

IgA ANTI-DENGUE PROFILE IN SAMPLES

by M Thohirin Ramadhani

Submission date: 23-May-2023 11:21AM (UTC+0800)

Submission ID: 2099752574

File name: IgA_ANTI-DENGUE_PROFILE_IN_SAMPLES.pdf (4.33M)

Word count: 342

Character count: 1287

INDONESIAN JOURNAL OF
**CLINICAL PATHOLOGY AND
 MEDICAL LABORATORY**

Majalah Patologi Klinik Indonesia dan Laboratorium Medik

CONTENTS

RESEARCH

Proportion of Isomorphic Erythrocyte Urine in Diabetic Kidney Disease with Flow cytometry Methods Erica Catarina, Coriejati Rita, Basti Andriyoko, Ida Parwati	1 - 6
Analysis of Ret-He in Chronic Kidney Disease Patients at Dr.Wahidin Sudirohusodo Hospital, Makassar Febrina Rovani, Asvin Nurulita, Mansyur Arif	7 - 10
Analysis of Red Blood Cell Distribution Width Coefficient of Variation on Stroke Patient Kartika Paramita, Agus Alim Abdullah, Mansyur Arif	11 - 15
IgA Anti-Dengue Profile in Samples with Positive Dengue PCR or NS1 M Thohirin Ramadhani, Aryati, M Vitanata Arfijanto	16 - 20
The Association of Insulin Resistance and Lipid Profile Ratio in Metabolic Syndrome Rini Rahmayani, Adi Koesoema Aman, Santi Safril	21 - 25
Correlation of Free Hemoglobin Level and Plasma Nitric Oxide in Packed Red Cell during Blood Bank Storage Period Ricca Fitria, Rismawati Yaswir, Zelly Dia Rofinda, Desywar	26 - 30
Correlation of Lipid Profile with Interleukin-12 in Type 2 Diabetes Mellitus Meri Ponda Sari, Hanifah Maani, Ellyza Nasrul, Zelly Dia Rofinda	31 - 34
Platelet Indices for Predicting Liver Fibrosis in Patients with Chronic Hepatitis B Infection Shendy Sherly Soelieuwan, Darwati Muhadi, Mutmainnah	35 - 37
The Relationship Between the Level of Interleukin-6 and Procalcitonin in Severe Sepsis Patients at the Adam Malik Hospital Sesity C Nainggolan, Adi Koesoema Aman, Achsanudin Hanafi	38 - 41
Spontaneous Platelet Aggregation in Third-Trimester Pregnancy at Adam Malik Hospital, Medan Rezqi Maulani Jusuf, Hotma Partogi Pasaribu, Herman Hariman	42 - 46
Correlation between Presepsin and Sequential [Sepsis-Related] Organ Failure Assessment (SOFA) Score as an Organ Dysfunction Marker in Sepsis Stevi Dwiyani, Agnes Rengga Indrati, Leni Lismayanti, Adhi Kristianto S	47 - 52
Correlation of Atherogenic Index of Plasma with Stenosis Level of Coronary Artery in Acute Coronary Syndrome Ilhamifithri, Rismawati Yaswir, Eugeny Alia, Efrida	53 - 57

The Compatibility of Neutrophil to Lymphocyte Count Ratio with Serum Procalcitonin as Bacterial Infection Markers in Sepsis Patients Elvinawaty, Hanifah Maani, Zelly Dia Rofinda, Husni	58 - 63
The Diagnostic Value of Troponin I Testing to Coronary Angiography with a Point of Care Testing Instrument in Patients with Acute Myocardial Infarction Riska Anton, Sheila Febriana, Asvin Nurulita, Uleng Bahrun	64 - 67
Comparisons of Fibro Q Index and FIB-4 in Various Stages of Chronic B Hepatitis Evy Adrianti, Liong Boy Kurniawan, Ibrahim Abdul Samad	68 - 72
Microorganism Pattern on Nasal Cavity of End Stage Renal Disease Patients with Regular Hemodialysis and Staffs in Hemodialysis Installation Adam Malik Hospital Medan Imelda Damayanti, Ricke Loesnihari, Syafrizal Nasution	73 - 78
The Correlation between the Mean Platelet Volume Values with Thrombocyte Aggregation in Nephropathy Diabetic Patients Agus Sunardi, Nadjwa Zamalek Dalimoenthe, Coriejati Rita, Adhi Kristianto Sugianli	79 - 85
The Role of Platelet Concentration Transfusion on The Correlation between Platelet Number and Maximum Amplitude with Bleeding Volume Post Cardiopulmonary Bypass Ryan Bayusantika Ristandi, Nida Suraya, Leni Lismayanti, Sylvia Rachmayati	86 - 90
The Relationship between Nitric Oxide and Glycemic Control in Controlled and Uncontrolled Type 2 Diabetes Mellitus Patients in the Adam Malik Hospital Medan Yessy Suziarty, Ratna Akbari Ganie, Santi Syafril	91 - 94
Analysis of Red Blood Cell Distribution Width Value Towards Fibrotic Stage in Chronic Hepatitis B Fatma Idris, Darwati Muhadi, Mutmainnah	95 - 98
Correlation of Serum High-Density Lipoprotein Cholesterol and Homocysteine Level in Patient with Acute Myocardial Infarction Yayie Dwina Putri, Rismawati Yaswir, Lillah, Tuty Prihandani	99 - 103
Correlation between Galectin 3, Creatinine and Uric Acid on Stage V Chronic Renal Failure Indranila KS, Guruh AI, Meita H	104 - 110
 LITERATURE REVIEW	
Role of Delta Check in Clinical Laboratory Services Osman Sianipar	111 - 114
 CASE REPORT	
Primary Myelofibrosis Muhammad Irhamsyah, Darwati Muhadi, Mansyur Arif	115 - 120
Malignant Lymphoma with Leukemic Phase in Children Sahriany S, Agus Alim Abdulah, Mansyur Arif	121 - 128

IgA ANTI-DENGUE PROFILE IN SAMPLES WITH POSITIVE DENGUE PCR OR NS1

M Thohirin Ramadhani¹, Aryati², M Vitanata Arfijanto³

¹Faculty of Medicine, Airlangga University, Surabaya, Indonesia. E-mail: m.thohirin.ramadhani@gmail.com

²Department of Clinical Pathology, Faculty of Medicine, Airlangga University/Dr. Soetomo Hospital, Surabaya, Indonesia

³Department of Internal Medicine, Faculty of Medicine, Airlangga University/Dr. Soetomo Hospital, Surabaya, Indonesia

ABSTRACT

Dengue Virus Infection (DVI) causes several clinical manifestations and requires varied diagnostic instruments. IgA anti-dengue as one of the diagnostic markers of DVI is suspected to have a shorter lifespan and greater sensitivity in detecting secondary infections compared to IgM anti-dengue. This study was conducted using 34 sera with positive RT-PCR or NS1 dengue virus. Samples were examined by a reverse flow immunochromatographic method using AIM Dengue IgA Assure Rapid Test and will be analyzed its profile toward the day of fever, serotype, severity, platelet count, and type of infection. The overall sensitivity of IgA anti-dengue was 61.76% (n=34); in which IgA anti-dengue detected 14.29% primary and 66.67% secondary cases. IgA anti-dengue detected DEN1, DEN2, DEN3, and Mixed DEN1 – DEN3 virus serotype respectively 55.56%, 22.22%, 16.67%, and 5.56% (n=20). The day of fever was dominated by day-4 and day-5 respectively 28.57% (n=21). IgA anti-dengue was detected in DD, DHF grade I, II, and III 42.86%, 28.57%, 19.05%, and 9.52% (n=21) respectively. IgA anti-dengue detected in all levels of platelet count, it detected 60% in < 50,000 cell/mm³, 30% in 50,000 - 100.000 cell/mm³ and 10% in > 100,000 cell/mm³ platelet count sample (n=20). In conclusion, IgA anti-dengue showed a good performance, applicable as a diagnostic marker of DVI.

Key words: Dengue virus infection, IgA anti-dengue, dengue virus serotype, type of infection dengue virus, dengue virus severity, AIM Dengue IgA Assure Rapid Test

INTRODUCTION

Dengue Virus Infection (DVI) is an infectious disease that has a high incidence and prevalence especially in tropical regions such as Indonesia. This disease is caused by the dengue virus and transmitted by *Aedes aegypti* and *Aedes albopictus*. This disease still becomes the major cause of morbidity and mortality in tropical and sub-tropical countries around the world.¹

The prevalence of DVI around the world is 50 to 100 million cases with 22,000 deaths.² The number DVI cases in Indonesia is increasing along the rainy season. In mid-December of 2014, 71,668 people were recorded suffering from DVI and 641 of them died.³ This number is lower than the previous year (2013) in which 112,511 people suffered from DVI with 871 death.³

Dengue virus infection causes symptomatic and asymptomatic DVI. Symptomatic of DVI consist of non-specific fever, Dengue Fever (DD) and Dengue Hemorrhagic Fever (DHF). Dengue hemorrhagic fever is divided into stage I and stage II based on the presence or absence of bleeding. While DHF is divided into stage III and stage IV based on the

presence or absence of shock.¹

Dengue virus infection patients are often found in a bleeding and shock stage that can lead to multiple organ failure and even death. Early diagnosis and appropriate treatment are the keys to DVI treatment. Currently, routine serological diagnosis of DVI is performed using IgM, IgG and NS1 dengue virus derived from blood or serum specimens. IgM anti-dengue used as a sign of acute dengue infection can be detected on the 6th day and can remain positive until the 10th day after fever which may lead to late diagnostic.⁴ In several cases, IgM anti-dengue can persist for several months after onset of fever that tends to cause a false-positive result.⁵

Currently, the use of Immunoglobulin A(IgA) anti-dengue as the diagnostic marker of DVI has been developed. A study conducted by Ahmed *et al.* showed that IgA anti-dengue had total 99.4% sensitivity rate.⁶ Another study conducted by Tan *et al.* showed IgA anti-dengue had been detected 92.8% in secondary infection, 77.4% in primary infection and had an 86.7% total sensitivity.⁷

IgA anti-dengue as a diagnostic marker as DVI is still not widely used in Indonesia although its diagnostic kit is available.⁸ This study aimed to find

out IgA anti-dengue profile towards days of fever, dengue virus serotype, platelet count, dengue severity and type of infection.

METHODS

This study was conducted during March-September 2017 using 34 RT-PCR or NS1 positive sera. IgA anti-dengue assay was then performed in these samples. Samples with positive IgA anti-dengue were analyzed about its profile towards days of fever, virus serotype, platelet count, severity and type of infection. Days of fever were determined when body temperature was increased above 37.5°C and counted from 1st till 7th day. Serotype dengue virus was classified into DEN-1, DEN-2, DEN-3, and DEN-4. The severity of DVI was determined based on 2011 WHO classification. Type of infection consisted of either primary or secondary infection.¹

Laboratory examinations were performed as the Infection Division of Clinical Pathology Department, Dr. Soetomo Hospital Surabaya. The RT-PCR assay was performed using Simplexa Dengue Real-Time PCR (Focus Diagnostic) while NS1 assay was performed using SD Bioline Dengue Duo (Standard Diagnostics). IgA anti-dengue assay was performed using AIM Dengue IgA Assure Rapid Test.

RESULTS AND DISCUSSION

This study revealed that IgA anti-dengue assay was positive in 21 (61.7%) samples (n=34), thus analyze its profile was only performed toward these 21 samples (Table 1).

Immune response begins when the dengue virus enters the bloodstream. IgM anti-dengue starts to rise around the 3rd to 5th day after a fever, and then increases in 1-3 weeks, and can be detected for up to 3 months, even for more than 8 months.⁹ IgG anti-dengue arises about 2 weeks after the onset of fever in primary infection while in secondary infection IgG begins to increase sharply on 3rd to 5th day after fever.¹ IgA anti-dengue starts on day 5 after fever but is shorter than IgM anti-dengue.⁹ A previous study by Decker *et al.* stated that IgA anti-dengue could be detected one day after the appearance of IgM anti-dengue.¹⁰

This study showed that the day of fever was dominated by the 4th and 5th day with 28.57% positive rate followed by the 3rd, 7th, and 6th day (Figure 1). IgA anti-dengue positivity decreased after the 5th day. A study conducted by Decker showed that IgA anti-dengue had a 45-day lifespan compared with anti-dengue IgM that has a 90-day lifespan, thus IgA

anti-dengue had a potential lower false positive value.¹⁰

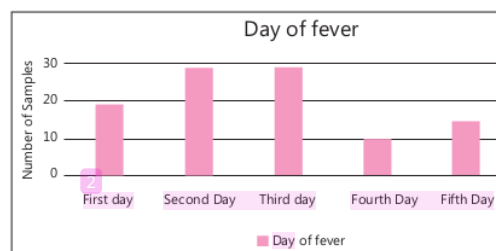


Figure 1. IgA anti-dengue profile toward day of fever on the 2nd day, 3rd day, 4th day, 5th day

Dengue Virus (DEN) has 4 strains (DEN 1, DEN 2, DEN 3, DEN 4). The structure of this serotype is very similar, but antibodies can not provide cross-protection.¹ All dengue serotypes are found in Indonesia. The dominance of the dengue virus serotype is somewhere dynamic and the shift of dominance takes place over time.⁹ Research by Ipain West Java showed that DVI was mostly caused by DEN-3 and DEN-2 serotypes.¹¹ Research by Andriyoko *et al.* using 27 samples found that dengue was dominated by DEN-3 followed by DEN-2.¹² Research conducted by Aryati *et al.* showed domination of DEN-1 followed by DEN-3 virus.¹³

This study showed dominance of 10 (55.56%) samples with DEN-3 serotype followed by 4 (22.22%) samples with serotype DEN-2 and 3 (16.67%) samples with serotype DEN-1 and 1 (5.56%) sample with mixed serotype DEN-1 and DEN-3 (Figure 2). The variation of serotype dominance proved that dengue virus has moved to its vector host.¹³ Research conducted by Aryati *et al.* showed that there was a change of serotype dominance occurring in Surabaya between 2005-2009 and 2012.¹³ Dengue virus infection was dominated by DENV-2 in 2009, while in 2012, it was dominated by DENV-1 serotype and finally in 2016-2017 it was dominated by DEN-3.¹⁴

Dengue severity is associated with secondary infection.¹ Halstead proposed a secondary heterologous infection hypothesis that said dengue occurred when a person was re-infected with dengue virus with different serotypes. This re-infection caused anamnestic antibody reactions resulting in high concentrations of immune complexes.¹⁵ This study showed IgA anti-dengue was found 9 (42.86%) in samples with DHF grade I followed by 6 (28.57%) DHF II and 4 (19.05%) DHF III and 2 (9.52%) DD (Figure 3).

Table 1. Characteristics of samples

IgA anti -dengue	Total (n=34)	Percentage (%)
Positive	21	61.76
Negative	13	38.24
Total	34	100.00
Samples characteristics	Total (n=21)	Percentage (%)
Day of fever		
3	4	19.05
4	6	28.57
5	6	28.57
6	2	9.52
7	3	14.29
Total	21	100.00
PCR and/or NS1		
PCR (+)	3	14.29
NS1 (+)	3	14.29
PCR dan NS1 (+)	15	71.43
Total	21	100.00
Virus serotype		
DEN -1	4	22.22
DEN -2	3	16.67
DEN -3	10	55.56
DEN -4	0	0.00
Mixed	1	5.56
Total	18	100.00
Severity		
DD	2	9.52
DHF Grade I	9	42.86
DHF Grade II	6	28.57
DHF Grade III	4	19.05
DHF Grade IV	0	0.00
Total	21	100.00
Platelets		
> 100.000	2	10
50.000 - 100.000	6	30
< 50.000	12	60
Total	20	100
Type of infection		
Primary	3	14.29
Secondary	14	66.67
Unknown	4	19.05
Total	21	100.00

This study showed decreasing platelet counts in a total of 20 samples with positive IgA anti-dengue. The platelet profile was dominated by 12 (60%)

samples with $<50,000$ cells/mm³, platelet counts followed by 6 (30%) samples with 50,000 - 100,000 cells/mm³ platelet counts, and 2 (10%) samples with

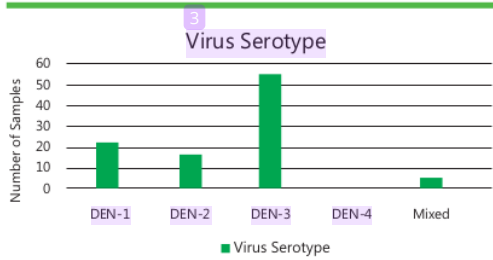


Figure 2. IgA anti-dengue profile toward dengue virus serotype

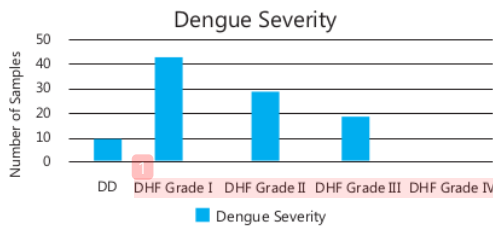


Figure 3. IgA anti-dengue profile toward dengue severity

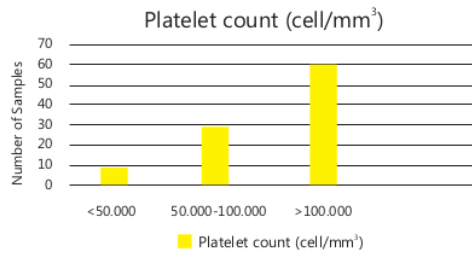


Figure 4. IgA anti-dengue profile toward platelet counts

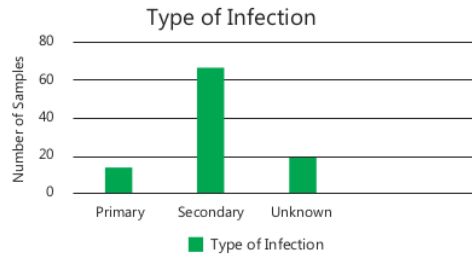


Figure 5. IgA anti-dengue profile toward types of infection

> 100,000 cells/mm³ platelet counts (Figure 4). This study showed that IgA anti-dengue could be found in samples with varying levels of platelet counts.

This study showed that IgA anti-dengue had a higher sensitivity (66.67%) in secondary infection compared to (14.29%) in primary infection. There were 4 (19.05%) samples with unknown dengue type of infection which means IgG and IgM anti-dengue both showed negative results (Figure 5). Whether the negative results of IgM and IgG anti-dengue could be caused by IgM/IgG was not established yet which mostly appeared at the beginning of primary infection.¹⁵ Decker *et al.* stated that IgA anti-dengue appeared at the same time or one day after the arise of IgM anti-dengue. This study showed that IgA anti-dengue could be detected even when IgG or IgM anti-dengue had not been formed.¹⁰

CONCLUSION AND SUGGESTION

Dengue virus infection has a broad spectrum of clinical manifestation. IgA anti-dengue has been developed to become one of its diagnostic markers. AIM Dengue IgA Assure Rapid Test showed a good performance and can be used as an early diagnostic instrument for DVI.

Based on the results of this study, it is recommended to classify the positivity level of IgA anti-dengue results to obtain more detailed data about IgA anti-dengue profile towards days of fever, serotype, severity, platelet count, and type of infection

REFERENCES

1. World Health Organization. Dengue guidelines for diagnosis, treatment, prevention, and control. 2011 cited on December 12, 2017. Available at: <http://www.who.int>.
2. Aaron L, Jeremias P, Matthias T. Outside of normal limits: False positive/negative anti TG2 autoantibodies. *International Journal of Celiac Disease*. 2015; 3(3): xx. cited on June 29, 2016. Available at <http://pubs.sciepub.com/ijcd/3/3/4>.
3. Primadi O, Sitohang V, Budijanto D, Soenardi TA. Data dan informasi tahun 2014 (profil kesehatan Indonesia). Kementerian Kesehatan Republik Indonesia. 2015 cited on December 13, 2017. Available at: <http://www.pusdatin.kemkes.go.id>.
4. Gubler DJ. Dengue and dengue hemorrhagic fever. *Clin Microbiol Rev*. 1998;11:480–96. cited on December 13, 2017. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/9665979>.
5. Chen WJ, Hwang KP, Fang AH. Detection of IgM antibodies from cerebrospinal fluid and sera of dengue fever patients. *Southeast Asian J Trop Med Public Health*. 1991;22:659–63. cited on December 13, 2017. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/1820657>.
6. Ahmed F, Mursalin H, Alam MT, Amin R, Sekaran SD, *et al.* Evaluation of assure dengue IgA rapid test using dengue positive and dengue negative samples. *Diagnostic Microbiology and Infectious Disease*. 2010; 68:339-44. cited on December 13, 2017.
7. Tan YY, Sekaran SD, Seok MW, Ahmed F, Hossain A, Sil BK. Development of Assure® Dengue IgA rapid test for the detection of Anti-dengue IgA from dengue

- infected patients. 2011; 3(3): 233–240. cited on December 13, 2017. Available at: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3162809>.
8. Resna Hermawati, Aryati, Puspa Wardhani, Triyono Erwin. Nilai diagnostik anti-dengue IgA, dan NS1 serta IgM/IgG di infeksi virus dengue. Indonesian Journal of Clinical Pathology and Medical Laboratory (IJCP&ML) 2014; 21(1): 82–89. cited on December 13, 2017.
 9. Aryati, Wardhani P. Profil virus dengue di Surabaya tahun 2008–2009. Indonesian Journal of Clinical Pathology and Medical Laboratory. 2010; 17(1): 21-24.
 10. De Decker S, Vray M, Sistek V, Labeau B, Enfissi A, Rousset D, Matheus S. Evaluation of the diagnostic accuracy of a new dengue IgA capture assay (Platelia Dengue IgA Capture, Bio-Rad) for dengue infection detection. PLoS Negl Trop Dis. 2015; 24;9(3): 35-96. cited on December 13, 2017. Available at : <https://www.ncbi.nlm.nih.gov/pubmed/25803718>.
 11. Ipa M, Astuti EP. Secondary infection and Den-3 serotype most common among dengue patients: A preliminary study. Health Science Indonesia, 2010; 1(1):14–9.
 12. Andriyoko B, Parwati I, Tjandrawati A, Lismayanti L. Penentuan serotipe virus dengue dan gambaran manifestasi klinis serta hematologi rutin pada infeksi virus dengue. Majalah Kedokteran Bandung. 2012; 44(4): 253-260.
 13. Aryati. Demam berdarah dengue (tinjauan laboratoris). Jilid 1. Surabaya, Airlangga University Press, 2011; 101-7. cited on December 13, 2017.
 14. Aryati, Trimarsanto H, Yohan B, Wardhani P, Fahri S, Sasmono RT. Distribusi serotype dengue di Surabaya tahun 2012. Indonesian Journal of Clinical Pathology and Medical Laboratory (IJCP&ML), 2012; 19(1): 41-4. cited on December 13, 2017.
 15. Aryati, Trimarsanto H, Yohan B, Wardhani P, Fahri S, Sasmono RT. Performance of commercial dengue NS1 ELISA and molecular analysis of NS1 gene of dengue viruses obtained during surveillance in Indonesia. 2013; 13: 611. cited on December 13, 2017.

IgA ANTI-DENGUE PROFILE IN SAMPLES

ORIGINALITY REPORT

12%

SIMILARITY INDEX

12%

INTERNET SOURCES

8%

PUBLICATIONS

0%

STUDENT PAPERS

PRIMARY SOURCES

1

es.scribd.com

Internet Source

3%

2

yahuwshua.org

Internet Source

3%

3

www.researchgate.net

Internet Source

3%

4

www.sabbathtruth.com

Internet Source

3%

Exclude quotes On

Exclude matches Off

Exclude bibliography On

IgA ANTI-DENGUE PROFILE IN SAMPLES

GRADEMARK REPORT

FINAL GRADE

/100

GENERAL COMMENTS

Instructor

PAGE 1

PAGE 2

PAGE 3

PAGE 4

PAGE 5

PAGE 6

PAGE 7
