Nutrient Intake of Dengue Hemorrhagic Fever Patients in Semarang City

Agustina Ratri Maharani1, Christina Tri Restuti1, Erna Sari1, Nur Endah Wahyuningsih1, Retno Murwani2,3, and MMDEAH Hapsari1

1Faculty of Public Health, Diponegoro University
2Faculty of Animal Science and Agriculture, Diponegoro University
3Center for Research and Service, Diponegoro University
4Faculty of Medicine, Diponegoro University

Jl. Prof. Soedharto, SH, Tembalang, Semarang 50275, Indonesia
E-mail: agustinaratrimaharani@gmail.com,wahyuningsihnew@gmail.com, rmurwani@gmail.com, christinatrirestuti@gmail.com, ernasari0411@gmail.com

Abstract. Dengue Hemorrhagic Fever (DHF) is an acute infectious disease caused by dengue virus and transmission of the virus is mediated by mosquitoes bites [1]. Host immunity against dengue infection is affected by nutrient adequacy which is depending on nutrient intake [2]. The aim of this study was to determine nutrient intake of DHF patients in Semarang city. The DHF sample cases were obtained from three hospitals in Semarang city (n=48), from the period of March to May 2016 and the control groups were obtained from healthy respondents with matched age, sex, and district location (n=48). Nutrient intake were obtained by food recall and calculated using Nutrisurvey Indonesia. Afterwards, the result of the nutrisurvey will be compared to Indonesian daily value according to Permenkes no. 75 about daily value based on age and gender. The results showed that both in cases and control groups the macro-energy, carbohydrate, protein, fat) and micro-nutrient (vitamins A, C, B1, B2, B6, calcium, magnesium, phosphorus, zinc, and Iron) intake were below 80% of nutrient adequacy. No correlation was found between nutrient adequacy and DHF cases. We find that macro and micronutrient intake in DHF case and control groups are the same and below 80% of nutrient adequacy. The nutrient intake was not related to DHF cases.

1. Introduction

Dengue Haemorrhagic Fever (DHF) is an acute infectious disease caused by dengue virus [1], mostly occurs through mosquito bites, especially species Aedes either aegypti or aedes albopictus. The highest case of dengue in Asia are Indonesia, Bangladesh, India, Maldives, Sri Lanka, Thailand and Timor Leste [2]. DHF cases in Indonesia during last 3 years (2013-2015) showed fluctuations in the number of cases, in 2013 the number of DHF patients reported as many as 112,511 which decreased to 110,347 in 2014 and increased in 2015 with 129,650 cases and the number of deaths were 1071 people. Provinces with highest DHF rates in 2014 and 2015 are still held by Bali of 257.75, East Kalimantan of 188.46 and North Kalimantan at 112.00 per 100,000 population [2-3]. The number of patients with DHF in Semarang were increased In 2015. Incidence Rate (IR) of 2015 increased from 92.45 to 98.61 and patients who died from 27 people in 2014 to 21 people in the year 2015. Incidence Rate of DHF Semarang in 2015 was ranked third IR DBD Central Java after Magelang city and Jepara regency. However, in 2016 there was a decreased in the number of cases to 448 from 1,737 cases in...
the previous year. The DHF IR in 2016 also decreased to 25.22 in 2016. However, the CFR of 2016 increased from 1.2 in 2015 to 5.12 in 2016 [4-5].

Research in Jepara and Ujungpandang shows that Aedes spp. associated with high rates of dengue virus transmission in the community; but the transmission does not always cause human dengue because it still depends on other factors such as vector capacity, virulence of dengue virus, and host immunity. The immune system has the function of helping repair human DNA; prevent transmission of diseases caused by fungi, bacteria, viruses, and other organisms; also produces antibodies to combat the attack of foreign bacteria and viruses that enter the body, the immune system one of which is influenced by nutritional status [6]. Nutritional status is a health condition due to the interaction of food, the human body and the environment which is the result of the interaction between nutrients which enter into the human body and its use [7]. Overall, the relationship between nutritional status and risk of DENV infection can not be clearly defined. There is no evidence to suggest that nutritional status can interfere with transmission or alter susceptibility to infection after the bite of dengue-infected mosquitoes; however, the nutritional status or supplement that a person consumes may decrease the probability of developing DENV infection into a severe disease or reduce the severity of the disease in the patient [8]. Several studies have found an association between nutritional status and the severity of DHF, such as Lukman’s study of 5-6-year-old DHF patients, who found that abnormal nutritional status was more likely to get dengue virus infection with a risk of 1,250 times compared with people with normal nutritional status [6]. Research in RSUD Tugurejo also shows that patients whose nutritional status is more easily infected and infected by dengue virus [9]. On the contrary, people who have normal or good nutritional status have a better immune system, thus avoiding the dengue fever [10] for it is necessary to do research to know the linkage of nutritional intake with the incidence of DHF. The aim of this study was to determine nutrient Intake (the macro nutrient include energy, carbohydrate, protein, fat and micro-nutrient include vitamins A, C, B1, B2, B6, calcium, magnesium, phosphorus, zinc, and Iron) of DHF patients in Semarang city.

2. Method
The study included an observational analytic study comparing case and control groups using case-control design. The case groups in this study were DHF patients who were hospitalized in three hospitals in Semarang city (RSUD) Dr.Adhyatma, MPH, (RSUP) dr.Kariadi and (RSUD) KRM Wongsonegoro period from March to May 2017 amounted to 48 people, while case group is the respondent who is neighbors who never suffer from DBD and have same characteristic covering age and gender so that the total of respondents in this research is 96 people. The approach used is data collection at one time (point time approach). Data collection of nutritional intake was done by using food recall questionnaire for 3 days and then the result of the questionnaire was processed using nutri survey program to be able to know exactly the amount of nutrients consumed. Afterwards it will be compared with the value of AKG at Permekes no 75 of 2013 on Nutrition Adequacy Rate for Indonesian Nation to know the nutritional adequacy of the respondents.

3. Results
3.1 Characteristics of Respondents
The majority of respondents were 0-14 years old aged 25 (52.1%) in case and control respondents while the lowest age was 50-65 years old which amounted to 2 (4.2%) in case and control respondents. The number of male respondents was more than female respondents (28.3%) in case respondents and 19 (39.6%) in control respondents. Majority of respondents had primary education (31.6%) in primary school and 27 (56.3%) in control respondents. The highest nutrient status among the respondents was normal nutritional status, in case respondents were 25 (52.1%) and control respondents were 22 (45.8%).
Table 1. Characteristics of Respondents

| Variables          | Dengue Incidence |           |         |
|--------------------|------------------|-----------|---------|
|                    | Case | %    | Control | %    |
| **Age**            |      |      |         |       |
| 0-14 years old     | 25   | 52,1 | 25      | 52,1  |
| 15-49 years old    | 21   | 43,8 | 21      | 43,8  |
| 50-65 years old    | 2    | 4,2  | 2       | 4,2   |
| **Gender**         |      |      |         |       |
| Man                | 28   | 58,3 | 19      | 39,6  |
| Woman              | 20   | 41,7 | 29      | 60,4  |
| **Education**      |      |      |         |       |
| SD                 | 31   | 64,6 | 27      | 56,3  |
| SMP                | 4    | 8,3  | 6       | 12,5  |
| SMA                | 11   | 22,9 | 11      | 22,9  |
| D3/S1              | 2    | 4,2  | 4       | 6,3   |
| **Nutritional Status** |    |      |         |       |
| Thin               | 18   | 37,5 | 20      | 42,6  |
| Normal             | 25   | 52,1 | 22      | 45,8  |
| Obesity            | 5    | 10,4 | 6       | 12,5  |

3.2 Macro Nutrients

Table 2. Macro Nutrients

| Macronutrients              | DHF incidence |           |         |
|                            | Case | %    | Control | %    |
| **Energy Sufficiency Level** |      |      |         |       |
| Less                         | 43   | 89,6 | 42      | 87,5  |
| Normal                       | 0    | 0,0  | 1       | 2,1   |
| Over                         | 5    | 10,4 | 5       | 10,4  |
| **Carbohydrate Adequacy Level** |    |      |         |       |
| Less                         | 20   | 41,7 | 18      | 37,5  |
| Normal                       | 5    | 10,4 | 8       | 16,7  |
| Over                         | 23   | 47,9 | 22      | 45,8  |
| **Protein Sufficiency Level** |    |      |         |       |
| Less                         | 24   | 50,0 | 26      | 54,2  |
| Normal                       | 6    | 12,5 | 9       | 18,8  |
| Over                         | 18   | 37,5 | 13      | 27,1  |
| **Fat Adequacy Level**      |      |      |         |       |
| Less                         | 38   | 79,2 | 35      | 72,9  |
| Normal                       | 3    | 6,2  | 7       | 14,6  |
| Over                         | 7    | 14,6 | 6       | 12,5  |
Based on the results table the majority of respondents both in cases and controls have sufficient levels of energy, protein and fat below 80% AKG. While the level of carbohydrate sufficiency of respondents more have more carbohydrate sufficiency level.

3.3 Micro Nutrients

**Table 3. Percentage Rate Adequacy Vitamin on the respondents**

| Micronutrients | Dengue incidence | Case | % | Control | f | % |
|----------------|------------------|------|----|---------|----|----|
| **Vitamin C**  |                  |      |    |         |    |    |
| Less           |                  | 43   | 89.6 | 39      | 81.2 |
| Over           |                  | 5    | 10.4 | 9       | 18.8 |
| Amount         |                  | 48   | 100  | 48      | 100  |
| **Vitamin A**  |                  |      |    |         |    |    |
| Less           |                  | 30   | 62.5 | 28      | 58.3 |
| Normal         |                  | 3    | 6.2  | 6       | 12.5 |
| Over           |                  | 15   | 31.2 | 14      | 29.2 |
| Amount         |                  | 48   | 100  | 48      | 100  |
| **Vitamin B1** |                  |      |    |         |    |    |
| Less           |                  | 47   | 97.9 | 42      | 87.5 |
| Normal         |                  | 0    | 0    | 1       | 2.1  |
| Over           |                  | 1    | 2.1  | 5       | 10.4 |
| Amount         |                  | 48   | 100  | 48      | 100  |
| **Vitamin B2** |                  |      |    |         |    |    |
| Less           |                  | 33   | 68.8 | 37      | 77.1 |
| Normal         |                  | 8    | 16.7 | 1       | 2.1  |
| Over           |                  | 7    | 14.6 | 10      | 20.8 |
| Amount         |                  | 48   | 100  | 48      | 100  |
| **Vitamin B6** |                  |      |    |         |    |    |
| Less           |                  | 34   | 70.8 | 37      | 77.1 |
| Normal         |                  | 7    | 14.6 | 5       | 10.4 |
| Over           |                  | 7    | 14.6 | 6       | 12.5 |
| Amount         |                  | 48   | 100  | 48      | 100  |

**Table 4. Percentage Rate for the minerals in the respondents**

| Micronutrients | Dengue incidence | Case | % | Control | f | % |
|----------------|------------------|------|----|---------|----|----|
| **Calcium**    |                  |      |    |         |    |    |
| Less           |                  | 41   | 85.4 | 38      | 79.2 |
| Normal         |                  | 2    | 4.2  | 1       | 2.1  |
| Over           |                  | 5    | 10.4 | 9       | 18.8 |
| Amount         |                  | 48   | 100  | 48      | 100  |
| **Magnesium**  |                  |      |    |         |    |    |
| Less           |                  | 31   | 64.6 | 31      | 64.6 |
| Normal         |                  | 6    | 12.5 | 4       | 8.3  |
| Over           |                  | 11   | 22.9 | 13      | 27.1 |
| Amount         |                  | 48   | 100  | 48      | 100  |
| **Phosphor**   |                  |      |    |         |    |    |
| Less           |                  | 25   | 52.1 | 29      | 60.4 |
| Normal         |                  | 9    | 18.8 | 5       | 10.4 |
| Over           |                  | 14   | 29.2 | 14      | 29.2 |


Vitamins intake from the respondents are vitamin A, vitamin C, vitamin B1, vitamin B2 and vitamin B6 and from the questionnaire foodrecall seen that many respondents have less intake of Vitamin. The intake of minerals that were examined in this study is the intake of calcium, magnesium, phosphorus, zinc and iron, from the questionnaire foodrecall seen that most respondents still have mineral intake AKG less of % daily.

The intake of minerals from the questionnaire foodrecall seen that most respondents still have mineral intake AKG less of % daily. Of the 96 respondents who examined 79 of them maashi intake of calcium below the% Daily, 62 of which have intake magnesium below the% Daily, 54 of which have intake phospor below the% Daily, 78 of which have intake phospor below the% daily and 80 which have zinc intake below the % daily.

4. Discussion
4.1 Macro Nutrients
Based on the results table the majority of respondents both in cases and controls have sufficient levels of energy, protein and fat below 80% AKG. While the level of carbohydrate sufficiency of respondents more have more carbohydrate sufficiency level. Nutritional status is influenced by the balance of nutrient intake and absorption [11]. Nutrition (nutrients) is a chemical bond to perform its functions, which produce energy, build and maintain the network, and regulate the processes of life. In addition to health, nutrition is associated with the economic potential of a person, because nutrients associated with brain development, learning, and productivity [12].

Energy in food is mainly obtained from carbohydrates, proteins, and fats. Energy is needed for the continuity of processes in the body such as circulatory processes and blood circulation, heart rate, breathing, digestion, other physiological processes, to move or do physical work. Energy in the body can arise because of the burning of carbohydrates, proteins and fats, so that sufficient energy needs to enter enough food by consuming enough and balanced food. Proteins are needed by the body to build damaged cells, form regulating substances such as enzymes and hormones, forming anti-energy substances where each gram of protein produces about 4.1 calories [12]. Fat is the most important energy store in the body, besides being a source of essential nutrients. Polyunsaturated fats contain essential fatty acids that are important for health but must be supplied through diet ie linoleic and linolenic acids. Polyunsaturated fats are important in the immune system response, and essential fatty acids in the cell membrane also maintain stability because of their role in regulating metabolism. Free fatty acids and fat on the skin surface also contribute to the ability of skin that is waterproof and can become bactericidal [13]. The results indicating the number of respondents who have the level of energy sufficiency, carbohydrates and fats tend to be a risk factor that along with other factors can be a causative factor Dengue Hemorrhagic Fever as it relates to the status of immunity. Host immunity against an infectious disease infection is closely related to age and nutritional status [11]. According to research conducted in Thailand, showed that dengue shock syndrome is more common in children less than the nutritional status of children of normal nutritional status [14].

Protein is the most important macro substance needed especially for children under five because amino acids (which are part of proteins) have benefits for child growth, water balance regulation,
transporting nutrients, as an energy source, and most importantly as forming antibodies effect on child defense system against infection attack [15]. When a person is deficient in protein will lower IgG circulation, tissue repair body cells and macrophages function [16]. Someone who has the nutritional status are less susceptible to dengue virus infection because it has a low cellular immunity because of immunologic memory is not fully developed [17]. Once the dengue virus enters the human body, the virus multiplies in reticuloendothelial cells followed by viremia that lasts 5-7 days. After that emerged immune response both humoral and cellular. Antibodies against dengue virus can be found in the blood around the 5th day of fever, increased in the first week to the third and disappears after 60-90 days. In the primary infection IgG antibodies increase around days 14 while in secondary infection IgG antibodies increase on the second day. Therefore, early diagnosis of primary infection can only be established by detecting IgM antibody after fifth day of illness, Diagnosis Secondary infection may be established early in the presence of rapid IgG and IgM antibody increases [18].

4.2 Micro Nutrients
Host immunity against infectious diseases is influenced by several factors, one of which is the age and nutritional status. Where some studies show that less / abnormal nutritional status is more susceptible to contracting and infected with dengue virus than people with normal nutritional status, while nutritional status is influenced by the balance of nutrient intake and absorption, especially the macronutrients that affect the immune system [6]. In addition to macro-nutrients, mentioned that micronutrients such as iron and zinc affects the immune response, if there is a deficiency of one micronutrient, it will damage the immune system [19]. Unfulfilled nutritional intake will cause the immune system to decrease. This is because the role of macro nutrition zaktis will not be optimal without the presence of micronutrients [20-21]. Micronutrient deficiencies can increase the risk of infectious disease, deaths from diarrhea, measles, malaria and lung [7]. Vitamin are complex organic substances needed in very small amounts, and generally can not be formed by the body. Vitamins play a role in several stages of the energy metabolism, growth and maintenance of the body. The body needs different types of vitamins in the right amount to react well in the body [7]. Vitamin C serves as a body's defense system that is fully responsible for any disorders of the body whether it is psychological disorders (eg stress, sadness, anger), physical (eg, injury, fatigue, pain), physiology (eg intake of nutrients with food, nutrition), and the environment (such as polluted air, tobacco smoke, noise) [22]. Vitamin C plays an important role in the process of absorption of iron. Iron in the body plays an important role in many biochemical reactions, among others in producing red blood cells in addition to the required n in the formation of blood, iron also plays a roleas part of several enzymes hemoprotein. Iron and zinc deficiency can reduce immune function, so it will be more susceptible to disease [23-24].

Vitamin A deficiency has been shown in many studies to interfere with humoral and cell-mediated immunity and the integrity of epithelial tissue of the eyes, lungs, and intestines, all of which lead to increased susceptibility to pathogens and infectious diseases. Specifically, vitamin A affects the activity of macrophages, the number and activity of NK cells and the function of lymphocytes, such as B cell proliferation and activation of T40 cells [8]. Vitamin B (in the form of folic acid) plays a major role in cell growth and development, as well as the establishment of a network. Lack of folic acid, the body will be susceptible to diseases such as depression, anxiety, fatigue, insomnia, difficulty remembering, red tongue and injury to indigestion. Vitamin B6 along with niacin, folic acid and cobalamin play a role in helping to move some of the vital functions of the human body. This vitamin is necessary when the body forms proteins by altering the amino acids present in the diet. Vitamin B6 helps the body form of energy by burning stored sugar reserves in the organs of the body and the formation of the protein hemoglobin [25]. The intake of minerals that were examined in this study is the intake of calcium, magnesium, phosphorus, zinc and iron, and from the questionnaire foodrecall seen that most respondents still have mineral intake AKG less from % daily. Of the 96 respondents who examined 79 of them maasih intake of calcium below the % Daily, 62 of which have intake magnesium below the % Daily, 54 of which have intake phosphor below
the Daily, 78 of which have intake phosphorus below the Daily and 80 which have zinc intake below the Daily. Less or low intake of calcium and iron can cause the body's metabolic disorders at the cell level. Calcium serves as a cell membrane transport acting as a membrane stabilizer and ion transmission through cell organ membranes [26].

5. Conclusion
The results showed that both in cases and control groups the macro- (energy, carbohydrate, protein, fat) and micro-nutrient (vitamins A, C, B1, B2, B6, calcium, magnesium, phosphorus, zinc, and Iron) intake were below 80% of nutrient adequacy. We find that macro and micronutrient intake in DHF case and control groups are the same and below 80% of nutrient adequacy.

6. Recommendation
The results of research can be forwarded by other researchers so that factors that have not been related can prove the relationship in accordance with the theory by increasing the number of sample research.

Acknowledgment
The research was supported by Nur Endah Wahyunningsih, Retno Murwani and MMDEAH Hapsari. We thank our respondents from dr. Adhiyatma Hospital, dr. Kariyadi Hospital and KRMT Wongsonogoro Hospital.

References
[1] World Health Organization (WHO). 2009. Dengue Guidlines For Diagnosis Treatment, Prevention and Control.
[2] Kementerian Kesehatan RI. 2016. Profil Kesehatan Indonesia 2015. 403.
[3] Kementerian Kesehatan RI. 2017. Data dan Informasi Profil Kesehatan Indonesia Tahun 2016.
[4] Dinas Kesehatan Kota Semarang. 2015. Profil Kesehatan Kota Semarang.
[5] Dinas Kesehatan Kota Semarang. 2016. Profil Kesehatan Kota Semarang 2016.
[6] Hakim L, Kusnandar AJ. 2012. Hubungan Status Gizi Dan Kelompok Umur Dengan Status Infeksi Virus Dengue. Aspirator. 4(1):34-45.
[7] Almatsier S. 2010. Prinsip Dasar Ilmu Gizi. 9, editor. Jakarta: PT. Gramedia Pustaka Utama.
[8] Ahmed S, Finkelstein JL, Stewart AM, Kenneth J, Polhemus ME, Endy TP, et al. 2014. Review article: Micronutrients and Dengue. Am J Trop Med Hyg. 91(5):1049–56.
[9] Devi Yanuar Permatasari, Galuh Ramaningrum AN. 2015. Hubungan Status Gizi, Umur, dan Jenis Kelamin Dengan Derajat Infeksi Dengue pada Anak. Jurnal Kedokteran Muhammadiyah. Volume 2 Nomor 1 Tahun 2015 24-2.pdf. J Kedokt Muhammadiyah. 2(1):24–8.
[10] Faktor A, Terjadinya R, Syok S, Pada D, Soebandi RSD, Regency J, et al. Risk Factor Analysis of Dengue Shock Syndrome Occuring to Children in RSD dr. Soebandi. 3(1):56–61.
[11] Departemen Kesehatan Republik Indonesia. 2003. Pedoman Tatalaksana Gizi Usia Lanjut untuk Tenaga Kesehatan. Jakarta: Ditjen Binkesmas.
[12] Almatsier S. 2002. Prinsip Dasar Ilmu Gizi. Jakarta: PT. Gramedia Pustaka Utama.
[13] Boyle, Maureen. 2009. Pemulihan Luka. Jakarta : EGC.
[14] Kalayanarooj S, Nimmannitya S. 2005. Is dengue severity related to nutritional status. South East Asian J Trop Med Public Health 36: 380.
[15] Almatsier, S. 2005. Prinsip Dasar Gizi. Jakarta: Gramedia Pustaka Utama.
[16] Chandra RK. 1997. Nutrition and Immune System: An Introduction. American Journal of Clinical Nutrition.
[17] Soedarmo SPS, Garna H, Hadinegoro SRS, Satari HI. 2008. Buku Ajar Infeksi dan Pediatri Tropis, Jakarta IDAI 155-181.
[18] Soegijanto S. 2006. Demam Berdarah Dengue. Edisi ke-2. Surabaya: Airlangga Press.
[19] Rosrnalina Y, Ernawati F. 2010. Hubungan Status Gizi Mikro Dengan Status Gizi Pada Anak Remaja SLTP. Puslitbang Gizi dan Makanan, Badan Litbang Kesehatan, Kemenkes RI. 33(1):14–22

[20] Widiastuti H. 2010. Standarisasi Vitamin C pada Buah Bengkuang (Pachyrhizus erosus) Secara Spektrofotometri UV-VIS. Fitofarmaka Indonesia. 2(1):72–5

[21] Putri Mp, Setiawati Yh. 2015. Analisis Kadar Vitamin C Pada Buah Nanas Segar (Ananas Comosus (L.) Merr) dan Buah Nanas Kaleng dengan Metode Spektrofotometri Uv-Vis Analysis Levels of Vitamin C In Fruit Fresh Pineapple (Ananas Comosus (L.) Merr) and Fruit Canned Pineapple With. 34–8.

[22] Arifin Z. 2008. Beberapa Unsur Mineral Esensial Mikro Dalam Sistem Biologi Dan Metode Analisisnya. J Litbang Pertan. 27(3):99–105

[23] CDC. 2012. Dengue and the Aedes aegypti mosquito. Aegypti Fact Sheet. 2.

[24] Muktar Y, Tamerat N, Shewafera A. 2016. Aedes aegypti as a Vector of Flavivirus Aedes aegypti as a Vector of Flavivirus 4(5).

[25] McBride CS, Baier F, Omondi AB, Spitzer SA, Lutomiah J, Sang R, et al. 2014. Evolution of mosquito preference for humans linked to an odorant receptor. Nature [Internet]. 515(7526):222–7

[26] Yuliwulandari R, Rochani JT, Indrawati I, Kunci K. 2010. Pengelompokan Genotip, Serologi dan Supertipe Gene HLA Kelas I pada Suku Jawa, Indonesia Genotype, Serology and Supertype Classification of HLA Class I in the Javanese, Indonesia. 18(2):86–93

[27] WHO. 2009. Dengue: Guidelines for Diagnosis, Treatment, Prevention and Control. New Edition. Geneva: World Health Organization

[28] Aspinall, R. 2004. Ageing and the Immune System in Vivo: Commentary on the 16th session of British Society for Immunology Annual Congress Harrogate December Vol 2: 5-1, (2005)