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THE RELATIONSHIP BETWEEN THE PRESENCE OF AEDES SPP. LARVAE WITH CASES OF DENGUE HERMORRHAGIC FEVER

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ABSTRACT

Dengue hemorrhagic fever is an infectious disease caused by dengue virus and transmitted through the *Aedes spp*. Prevention of dengue hemorrhagic fever can be done by eradicating the presence of *Aedes spp.* larvae in their breeding sites. This study aimed to determine whether there was a relationship between the presence of *Aedes spp.* mosquito larvae with the incidence of dengue hemorrhagic fever in the working area of Puskesmas Padang Selasa Kecamatan Ilir Barat I Palembang in 2019. This study was an analytic observational study with cross-sectional design. The research sample consisted of 110 houses, along with water reservoirs and mosquito larvae in it, which were chosen with purposive and simple random sampling technique. Research respondents were residents of the house chosen as the sample. Data collected by interview, observation, and microscopic identification. Data was processed and analyzed with the chi-square statistical test. Out of 110 houses visited, 26 (23.6%) of the respondents stated that they themselves or their household relatives had experienced DHF in the last two years. Out of the 332 water reservoirs observed, 36 (32.7%) were positive for *Aedes spp.* larvae, 14 (53.8%) of them were found in houses where residents had a history of DHF in the last 2 years. Chi-square statistical test results with a degree of confidence of 95% and α 0.05 showed a significant relationship between the two variables with a *p* value = 0.017 and PR (prevalence rate) 2.339 (95% CI = 1.239-4.61). There was a significant relationship between the presence of *Aedes spp.* mosquito larvae with the incidence of dengue hemorrhagic fever in the working area of the Puskesmas Padang Selasa Kecamatan Ilir Barat I Palembang in 2019.

Keywords: *dengue hemorrhagic fever, dengue vector, mosquito larvae, Aedes spp.*

1. INTRODUCTION

Dengue hemorrhagic fever (DHF) is a viral infection disease with clinical manifestations of acute fever, muscle aches and / or joint pain, leukopenia, rash, lymphadenopathy, thrombocytopenia, hemorrhagic diathesis, and increased levels of hematocrit and/or accumulation of fluid in the body cavities due to plasma leakage (Suhendro, et al., 2014). Dengue virus, virus of DHF, is transmitted through the vector of the genus Aedes, subgenus Stegomyia (Zuckerman, et al., 1987). The Aedes aegypti and Aedes albopictus mosquitoes are the most common DHF vectors found in Indonesia.

Approximately 50-100 million new infections are estimated to occur each year in more than 100 DHF endemic countries. The distribution of DHF covers all regions in Indonesia, including Palembang City (Suhendro, et al., 2014). Based on the health profile data of South Sumatra Province over the last few years, Palembang City has the highest incidence of DHF cases in South Sumatra Province (Dinkes Kota Palembang, 2018; Dinkes Kota Palembang, 2017; Dinkes Kota Palembang, 2016) .

The latest report from the Indonesian Ministry of Health (2019) from the beginning of the year to 3 February 2019, there were 16,692 DHF cases in Indonesia with a death rate of 169 people (Kemenkes, 2019). In line with the rapid increase in cases of DHF at the beginning of the year, the Indonesian Ministry of Health

appealed to all regions to watchful for DHF and maximize the practice of eradicating mosquito nests (Pemberantasan Sarang Nyamuk/PSN) as a precaution for DHF (Kemenkes, 2019).

Prevention that has been proven to reduce the incidence of DHF at this time is by eradicating the mosquito vector that spreads the dengue virus (WHO, 2000). Environmental control vector carried out with the 3M plus program aims to eradicate the presence of mosquito larvae.

Research conducted in Banjar Graha Kerti and Banjar Kerta Petasikan, Denpasar, shows a significant relationship between the presence of mosquito larvae and the incidence of DHF (Widjana, et al., 2012). This research was conducted to determine whether there was a relationship between the presence of *Aedes spp*. larvae with the incidence of DHF in the working area of Puskesmas Padang Selasa, Ilir Barat I, Palembang City in 2019.

2. METHOD

This study was an observational analytic study with a cross sectional design. The study was conducted from July to Decpail 2019. The research sample was purposive sampling and simple random sampling consisting of 76 houses in Bukit Lama and 34 houses in Bukit Baru. After passing the informed consent procedure, data collection was continued with interviews, observation of mosquito larvae in water reservoirs, and microscopic observation of mosquito genus or species of larvae. Univariate and bivariate data analysis using the SPSS application. Hypothesis testing in bivariate analysis using the chi-square test (CI 95% and $\alpha = 0.05$).

3. RESULT

3.1 Habitat for the development of mosquitoes

The number of water reservoirs (WR) observed was 332 WR (232 indoor WR and 100 outdoor WR) with the presence of mosquito larvae can be seen in Table 1 and Table 2.

Table 1. Identification of indoor WR (n = 232)

No	Type of Indoor WR	Total		Presence of larvae			
				Yes		No	
		n	%	N	%	N	%
1	Aquarium	2	0,86	0	0,00	2	0,86
2	Bath tub	124	53,45	32	13,79	92	39,66
3	Bottle	2	0,86	1	0,43	1	0,43
4	Dispenser	7	3,02	0	0,00	7	3,02
5	Drum	16	6,90	3	1,29	13	5,60
6	Pail	78	33,62	5	2,16	73	31,47
7	Cans	1	0,43	0	0,00	1	0,43
8	Flower pot	1	0,43	0	0,00	1	0,43
9	Pet bowl	1	0,43	0	0,00	1	0,43
	Total	232	100	41	17,67	191	82,33

The most indoor water reservoirs of each house is a tub, 124 (53.45%). Of the 232 water reservoirs, 41 (17.67%) contained mosquito larvae and 191 (82.33%) no mosquito larvae were found. Most mosquito larvae in indoor WR were found in tubs (13.79%).

Table 2. Identification of outdoor WR (n = 100)

No	Type of outdoor WR	Total		Presence of larvae			
				Yes		No	
		N	%	N	%	n	%
1	Tub	6	6	0	0	6	6
2	Tire	1	1	0	0	1	1
3	Basin	5	5	0	0	5	5
4	Bottle	3	3	0	0	3	3
5	Drum	9	9	4	50	5	5
6	Pail	49	49	2	25	47	47
7	Fish pond	5	5	2	25	3	3
8	Flower pot	21	21	0	0	21	21
9	Bowl pet	1	1	0	0	1	1
	Total	100	100	8	8	92	92

Table 2 shows the identification results of mosquito larvae in outdoor water reservoirs. The most number of outdoor water reservoirs was pails, 49 (49.00%). 8 (8.00%) outdoor WRs were present with positive mosquito larvae. Most mosquito larvae in outdoor WR were found in drums (50.00%).

3.2 Distribution of larva postitf WR and the number of larva

Mosquito larvae were found in 41 houses of a total 110 houses where water reservoirs were observed. From the outdoor and indoor observations in each house, a total of 576 mosquito larvae were obtained. The distribution and number of mosquito larvae can be seen in Table 3.

Table 3. Distribution of positif larva WR and the number of larva (n=576)

No.	Type of (+) larva WR	Location	∑ Larva
1.	Tub	Indoor	26
2.	Tub	Indoor	18
3.	Tub	Indoor	3
4.	Pail	Indoor	3
5.	Tub and pail	Indoor	3
6.	Pail	Outdoor	13
7.	Tub	Indoor	35
8.	Tub	Indoor	2
9.	Drum	Indoor	7
10.	Tub dan drum	Indoor	8
11.	Pail dan drum	Indoor	179
12.	Drum	Outdoor	18
13.	Pail	Outdoor	1
14.	Tub	Indoor	20
15.	Pail dan kolam ikan	Outdoor	7
16.	Fish pond	Outdoor	71
17.	Drum	Outdoor	3
18.	Drum	Outdoor	2
19.	Tub	Indoor	2
20.	Tub	Indoor	24
21.	Tub	Indoor	16
22.	Tub	Indoor	5
23.	Tub	Indoor	4
24.	Tub	Indoor	7
25.	Bottle	Indoor	30
26.	Tub	Indoor	3
27.	Tub	Indoor	9
28.	Tub	Indoor	5
29.	Tub	Indoor	1
30.	Tub	Indoor	5
31.	Tub	Indoor	1
32.	Drum	Indoor	4
33.	Drum	Indoor	6
34.	Tub	Indoor	2
35.	Tub	Indoor	5
36.	Tub	Indoor	3
37.	Tub	Indoor	6
38.	Tub	Indoor	1
39.	Tub	Indoor	6
40.	Tub	Indoor	7
41.	Tub	Indoor	3
42.	Tub	Indoor	2
	Total		576

Table 3 shows the uneven distribution of mosquito larvae in each house. In house number 11, the most mosquito larvae were found with 179 (31.08%) in indoor pails and drums. The lowest number of mosquitoes, 0.17%, was found in houses number 13, 29, 31, and 38, 1.

3.3 Mosquito larvae density index

From the 110 houses, there are 41 houses whose water reservoirs contain mosquito larvae (House index/HI = 37.27%) and 69 houses where mosquito larvae are not found (Angka Bebas Jentik/ABJ = 62.73%). Mosquito larvae were found in 49 water reservoirs out of 110 observed houses (Breteau Index/BI = 44.54) of the total WR observed as many as 332 (Container Index/CI = 14.76%). After obtaining HI, BI and CI values, it can be determined that the density figure (DF) value in the Puskesmas Padang Selasa work area is 5 (Table 4). This value indicates that the density of mosquito larvae in the working area of Puskesmas Padang Selasa is in the medium category.

Table 4. Mosquito larva index

Indicator	Parameter of value
Angka Bebas Jentik/ABJ (%)	62,73
House Index/HI (%)	37,27
Container Index/CI (%)	14,76
Breteau Index/BI (Container/100 Bangunan)	44,54
Density figure (DF)	5,0

3.4 Genus and spesies of mosquito larva

From the observations, no larvae were found with a resting position parallel to the air surface which is a larva characteristic of Genus Anopheles. An illustration of larva resting position that forms an angle on the air surface can be seen in Figure 1. Mosquito larvae found are white, brown, to black with various sizes (instar 1-4). The movement of the mosquito larvae in the water looks twisted.

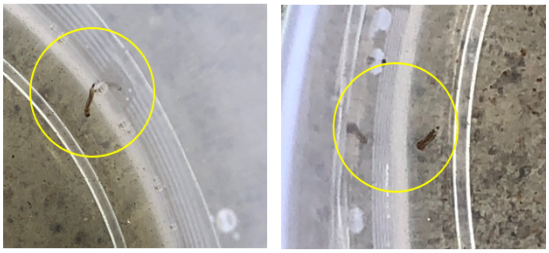

Figure 1. The resting position of the mosquito larvae forms an angle on the water surface in the outdoor pail.

One of larva from positive WR was made a dry preparation to be micorscopic observed the morphology of the head, chest (thorax), stomach (abdomen), and siphon, which were matched with the identification key.

The head of *Aedes aegypti* larvae is characterized by a pair of brush-like hairs on the tip of the head and a pair of hairless antennae (Figure 2).

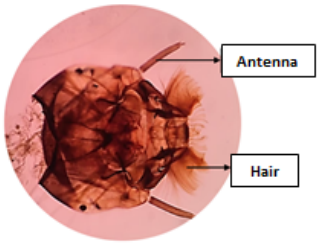

Figure 2. Head of *Aedes aegypti* larva (100x magnification)

The abdominal sections of the *Aedes aegypti* larvae are shown in Figure 3. There are lateral hairs that are curved on each side of the abdominal segment.

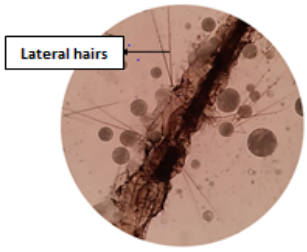

Figure 3. Abdomen (sections 4-8) of *Aedes aegypti* larva (100x magnification)

The picture of the siphon in *Aedes aegypti* larvae can be seen in Figures 4, 5, and 6. They show the characteristics of the siphon which is fat and short, the presence of a pair of siphon hairs, pecten on the siphon, open saddle on the anal segment, and a row of comb scales on the last segment in abdomen (8th segment). The presence of lateral spines on the comb scale which is a characteristic of *Aedes aegypti* larvae, a differentiator from *Aedes albopictus,* was more clearly shown in Figure 6. All mosquito larvae identified as *Aedes spp*. In this study, lateral spines were found on the comb scale. From these results, it was found that no *Aedes albopictus* larvae from 576 mosquito larvae were found.

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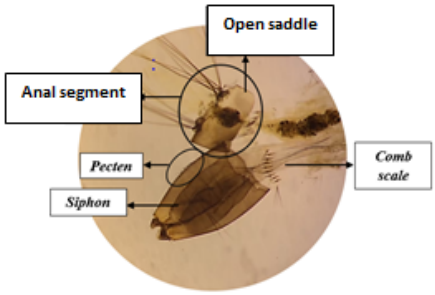

Figure 4. The last segment of the abdomen and siphon of the *Aedes aegypti* larva (100x magnification)

Figure 5. *Siphon* and *anal gill*of *Aedes aegypti* larva (100x magnification)

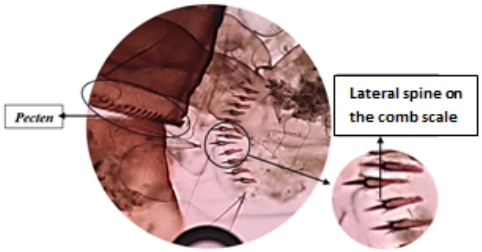

Figure 6. Comb scale with lateral spines on the last segment of the abdomen of *Aedes aegypti* larvae (400x magnification)

Figure 7 shows the large head of the mosquito larvae with long antennae and hair on the antennae that are characteristic of the genus *Culex*.

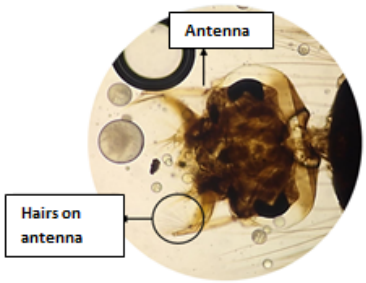

Figure 7. The head of genus *Culex* larva (100x magnification)

Figures 8, 9, and 10 show a long slender siphon, some hair on the sides of the siphon, and a closed saddle on the anal segment. These findings are consistent with the key identification for the genus *Culex* larvae.

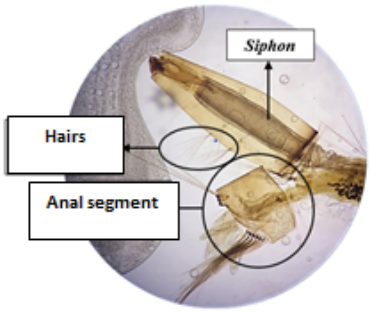

Figure 8. The siphon of genus *Culex* larva (100x magnification)

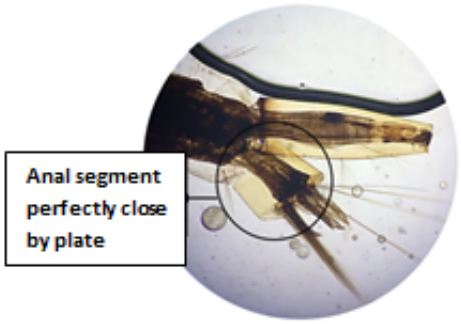

Figure 9. The siphon of genus *Culex* larva (100x magnification)

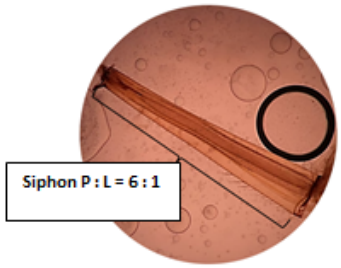

Figure 10. The siphon of genus *Culex* larva (100x magnification)

From the 576 mosquito larvae scattered in 41 houses, almost all of them are *Aedes aegypti* species (86.98%) which is the main vector of DHF. The frequency distribution of the types of larvae can be seen in Table 5. In this study, there were no *Aedes albopictus* larvae, which are potential vectors of DHF. 75 larvae of the genus *Culex* were found scattered in 1 WR indoor and 2 WR outdoor.

Table 5. Frequency distribution of mosquito larvae types (n=576)

Genus and Species	Amount		Location of WR			
	N	%	*In door*	%	*Out door*	%
Aedes aegypti	501	86,98	466	80,90	35	6,08
genus *Culex*	75	13,02	2	0,35	73	12,67
Total	576	100	468	81,25	108	18,75

3.5 Respondent characteristic

Respondents in this study were 110 people from each house that became the research sample.

Table 6. Frequency distribution of respondent characteristic (n = 110)

Respondent Characteristic	Amount (n)	%
Age (Years)		
18-25	7	6,4
26-33	24	21,8
34-41	26	23,6
42-49	14	12,7
50-57	17	15,5
58-65	16	14,5
66-73	4	3,6
≥74	2	1,8
Sex		
Female	70	63,6
Male	40	36,4
Degree of School		
No Primary Junior	22	20
Senior Bachelor	88	80
History of DHF in last 2 years		
Positive	26	23,6
Negative	84	76,4
Total	**110**	**100**

Based on Table 6, most respondents were in the range 34-41 years (23.6%). Respondents with age above or equal to 74 years are at least 2 people (1.8%). Of the 110 respondents, 70 (63.6%) of them were female.

The most respondents were in high school or bachelor degree, 88 respondents (80%). Meanwhile, the number of respondents with the latest education level did not go to school, primary and junior high school amounted to 22 people (20%).

Based on respondents' interviews accompanied by evidence of diagnosis, it was found that 26 (23.6%) respondents had a history of DHF in the last two years. Evidence of the diagnosis was obtained from data on DHF sufferers in the Puskesmas Padang Selasa, 2017-2019.

3.6 The relationship between the presence of mosquito larvae and DHF cases

From the results of the study, the water reservoir owned by the respondent or member of the respondent's house with a history of DHF found that there were more *Aedes spp*. larvae. (53.8%) compared to the absence of *Aedes spp*. (46.2%) (See Table 7).

Table 7. Relationship between DHF case history and the presence of mosquito larvae

Larva	DHF History				Total		PR	*p-value*
	(+)		(-)					
	n	%	n	%	N	%		
Yes	14	53,8	22	26,2	36	32,7	2,398	0,017
No	12	46,2	62	73,8	74	67,3		

Total	26	100	84	100	110	100

In Table 7, based on the results of the Chi-Square statistical test (CI 95% and α 0.05), it was found that *p value* = 0.017 (p <α) and PR 2.398 (95% CI = 1.239-4.641). There is a significant relationship between the presence of *Aedes spp.* larvae. with cases of DHF. The PR value shows that the presence of *Aedes spp.* can increase the risk of DHF cases by 2.398 times compared to the absence of *Aedes spp.* in the water reservoir.

4. DISCUSSION

The results of this study are consistent with the research of Yotopranoto (2008) and Ridha et al. (2013) in Surabaya and Banjarbaru which showed that water reservoirs that are potential for breeding mosquitoes are containers used for daily needs such as drums, tubs, and pails (yotoptanoto, et al., 2008; Ridha, et al., 2013). Research conducted by Purwaningrum et al. (2016) showed a significant relationship between the presence of breeding places for *Aedes aegypti* and DHF with a *p value* 0.001 and OR 10.524 (95% CI = 2.271-48.757) (Purwaningrum, 2016). Potential water reservoirs for breeding *Aedes aegypti* is containers with clear water, close to settlement, and not directly related to the soil (Kemenkes, 2013; Djakaria & Sungkar, 2008).

Index of larvae in this research shows that the working area of Puskesmas Padang Selasa, Ilir Barat I, was an area with a high risk of dengue fever transmission but does not potential to dengue fever outbreaks. The density figure indicated that the density of mosquito larvae in the working area of Puskesmas Padang Selasa, Ilir Barat I was in the medium category. This value also shows that the presence of mosquito vectors, including *Aedes spp.* as a vector of DHF, needs to be watched out and eradicated to prevent the increase in the density of mosquito larvae which can lead to DHF outbreaks.

Based on statistical tests, this study was in line with the cross sectional study conducted by Tirtasari, et al. (2016) who examined the relationship between the presence of larvae in containers with the incidence of dengue fever in 19 Novpail, Wundulako, Kolaka in 2016. She found p-value of 0.003 (p <α) which means that there is a significant relationship between the two test variables (Tirtasari, et al., 2016). Furthermore, PR value of 2.398 (95% CI = 1.239-4.641) indicates that the respondent with the presence of *Aedes spp.* in the water reservoir has a risk 2.398 times greater than that of respondents who were not found larvae of *Aedes spp*. in the water reservoir. This is also accordance with the results of a case control study conducted by Purwaningrum, that there is a significant relationship between the two variables (p value 0.002 and OR 11 with 95% CI = 1.998-60.572) (Purwaningrum, et al., 2016). The OR value in this study shows that the respondent with the presence of larvae. *Aedes aegypti* has 11 times greater risk of suffering dengue fever compared to respondents who were not found *Aedes aegypti* larvae in their house.

5. CONCLUSION

The working area of Puskesmas Padang Selasa, Ilir Barat I was an area with a high risk of DHF transmission but does not have the potential to dengue outbreaks. It is necessary to implement a mosquito nest eradication program with 3M Plus practices that are complete, correct, and routine in every home to prevent cases of DHF. In addition, we also found that there was a significant relationship between the presence of mosquito larvae and the incidence of DHF.

REFERENCES

[1]. Aji, H. R. (2016). Lingkungan Non-TPA Dalam Rumah dengan Indeks Larva *Aedes Aegypti* di Kabupaten Rejang Lebong. *Jurnal Vokasi Kesehatan*. 7(2), 92-97.

[2]. Aulia, S., Djamahar, R., Rahmayanti, R. (2017). Deskripsi Tempat Penampungan Air Positif Larva Aedes aegypti di Kelurahan Cakung Timur. *Bioma*. 10(1), 25.

[3]. CDC. (2014). Life Stages of Aedes Mosquito. Retrieved from : https://www.cdc.gov/dengue/resources/factSheets/MosquitoLifecycleFINAL.pdf.

[4]. Dinas Kesehatan Kota Palembang. (2016). Profil Kesehatan Kota Palembang tahun 2015. Dinas Kesehatan Kota Palembang, Palembang, Indonesia.

[5]. Dinas Kesehatan Kota Palembang. (2017). Profil Kesehatan Kota Palembang tahun 2016. Dinas Kesehatan Kota Palembang, Palembang, Indonesia.

[6]. Dinas Kesehatan Kota Palembang. (2018). Profil Kesehatan Kota Palembang tahun 2017. Dinas Kesehatan Kota Palembang, Palembang, Indonesia.

[7]. Djakaria, S. & Sungkar, S. (2008). Vektor Penyakit Virus, Riketsia, Spiroketa, dan Bakteri. In Sutanto, et al. (Eds), *Buku Ajar Parasitologi Kedokteran* (4: pp.265-269). Jakarta, Indonesia : FK UI.

[8]. Kementerian Kesehatan Republik Indonesia. (2019). Kasus DBD Terus Bertambah, Anung Imbau Masyarakat Maksimalkan PSN. Retrieved from http://www.depkes.go.id/article/view/19020600004/kasus-dbd-terus-bertambah-anung-imbau-masyarakat-maksimalkan-psn.html

[9]. Kemendagri. Kode dan Data Wilayah Administrasi Pemerintahan (2017). Permendagri No.137-2017. Retrieved from https://www.kemendagri.go.id

[10]. Kementerian Kesehatan RI DITJEN PP&PL. (2013). RI. Pedoman Pengendalian Demam Berdarah Dengue di Indonesia. Jakarta, Indonesia.

[11]. Mutiara, H. (2019). Analisis Spasial Kepadatan Larva, Maya Index Dan Kejadian Demam Berdarah Dengue (Studi Kasus di Kelurahan Sendangmulyo Kota Semarang). *Jurnal Kesehatan Masyarakat*. 7(2). Retrieved from : http://ejournal3.undip.ac.id/index.php/jkm6

[12]. Pratt, Harry, D. (2005). Mosqiutoes: Pictorial key to U.S Genera of Larvae. Retrieved from : https://www.cdc.gov/nceh/ehs/docs/pictorial_keys/mosquitoes.pdf.

[13]. Purwaningrum S., Widyanto A., Widiyanto T. (2016). Faktor-Faktor Lingkungan yang Berhubungan dengan Kejadian Demam Berdarah Dengue (DBD) di Wilayah Puskesmas Banjarnegara 1 Kabupaten Banjarnegara Tahun 2016. Retrieved from http://ejournal.poltekkes-smg.ac.id/ojs/index.php/keslingmas/article/viewFile/2964/598

[14]. Queensland Government. (2011) Queensland Dengue Management Plan 2010-2015. Retrieved from http://s3.amazonaws.com/zanran_storage/www.health.qld.gov.au/ContentPages/2508518310.pdf

[15]. Ridha, M. R., Rahayu, N., Rosvita, N.A., & Setyaningtyas, D. E. (2013). Hubungan kondisi lingkungan dan kontainer dengan keberadaan jentik nyamuk *Aedes aegypti* di daerah endemis demam berdarah dengue di Kota Banjarbaru. *Jurnal Epidemiologi dan Penyakit Bersumber Binatang* 4(3), 133 - 137. Retrieved from

http://ejournal.litbang.depkes.go.id/index.php/buski/article/view/3231/3202

[16]. Sari, I. P., Adrial, Nofita, E. (2017). Hubungan Kepadatan Larva *Aedes spp.* dengan Kejadian Demam Berdarah Dengue di Kelurahan Lubuk Buaya Kecamatan Koto Tangah Kota Padang. *Jurnal Kesehatan Andalas*. 6(1), 41–8.

[17]. Suhendro, Chen K., Nainggolan L., and Pohan H. (2014). Demam Berdarah Dengue. In *Buku Ajar Ilmu Penyakit Dalam (Part I)*. (pp. 539). Jakarta, Indonesia : FK UI.

[18]. Stojanovich, C. J. (2005). General characteristics of mosquitoes in the genera Anopheles, Aedes, and Culex. Retrieved from : https://www.cdc.gov/nceh/ehs/docs/pictorial_keys/mosquitoes.pdf

[19]. Tirtasari, E., Asfian, P., Ainurafiq. (2016). Faktor-Faktor yang Berhubungan dengan Kejadian Demam Berdarah Dengue (DBD) di Kelurahan 19 Novpail Kecamatan Wundulako Kabupaten Kolaka Tahun 2016. *Jurnal Ilmiah Mahasiswa Kesehatan Masyarakat UHO*. Retrieved from : http://ojs.uho.ac.id?index.php/JIMKESMAS/article/viewFile/1248/895.

[20]. World Health Organization. (2000). Strengthening implementation of the global strategy for dengue fever/dengue haemorrhagic fever prevention and control. Geneva.

[21]. Widjana, D. P., Sudarmaja, M., & Sutisna, P. (2012). Fauna Nyamuk Aedes dan Kemungkinan Perannya dalam Penularan Demam Berdarah Dengue di Banjar Graha Kerti dan Banjar Kerta Petasikan, Denpasar. *Jurnal Kesehatan Yarsi 20*. Denpasar, Indonesia.

[22]. Yotopranoto, S., Subekti, S., Rosmanida, & Sulaiman. (2008). Dinamika Populasi Vektor pada Lokasi dengan Kasus Demam Berdarah Dengue yang Tinggi di Kotamadya Surabaya.

[23]. Zuckerman, A. J., Banatvala, J. E., Pattison, J. R., Griffiths, P. D., & Schoub, B. D. (1987). Principles and Practice of Clinical Virology (Eds. 5). Retrieved from www.wileyeurope.com