan waktu pemeriksaan dan gejala yang didapati pada pasien untuk menginterpretasikan hasil serologi.

Kata kunci: Demam berdarah dengue, Lama demam, Pemeriksaan NS1, IgM dan IgM

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INTRODUCTION

Dengue hemorrhagic fever (DHF) is caused by arbovirus with help of mosquito Aedes aegypti. Incident of DHF is predicted to rise and spreading to wider area due to climate changing, behavioral change, economic rising and clean water availability. Until now, there are neither specific drug nor vaccine. [1]

World Health Organization (WHO) predicted annually there would be 100-400 million cases DHF globally. According to Minister of Health (2020), DHF cases in Indonesia accounted to 95.893 cases and 661 mortality cases. That was spread in 472 cities and districts in 34 provinces while mortality cases were in 219 cities and districts. Incident rate (IR) rose up to 49/100.000 people. [2,3]

Early detection should be done to avoid worsening clinical condition. Non-structural protein 1 antigen (NS1) examination can be performed early as it circulated in blood with high concentration. NS-1 antigen is glycoprotein and has ability to replicate virus. [3,4]

Dengue infection stimulates specific antibody production and cellular immune response. IgM and IgG antibody vary based on onset of fever. Fever itself is a body mechanism to battle infection by activating immune system.

A study by Puspitasari in Soetomo Hospital, Surabaya, showed the highest concentration of NS-1 antigen could be seen in fever day-2 until it lowered and being non-reactive before or simultaneously to decreasing body temperature in day 5.[5] In 2021, there was a significant rise of

DHF cases in Karawang Health Center, Sukabumi, and its peak was in November with 38% rise and December with 34% rise and 28% mortality case.

NS1 antigen, IgM and IgG examination related to onset of fever could optimize the result. Onset of fever was defined as average number of days from the day fever appear to the day of NS1, IgM and IgG examined. High IR and Case Fatality Rate (CFR) of DHF in Indonesia related to onset of fever as main symptom of the disease motivated the writer to study this topic.

MATERIAL AND METHODS

The study was a descriptive analytic study. Primary data such as laboratory results NS1, IgM and IgG Dengue was collected. The study was held in May- July 2022 in Laboratory Karawang Health Center, Sukabumi. Samples were taken from patients who had pathognomonic symptom of DHF. We used purposive sampling which the process was decided by the researcher. We then performed NS1, IgM and IgG examination to the samples. Inclusion criteria was positive results of NS1, IgM and IgG Dengue examination. Exclusion criteria was sample from patient with co-infection or comorbid disease which could misinterpret the main results, as example was typhoid fever.

We used rapid test dengue combo *Indec Diagnostic* which NS1, IgM and IgG Dengue were examined simultaneously. Baseline tests were performed when patient came to the health center. On the 5th day of fever, we re-examined the tests. Samples was blood plasma to performed NS1 test and 15-minutes centrifugated serum for IgM and IgG Dengue. We collected 50 samples. Data was analyzed using IBM SPSS 25. We performed Chi-Square analysis to prove correlation among days of fever, NS1, IgM and IgG Dengue

RESULT

We collected 50 patients. Out of all patients, 62% of them were females and most of them were children 6-11 years old (30%). At the baseline, most of them had already experienced fever for 2 days (46%), reactive NS1 (94%), non-reactive IgM (94%), and non-reactive IgG (100%). Five days later, we re-examined all the test. All of them were non-reactive NS1, 92% of them were non-reactive IgM and 96% were reactive IgG.

Tabel 1. Respondent's Demography Data

Variable	Frequency	Percentage (%)
Gender		
Male	19	38%
Female	31	62%
Age (years old)		
0-5	3	6%
6-11	15	30%
12-16	2	4%
17-25	7	14%
26-35	9	18%
36-57	14	28%
Baseline Days of Fever		
1 day	6	12%
2 days	23	46%
3 days	21	42%
Baseline NS1		
Reactive	47	94%
Non Reactive	3	6%
Baseline IgM		
Reactive	3	6%
Non Reactive	47	94%
Baseline IgG		
Reactive	0	0%
Non Reactive	50	100%
Follow Up Days of Fever		
5 days	44	88%
6 days	4	8%
7 days	2	4%
Follow Up NS1		
Reactive	0	0%
Non-Reactive	50	100%
Follow Up IgM		
Reactive	4	8%
Non Reactive	46	92%
Follow Up IgG		

Reactive	48	96%
Non Reactive	2	4%

We performed Chi Square test to analyze correlation days of fever to NS1, IgM and IgG Dengue examination. Table 2 and 4 showed days of fever were significantly correlated to NS1 and IgG Dengue ($p<0,01$), while we didn't find any correlation between days of fever and IgM Dengue ($p >0,01$) as shown in Table 3.

Tabel 2. Correlation Days of Fever to NS1 Dengue Examination

Days of Fever	NS1		Total	*p- value*
	Reactive	Non- Reactive		
3 days	47	3	50	0.0001
>5 days	0	50	50	

Tabel 3. Correlation Days of Fever to IgM Dengue Examination

Days of Fever	IgM		Total	*P value*
	Reactive	Non- Reactive		
3 days	3	47	50	0.695
>5 days	4	46	50	

Tabel 4. Correlation Days of Fever to IgG Dengue Examination

Days of Fever	IgG		Total	*P value*
	Reactive	Non- Reactive		
3 days	0	50	50	0.0001
>5 days	48	2	50	

DISCUSSION

The participants were dominated by female (62 %). It was in line to Irwadi's study that was also dominated by female. He stated that females were put in higher risk to get infected than males.[6] Other study by Nguyet et al also showed female was put in higher risk. Permatasari proved, based on statistical analysis, there was significant correlation between gender and DHF incidence. She stated that female had chance 3,333x more than male to be infected DHF. [7]

We collected 0-60 years old participants, mainly 6-11 years old (30%). This is in line to a study by Sudarmo that found more than 5 years old children or more in higher risk to get infected as they were actively being outdoor as the reservoir activity.[8,9] DHF transmission could spread widely. Generally, all age group and gender are in risk to get infected. Prevention program in residential area, school and workplace should be hold in order to avoid the transmission.[10]

Our study showed NS1 was mainly reactive at the baseline (94%) and 5 days later was non-reactive (100%). Our study also described difference result based on the day NS1 examination. Ahmed and Shobha found efficiency of NS1 antigen was dependent to onset of fever. In day 1 of fever sensitivity was 50% and maximum sensitivity was seen in two days of fever. In day 3 and 4 if fever, it decreased to71,4%, dan 75%. Specificity NS1 antigen dengue reached 100%. [11,12] We found that days of fever were significantly correlated to NS1 Dengue (p value = 0,0001). We didn't find any patient who experienced fever day 4-7 with reactive NS1. It was shown NS1 was initiated only in acute phase and being non-reactive as the disease resolute. [13]This study described decreasing positivity of NS1 examination begin at the third day of fever as a result of absence of dengue virus in blood as NS1 antigen was sensitized in viremia phase.

At baseline, IgM wasn't detected in most participants (97%). This result was in line to Indasari's study. This described importance of examination timing. Other study stated negative correlation related to IgM and day of fever. [14]Our data showed based on Chi Square analysis, no correlation occurred between day of fever to IgM antibody (p>0,05). Other study held by Agarwal et al demonstrated IgM, combined to IgG dengue (IgM/IgG ratio), as laboratory parameter to predict severe infection and dengue shock syndrome, mainly in secondary infection. [15,16]

We found most IgG reactive in >5 days of fever, while at baseline mostly were non-reactive. IgM/IgG serologic test could be used to classified primary and secondary infection. Primary infection was dengue virus infection without any history of dengue infection, while secondary infection was with prior dengue infection. IgG in primary infection appear slower with low titer thus in some cases it couldn't be detected using combo dengue rapid test. In this study, 48 participants experienced secondary infection. IgG was detected clearly while IgM was really low so that was not detected by combo dengue rapid test. Chi Square analysis showed significant difference between IgG performed in day 3 and day >5 of fever (p value <0,05). Timing of serologic test was essential to interpret the result. Day 3-5 of fever is the best timing to perform the test since production of

antibody had been able to detected in the blood. In day 0-2 of fever, there are no hemodynamic change that are able to be detected. IgG dengue was mostly detected in Day 5 of fever.[17,18]

CONCLUSION

We found NS1 and IgG dengue examination to be significantly related to days of fever. NS1 were detected mostly in the first three days of fever while IgG were reactive in more than five days of fever. This showed importance of timing to perform the tests and its interpretation.

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Conflict of Interest

We declare there was no conflict of interest

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