

ORIGINAL ARTICLE

SPACE TIME CLUSTERS OF DENGUE FEVER IN MEDAN MUNICIPALITY, NORTH SUMATERA, INDONESIA

Zulfikar^{1*}, Frans Yosep Sitepu^{2**}, Elpiani Depari³ and Boy Debatardja⁴¹Department of Environmental Health, Banda Aceh Polytechnic of Health of the Ministry of Health, Indonesia²Provincial Health Office, North Sumatera, Indonesia³GrandMed Hospital, Deliserdang, Indonesia⁴Medan Health Office, North Sumatera, Indonesia

Corresponding author 1: Zulfikar

Email: zulfikarkawe@gmail.com

Correspondence author 2: Frans Yosep Sitepu

Email: franz_sitepu@yahoo.co.uk

ABSTRACT

Dengue fever (DF) infection continues to present as a serious public health problem in Medan municipality, North Sumatera, Indonesia. The number of DF cases continuously increasing recently. However, space time clusters of DF have not been investigated yet. A study was undertaken to detect clusters of DF incidence during 2015-2018 in Medan. Spatial geo-reference was conducted to 151 village coordinates by geocoding each village's offices. A retrospective space-time scan statistic analysis based on population data and monthly DF incidence was performed using SaTScan™ v9.4.4. Data of DF during 1 January 2015-31 December 2018 were analyzed using Poisson model to identify the villages at high risk of DF. The test of significance of the identified clusters of DF was based on comparing the likelihood ratio (LLR) against the null distribution obtained from Monte Carlo hypothesis testing. Total number of permutation was set to 999 and the significance level was set as 0.05. The highest LLR number was determined as the most likely cluster, while the rests were as the secondary clusters. This analysis identified 13 significant clusters. These DF clusters were initially spatially concentrated in the southwest and center of Medan and the last two years of study moved towards the northern part and identified in the last four months (September-December) of each year, which were the rainy seasons in the area. Most likely clusters were most frequently detected in the last three-year period of study in Anggrung village. Thirteen statistically significant DF clusters were identified in the 2015-2018 period. This may assist health authorities to improve the DF preventive strategies and develop public health interventions especially in the cluster's area.

Keywords: space time; dengue fever; clusters; Indonesia

INTRODUCTION

Dengue fever (DF) is an emerging infectious disease that remains a serious public health problem globally.⁽¹⁾ It is one of arboviral diseases caused by four distinct serotypes of dengue virus (DEN 1-4).^(1,2) The disease is transmitted among people through the bite of infective female *Aedes* mosquito.^(1,3) The spread of DF tends to be increasingly widespread, especially in developing countries.⁽⁴⁾ The incidence of DF has increased more than 30-fold over the past decades. The attacks of the disease can have a widespread consequence that cause the most fatal material and moral losses and resulted in loss of life or death. The disease often occurs in tropical and subtropical countries, including in Indonesia.^(1,3)

In Indonesia, DF is one of the emerging diseases and remains a major and growing public health problem.^(1,5) It was first reported in Surabaya and Jakarta in 1968, and the number its cases were increasing from year to year. In 1997 all provinces in Indonesia already reported the DF cases.^(5,6) North Sumatera is one of DF endemic provinces in Indonesia, and the disease continues as a public health problem. As much as 31 out of 33 districts

are DF endemic districts including Medan Municipality.^(6,7)

Medan municipality is one of the endemic of DF districts in North Sumatera. It is the third largest city in Indonesia with the number of population more than 2.2 million people. Population distribution that is not supported by environment and development would have complex social problems, where residents will be a burden for the environment and vice versa.⁽⁸⁾ This condition creates Medan more vulnerable to DF incidence due to high population density provides human virus reservoirs which allow rapid DF transmission among the community.⁽⁹⁾

In the absence of dengue vaccine and specific antiviral therapy, the only and effective way to prevent DF cases in the community is by conducting vector control management.^(10,11) In addition, surveillance should be prioritized in the face of the DF threat.^(1,7) Surveillance can be conducted by spatial analysis of DF in detecting space-time clusters, distribution, and trends of DF over time. Therefore, these approaches are useful for prioritizing DF surveillance and vector control.^(12,13) Therefore, it is needed to discover

the distribution pattern of DF cases and determine the spread of the disease spatially in Medan Municipality. This study aimed to investigate the presence of DF clusters in Medan Municipality and the temporal distribution pattern of detected such cluster over the four years.

METHOD

Study area

The study area was in Medan Municipality which is consisting of 21 sub-districts. The sub-districts consist of 151 *kelurahan* (villages). The population density varies in each village, from 359.7 to 52,767.7 people per km².⁽⁸⁾ Medan municipality is located around 3°35'N 98°40'E and 3.583°N 98.667°E (Figure 1).

Data

The monthly numbers of clinically confirmed DF cases from 1 January 2015 to 31 December 2018 were obtained from the Medan Municipal Health Office. Data of villages population were obtained from the Medan Municipal Bureau of Statistics.

Spatial geo-reference to 151 village coordinates (latitude/longitude) were obtained by geo-coding each village offices to represent each geographic location on a Google Maps application.

Space time scan statistic

We downloaded the free space time statistic software SaTScan™ v9.4.4 to conduct the retrospective space-time scan statistic to detect clusters.⁽¹⁴⁾ A Poisson model was used to identify villages at high risk of DF during 1 January 2015-31 December 2018. The test of significance of the identified clusters of DF was rested on comparing the likelihood ratio (LLR) against the null distribution obtained from the Monte Carlo hypothesis testing.^(14,15) The number of permutation was conducted to 999 and the significance level was 0.05. The null hypothesis of this study assumed that the relative risk of DF was the same within the window compared to outside. The most likely cluster determined as the highest LLR number, while the others were determined as the secondary clusters of DF.^(12,14,15)

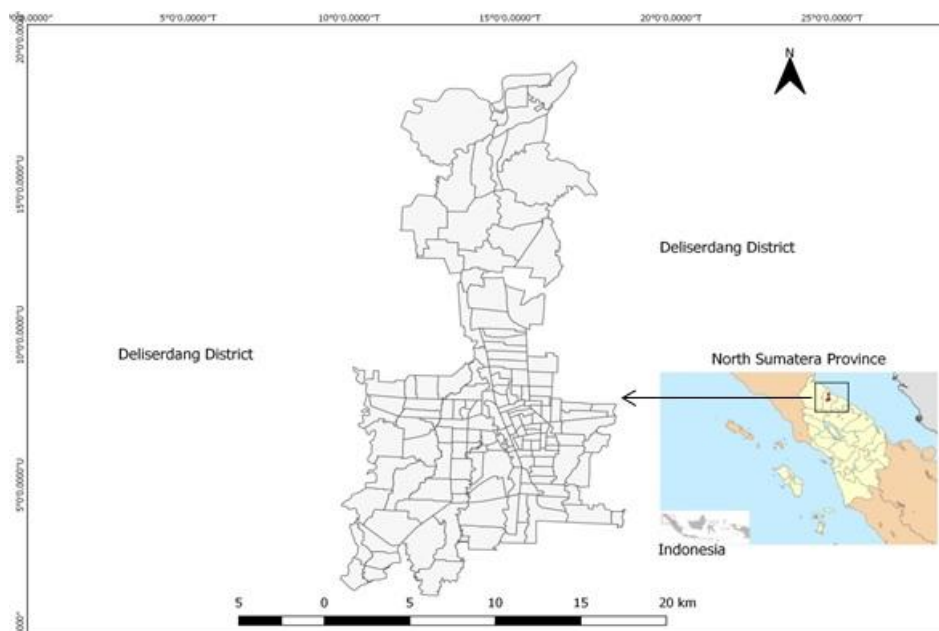


Figure 1. Location of the study area

RESULTS

Descriptive analysis of DF in Medan Municipality

In the four years DF data analysis, there were 5,839 DF cases reported in Medan Municipality. The annual average incidence rates (IR) of DF ranges from 0 to 269 per 100,000 population (Figure 2). Out of 151 villages, 17 were found as non-endemic with zero incidences whereas 134 were found endemic of DF. Among 134 villages, 11 were low endemic (IR <20 per 100,000 population), 31 were medium endemic (IR: 21-40), 29 were high endemic (IR:41-60), and 63 were very high endemic (IR>60). *Baru Ladang Bambu* village was the highest IR in the three-year period (269 per 100,000 population).

Space-time analysis of DF in Medan Municipality

The result of the space-time scan statistic analysis of DF for the period 2015-2018 are shown below (Figure 2). The analysis detected a total of 13 clusters based on monthly DF data (Table 1). These DF clusters were initially spatially concentrated in the southwest and center of Medan Municipality and at the last two year of study moved towards to the northern part. They were identified in the last four months (September-December) of each year, which were the rainy seasons in the area. In 2015, the most likely cluster was detected in the southwest of Medan, and the last three years were detected in the center of Medan Municipality (Figure 2)

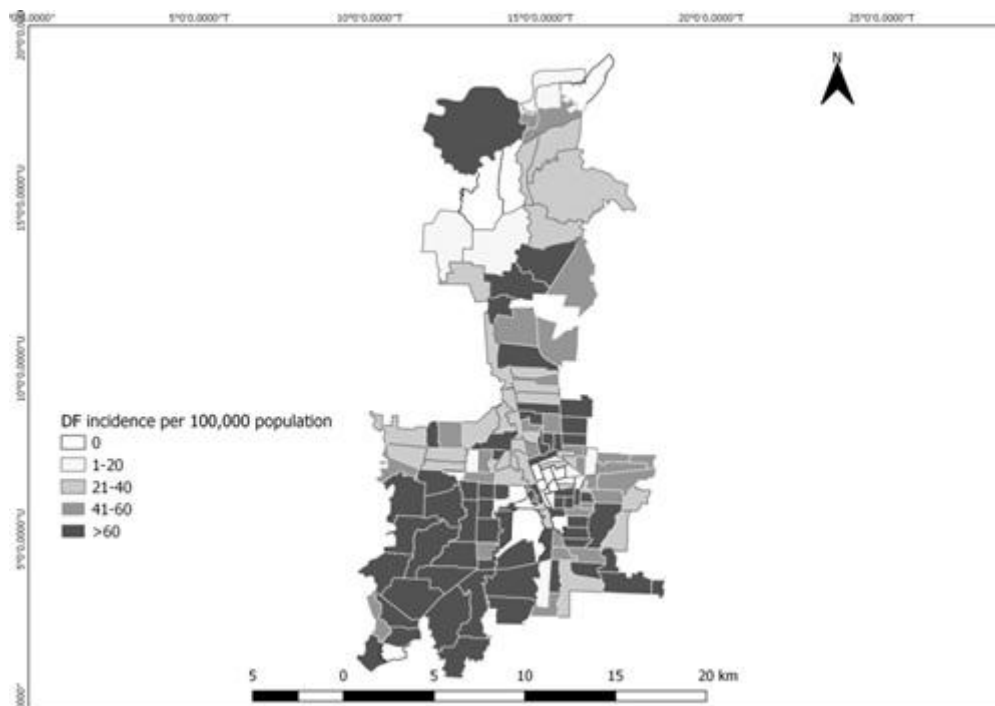


Figure 2. Annualized average DF incidence in Medan municipality (2015-18)

We identified that the highest number of DF clusters was in 2015 and 2018. In 2015, we found four significant DF clusters. The most likely cluster, with RR of 11.1 ($p < 0.001$) identified in the southwest of Medan Municipality (center of coordinate: 3.498906 N / 98.603214 E) which was the highest IR in 2015. There were three secondary clusters identified in the center of the city. In 2016-2018, the most likely clusters moved to the center part (*Anggrung* village) and in the last two years of study, the secondary clusters were localized in the northern part.

DISCUSSION

Exploratory data analysis and space time scan statistics of DF were conducted at village level of Medan Municipality. We mapped DF in terms of IR data from 1 January 2015 to 31 December 2018. We analyzed the patterns of spatiotemporal variation pattern and explored the significant clusters of DF. To our knowledge, this is the first study to investigate the space-time scan statistic of DF in Medan Municipality. In Indonesia, especially in North Sumatera province the use of spatial analysis of infectious diseases is still limited. It could be conducted to understand spatial risk factors of DF based on environmental risk factors.⁽¹⁶⁻¹⁹⁾

In the four-year period of space-time scan statistic discovered various statistically significant high-risk of DF clusters with various RR in Medan

Municipality. It showed the significant spatiotemporal variation pattern of DF in the study area. Our finding is in line with other studies of space time scan statistic of DF carried out by Dhewantara et al in Indonesia⁽¹²⁾, Anno et al in Sri Lanka⁽¹³⁾, Chuang et al in Taiwan⁽²⁰⁾, Acharya et al in Nepal⁽²¹⁾, and Hamer et al in Suriname⁽²²⁾ confirmed that DF cases tend to cluster.

Anggrung village identified as a secondary cluster in 2015. It was consistently identified as the most likely cluster in the last three-year period of study (2016-2018). Anggrung village is one of the business areas and has many public spaces that will impact the highly interacted people with each other with different health status background. Potential explanation for this phenomenon is that DF transmission might have occurred in the village.⁽²³⁻²⁵⁾ The existence of potential breeding sites of *Aedes* mosquito in the public spaces, high vector density and highly mobile people were associated with the incidence of DF.^(3,23,26) In addition, this phenomenon is also possible due to lack of preventive practices of DF incidence in the community level^(7,27-29) and insecticide resistance.^(10,23) A study on DF vector resistance found that some insecticides such as organophosphate and pyrethroid were no longer effective when used to control *Aedes aegypti* populations in some villages in Medan Municipality.⁽⁶⁾ Thus, further study is required to determine potential risk factors in these high-risk clusters including individual risk factors.

Table 1. Dengue clusters (2015-18) based on spatial temporal analysis under the Poisson Discrete

Year	Cluster type	Coordinates (latitude/longitude)	Period	Radius (km)	Cases (n)	Expected cases (n)	People at risk (n)	RR	LLR	p
2015	Most likely	3.498906 N / 98.603214 E	1/9/2015-31/12/2015	1.93	19	1.7	1,273	11.1	28.3	<0.01
	1st Secondary	3.576067 N / 98.656169 E	1/9/2015-30/11/2015	1.27	70	30	22,327	2.4	19.3	<0.01
	2nd secondary	3.587125 N / 98.692006 E	1/10/2015-30/11/2015	2.06	87	49	36,358	1.8	12.1	<0.01
	3rd secondary	3.554267 N / 98.697881 E	1/11/2015-31/12/2015	1.17	81	51	37,686	1.6	7.6	0.037
2016	Most likely	3.573836 N / 98.683597 E	1/9/2016-30/11/2016	3.41	523	347	237,721	1.7	49.3	<0.01
	1st Secondary	3.506039 N / 98.616708 E	1/9/2016-31/12/2016	4.73	208	113	77,687	1.9	34.0	<0.01
2017	Most likely	3.577400 N / 98.681228 E	1/10/2016-31/12/2017	3.41	248	152	130,556	1.8	29.3	<0.01
	1st secondary	3.768803 N / 98.675972 E	1/9/2016-31/12/2017	2.42	72	30	25,719	2.5	21.6	<0.01
	2nd secondary	3.506039 N / 98.616708 E	1/9/2016-31/10/2017	1.36	8	1.36	1,161	5.9	7.6	<0.01
2018	Most likely	3.565461 N / 98.688928 E	1/9/2018-31/12/2018	2.57	228	121.1	54,538	2.1	41.7	<0.01
	1st secondary	3.506039 N / 98.616708 E	1/9/2018-31/10/2018	1.69	25	6.11	2,752	4.1	16.4	<0.01
	2nd secondary	3.768803 N / 98.675972 E	1/10/2018-31/10/2018	1.14	24	11.5	5,184	2.1	5.2	0.025
	3rd secondary	3.602050 N / 98.697492 E	1/11/2018-31/12/2018	1.34	78	58.3	26,259	1.3	3.1	0.047

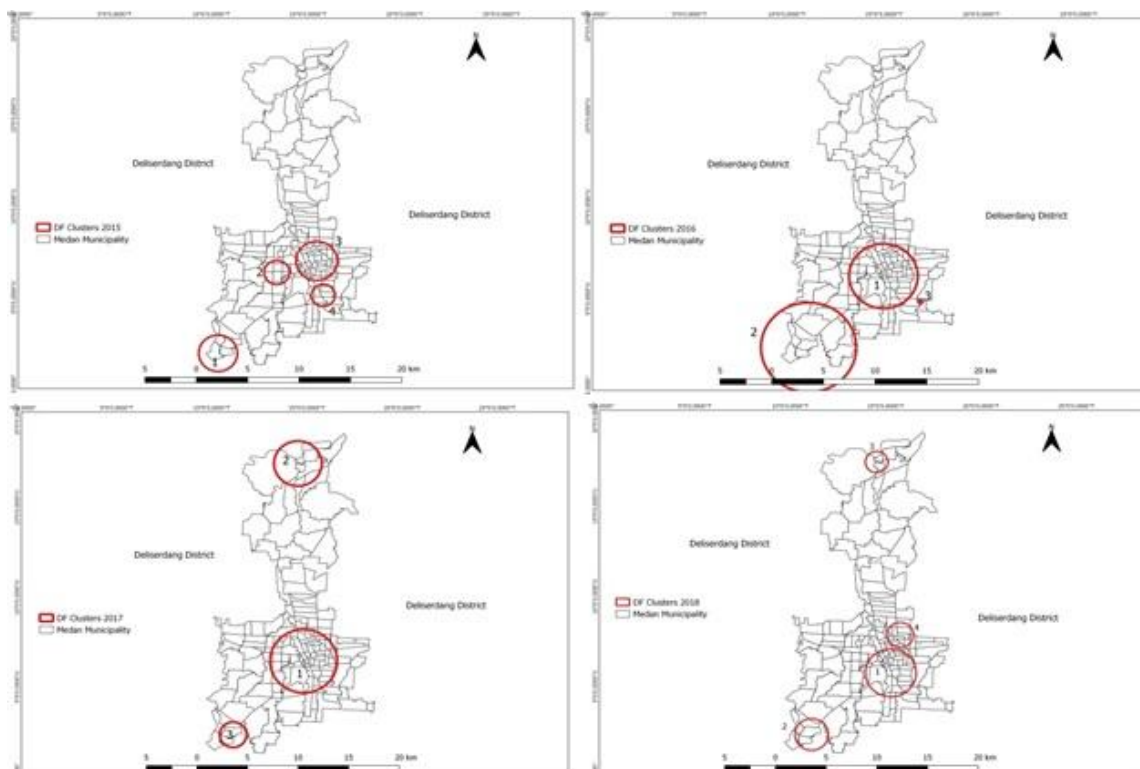


Figure 3. Clusters of dengue fever identified during the study period

The spread of clusters areas within Medan Municipality during the four-year study indicates that there was a closely association between human host, infectious agent, vector, the environment with DF incidence.⁽³⁰⁾ The DF clusters in Medan identified in the rainy season. Seasonal variation have strongly associated with the incidence of DF in Medan municipality. Some studies found that higher DF incidence occurred in the rainy season.^(9,31) Setiawati *et al* found that the highest risk of DF was located in the center of Medan, where the population density are high and the climate condition was favourable for all stages of mosquito life cycle.⁽⁹⁾

The spatio temporal statistical and space time clustering analyses implemented in this research identified DF spacetime clusters with a higher DF burden and greater risks for DF transmission. It is also identified the geographic areas and time periods associated with highest DF risk at the village level in Medan Municipality. These clusters and surrounding areas should be targeted for DF prevention and control interventions.⁽³²⁾

Strength and limitation

Our findings contribute to a better comprehension of the spatial analysis of dengue fever by assessing its clusters. These results can inform health authorities in the design of surveillance and control activities. However, there are some limitations of the study. First, our study only conducted spatial geo-reference to the village offices' coordinate, it would be better if we collected all dengue fever cases' coordinate and potential individual and environmental risk factors. Second, we could not get entomological data in every village, analysis of entomological data will enrich the discussion of our study.

CONCLUSIONS

Thirteen statistically significant DF clusters were identified in the 2015-2018 period. Most likely clusters were most frequently detected in the last three-year period of study in *Anggrung* village. The space time scan statistic method can be used for other communicable diseases and a higher spatiotemporal scale. This may assist health authorities to improve the DF preventive strategies and develop public health interventions especially in the cluster's area.

CONFLICT OF INTEREST

None

ACKNOWLEDGEMENTS

The authors would like to acknowledge all the surveillance of arbovirolosis staff in all Puskesmas, Medan Municipality.

REFERENCES

1. WHO. Prevention and Control of Dengue and Dengue Hemorrhagic Fever. WHO Reg Publ SEARO. 2009;29.

2. Guzman MG, Harris E. Dengue. Lancet. 2015;385:453-65.
3. Malavige GN, Fernando S, Fernando DJ, Seneviratne SL. Dengue viral infections. 2004;588-601.
4. Rossi G, Karki S, Smith RL, Brown WM, Ruiz MOH. Spatial and Spatio-temporal Epidemiology The spread of mosquito-borne viruses in modern times : A spatio-temporal analysis of dengue and chikungunya. Spat Spatiotemporal Epidemiol. 2018;26:113-25.
5. Ministry of Health Indonesia. Guideline for prevention and control of dengue fever. 2017.
6. Sitepu FY, Supriyadi T. Evaluation of dengue hemorrhagic fever control and prevention program in North Sumatra, 2010-2012. BALABA. 2013;9(01):1-6.
7. Sitepu FY, Nasution H, Supriyadi T, Depari E. Epidemiological and Entomological Investigation of Dengue Fever Outbreak in South Nias District, North Sumatera Province, Indonesia, 2016. OSIR. 2018;Sep;11(3):8-12.
8. Statistics MB of. Medan Municipality in Figures 2017. Medan Bureau of Statistic; 2018.
9. Setiawati MD. The Influence of Climate Variables on Dengue in Medan , Indonesia The Influence of Climate Variables on Dengue in Medan , Indonesia. 2017;(January).
10. Ghosh A, Dar L. Dengue vaccines: challenges, development, current status and prospects. Indian J Med Microbiol. 2015;33(1):3-15.
11. Hadisoemarto PF, Castro MC. Public Acceptance and Willingness-to-Pay for a Future Dengue Vaccine : A Community-Based Survey in Bandung , Indonesia. 2013;7(9).
12. Dhewantara PW, Ruliansyah A, Fuadiyah MEA, Astuti EP, Widawati M. Space-time scan statistics of 2007-2013 dengue incidence in Cimahi city, Indonesia. Geospat Health. 2015;10(373):255-60.
13. Anno S, Imaoka K, Tadono T, Igarashi T, Sivaganesh S, Kannathasan S, et al. Space-time clustering characteristics of dengue based on ecological, socio-economic and demographic factors in northern Sri Lanka. Geospat Health. 2015;10(376):215-22.
14. Kulldorff M. SaTScan User Guide. <http://www.satscan.org/>; 2018. 1-118 p.

15. Jerrett M, Gale S, Kontgis C. Spatial Modeling in Environmental and Public Health Research. *Int J Environ Res Public Health*. 2010;7:1302-29.
16. Velasco-salas ZI, Vincenti-gonzalez MF, Lizarazo F, Amarista MA, Sierra GM, Comach G, et al. Spatial Analysis of Dengue Seroprevalence and Modeling of Transmission Risk Factors in a Dengue Hyperendemic City of Venezuela. *PLoS Negl Trop Dis*. 2017;1-21.
17. Yue Y, Sun J, Liu X, Ren D, Liu Q, Xiao X, et al. International Journal of Infectious Diseases Spatial analysis of dengue fever and exploration of its environmental and socio-economic risk factors using ordinary least squares : A case study in five districts of Guangzhou City ,. *Int J Infect Dis [Internet]*. 2018;75:39-48. Available from: <https://doi.org/10.1016/j.ijid.2018.07.023>
18. Endy TP, Nisalak A, Chunsuttiwat S, Libraty DH, Green S, Rothman AL, et al. Spatial and Temporal Circulation of Dengue Virus Serotypes : A Prospective Study of Primary School Children in Kamphaeng Phet , Thailand. 2002;156(1):52-9.
19. Luz PM, Mendes BVM, Codeço CT, Struchiner CJ, Galvani AP. Time Series Analysis of Dengue Incidence in Rio de Janeiro , Brazil. 2008;79(6):933-9.
20. Chuang T, Ng K-C, Nguyen TL, Chaves LF. Epidemiological Characteristics and Space-Time Analysis of the 2015 Dengue Outbreak in the Metropolitan Region of Tainan City , Taiwan. *Int J Environ Res Public Health*. 2018;15(396).
21. Acharya BK, Cao C, Lakes T, Chen W, Naeem S. Spatiotemporal analysis of dengue fever in Nepal from 2010 to 2014. *BMC Public Health*. 2016;16(August).
22. Hamer D, Lichtveld M. Spatial Distribution of Epidemiological Cases of Dengue Fever in Suriname, 2001 – 2012. *West Indian Med J*. 2015;64(4):344-50.
23. Satoto T, Alvira N, Wibawa T, Diptyanusa A. Controlling Factors that Potentially against Transmission of Dengue Hemorrhagic Fever at State Elementary Schools in Yogyakarta. *Kesmas Natl Public Heal J*. 2017;11(4):178-84.
24. Cordeiro R, Donalisio MR, Andrade VR, Mafra ACN, Nucci LB, Brown JC, et al. Spatial distribution of the risk of dengue fever in southeast Brazil, 2006-2007. *BMC Public Health*. 2011;11(355).
25. Prayitno A, Taurel A-F, Nealon J, Satari HI, Karyanti MR, Sekartini R, et al. Dengue seroprevalence and force of primary infection in a representative population of urban dwelling Indonesian children. *PLoS Negl Trop Dis*. 2018;11(2017):1-9.
26. Dom NC, Madzlan MF, Hasnan SNA, Misran N. Water quality characteristics of dengue vectors breeding containers. *Int J Mosq Res*. 2016;3(January):25-9.
27. Harapan H, Anwar S, Bustaman A, Radiansyah A, Darmayanti D, Pratama R, et al. Community Willingness to Participate in a Dengue Study in Aceh Province , Indonesia. 2016;1-15.
28. Siregar FA, Abdullah MR, Omar J, Sarumpaet SM, Supriyadi T, Makmur T, et al. Social and Environmental Determinants of Dengue Infection Risk in North Sumatera Province , Indonesia.
29. Sarfraz MS, Tripathi NK, Tipdecho T, Thongbu T, Kerdthong P, Souris M. Analyzing the spatio-temporal relationship between dengue vector larval density and land-use using factor analysis and spatial ring mapping. *BMC Public Health*. 2012;12(853):1-19.
30. Gordis L. *Epidemiology*. Fourth. Saunders Elsevier; 2008.
31. Fazidah SA, Abdullah MR, Omar J, Sarumpaet SM. Climate Variability and Disease Forecasting Model for Dengue Hemorrhagic Fever in North Sumatera Province , Indonesia. 2015;(August).
32. Tonini M, Tuia D, Ratle F. Detection of clusters using space - time scan statistics. *Int J Wildl Fire*. 2009;18(18):830-6.