

# GLOBAL MEDICAL & HEALTH COMMUNICATION

**AUG** 2018 VOL. 6 NO. 2

# Global Medical & Health Communication

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### Accredited by:

Ministry of Research, Technology and Higher Education of the Republic of Indonesia  
(Kemenristekdikti) Number: 2/E/KPT/2015, 1<sup>st</sup> December 2015

### This journal is indexed on:



### Published by:

Faculty of Medicine Universitas Islam Bandung;  
Pusat Penerbitan Universitas-Lembaga Penelitian dan Pengabdian kepada Masyarakat (P2U-LPPM)  
Universitas Islam Bandung

### Publish Every 4 Months

April, August, December

# Global Medical & Health Communication

pISSN 2301-9123 | eISSN 2460-5441

Volume 6 Number 2, August 2018

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The submitted manuscript must be the article that has never been published, and the author must ensure that all co-authors have agreed by signing a statement on the seal. Download template of the ethical statement (free plagiarism) here. The manuscript is an original article free from plagiarism. When the article published in another journal then in the next journal, the article will be disallowed.

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The article contains results of original research in the field of basic medical or applied, and health. The article format consists of Title & Abstract (English) and *Judul & Abstrak* (Indonesian), Introduction, Methods, Results, Discussion, Conclusion(s), Conflict of Interest, Acknowledgments, and References.

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The introduction is written succinctly to stimulate the reader's interest include all the necessary information. At the end of the introduction was written the purpose of the study.

## Methods

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The result is the core of scientific writing. This section presents data and information that will be used as

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**EDITORIAL**

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## Stepping Up to New and Better Us

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*“In a progressive country, change is constant;  
change is inevitable.”*

-Benjamin Disraeli

This is another milestone for our Journal, Global Medical and Health Communication (GMHC). Starting from this volume in August 2018, GMHC will only publish in English. This move is following our mission to be involved in the global arena.<sup>1</sup> The best approach is by publishing in one of United Nation Language official and working languages, and we choose English.

This month is chosen because this month, more accurately on August 17, 2018, our country celebrates the 73rd anniversary of our Independence Day. It is the best moment for us to stepping up, to be better at what we do.

The journal need to reconfiguring itself to

catch up with the demand of our time. It has to leave its comfortable environment to navigate a newer and better way. Challenges face us in every direction. Hopefully, with the new approach, GMHC will be expanding its level of influence.

Our gratitude to all researchers, lectures and other health practitioners who support us from the very beginning by submitting their original research articles and also to our reviewers which contributed to make GMHC a better journal.

Let's embraces our new challenges by prepared to think differently.

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## RESEARCH ARTICLE

## The Upregulation of *Carnitine Palmitoyltransferase 1a (CPT1a)* Expression under Prolonged Fasting in CD36 Knockout Mice

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### Abstract

Food deprivation is one of the extreme conditions that mammals have to survive. The majority of the tissues, excluding the brain and red blood cells, depend on the fatty acids (FA) utilization to produce energy. We recently showed in mice lacking for CD36 (CD36<sup>-/-</sup>), the uptake of FA is limited with dramatically increased of glucose uptake in heart and skeletal muscle in fasted condition, indicating a compensatory mechanism of organ to fulfill an energy demand. The liver is the central tissue maintaining metabolic homeostasis in fasted state. Synthesize adenosine triphosphate (ATP) in the mitochondria via beta-oxidation was mediated by *carnitine palmitoyltransferase 1a (CPT1a)*. The objective of this research was to explore the role of CD36 in *CPT1a* expression in the fasted state. This research was conducted at Gunma University Japan in 2015. The method was in vivo-experimental, that we used CD36<sup>-/-</sup> and wild-type (WT) mice, as a control. The gene expression of *CPT1a* was measured by real-time PCR. Fasting condition up regulated mRNA expression of *CPT1a* in both WT and CD36<sup>-/-</sup> mice in 24 h and 48 h. However in CD36<sup>-/-</sup> mice, the mRNA expression of *CPT1a* in 24 h fasted state was lower very significantly than WT mice (p<0.01). We demonstrate that CD36 deficiency up regulate *CPT1a* gene expression, suggested that CD36 is essential for nutrient homeostasis when requirement for FA is increased and obtainability of nutrient is inadequate.

**Keywords:** CD36, *CPT1a*, fasted, fatty acid

## Peningkatan Ekspresi Gen *Carnitine Palmitoyltransferase 1a (CPT1a)* pada CD36 Knockout Mice dalam Keadaan Puasa

### Abstrak

Kekurangan makanan adalah salah satu kondisi ekstrem yang harus dihindari oleh mamalia. Sebagian besar jaringan, kecuali otak dan sel darah merah sangat bergantung pada pemanfaatan langsung asam lemak untuk menghasilkan energi. Penelitian kami sebelumnya menunjukkan pada mencit dengan defisiensi CD36 (CD36<sup>-/-</sup>), serapan asam lemak terbatas karena peningkatan pengambilan glukosa hati dan otot rangka secara signifikan dalam kondisi puasa yang mengindikasikan mekanisme kompensasi organ untuk memenuhi kebutuhan energi. Hati adalah jaringan sentral yang menjaga homeostasis metabolik tubuh dalam keadaan berpuasa. Sintesis *adenosine triphosphate (ATP)* di mitokondria melalui beta-oksidasi dimediasi oleh *carnitine palmitoyltransferase 1a (CPT1a)*. Tujuan penelitian ini mengetahui peran CD36 dalam ekspresi *CPT1a* dalam keadaan puasa. Penelitian ini dilakukan di Universitas Gunma Jepang pada tahun 2015. Metode penelitian ini adalah eksperimental *in vivo* dengan menggunakan mencit CD36<sup>-/-</sup> dan *wild type* (WT) sebagai kontrol. Ekspresi gen *CPT1a* diukur dengan *real-time* PCR. Puasa meningkatkan ekspresi mRNA *CPT1a* pada mencit WT dan CD36<sup>-/-</sup> baik setelah puasa selama 24 jam dan 48 jam. Namun, pada mencit CD36<sup>-/-</sup>, ekspresi mRNA *CPT1a* dalam keadaan setelah dipuasakan 24 jam lebih rendah daripada mencit WT (p<0,01). Penelitian ini menunjukkan bahwa defisiensi CD36 mengatur ekspresi gen *CPT1a* sehingga CD36 sangat diperlukan untuk homeostasis nutrisi ketika kebutuhan asam lemak meningkat dan kemungkinan ketersediaan nutrisi terbatas.

**Kata kunci:** Asam lemak, CD36, *CPT1a*, puasa

Received: 15 December 2017; Revised: 28 July 2018; Accepted: 31 July 2018; Published: 30 August 2018

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## Introduction

Food deprivation is one of the extreme conditions that mammals have to survive. This action includes many metabolic processes at numerous levels. In generating energy, mainly the tissues in mammals rely greatly on the direct utilization of fatty acids (FA), except the brain and red blood cells. Elongated fasting stimulates the hydrolysis of triacylglycerol (TG) in adipose tissue; followed by up regulating of the non-esterified FA (NEFA) concentration in plasma, and then liver takes up the circulating FAs.<sup>1</sup>

Heart, adipose tissues and skeletal muscle (SkM) are FA consuming organs, where a membrane protein, namely CD36 or FA translocase (FAT), transport long-chain FA from circulation into tissues.<sup>2</sup> Our previous study showed that the FA uptake by CD36 is essential for thermogenesis with prior fasting. In mice deficient for CD36 (*CD36*<sup>-/-</sup>), the uptake of FA is limited with dramatically increased uptake of glucose in heart and skeletal muscle in fasted condition, suggesting a compensatory mechanism of organ to fulfill an energy demand.<sup>3</sup> Moreover, fasted *CD36*<sup>-/-</sup> mice showed the disturbance of thermogenesis related genes expression in brown adipose tissue (BAT), an organ that responsible to generate heat.<sup>4</sup>

The liver is the central tissue preserve metabolic homeostasis in the fasted state, where NEFA will through several processes. Either re-esterification process from NEFA to TG and secreted as very low-density lipoprotein (VLDL), adenosine triphosphate (ATP) synthesis in the mitochondria of hepatocytes by beta-oxidation or change into ketone bodies that is utilized by organs.<sup>5-8</sup> The increase in serum ketone bodies is resulted from the increased of capacity for FA flux via beta oxidation and shunting of acetyl-CoA continue to synthesize of ketone body, marked by increasing carnitine palmitoyltransferase 1a (*CPT1a*). The flux of FA by beta-oxidation and acetyl-CoA through the tricarboxylic acid cycle increases production of hepatic mitochondrial nicotinamide adenine dinucleotide (NADH).<sup>1,8,9</sup>

*CPT1a* is a mediator for beta-oxidation. The capacity for mitochondrial beta oxidation is primarily regulated at the level of *CPT1* in gene level in reaction to various stimuli either physiologic or pathologic example, as fat feeding, fasting, induction of diabetes or treatment using peroxisomal/mitochondrial proliferating agents.<sup>6</sup> Palou et al.<sup>10</sup> 2008 showed increasing of *CPT1a*

levels after 8 h fasting and greater after 24 h. The objective of this research was to explore the role of CD36 in *CPT1a* expression in the fasted state. We used *CD36*<sup>-/-</sup> and wild-type (WT) mice as a control to explore the crucial role of CD36 in the liver when nutrient supply were limited.

## Methods

This research was conducted at Gunma University Japan in 2015. Ten to twelve-week old male mice with a homozygous null mutation in CD36 (*CD36*<sup>-/-</sup> mice) were generated as previously described,<sup>11,12</sup> and control male wild-type C57BL6j mice were purchased from Japan SLC, Inc. with body weights 22 to 27 grams. Mice were housed in a temperature-controlled room (22°C), exposed to a 12-h light/12-h dark cycle and given ad libitum access to water and standard chow (CE-2, Clea Japan, Inc.).<sup>13</sup> For the fasting experiments, mice were individually housed and the food was withdrawn for 0, 24 h and 48 h; water was provided ad libitum, as previously described.<sup>1</sup> Samples of liver were snapped frozen in liquid nitrogen and conserved at -80°C until further use. The study protocol was approved by The Institutional Animal Care and Use Committee (Gunma University Graduate School of Medicine, Japan) number: 15-024.

Total RNA was isolated from liver using the RNAiso Plus reagent (Takara, Japan). Semi-quantitative RT-PCR was performed with RT-PCR kit (Takara, Japan) according to manufacturer's protocol. RNA was prepared by reverse transcription using oligo-dT and dNTP, and each sample was processed with the RT-PCR kit (TAKARA, Japan). Quantitative real time-PCR was performed using the SYBR Green PCR Master Mix (Applied Biosystems, CA, USA) according to the manufacturer's instructions, and then evaluated using the LightCycler 480 Real-Time PCR system (Roche, CA, USA). The expression level of the target gene was normalized to the glyceraldehyde-3-phosphatase dehydrogenase (GAPDH) mRNA level. The sequences of primers for quantitative real-time PCR used in this study are listed in Table.

Statistical analysis was performed using one-way ANOVA with Bonferroni's post-hoc multiple comparison. A p value <0.05 was considered statistically significant. The data are presented as the means ± S.E. Statistical analysis of the data was performed with IBM SPSS (version 20.0 for Windows, IBM, NY, USA).



**Table Primers for Quantitative Real-Time PCR**

	Forward	Reverse
<i>mCPT1a</i>	CCATGAAGCCCTCAAACAGATC	ATCACACCCACCACCACGATA
<i>mGAPDH</i>	AGCCCCAGTCTGTATCCTT	TCCACCACCCTGTTGCTGTA

*CPT1a*: carnitinepalmitoyltransferase 1a, *GAPDH*: glyceraldehyde-3-phosphatase dehydrogenase

## Results

We examined the expression levels of the *CPT1a* gene in response to fasting conditions (Figure). Fasting condition increased mRNA level of *CPT1a* in both WT and CD36<sup>-/-</sup> mice. The dramatically increased of *CPT1a* gene expression seen in 24 h fasted CD36<sup>-/-</sup> mice. It was nearly two times higher than fed CD36<sup>-/-</sup> mice or 24 h WT mice. The same pattern also seen in mice with 48 h fasting. After 48 h fasting, the expression of *CPT1a* tends to be higher in CD36<sup>-/-</sup> mice compared to WT mice.

## Discussion

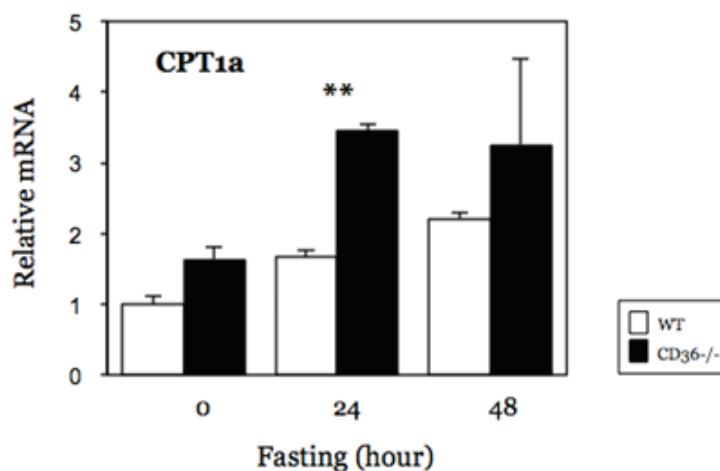
In this study, we reveal an essential role of CD36 to regulate the expression of *CPT1a* in fasting condition. Our previous study underscored the role of FA binding carrier such as fatty acid binding protein 4 and 5 (FABP 4/5) and FA membrane transporter CD 36 in FA voracious organs, example as not just the heart but also the BAT and oxidative skeletal muscle for preserving nutrient homeostasis. When FA uptake is

interrupted in these tissues, as a compensating process, there is an increase of glucose uptake and utilization further corrupts the homeostasis of nutrient in the extreme environment such as fasting condition.<sup>1,3,13</sup>

We suggested that in highly restrictive of nutrient availability such as in CD36<sup>-/-</sup> mice, the liver needs an extra energy to allowing the maintenance of energy homeostasis. Beta-oxidation in liver under low nutrition has two purposes, to fulfill energy demand for glucose product, a process called gluconeogenesis and to produce ketone bodies. Thus, the increased of *CPT1a* gene expression might be a compensatory mechanism to enhance FA influx to mitochondrial membrane. Further experiments, including FA uptake by the liver and TG liver concentration are necessary to confirm our hypothesis.

## Conclusion

In conclusion, we demonstrate that CD36 deficiency up regulate *CPT1a* gene expression, indicated that CD36 is essential for the homeostasis of nutrient when requirement for



**Figure Induction of *CPT1* Gene in Liver of Fasted WT and CD36<sup>-/-</sup> Mice**

The mice were maintained at room temperature for 0, 24 and 48 h fasted state. The total RNA from liver was extracted for quantitative real-time PCR. n=4-5/group, \*\*p<0.01

FA is increased and obtainability of nutrient is restricted.

### Conflict of Interest

All the authors have read the manuscript and have agreed to submit it in its current form for consideration for publication in the journal. There are no conflicts of interest to declare.

### Acknowledgements

We thank Miki Matsui, Yukiyo Tosaka, Keiko Matsukura and Takako Kobayashi for excellent technical help. This work was supported in part by a Grant-in-Aid for Scientific Research from the Japan Society for the Promotion of Science (to MK and TI), a grant from the Japan Cardiovascular Foundation (to MK) and a grant from the Vehicle Racing Commemorative Foundation and to TI.

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## RESEARCH ARTICLE

## The Effects of Fermented Rice *Monascus purpureus* *JmbA3'K* to Blood Pressure and Heart Rate Elderly Woman

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### Abstract

Incidence of hypertension is increasing rapidly, in 2000 more than 25% of the world's population of hypertension estimated in 2025 increased to 29%. The incidence of hypertension, especially in women will increase at the age of post menopause so it needs to be prevented in elderly women, especially with giving functional food that has effect to lowering blood pressure. Gamma-aminobutyric acid (GABA) is a compound that has the properties of lowering blood pressure through the regulation of smooth muscle tone of blood vessels contained in seeds fermented by *Monascus purpureus* sp. This research was a case control study which conducted in June 2013 to 19 women within age range 60–80 years who life in Santana Nursing Home, Cirebon to find out the influence of giving fermented rice *M. purpureus JmbA3'K* to systolic/diastolic blood pressure and heart rate of elderly women. Subjects were given 3 g of fermented rice *M. purpureus JmbA3'K*. Blood pressure and heart rate was monitored daily. The Wilcoxon signed-rank test was done to see whether the effect of giving fermented rice from the local *M. purpureus JmbA3'K* to the systolic and diastolic blood pressure of the elderly and the mean difference test using paired t test was done to see if the effect of fermented rice from *M. purpureus JmbA3'K* local to the heart rate of the elderly women. At the end of research, blood pressure and heart rate were compared before and after the treatment. At the end of the study there were no significant treatment side effects. There were improvements in aging syndrome such as: anxiety to depression, insomnia, overactive bladder (especially at night), neuralgia, and myalgia. In treatment group was found decrease in sistolic (176 to 152 mmHg) and diastolic blood pressure (90 to 83 mmHg) ( $p < 0.05$ ) without any changing in heart rate (81.68 to 79.32 b/sec) ( $p > 0.05$ ). The conclusion of this research is giving 3 grams of fermented rice *M. purpureus JmbA3'K* every evening meal for fourteen days decrease the sistolic and diastolic blood pressure of the elderly without any changing in heart rate.

**Keywords:** Blood pressure, fermented rice, gamma-aminobutyric acid (GABA), heart rate, *Monascus purpureus*

## Efek Pemberian Beras Fermentasi *Monascus purpureus* *JmbA3'K* terhadap Tekanan Darah dan Frekuensi Nadi Usila Wanita

### Abstrak

Peningkatan angka kejadian hipertensi sangat pesat, pada tahun 2000 lebih dari 25% populasi dunia penderita hipertensi yang diperkirakan pada tahun 2025 meningkat menjadi 29%. Angka kejadian hipertensi khususnya pada wanita akan meningkat pada usia posmenopause (usila) sehingga perlu diupayakan pencegahan hipertensi pada wanita usila, khususnya pemberian makanan yang mempunyai efek menurunkan tekanan darah. *Gamma-aminobutyric acid* (GABA) mempunyai sifat menurunkan tekanan darah melalui pengaturan tonasi otot polos pembuluh darah terkandung pada biji-bijian yang ditumbuhi kapang *Monascus purpureus* sp. Penelitian ini merupakan penelitian *case control* yang dilakukan Juni 2013 terhadap 19 orang subjek wanita usila rentang usia 60–80 tahun penghuni Panti Wreda Santana, Cirebon untuk mengetahui efek pemberian beras fermentasi *M. purpureus JmbA3'K* terhadap tekanan darah dan frekuensi nadi. Subjek diberikan 3 g beras fermentasi *M. purpureus JmbA3'K* selama 14 hari. Tekanan darah dan frekuensi detak jantung dimonitor setiap hari. Pada akhir penelitian tekanan darah dan frekuensi nadi dibandingkan antara sebelum dan sesudah perlakuan. Uji beda Wilcoxon untuk melihat apakah efek pemberian beras fermentasi dari kapang *M. purpureus JmbA3'K* lokal terhadap tekanan darah sistole dan diastole usila dan uji beda rata-rata menggunakan *paired t test* dilakukan untuk melihat apakah efek pemberian beras fermentasi dari kapang *M. purpureus JmbA3'K* lokal terhadap frekuensi nadi usila. Pada akhir penelitian tidak didapatkan efek samping perlakuan yang berarti. Didapatkan perbaikan sindrom penuaan seperti ansietas sampai depresi, insomnia, *overactive bladder* (terutama malam hari), neuralgia, dan mialgia. Terdapat perbedaan tekanan darah sistole dengan diastole sebelum (176/90 mmHg) dengan sesudah diberi perlakuan (152/83 mmHg) ( $p < 0,05$ ) tanpa perbedaan frekuensi nadi sebelum (81,68 kali/menit) dengan sesudah diberi perlakuan (79,32 kali/menit) ( $p > 0,05$ ). Simpulan, pemberian beras IR-42 fermentasi *M. purpureus JmbA3'K* menurunkan tekanan darah sistole dan diastole usila tanpa perubahan frekuensi nadi.

**Kata kunci:** Beras fermentasi, frekuensi nadi, *gamma-aminobutyric acid* (GABA), *Monascus purpureus*, tekanan darah

Received: 14 February 2017; Revised: 7 August 2018; Accepted: 25 August 2018; Published: 30 August 2018

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## Introduction

According to the National Institute of Health Research and Development (NIHRD), Ministry of Health of the Republic Indonesia in year the 2000, the Indonesian population is currently the fifth largest in the world with a population shift pyramid in Indonesia. Economic progress and health degrees cause life expectancy to increase from 60–62 years to 66 years.<sup>1</sup>

According to the results of *Survei Kesehatan Rumah Tangga Indonesia* (SKRT) (Indonesian Household Health Survey), cardiovascular disease (CVD) is increasing and is the main cause of death as much as 16% (SKRT 1992), 1995 as much as 18.9%, and in 2001 reached 26.9%.<sup>2</sup> According to *Riset Kesehatan Dasar* (Riskesmas) (Basic Health Research) in the year 2007 the prevalence of heart disease in Indonesia reached 7.2% (diagnosed and with symptoms), whereas deaths caused by ischemic heart disease 5.1%, stroke 15.4%, and other heart disease 4.6%.<sup>2</sup>

The incidence of hypertension is increasing rapidly, recorded in the year 2000, more than 25% (about 1 billion people) of the world's population is hypertensive, and two-thirds of people with hypertension is in developing countries. If we not done any right effort, this number will continue to increase, and by the year 2025 the number of hypertension patients is predicted to 29%, or about 1.6 billion people worldwide.<sup>3</sup>

The majority of CVD problems are caused by hypertension, whereas to date hypertension remains a major challenge in Indonesia, the prevalence of hypertension is 25.8%.<sup>4</sup> In addition, hypertension control is inadequate even though effective drugs are widely available.

Women are more protected from cardiovascular disease due to hormonal effects, therefore the incidence of cardiovascular disease increases in the postmenopausal period.<sup>5,6</sup> This is caused by a drastic decrease in sex hormones, especially estrogen, which maintains smooth muscle tone smoothness of blood vessels.<sup>7</sup>

Regulation of vascular sympathetic tone is influenced by the hypothalamic paraventricular (PVN) nucleus. Impaired control of GABAergic PVN neurons contributes to an increase in sympathetic muscle tone sympathetic blood vessels leading to hypertension.<sup>8</sup> Arrangements and administration of gamma-aminobutyric acid (GABA) foods should be sought in order to protect elderly women from hypertension.

Gamma-aminobutyric acid or GABA is a

compound that has the nature of lowering blood pressure through regulation of smooth muscle tone of blood vessel especially vein.<sup>8</sup> Grain covered with mold *Monascus purpureus* sp. can produce GABA.<sup>9–11</sup> GABA administration to patients with mild hypertension can lower blood pressure.<sup>12–15</sup>

This study aimed to measure the effect of fermented rice from local *M. purpureus JmbA3'K* to blood pressure level of systolic/diastolic and pulse frequency in elderly women.

## Methods

Materials which used in this study are *Monascus purpureus JmbA3'K* microorganisms from the collections of the Biology Laboratory of the Center for Biological Research-LIPI, Cibinong Science Center and IR-42 low quality rice, from the Bogor market in January 2013.

The subjects of this study were elderly women (60–80 years old) of the Santana Nursing Home, Cirebon. Prior to the study, adaptation was performed with standard daily feeding (55% carbohydrate, 20% protein, 25% fat) without drinking water restriction during adaptation (seven days).

The inclusion criteria of this study were healthy elderly women, aged 60–80 years. Exclusion will performed if anorexia and liver, kidney, or other health problems occurs during the treatment period.

The sample size can be determined based on the formula of unpaired numerical analytical samples, 17 required 17 people, to keep the high representative level in case of drop out, we add the number of samples to 19 people.

Before blood sampling, homogenization of food input was performed at least 7 days before treatment with feed intake of 55% carbohydrate, 20% protein, and 25% fat. In the evening before sampling, the subject was fasted for 12 hours. The morning after in a state of fasting (allowed to drink enough water) the blood was taken by means of a puncture vein in the right brachial vein.

Blood pressure checking was done every day, at 7:30 am, at the right arm position with blood pressure measuring device Omron HEM 907. Before subject examination was rested from activity for 15 minutes.

The GABA dose used for hypertension ranges from 10 mg per day,<sup>14,15</sup> referring the dose of GABA, fermented rice powder of *M. purpureus*

**Table 1 Normality Test of Variables Measured on Study**

Variable	Normality Test	
	p Value	Data Distribution
Systolic blood pressure before treatment	0.978	Normal
Systolic blood pressure after treatment	0.040	Abnormal
Diastolic blood pressure before treatment	0.046	Abnormal
Diastolic blood pressure after treatment	0.206	Normal
Heart rate before treatment	0.130	Normal
Heart rate after treatment	0.150	Normal

Shapiro Wilk normality test

sp. given as much as 3 g,<sup>16</sup> after dinner mixed and stirred in 200 mL reverse osmosis water {Advance P-5200R (APIT-003)} was boiled at 100°C for 3 min, then cooled.

During the treatment, the subjects continued to be fed similar foods to the carbohydrate composition of 55%, 25% fat and 20% protein.

Prior to statistical analysis, for numerical data type, normality test is done by using Shapiro-Wilk test to see the distribution of data whether the data is normal distribution or not, the result of normality test can be explained in Table 1.

Shapiro Wilk normality test showed that for heart rate variables in normal distribution ( $p > 0.05$ ) so that the data were analyzed using parametric tests. The variables of systolic and diastolic blood pressure were not normally distributed ( $p < 0.05$ ) so the data were analyzed using non-parametric tests.

Wilcoxon signed-rank test was conducted

to see whether the effect of local *M. purpureus JmbA3'K* fermented rice administration on systolic and diastolic elderly blood pressure. The average difference test used paired t test to see whether the effect of fermented rice is given by the local *M. purpureus JmbA3'K* mold to the elderly pulse frequency. This test was conducted to see whether there was or not a significant effect of GABA content in IR-42 fermented rice with *M. purpureus JmbA3'K* on heart rate of elderly.

## Results

Based on the calculation, both of systolic and diastolic blood pressure obtained p value  $< 0.05$  (Table 2). Therefore, it can be concluded that there was a difference in blood pressure of systolic and diastolic before and after treatment.

Based on the calculation results obtained p value  $> 0.05$ , there was no difference in pulse

**Table 2 Comparison of Systolic and Diastolic Blood Pressure Before the Treatment**

Sistolic and Diastolic		n	Median	Range	Zwx	p
Sistolic	Before	19	176	118–217	-3.283	0.001
	After	19	152	121–206		
Diastolic	Before	19	90	62–138	-3.137	0.001
	After	19	83	60–94		

**Table 3 Comparison of Pulse Frequency Before with Treatment**

Heart Rate	Median	t Count	df	t Table	p
Before	81.684	1.513	18	1.73	0.074
After	79.316				



frequency before and after treatment (Table 3).

## Discussion

From the nineteen subjects, there were no significant side effects of treatment (rhabdomyolysis and impaired liver and kidney function). A small side effect that occurs is a complain of headache after treatment so it is overcome by gradual administration (50 mL per 15 min).

The result of the prehistory and the post treatment in this study found another improvement in the complaints of the research subjects. As is known in the elderly almost get aging syndrome such as anxiety to depression, insomnia, overactive bladder (especially the night), neuralgia, and myalgia. In the treatment group, the symptoms of aging are almost completely reduced. Lydiard<sup>18</sup> states this may be caused by GABA having an antianxiety effect. GABA is the main transmitter inhibitor in the central nervous system (CNS). A balance between GABA and glutamate transmitter inhibitors in the CNS that maintains anxiety levels. GABA proven to reduce anxiety.

At baseline examination, almost all subjects (median systolic blood pressure 176 mmHg and diastolic blood pressure 90 mmHg) suffered from class II hypertension (JNC 7, 2003).<sup>19</sup> This is consistent with research conducted by Lima et al.,<sup>5</sup> Maas & Franke,<sup>6</sup> and Yanes & Reckelhoff<sup>7</sup> which states that hypertension often occurs in the postmenopausal period. Several studies have shown that changes in the ratio of estrogens to androgens support the increase of androgens, activation of the renin-angiotensin system and endothelin, activation of the sympathetic nervous system, metabolic syndrome and obesity, inflammation, increased eicosanoid vasoconstrictor, and anxiety and depression are important factors in the pathogenesis of postmenopausal hypertension. This causes hypertension to be difficult to control in elderly women than in elderly men.<sup>5-7</sup> GABA provision is proven to prevent anxiety and smooth muscle tone of blood vessels through inhibition of sympathetic nervous activity.

After fourteen days observation on the subjects, it was found out that the administration of *Monascus purpureus JmbA3'K* fermented rice, could decrease systolic ( $p=0.001$ ) and diastolic ( $p=0.001$ ) blood pressure without interruption to heart rate. Research conducted by Li and Pan<sup>8</sup>

and Shimada et al.<sup>12</sup> used chlorella containing GABA in patients with mild hypertension and borderline proven to lower blood pressure. Hypothalamic paraventricular nucleus (PVN) is involved in regulation of smooth muscle tonics. Disorders of GABAergic control of PVN neurons can contribute to the sympathetic drive that increases blood smooth muscle tone in hypertension. GABA proved to decrease the smooth muscle tone of blood vessel that occurs in hypertension.<sup>8,12</sup> The difference in this study was used 3 grams of fermented rice *Monascus purpureus JmbA3'K*, collection from the LIPI Cibinong Research Center, which contains enough GABA to lower blood in elderly women.

Nonetheless, this study has several susceptibility, which are the subject was elderly women that have experienced a decline in cleansing of nutrients or drugs taken, metabolism, and homeostasis that are different from young adults. For further research can be done on young adults and also in men. Another disadvantage is the taste of the *Monascus purpureus JmbA3'K* fermented rice solution which is less tasty so that cause the level of compliance in this study decreased. Higher doses of divided doses may be given for further research to find the optimal dose.

Suggestions for further research are necessary measurements that still need to be done to determine the optimal dose needed and can be used in long-term use.

## Conclusion

The results of this study that has been described, it is concluded that giving IR-42 rice fermentation *Monascus purpureus JmbA3'K* at 3,000 milligrams once a day for 14 days can lower systolic and diastolic blood pressure without changes in heart rate.

## Conflict of Interest

The authors declare no conflict of interests.

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## RESEARCH ARTICLE

**Obesity as Risk Factor of Type 2 Diabetes Mellitus  
in Women of Childbearing Age****Hanifah Ardiani,<sup>1</sup> Soeharyo Hadisaputro,<sup>2</sup> Djoko Trihadi Lukmono,<sup>2</sup>  
Heri Nugroho,<sup>3</sup> Antono Suryoputro<sup>4</sup>**<sup>1</sup>Study Program of Public Health, STIKES Bhakti Husada Mulia, Madiun, Indonesia, <sup>2</sup>Study Program of Master of Epidemiology, Postgraduate School, Universitas Diponegoro, Semarang, Indonesia, <sup>3</sup>Department of Internal Medicine, Faculty of Medicine, Universitas Diponegoro/Dr. Kariadi General Hospital, Semarang, Indonesia, <sup>4</sup>Department of Health Policy and Administration, Faculty of Public Health, Universitas Diponegoro, Semarang, Indonesia**Abstract**

Women of childbearing age with type 2 diabetes mellitus (DM) are more at risk of having pregnancy complication (in both the mother and the baby) at twice the risk for sexual dysfunction and three times more likely to die than women of childbearing age without DM. The purpose of this study was to prove obesity as the risk factor of type 2 DM in women of childbearing age. The study design was a case-control and a qualitative analysis using the in-depth interview. This study conducted in Internal Medicine Polyclinic and Eye Polyclinic in Regional General Hospital Madiun, June–July 2017. The population in this study was women of childbearing age 20–49 years old and married who check blood sugar in Regional General Hospital Madiun. The samples of this study were 54 cases and 54 controls using consecutive sampling. Data analyzed by chi-square and logistic regression. The results showed that obese women of childbearing age had risk 2.63 times greater for type 2 DM than non-obese ( $p=0.016$ , 95% CI=1.06–6.53). In conclusion, obesity was a risk factor of type 2 DM in the women of reproductive age.

**Keywords:** Diabetes, obesity, women of childbearing age**Obesitas sebagai Faktor Risiko Diabetes Melitus Tipe 2  
pada Wanita Usia Subur****Abstrak**

Wanita usia subur (WUS) dengan diabetes melitus (DM) tipe 2 lebih berisiko mengalami komplikasi kehamilan (baik pada ibu maupun bayinya), berisiko 2 kali lebih besar untuk menderita gangguan fungsi seksual, dan 3 kali lebih besar untuk mengalami kematian dibanding dengan WUS tanpa DM. Tujuan penelitian ini membuktikan obesitas sebagai faktor risiko DM tipe 2 pada WUS. Desain studi dalam penelitian ini adalah kasus kontrol yang diperdalam dengan analisis kualitatif menggunakan wawancara mendalam. Penelitian ini dilakukan di poliklinik penyakit dalam dan poliklinik mata RSUD Kota Madiun Juni–Juli 2017. Populasi dalam penelitian ini adalah WUS berusia 20–49 tahun dan sudah menikah yang diperiksa gula darah di RSUD Kota Madiun. Sebanyak 54 kasus dan 54 kontrol dipilih menggunakan *consecutive sampling*. Data dianalisis dengan *chi square* dan regresi logistik. Hasil penelitian menunjukkan bahwa WUS yang obesitas memiliki risiko 2,63 kali lebih besar untuk mengalami DM tipe 2 dibanding dengan yang tidak obesitas ( $p=0,016$ ; 95% IK=1,06–6,53). Simpulan, obesitas merupakan faktor risiko DM tipe 2 pada WUS.

**Kata kunci:** Diabetes, obesitas, wanita usia subur

Received: 14 July 2017; Revised: 23 July 2018; Accepted: 27 August 2018; Published: 30 August 2018

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## Introduction

Women of childbearing age are women aged 15–49 years who have reproductive organs which still works fine easier to get pregnancy.<sup>1</sup> If the women of childbearing age to suffer from type 2 diabetes mellitus, then it will be more at risk to experience complications of pregnancy, both in the mother or her baby.<sup>2–4</sup> Data January 2016–March 2017 in Regional General Hospital Madiun, showed 11 women of childbearing age with type 2 diabetes mellitus (DM type 2) that maternity in Regional General Hospital Madiun and everything maternity with a cesarean section.

Some women of childbearing age also to suffer complications, including five women, have hypertension and one person suffered amniotic rupture early. Also, there are complications in infants, namely two abortion, a baby is born with high weight, one baby has a low Apgar score, one baby undergoes intrauterine fetal death (IUFD), and one baby undergoes intrauterine growth restriction (IUGR).<sup>5</sup> Women of childbearing age two times greater to suffer from sexual dysfunction than women of childbearing age without DM with the incidence of 23.8%.<sup>6</sup> DM is also the leading cause of death in the United States in the women of childbearing age. Women of childbearing age with DM have three times greater risk for death compared with women of childbearing age that have not experienced DM.<sup>7</sup> Fifty four percent of women of childbearing age not pregnant in Pennsylvania (15–45 years) experiencing overweight and obesity.<sup>8</sup> Obesity associated with an increase in the release of free fatty acids secreted from adipose tissue and can interfere with the absorption of glucose into muscle cells because of the competitive barriers.<sup>9</sup> Obesity also associated with the secretion of adipokines which regulates insulin sensitivity through the tumor necrosis factor alpha, interleukin-6, adiponectin, resistin, and leptin.<sup>10</sup> According to research conducted in Indonesia, the women of childbearing age are obese have 2.8 times greater risk for suffering a DM than women of childbearing age, not obesity (95% CI=2.20–3.50).<sup>11</sup>

Type 2 DM on the women of childbearing age is an important issue because it has a significant impact. Research on the relationship of obesity with type 2 DM on women of childbearing age still rarely performed, even the research that has been conducted in Indonesia still cross-sectional study design. Thereby, studies the relationship

of obesity with type 2 DM on the women of childbearing age with a design case study with qualitative analysis deepened control using in-depth interviews. The purpose of this research was to prove obesity as a risk factor for incidence of type 2 DM on women of childbearing age.

## Methods

This study used the mixed method with case-control design study and the qualitative analysis using in-depth interviews. This research was conducted at the Eye Clinic and Internist Clinic in the Regional General Hospital Madiun in June–July 2017. The population of this research were all the women of childbearing age aged 20–married 49 years and had blood sugar examined in the Regional General Hospital Madiun. The sample in this study newly diagnosed DM in an internal medicine clinic based upon examination of the blood sugar as the case group and who have not diagnosed DM as the control group. The sample was selected using consecutive sampling method with 54 cases and 54 controls. Samples for qualitative analysis, i.e., respondents from the closest person (family) to confirm the answers of the respondents for validating through triangulation method. The simple random sampling method for qualitative analysis. The number of samples for qualitative analysis is 10% of the total sample for the quantitative method, six from the cases group and six people from the control group.<sup>12</sup>

DM was diagnosed based upon the criteria Perkeni years 2015, namely blood glucose during the examination (GDS)  $\geq 200$  mg/dL with a classic complaint (polyphagia, polyuria, polydipsia and weight loss without definite cause) to the group case. The control group upheld the results of blood sugar during capillary  $< 90$  mg/dL as well as without the classic complaint.<sup>13</sup> Obesity is enforced using a body mass index (BMI), with the formula weight in pounds divided height squared in meters.<sup>14</sup> BMI in research is categorized into three, that is normal ( $\leq 25$  kg/m<sup>2</sup>), overweight ( $> 25$ – $27$  kg/m<sup>2</sup>), and obesity ( $> 27$  kg/m<sup>2</sup>).<sup>15</sup> Data analyzed using chi-square to bivariate followed by regression logistics by the method of Backward LR to see the influence of several factors together (multivariate). The content analysis used for qualitative analysis.

This research has got ethical clearance from Health Research Ethics Commission (KEPK) of Faculty of Medicine, Universitas Diponegoro

Semarang with number: 333/EC/FK-RSDK/VI/2017.

**Results**

Characteristics of respondents in this study are shown in Table 1. Table 1 shows that respondents aged ≥35 years and respondents with hypertension found more on groups of cases compared to the control group (28% vs 24%). Likewise with respondents who have a family history of DM (63% vs 37%) and respondents with obesity (46% vs 24%).

Table 2 shows that there was a relationship on the history of gestational diabetes mellitus (GDM) and obesity with type 2 DM on women of childbearing age. Obese reproductive age women had 2.7 times greater (95% CI=1.19–6.18) risk to suffer type 2 DM compared to reproductive age women with healthy weight. Women of childbearing age that have a history of GDM had a risk of 2.15 times higher (95% CI=1.74–2.65) suffering from type 2 DM compared with women of childbearing age which did not have a history of GDM. Variable hypertension, overweight, and age did not correlate with the incidence of type 2 DM on women of childbearing age. The variable to be included in the analysis of multivariate is a variable that has a value of 0.25, i.e.,  $p < 0.05$ , i.e.,  $p < 0.05$  GDM history, obesity, and age.

Table 3 shows that obesity and age was a risk factor of Genesis of type 2 DM on reproductive age women. Obese reproductive age women had 2.63 times greater risk of experiencing a DM type

**Table 2 Factors Related to the Incidence of Type 2 DM on Childbearing Age Women**

Variable	OR	95% CI	p Value
Hystory of GDM	2.15	1.74–2.65	0.006**
Hypertension	1.21	0.51–2.87	0.661
BMI status			
Overweight	0.78	0.29–2.07	0.620
Obesity	2.72	1.19–6.18	0.016**
Age ≥35 years	2.06	0.88–4.80	0.092*

Description: \* =variables become candidates in logistic regression test ( $p < 0.25$ ), \*\* =variable associated with the dependent variables ( $p < 0.05$ ) and was a candidate in the logistic regression test

2 compared to the normal (95% CI=1.06–6.53). Women aged ≥35 years had 6.63 times greater risk experiencing than type 2 DM with the <35 years old (95% CI=2.23–19.70).

Finding of the qualitative analysis show the reason as stated by one of the respondents:

*“Before diagnosed of diabetes, I never diet. Indeed fatter anyway, but it’s very hard to diet. I am easy hungry, eating potluck, and also can not be picky. I started controlling the food since diagnosed diabetes. I reduced the portion of rice and reduce sweet drinks. I’m still not exercise, due to illness of diabetes so easily tired. I also do not know if that excess weight can trigger diabetes.”*

**Table 1 Characteristics of Respondents**

Characteristics	Cases		Controls	
	Frequency (f=54)	Percentage (%)	Frequency (f=54)	Percentage (%)
Age (years)				
≥35	47	87	29	54
<35	7	13	25	46
Hypertension				
Yes	15	28	13	24
No	39	72	41	76
Family history of DM				
Yes	34	63	20	37
No	20	37	34	63
BMI status (kg/m <sup>2</sup> )				
Obesity (>27)	25	46	13	24
Overweight (>25–27)	9	17	11	20
Normal (≤25)	20	37	30	56

**Table 3 Factors with Effect on the Incidence of Type 2 DM on Reproductive Age Women**

Variable	B Value	p Value	ORadj	95% CI
Obesity	0.968	0.037	2.63	1.06–6.53
Age ≥35 years	1.892	0.001	6.63	2.23–19.70
Constanta	-1.893			

## Discussion

Results showed that obesity associated with the incidence of type 2 DM on women of childbearing age, but overweight did not show any relation. The results of the multivariate analysis showed that the risk of having obese women of childbearing age 3.09 times more likely to suffer from type 2 DM compared with the women of childbearing age BMI-his normal or overweight.

The results of this study following research conducted in Indonesia. Women of childbearing age with obesity have 2.8 times greater risk of suffering from type 2 DM compared with women of childbearing age are not obese (95% CI=2.20–3.50).<sup>11</sup> The results are also consistent with research conducted in Norway, women with BMI 25.0–29.9 kg/m<sup>2</sup> and ≥30.0 kg/m<sup>2</sup> has a risk of 3.52 times (95% CI=2.63–4.73) and 9.97 times greater (95% CI=7.38–13.00) experienced DM type 2 compared with women of childbearing age that have the BMI 14.5–24.9 kg/m<sup>2</sup>.<sup>16</sup> A case-control study conducted in the United States suggests that women who have the BMI >25 kg/m<sup>2</sup> have a 3.57 times greater risk of experiencing a DM type 2 compared to women who have the BMI ≤25 kg/m<sup>2</sup> (95% CI=3.52–3.63).<sup>17</sup> A prospective cohort study also proved that the BMI associated with the incidence of type 2 DM. Asian race women experience increased BMI 5 kg/m<sup>2</sup> for 20 years had a risk of 2.36 times to suffer from type 2 DM (95% CI=1.83–3.04).<sup>18</sup> Someone experiencing overweight will have a mass of cells that insulin needs more so that is also a lot more than people who are not obese. If the pancreas that produces insulin then the damage could not be produced in sufficient quantities. Therefore, an increase in insulin requirements will not be met so that the blood glucose concentration being high.<sup>19</sup>

People with obesity will experience an increased secretion of resistin. Resistin is a member of cysteine-rich proteins. A study in mice suggests that a decrease in serum resistin

associated with increased insulin sensitivity. Studies in humans also show the same thing, that resistance associated with insulin sensitivity. Some studies show a positive correlation between resistin levels and insulin resistance.<sup>19</sup>

Obesity also associated with an increase in the release of free fatty acids. Free fatty acids will interfere with the absorption of glucose into muscle cells.<sup>20</sup> Besides, obesity also associated with adipose tissue that acts as an endocrine secretion organ including the secretion of adipokines. Adipokine regulates insulin sensitivity through the tumor necrosis factor alpha, interleukin-6, adiponectin, resistin, and leptin.<sup>10</sup>

The results of the in-depth interview show that almost all respondents (11 out of 12 respondents) stated that never go on a diet to reduce his weight. For groups of cases, they go on a diet after being diagnosed with type 2 DM, a diet that was only done to control eating patterns, accompanied by sports. They have resigned with her weight. They also did not know that obesity may be a risk factor for DM.

The results of this research also show that age was a risk factor for type 2 DM on women of childbearing age. Women of fertile age aged ≥35 years had a higher risk of experiencing 6.63 times DM type 2 compared to the <35-year-old. An increased incidence of DM closely associated with age. Influence of aging on Genesis DM type 2 occurs because of changes in the pancreatic β cells. The changes cause changes in insulin secretion and glucose metabolic changes associated with old age.<sup>20</sup> A research was done in the area of urban in Indonesia suggesting that women of childbearing age aged 35–49 years has 5.4 times greater risk of experiencing a DM compared with women of childbearing age aged 15–34 years.<sup>11</sup>

Obese women of childbearing age had a 2.63 times greater risk of developing type 2 diabetes than those who are not obese. Obese women of childbearing age should try to lose weight through regular diet and exercise regulation to avoid the risk of type 2 diabetes mellitus.



## Conclusion

Obesity was a risk factor for DM type 2 in women of childbearing age.

## Conflict of Interest

The authors declare no conflict of interests.

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## RESEARCH ARTICLE

## The Effects of Physical Exercise on Spatial Learning and Serotonin Levels in the Brain of Adult Rats

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### Abstract

Physical exercise can enhance tryptophan transport into the brain so that it will also increase serotonin levels in the brain. Therefore, it may influence many brain functions, such as learning and memory. This study aimed to determine the effect of physical exercise on spatial learning and serotonin levels in the brain of adult male Wistar rats. Biochemistry Laboratory of Department of Biochemistry & Molecular Biology, Faculty of Medicine, Universitas Indonesia was the study place which conducted in January–April 2013. Sixteen adult male rats randomly divided into two groups, the control group, and the treatment group. Physical exercise for the treatment group for four weeks using the animal treadmill at 15 m/min in speed for 15 minutes in the 1st week and 25 minutes for the next three weeks. Learning and memory test using water-E maze apparatus once a week. At the end of the exercised period, animals were sacrificed, and the brains were isolated. The measurement of serotonin and tryptophan levels was done using high-performance liquid chromatography (HPLC). The results showed that physical exercise improved animals performance in learning and memory test, exercised group made fewer errors at third and fourth week ( $p < 0.05$ ). Serotonin levels in the brain of exercised group was significantly higher than that in control group ( $p < 0.05$ ). These results indicated that the enhancement of serotonin levels in the brain induced by physical exercise is involved in improving spatial learning and memory.

**Keywords:** Brain, learning and memory, physical exercise, serotonin

## Pengaruh Latihan Fisik terhadap Kemampuan Belajar Spasial dan Kadar Serotonin pada Otak Tikus Dewasa

### Abstrak

Latihan fisik diketahui dapat meningkatkan transpor triptofan melewati sawar otak sehingga dapat meningkatkan kadar serotonin di otak. Oleh karena itu, latihan fisik berperan memengaruhi berbagai fungsi otak termasuk proses belajar dan memori. Penelitian ini bertujuan mengetahui pengaruh latihan fisik aerobik dengan intensitas yang ringan terhadap kemampuan belajar spasial serta kadar serotonin pada otak tikus Wistar dewasa. Penelitian ini dilakukan di Laboratorium Biokimia, Departemen Biokimia & Biologi Molekuler, Fakultas Kedokteran, Universitas Indonesia, Jakarta periode Januari–April 2013. Enam belas ekor tikus jantan dewasa dibagi secara acak menjadi dua kelompok, yaitu kelompok kontrol dan kelompok perlakuan. Latihan fisik diberikan kepada kelompok perlakuan selama 4 minggu menggunakan *animal treadmill* dengan kecepatan 15 m/menit selama 15 menit pada minggu pertama dan 25 menit pada 3 minggu berikutnya. Uji belajar dan memori dengan perangkat *water-E maze* dilakukan satu kali/minggu. Setelah masa latihan fisik selesai, hewan coba dikorbankan dan jaringan otak diisolasi. Pengukuran kadar serotonin dan triptofan pada otak dilakukan menggunakan kromatografi cair kinerja tinggi (KCKT). Hasil penelitian menunjukkan bahwa jumlah kesalahan yang dilakukan oleh kelompok perlakuan lebih sedikit secara signifikan pada uji belajar dan memori ke-3 dan ke-4 ( $p < 0,05$ ). Kadar serotonin lebih tinggi secara signifikan pada otak kelompok perlakuan ( $p < 0,05$ ). Hasil penelitian ini mengindikasikan bahwa peningkatan kadar serotonin pada otak yang diinduksi oleh latihan fisik aerobik intensitas ringan terlibat dalam meningkatkan kemampuan belajar dan memori spasial.

**Kata kunci:** Belajar dan memori, latihan fisik, otak, serotonin

Received: 26 May 2017; Revised: 8 August 2018; Accepted: 27 August 2018; Published: 30 August 2018

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## Introduction

Physical exercise defined as any structured physical activity undertaken in a certain period to maintain or improve body health and physical fitness. Regular physical exercise contributes to maintaining muscle tone, ideal body weight, and cardiovascular fitness.<sup>1</sup> It also plays a vital role in improving mental health, maintaining positive self-esteem, preventing stress and depression. Moreover, physical exercise has a beneficial effect on improving cognitive function, including learning and memory.<sup>2,3</sup>

The physical exercise involved in improving cognitive function through several mechanisms, such as increased nutrients and oxygen distribution into the brain, enhancing neurogenesis, increasing neurotrophic and neuroprotective levels that induce nerve cells growth, maintaining synapses plasticity, activating antioxidant systems, and formatting long-term potentiation (LTP).<sup>4-11</sup> Moreover, physical exercise also improves cognitive function by affecting the neurotransmitter systems, such as serotonin (5-HT),<sup>12-14</sup> dopamine (DA),<sup>14</sup> epinephrine (E), two norepinephrine (NE),<sup>4,14</sup> glutamate (Glu),<sup>6</sup> and acetylcholine (ACh).<sup>14</sup>

Physical exercise can enhance serotonin levels in the brain by increasing the transport of plasma tryptophan (Trp) into the brain as a consequence of the increased fat catabolism during the physical exercise. Physical exercise also enhances the uptake of branched-chain amino acids (BCAA) by the skeletal muscles so that BCAA levels in the plasma decreased. Since BCAA and tryptophan using the same protein carrier (sizeable neutral amino acid, LNAA, protein carrier), the increased of free tryptophan levels along with the decreased of BCAA levels in plasma will enhance the utilization of LNAA protein carrier by tryptophan. Therefore, more tryptophan can pass through the blood-brain barrier. Increased tryptophan availability in the brain provides more abundant substrates for serotonin synthesis and release by serotonergic neurons.<sup>15-18</sup>

Increased serotonin levels in the brain will be able to affect various brain functions, including learning and memory. Serotonin is known as a neurotransmitter that involved in the learning and memory processes due to serotonergic neurons innervate different regions of the central nervous system, such as the cerebellum, neocortex, thalamus, limbic system, medulla oblongata, and medulla spinalis. In addition, various

serotonin receptors can be found in almost all parts of the brain that enables serotonin affects learning and memory processes through several mechanisms depend on the receptor-activated, among others, depolarizing neurons directly via activation of 5-HT<sub>3</sub> receptor, increasing certain neurotransmitters release through cyclic adenosine monophosphate (cAMP) cascade, involving in neurogenesis, and formatting LTP.<sup>19-25</sup> It mentioned earlier that serotonergic neurons innervate different regions of the central nervous system, one of the densest parts innervated by serotonergic neurons is hippocampus, which is part of the limbic system. The hippocampus plays a vital role in learning and memory, emotion, and spatial navigation.<sup>26</sup> Therefore, increased levels of serotonin in the brain induced by physical exercise implicated in increasing this neurotransmitter levels in the hippocampus. Furthermore, it will also improve hippocampal-dependent learning and spatial memory. Therefore, this research aimed to determine the effect of physical exercise on spatial learning and serotonin levels in the brain of adult male Wistar rats.

## Methods

This study was experimental in vivo research. Sixteen adult male Wistar rats (*Rattus norvegicus*), age 8–10 weeks, initial weight 150–200 g, were used. This study was done at the Biochemistry Laboratory of Biochemistry & Molecular Biology, Faculty of Medicine, Universitas Indonesia in January–April 2013. Rats obtained from the Department of Biochemistry & Molecular Biology, Universitas Indonesia. Animals maintained under the controlled condition of light (12 hours light:12 hours dark), temperature 24±1°C, and humidity 60–85%. They fed on standard food produced by PT Charoen Pokphand Indonesia and allowed to have free access to food and tap water ad libitum. This study had been reviewed and approved by the Health Research Ethics Committee, Faculty of Medicine, Universitas Indonesia-Dr. Cipto Mangunkusumo General Hospital Jakarta, with ethical approval number: 759/H2.F1/ETIK/2012.

Animals randomly divided into two groups of eight animals each. The control group and the exercised group that performed a low intensity of aerobic exercise. The exercise was done for four weeks (5 days/week). The animals of the exercised group ran on a motorized treadmill with a slope of 0° at 15 m/min in speed for 15 minutes in the

1<sup>st</sup> week and 25 minutes for the next three weeks. In the first two minutes of every exercise session, the speed of motorized treadmill set at 10 m/min in order to warm up the animals.

Learning memory test in this study was done once a week. Water-E maze apparatus was used to assess the animal's learning and memory capability. The apparatus was made up of E shaped glass, with the main ditch, center ditch, and two side ditches (left and right). Stairs used as the goal (finish point) and placed in one side of the ditch. The animals placed at the end part of the center ditch as the start point of a water-E maze. The number of errors and the duration to finish the test recorded. The test was repeated three times for each animal without resting.

By the end of the treatment period, animals sacrificed, and the brains isolated in order to measure tryptophan and serotonin levels using HPLC. The brain of each individual rat was homogenized at 10,000 rpm in HClO<sub>4</sub> 0.1 M, 0.025% Na<sub>2</sub>EDTA, and 0.025% L-cystine. Homogenates centrifuged at 12,500 g, 4°C, for 15 minutes. The supernatants from the centrifugation were ready for analysis using HPLC. Chromatographic separation performed with octadecyl (C18) column, 5 µm, 4.6 × 250 mm. Flow rate set at one mL/min and UV detection at 210–400 nm. The mobile phase was KH<sub>2</sub>PO<sub>4</sub> 10 mM : acetonitrile (9:1). 50 µL sample injected into the column. The external standard of tryptophan and serotonin produced by SIGMA, USA.

The results of the study presented as mean ± standard deviation (SD). T test independent with α=0.05 was performed to analyze all parameters in the study, except the number of errors at the fourth week was analyzed using Mann-Whitney

with α=0.05.

## Results

The results of the learning and memory test presented in Table 1. The number of errors and duration needed by the animals to finish the test assessed. The average travel time required to reach the target (stairs) and the average number of errors made by the animals in completed learning and memory test decreased in both groups (control and exercised groups). However, the exercised group was able to show better progress than the control group in resolving water-E maze test. The results showed that physical exercise could improve animals performance in learning and memory tests, exercised group made fewer errors at third (p<0.05) and fourth week (p<0.05). Although there was no significant difference in duration needed by both groups to complete learning and memory tests (p>0.05).

The results of the measurement of tryptophan and serotonin levels in the brain presented in Table 2. Serotonin levels in the brain of exercised group significantly higher than that in control group (p<0.05). Meanwhile, tryptophan levels were not significantly different in both group (p>0.05). By observing the levels of serotonin in the brain, it concluded that tryptophan levels were not significantly different might be caused by more tryptophan in the exercised group has been converted into serotonin.

## Discussion

The results showed that exercised group was able to show better performance than the control

**Table 1 Duration and Number of Errors in Learning and Memory Test**

Parameters	Week	Control Group	Exercised Group	p Value
Duration (second)	0	24.63±16.07	27.43±12.50	0.704
	1 <sup>st</sup>	15.36±5.62	15.83±5.06	0.847
	2 <sup>nd</sup>	14.50±7.54	12.48±3.90	0.604
	3 <sup>rd</sup>	13.13±6.11	9.50±3.57	0.900
	4 <sup>th</sup>	8.62±4.02	5.78±2.75	0.118
Number of errors (times)	0	1.42±1.15	1.46±0.53	0.928
	1 <sup>st</sup>	1.08±0.83	0.96±0.55	0.728
	2 <sup>nd</sup>	1.13±1.08	0.71±0.42	0.642
	3 <sup>rd</sup>	1.04±0.74	0.37±0.45*	<b>0.039</b>
	4 <sup>th</sup>	0.62±0.55	0.04±0.12*	<b>0.008</b>

\*Showed significantly different from the control group (t test independent for all paramater, Mann-Whitney test for number of errors at 4<sup>th</sup> week, p<0.05)

**Table 2 Tryptophan and Serotonin Levels in the Brain**

Parameter (ppm/g brain tissue)	Control Group	Exercised Group	p Value
Tryptophan	2.54±0.97	3.41±1.26	0.115
Serotonin	9.90±2.46	15.88±3.93*	<b>0.003</b>

\*Showed significantly different from the control group (t test independent,  $p < 0.05$ )

group in finishing learning and memory test, especially after three weeks of exercising. The exercised group was able to resolve learning and memory test with fewer errors than the control group at the third and fourth week. It concluded that low intensity of aerobic exercise in this study improved learning and spatial memory assessed with the water-E maze. The results of this study were consistent with other studies which showed that physical exercise has a positive contribution to cognitive functions, including learning and memory ability. Van Praag et al.<sup>6</sup> showed that running enhances learning and spatial memory with the Morris water maze, increase neurogenesis in the hippocampus and improve LTP at medial perforant path synapses toward the dentate gyrus (DG). The increased in neurogenesis and synaptic plasticity in the runner mice thought to contribute to improving spatial navigation ability. Another study showed that low intensity of aerobic exercise could improve spatial learning and memory ability of elderly rats, but the exercise procedure had not been able to increase brain-derived neurotrophic factor (BDNF) and nerve growth factor (NGF) in the forebrain.<sup>27</sup>

The study by Borght et al.<sup>8</sup> showed that running could increase neurogenesis in rat's hippocampus which allegedly associated with the improvement of animal performance in completing learning and memory test with Y-maze. Liu et al.<sup>28</sup> concluded that both, voluntary exercise and forced exercise on a treadmill, can improve spatial navigation of mice on the Morris water maze. Those exercise procedures also increase BDNF and synaptotagmin one levels in the hippocampus. The increased BDNF levels positively correlated with improvement of learning and memory ability, mainly through neurogenesis, synaptogenesis, and activation of another neurotrophic factor. While synaptotagmin is a molecule that required in synaptic vesicles aggregation when new synapses formation take place. In their study, Kobilo et al.<sup>29</sup> showed that running could increase

BDNF levels in the hippocampus. BDNF plays a role in increasing neurogenesis in that brain region. Their study also showed that running could improve animals (mice) performance in the open-field test which reflects the improvement in processing information and decreasing anxiety levels in new environments. Another research by Ke et al.<sup>30</sup> concluded that voluntary exercise was the most effective exercise in increasing BDNF levels in the hippocampus and improving motor function in rats with ischemic stroke.

Exercise also affects brain functions by modulating neurotransmitter systems. Chaouloff et al.<sup>17</sup> showed that light intensity of running increased tryptophan levels in mice's brain, without affect the total tryptophan levels in the body. According to Chaouloff et al.<sup>17</sup> results, it was clearly indicated that fat catabolism which occurred during the physical exercise was the factor that responsible for the enhancement of tryptophan transport into the brain so that this amino acid levels increased in the brain. More free fatty acids (FFA) was available in the plasma when fat catabolism occurred. FFA and tryptophan had the same binding sites on albumin so that the enhancement FFA levels in plasma disrupted chemical bond between tryptophan and albumin. As a result, there would be more free tryptophan found in plasma. Along with the increased free tryptophan levels and the increased of FFA concentrations, there was also an increased BCAA uptake by the skeletal muscles. Therefore BCAA levels in the plasma decreased, and the number of competitors for tryptophan to pass through the brain barrier decreased because LNAA (including BCAA) used the same protein carrier. Increased free tryptophan levels along with decreased BCAA levels in plasma resulted in enhancing tryptophan transport into the brain so that more tryptophan available in the brain. Tryptophan is an essential amino acid which is a precursor of serotonin. Increased levels of tryptophan providing more substrate for serotonin synthesis by the serotonergic



neurons in the brain, including the hippocampus. Increased serotonin levels in the brain may affect various brain functions, including learning and memory.<sup>15-18</sup>

In line with Chaouloff et al.,<sup>17</sup> this study showed that tryptophan levels in the brain of the exercised group were higher than that in the control group although not significantly different. The average tryptophan levels were not significantly different can be explained by observing serotonin levels in the brain. The results showed that serotonin levels in the brain of exercised group significantly higher than that in the brain of the control group. Tryptophan levels were not significantly different might be caused by more tryptophan in the exercised group had been converted into serotonin. These results indicated that low intensity of aerobic exercise in this study not only enhanced serotonin levels in the brain but also improved learning and spatial memory. The enhancement of serotonin levels in the brain implicated in the enhancement of this neurotransmitter in the hippocampus. Hippocampus is a small region of the brain that forms part of the limbic system and associated with learning processes, memory, and spatial navigation.<sup>20</sup>

The increased levels of serotonin in the hippocampus induced by physical exercise played essential roles in improving hippocampus structures and functions through several mechanisms, such as increase neurogenesis, increase other neurotransmitters production and their release, synaptogenesis, and synapses facilitation. Improvement of hippocampus structure and function enhanced hippocampal-dependent learning and memory.<sup>23-25</sup> Activation of the 5-HT<sub>3</sub> receptor involved in increasing some neurotransmitters release by activated cAMP cascade, depolarize neurons directly so that the transmitting of information will move quicker in the nervous system. Activation of this receptor may also increase the release of other neurotransmitters, especially the excitatory neurotransmitter, encephalin, and gamma-aminobutyric acid (GABA).<sup>31,32</sup> Physical exercise can also increase neurotrophic levels, such as NGF, BDNF, synaptotagmin I, insulin-like growth factor I (IGF-I), vascular endothelial growth factor (VEGF) that involve in increasing neurogenesis, synaptogenesis, and angiogenesis in the brain and also hippocampus.<sup>28-30,33-36</sup>

Activation of 5-HT<sub>2A</sub> receptor on cholinergic

and glutamatergic axon terminals can increase the release of acetylcholine and glutamate. Increased levels of both neurotransmitters are significant in memory formation, the process of LTP, and the learning process.<sup>22</sup> 5-HT<sub>2A</sub> is also involved in neurogenesis, increased levels of 5-HT<sub>2A</sub> are increasing proliferation rate of precursor cells in the DG of the hippocampus. Activation of 5-HT<sub>1A</sub>, 5-HT<sub>2A</sub>, and 5-HT<sub>2C</sub> receptors were involved in the regulation of neurogenesis in the DG.<sup>22,25,37</sup> Activated 5-HT<sub>4</sub>, 5-HT<sub>6</sub>, and 5-HT<sub>7</sub> receptors are also involved in enhancing cell proliferation in the DG indirectly through cAMP cascade, activation of cAMP can increase the expression of cAMP response element-binding protein (CREB), cAMP-CREB complex is capable of increasing the expression of BDNF.<sup>24,25,38</sup> BDNF involved in enhancing serotonin release in the hippocampus, as a result, it is also enhancing neurogenesis in that region.<sup>7-9</sup> The DG of the hippocampus also contributes to anxiety. Modulating the activity of the ventral dentate gyrus by stimulating neurogenesis in that area is suggested can lower anxiety.<sup>20</sup>

The enhancement of serotonin levels has essential roles in improving hippocampus structure so that it will also improve hippocampus function, including hippocampal-dependent learning and spatial memory. This study showed that low intensity of aerobic exercise involved in modulating serotonin levels in the brain. Moreover, it was also improved learning ability and spatial memory of rats with the water-E maze.

## Conclusion

The enhancement of serotonin levels in the brain induced by low intensity of aerobic exercise is involved in improving learning ability and spatial memory.

## Conflict of Interest

The authors declare no conflict of interests.

## Acknowledgement

The authors would like to express gratitude to the Department of Physiology, Department of Biochemistry & Molecular Biology, and Laboratory of Bioavailability & Bioequivalence, Universitas Indonesia, for the support and

cooperation. We would also like to thank the Tanoto Foundation which had partly funded this research.

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## RESEARCH ARTICLE

**Difference Duration of Labor at BC-MK15 Birth Chair with Conventional Bed in Multiparous**Fitriani,<sup>1,2</sup> Johaness Cornelius Mose,<sup>3</sup> Herry Herman<sup>4</sup><sup>1</sup>Dinas Kesehatan Kabupaten Bireuen, Bireuen, Indonesia, <sup>2</sup>Midwifery Master Study Program,<sup>3</sup>Department of Obstetrics and Gynecology, <sup>4</sup>Department of Orthopaedics and Traumatology, Faculty of Medicine, Universitas Padjadjaran, Bandung, Indonesia**Abstract**

Prolonged labor increases the mortality and morbidity of mother and baby. The philosophy of childbirth is a natural process by taking the upright positions. The BC-MK15 birth chairs can facilitate the vertical position of the delivery mother. This study aims to analyze the difference of childbirth duration in the BC-MK15 birth chair with the conventional bed in multiparous. This research was an experimental study of posttest-only control group design. Experimented at *Pelayanan Obstetri Neonatal Emergensi Dasar/PONED* (Basic Emergency Obstetric and Neonatal Care/BEONC) Puskesmas (Public Health Center) Garuda, Puter, and Ibrahim Aji Bandung from 17 April–26 May 2017. The research samples were 30 multiparous on their first stage active phase of treatment and control group. Sampling method using a random permuted block. Birth measurements using the digital Q & Q stopwatch. The results of the duration during the active phase of first stage BC-MK15 was shorter 250.44 minutes than conventional bed 271.61 minutes ( $p=0.038$ ). The second stage of the BC-MK15 birth chair was shorter  $20.67\pm 2(1.02)$  minutes than the conventional beds of  $26.06\pm 2(1.08)$  minute ( $p=0.001$ ). The total duration of the labor of BC-MK15 was 269.42 minutes shorter than conventional bed 299.09 minutes ( $p=0.011$ ). In conclusion, the duration of childbirth is shorter in the BC-MK15 birth chair than the conventional bed in multiparous.

**Keywords:** BC-MK15 birth chairs, conventional bed, duration of labor**Perbedaan Lama Persalinan di Kursi Persalinan BC-MK15 dengan Tempat Tidur Konvensional pada Multipara****Abstrak**

Persalinan lama meningkatkan mortalitas dan morbiditas ibu dan bayi. Upaya yang dapat dilakukan sesuai filosofi persalinan adalah proses alamiah dengan memanfaatkan posisi tegak. Kursi persalinan BC-MK15 dapat memfasilitasi posisi tegak pada ibu bersalin. Penelitian ini bertujuan menganalisis perbedaan lama persalinan di kursi persalinan BC-MK15 dengan tempat tidur konvensional pada multipara. Penelitian ini merupakan studi eksperimental *posttest-only control group design*. Sampel penelitian multipara kala I fase aktif di Puskesmas Pelayanan Obstetri Neonatal Emergensi Dasar (PONED) Garuda, Puter, dan Ibrahim Aji Kota Bandung. Penelitian dilakukan pada 17 April–26 Mei 2017 yang memenuhi kriteria inklusi berjumlah 30 sampel tiap-tiap kelompok perlakuan dan kontrol. Pengambilan sampel menggunakan *random permuted block*. Pengukuran lama persalinan menggunakan *stopwatch* digital merek Q&Q. Hasil penelitian lama persalinan kala I fase aktif kursi persalinan BC-MK15 lebih singkat 250,44 menit daripada tempat tidur konvensional 271,61 menit ( $p=0,038$ ). Kala II kursi persalinan BC-MK15 lebih singkat  $20,67\pm 2(1,02)$  menit daripada tempat tidur konvensional  $26,06\pm 2(1,08)$  menit ( $p=0,001$ ). Total lama persalinan kursi persalinan BC-MK15 lebih singkat 269,42 menit daripada tempat tidur konvensional 299,09 menit ( $p=0,011$ ). Simpulan, lama persalinan lebih singkat pada kursi persalinan BC-MK15 daripada tempat tidur konvensional pada multipara.

**Kata kunci:** Kursi persalinan BC-MK15, lama persalinan, tempat tidur konvensional

Received: 15 August 2017; Revised: 20 August 2018; Accepted: 27 August 2018; Published: 30 August 2018

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## Introduction

Childbirth is a physiological process, the World Health Organization (WHO) estimates that 70–80% of pregnant women have low risk from delivery to birth.<sup>1</sup> The progress of childbirth is effected by 5 P namely passage, passanger (fetal or infant), power (strength of uterine contractions), psyche (psychological condition), and position (position).<sup>2</sup> Prolonged labour or dystocia may increase mortality and morbidity of mother and baby with prevalence 33% occurs in primiparas and 7% in multiparas.<sup>3</sup> In Indonesia, 90% of maternal deaths occur at the time of labor and soon after labor, one of the causes of maternal death is prolonged labor as much as 5%.<sup>4</sup>

Efforts that can be done as a form of the application of maternal love care and in accordance with the concept or philosophy that pregnancy and childbirth is a natural process, is by using the upright position that supports the childbirth so that it runs physiologically.<sup>5</sup> The advantage of upright position is the utilization of the effects of gravity, causing stimulation at the pituitary gland that can increase the release of oxytocin so that uterine contractions become more intensive, and affect the cervical dilation, upright position can also reduce the compression of the aortocaval, fetal conformity and the birth canal, and to increase pelvic outlet diameters. Stretch occurring in the posterior vagina causes endogenous oxytocin release resulting in a Ferguson reflex that triggers the mother's mother's desire to bearing down.<sup>6,7</sup>

The results of meta-analysis on 25 studies of 5,218 mother was in active phase of first stage labor in the upright position were shorter 1 hour 22 minutes than the recumbent position.<sup>6,8–11</sup> The results of the meta-analysis on 12 studies of 1,486 first stage labor on multiparous approximately 30 minutes in the upright position,<sup>9</sup> where as Jahanfar et al.<sup>12</sup> study on 50 samples of second stage labor on multiparous at upright position 10.78 (9.85) minutes and at recumbent position 16.52 (14.98) minutes.

Supine position is commonly used in contemporary obstetric care. The main advantage of this position is the convenience of the health worker in performing an abdominal examination to monitor the fetal heart rate.<sup>13</sup> The disadvantages that must be observed in the supine position, namely the high pain due to the duration of prolonged labor, the effort of the mother straining 30% heavier than the

upright position, diminished maternal blood flow in infants because aortic pressure, inferior vena cava, and umbilical cord compression, supine position also did not occur pelvic mother mobilization.<sup>1,8,14</sup>

The development of science and technology facilitates the upright position during delivery through the delivery of birth chairs designed to facilitate the delivery process in order to walk physiologically.<sup>15</sup> Currently innovation of the latest generation of birth chairs is one of AVE birthing bed that has been exported to 80 countries.<sup>16</sup> Previous research about the EZ birth seat birth chair duration of second stage labor is shorter with pvalue <0.01.<sup>7</sup> The research of Swedish birth seat duration of 1<sup>st</sup> labor and 2<sup>nd</sup> stage labor is also shorter with p=0.01.<sup>17</sup> Birthing Chairs-Magister Kebidanan 2015 (BC-MK15) was designed in accordance with the concept of EZ birth chair, Swedish birth seat and AVE birthing bed has been awarded by the Red Dot Design Award in 2003 and 2017 for AVE 2 which facilitates the physiological process of birth by using upright positions.<sup>16,18</sup> This study aims to analyze the difference duration in labor between births in BC-MK15 and conventional beds in multiparous.

## Methods

This research was an experimental research with posttest-only control group design done at *Pelayanan Obstetri Neonatal Emergensi Dasar/ PONE*D (Basic Emergency Obstetric and Neonatal Care/BEONC) Puskesmas (Public Health Center) Garuda, Puter, and Ibrahim Adjie Bandung from April 17 until May 26, 2017. How to select sample with consecutive sampling according to inclusion criteria, multiparous age 20–35 years, gestational age  $\geq 37$  to <42 weeks, cervical 4 cm dilated, single live fetus with fetal occiput is in occiput anterior position (OA), intact amniotic fluid, uterine contraction effective; regular rhythm, frequency 3 times/10 minutes, no acceleration of labor with drugs, estimated fetal weight 2,500 to 4,000 g, had a history of normal labor, BMI 18.5 to 24.9, and willing to be respondents. Exclusion criteria, cephalo pelvic disproportion, HB <11 g/dL, gestational distance <2 years and  $\geq 10$  years, pregnancy history with complications such as preeclampsia, eclampsia, antepartum bleeding (any contagious labor vaginal delivery), and no maternity assistant.

The study sample allocation used random

permuted blocks to determine the admission sample in the treatment group (BC-MK15 birth chair) or control (conventional bed). Criteria for drop out, which is a maternal who can not continue vaginal delivery (labor with acts such as extraction vacuum and cesarean delivery), partus precipitus labor that lasts less than 3 hours since the onset of regular contractions, prolonged labor, cannot with holding labor pain, and being in a BC-MK15 birth chair or a conventional bed less than 80% during labor. Birth measurement using digital stopwatch Q & Q brand.

The independent variable was the BC-MK15 birth chair and the conventional bed, the dependent variable was the duration of labor. Characteristics of respondents based on maternal education, economic status, parity, station, rupture of amniotic membrane, cervical dilation when rupture of amniotic membrane and the weight of newborns. Test the normality of data

using Shapiro-Wilk ( $p > 0.05$ ). Characteristics of the respondents were analyzed by chi square test ( $p < 0.05$ ), active phase of 1st stage of labor duration and total duration of labor were analyzed by Mann-Whitney test ( $p < 0.05$ ), the 2nd stage duration was analyzed by unpaired t test ( $p < 0.05$ ).

The protocol has been approved by the Health Research Ethics Committee, Faculty of Medicine, Universitas Padjadjaran, Bandung number: 294/UN6.C.10/PN/2017.

## Results

Table 1 presents characteristic of respondents. The result of statistical test of respondent characteristic was found, there was no significant difference between the two groups ( $p > 0.05$ ).

The duration of the active phase of first stage labor in the BC-MK15 birth chair group was

**Table 1 Statistical Analysis of Respondent's Characteristic**

Characteristic	Groups		p Value*
	BC-MK15	Conventional Bed	
	n=30	n=30	
Last education			
Low	18	15	0.529
Medium	10	14	
High	2	1	
Income every month (IDR)			
≤2,626,940.00	22	20	0.573
>2,626,940.00	8	10	
Parity			
2	18	18	0.881
3	9	10	
4	3	2	
Station			
0	9	6	0.618
+1	16	17	
+2	5	7	
Rupture of amniotic membrane			
Spontaneous rupture	28	27	1.000
Amniotomy	2	3	
Cervical dilation when rupture of amniotic membrane			
Cervical 7–8 cm dilatated	28	26	0.671
Cervical 9–10 cm dilatated	2	4	
Newborn body weight (g)			
2,500–2,999	13	8	0.371
3,000–3,499	14	17	
3,500–4,000	3	5	

IDR: Indonesian rupiah, \*chi-square

**Table 2 Statistical Analysis Comparison Duration of Labor**

Duration of Labor	Groups		p Value
	BC-MK15	Conventional Bed	
Active phase of 1 <sup>st</sup> stage			
Mean (SD)	250.75 (24.92)	265.38 (31.89)	0.038**
Median	250.44	271.61	
Range	204.17–303.35	216.57–312.28	
2 <sup>nd</sup> stage			
Mean±2(SE)	20.67±2(1.02)	26.06±2(1.08)	0.001*
Median	19.32	27.55	
Range	10.05–32.47	10.05–34.12	
Total labor duration (active phase of 1 <sup>st</sup> stage–2 <sup>nd</sup> stage)			
Mean±SD	271.42 (26.50)	291.44 (32.99)	0.011**
Median	269.42	299.09	
Range	226.07–334.62	231.62–336.40	

\*\*Mann-Whitney test, \*t test

250.44 minutes shorter than the conventional bed group of 271.61 minutes with  $p < 0.05$ . The result indicates that there was a significant difference in the duration of the active phase of first stage labor in the group of BC-MK15 birth chair was shorter than in the conventional bed group (Table 2).

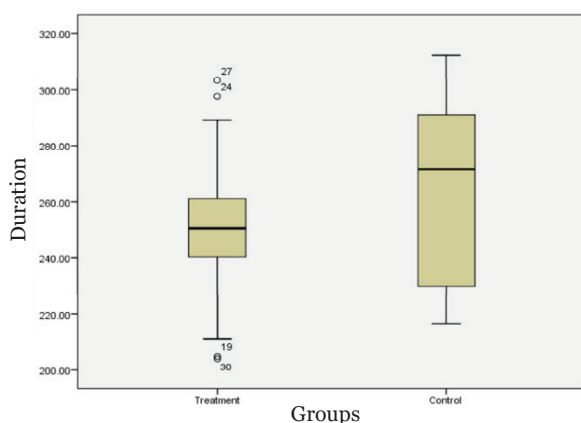
The mean duration of second stage labor in the group of BC-MK15 birth chairs was shorter  $20.67 \pm 2(1.02)$  minutes than in the conventional bed group of  $26.06 \pm 2(1.08)$  minutes with  $p < 0.05$ . There was a significant difference in that duration of labor order II in BC-MK15 birth chairs group was shorter than the conventional bed group.

Total labor duration in the group of BC-MK15 birth chairs had the median value of 269.42 minutes shorter than the conventional bed group

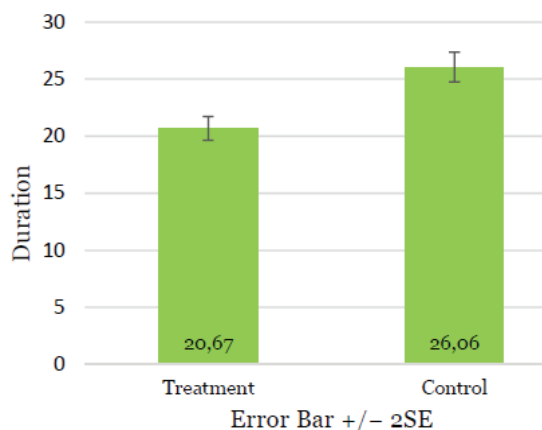
of 299.09 minutes with  $p < 0.05$  indicates that there was a significant difference between total labor duration with the group of BC-MK15 birth chairs shorter than in the conventional bed group.

Presentation of data with box plot in Figure 1, shows median line (Q2) in the control group not in the center of the box, whisker not symmetric in the control group. The data has a broader range (IQR/Q3-Q1) the higher control group showed that the data is spreading. In the treatment group, there were outlier data (symbol o) illustrates the distribution of the data is not normal.

Figure 2 showed 95% of respondents in the BC-MK15 birth chairs were between the mean of  $20.67 \pm 2(1.02)$  and in the conventional bed group, 95% were between the mean of  $26.06 \pm 2(1.08)$ .

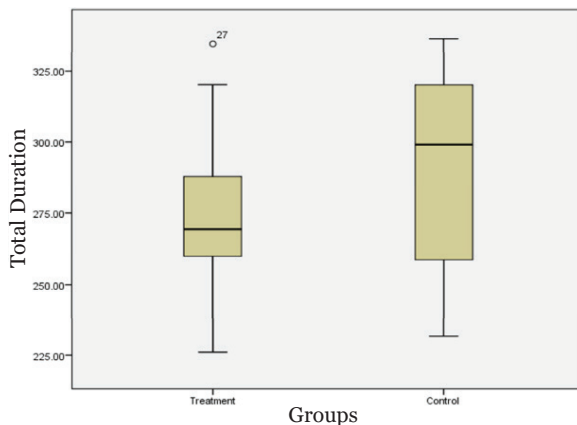


**Figure 1 Duration of Active Phase of First Stage Labor**



**Figure 2 Mean Duration of Second Stage Labor**





**Figure 3 Total Labor Duration**

Short bars indicate high precision and differences between the two groups are meaningful.

Figure 3 shows median line (Q2) in the control group not in the center of the box, whisker not symmetric in the control group. The data had a broader range (IQR/Q3-Q1) in the higher control group. In the treatment group, there were outlier data (symbol o) which illustrates the distribution of the data is not normal.

## Discussion

Respondents are multiparous during the active phase of first stage labor in work area 3 PONED Puskesmas Bandung. Characteristics observed were economic status, parity, station, rupture of amniotic membrane, cervical dilation when rupture of amniotic membrane and the weight of newborns. The characteristics of the two homogeneous groups are therefore comparable.

A study of differences in labor duration between the BC-MK15 birth chairs and conventional beds was significantly different, labor duration in the BC-MK15 birth chair is shorter than conventional bed group. This is supported by the results of the analysis which can be seen at stage of active phase of 1<sup>st</sup> stage and 2<sup>nd</sup> stage labor, the statistical analysis also shows significant differences, the duration of active phase of 1<sup>st</sup> stage and 2<sup>nd</sup> stage labor is shorter in the group of BC-MK15 birth chair than the conventional bed groups. This study is in line with previous research, the meta-analysis result of 12 studies to 1,486 first stage labor on multiparous about 30 minutes shorter in an upright position.<sup>9</sup> At the second stage labor of Jahanfar et al.'s study in 2004 on 50 samples of second stage labor in multiparous at

upright position 10,78 (9.85) minutes and at the recumbent position of 16.52 (14.98) minutes.<sup>12</sup>

The BC-MK15 birth chair can facilitate upright positioning during childbirth. Anatomically the upright position forms a hip angle between 60° to 90° compared to the hip angle at 30° recumbent position. Dimensions of the pelvic inlet and pelvic outlet also increased. The upright position results in the amount of pressure on the ischial tuberosities resulting in a passive stretching of the magnus of the muscle adapter. Muscle stimulation causes the shaft of the sacroiliaca joint to move backward to the lower sacrum, resulting in dilation of the intertuberos diameter.<sup>19</sup> The upright position widens the sagittal diameter under the pelvis 2±5 mm, the interspine diameter is 7±8 mm, the intertuberos diameter is 3±7 mm to facilitate childbirth.<sup>20</sup>

The BC-MK15 birth chair can also facilitate position changes with a reclining design that can support the back strongly.<sup>8,15</sup> The fowler position is an upright position with the head of the bed at an angle 80° to 90°, while the semi-Fowler's position of the head of the bed at an angle 45° to 60°. This position is a safe choice for maternal activity during the first order of childbirth.<sup>21</sup>

The upright position will reduce pressure on the blood vessels, and the blood flow becomes smooth which make contraction of the uterus better.<sup>6</sup> The contraction of the uterus has a vital role in obstetric mechanics and modify intrauterine pressure, which in turn provides a force that allows fetal movement. The force given by the fetus in the soft tissues changes shape depending on uterine contractions.<sup>22</sup>

The pelvic soft tissues also play a role in childbirth, the lower segment of the uterus will expand to accommodate intrauterine contents as well as with the thickened upper segment walls. The cervix will be pulled up and past the presenting part as this section moves down. The vaginal canal will be distended to accommodate the fetal passage.<sup>2</sup> Gravity of the pressure forces on the cervix will stimulate the proprioceptive nerves that will increase the Ferguson reflex and cause the pituitary gland to release oxytocin, thus increasing the contraction effectiveness. Active contractions and the magnitude of fetal head pressure will increase pressure on the cervix; the cervix will be pulled upwards so that thinning and opening this will have an impact on the shortening of first stage labor.<sup>6,7</sup>

Upright position also cause the fundus leading to the front, causing the alignment of the axis

extend the birth canal and directing the fetal head toward the pelvic outlet. The pelvic tilt adjusts the fetus forward to the birth canal from the abdomen to the pelvis so that during the labor process it facilitates the fetus to perform a series of movements to pass through the flanks (seven cardinal movements of labor).<sup>6,19</sup>

Second stage labor takes place at the time of complete opening until the baby is born, the physiological benefits of maternity and childbirth in an upright position, namely the presence of intra-abdominal pressure due to contraction of the abdominal muscles and diaphragm pressure. Increased intrauterine pressure due to uterine contractions that cause pressure on the fetal decline and when the fetal presentation section reaches the perineal base, mechanical stretching of the cervix occurs. Stretching in the posterior vagina causes endogenous oxytocin release and a Ferguson reflex that triggers the mother's desire to bearing down.<sup>6</sup>

The role of gravity in the sitting position when straining can increase the pelvic pressure of 30–50 mmHg higher than the supine position so that the upright position at childbirth may increase the effectiveness of straining.<sup>8</sup> Other theories state that strength at the pelvic floor of 54 Newton when the contraction and the force of gravity that working when voluntary pushing 120 Newtons. As for the contribution of gravity to forces acting on fall of the fetus through the birth canal is the force acting on the fetal derivatives most effectively when it is close to the direction of gravity, so gravitational use is instrumental in the labor process.<sup>22</sup>

The slope of the chair facilitates features of the BC-MK15 birth chair following the principle of upright position (avoiding the supine position) 45° from the horizontal. Legs rest and handgrip can be used in the second stage labor so that will help balance the posture of the body during childbirth which will ultimately increase the effectiveness of bearing down.<sup>8</sup> Legsrest with the buffer connection on the knee folds provides support to the patient during labor and widens the birth canal in labor.<sup>15</sup> Handgrip on each side act as a support for the hand, maximizing pressure while stretching and increasing comfort at the second stage labor.<sup>16,23</sup> The strength at hand is when the wrist is in a neutral position, so the mechanical load on the muscle is not substantial because it is in a neutral position.<sup>24</sup>

Various factors in this study can influence the duration of labor. Although the characteristics

of the respondents are already homogeneous, the characteristics of uterine contractions only observe retreats on uterine contractions in the BC-MK15 birth chairs group and the conventional bed. Which is the inclusion criterion is three times uterine contractions per 10 minutes, the researchers did not follow up for observation of uterine contractions in the later stage. In the control group using the conventional bed, women may choose a skewed position in the first and second stage. The sloping position makes uterine contractions more effective. Also, contractions can also be affected by fatigue, fear, and anxiety that cause stress that affects the weakness of uterine contractions.

Uterine contraction (power) is one determinant of the progress of labor that is the source of strength resulted in opened cervical, baby expenditure, and placental release. The contraction pattern is significant, and good uterine contractions will show progress on cervical dilation and baby descent.<sup>25</sup> Women who are in a tilted position of uterine contractions are more effective,<sup>26</sup> because in the oblique position there is no emphasis on the aorta-caval that blood flow to the uterus smoothly. The birth path is parallel between the pelvis and the presentation of the fetus. The sloping position forms C curve causing the uterus and fetus to fall toward the abdomen so that the uterus, pelvis and fetal presentation form the angle between the spine and the uterus. The contraction of the uterus directing the baby that posterior pelvic facilitate the decline of the fetal head, sacrum and cogsigeus free to move backward thus increasing the anterior-posterior diameter of the pelvis.<sup>27</sup>

Pain that occurs can affect the condition of the mother in the form of fatigue, fear, and anxiety that cause stress. Similarly, fatigue due to sleeplessness, lack of rest experienced by the mother before delivery will cause increased pain sensation and increased anxiety, this will affect the pattern of uterine contractions.<sup>28</sup> Cross-sectional research results by Ebrahimzadeh et al.<sup>25</sup> in Iran in 100 samples showed a significant correlation between severe fatigue with uterine contraction patterns ( $r=0.22$ ,  $p=0.026$ ), and duration first stage increased in severe fatigue ( $r=0.25$ ,  $p=0.014$ ).

Fear and anxiety during labor can stimulate increased secretion of catecholamines that lead to elevated levels of hormones such as epinephrine so that uterine contractions are not in line with the cervical opening. Increased

hormone epinephrine intensifies the pain that can affect the beta receptor that affects the fall in uterine blood flow resulting in uterine in coordinates and weak uterine contractions.<sup>26,29</sup> Women who experience anxiety in childbirth 30% experience fear in childbirth. The traumatic experience of labor causes a longer time interval in subsequent labor. The results of a case-control study by Sydsjö et al.<sup>30</sup> in southeastern Sweden from 2001–2007 in 23,000 samples showed that women experiencing fear during labor increased the duration of labor 40 minutes in the active phase ( $p < 0.001$ ). Therefore, the uterine contraction should be observed.

Research on the differences in labor duration between the BC-Mk15 birth chairs and conventional bed, found shorter labor in BC-MK15 birth chairs with a total length of labor 269.42 min (4 h 49 min), this included in the normal category and not dangerous, because the partus precipitates lasted less than 3 hours since the onset of regular contractions.<sup>31</sup> So, the BC-MK15 birth chair may facilitate intrapartum care, and labor can do physiologically.

### Conclusion

The duration of labor is shorter in the BC-MK15 birth chair than in conventional bed in multiparous.

### Conflict of Interest

The authors declare no conflict of interests.

### Acknowledgement

Thanks to Center for Quality Improvement of Human Resources for Health, Board of Development and Empowerment on Human Resources for Health, Ministry of Health Republic of Indonesia which has assisted the research fund, Politeknik Manufaktur Bandung, and PT Kramatraya Sejahtera Cimahi that has helped design and manufacture BC-MK15 birth chairs.

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## RESEARCH ARTICLE

## Profile of Late Adolescent Performance of Papua in Persipura U-21 Athlete Selection

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### Abstract

The enthusiasm of the people of Papua for football is in harmony with the emerging numbers of talented football athletes from Papua. It reflected in the selection of athletes football Persipura U-21 (aged 21 years and under) for the late adolescent. This study aims to determine the performance profile of late adolescents of Papua at the selection of Persipura U-21 football athletes. The result can be a material of strategic evaluation for improving the achievements of football sport in Papua. A descriptive study with the cross-sectional design conducted on total samples of 97 late adolescents (ages 16–21 years) of men from all provinces of Papua on Persipura U-21 January 2016 selection. Performance data consisted of body mass index (BMI), subcutaneous fat, cardiorespiratory fitness, anaerobic capacity, muscle endurance, flexibility, power, strength, balance, reaction time, and concentration levels. The results showed that all subjects were in healthy condition and most subjects (85%) had normal BMI. Physical characteristics of subcutaneous fat showed most of the subjects were lacking in the triceps (83%) and supraciliary (58%) fat. The basic physical ability for soccer is in good category whereas cognitive ability is in the less category. The research conclusions indicate the urgency to improve basic physical components of the athlete through a well-scaled and well-programmed exercise plan, as well as mental and cognitive development to improve athlete performance.

**Keywords:** Characteristic, football, late adolescent, performance

## Profil Performa Remaja Akhir Papua pada Seleksi Atlet Sepak Bola Persipura U-21

### Abstrak

Antusiasme masyarakat Papua terhadap olahraga sepak bola selaras dengan munculnya banyak atlet sepak bola bertalenta dari Papua. Hal tersebut terlihat pada seleksi atlet sepak bola Persipura U-21 (usia 21 tahun ke bawah) kategori remaja akhir. Penelitian ini bertujuan mengetahui profil performa remaja akhir Papua pada seleksi atlet sepak bola Persipura U-21 sehingga dapat menjadi bahan evaluasi yang strategis dalam meningkatkan prestasi cabang olahraga sepak bola di Papua. Penelitian deskriptif dengan desain potong lintang dilakukan terhadap seluruh sampel berjumlah 97 remaja akhir (usia 16–21 tahun) laki-laki dari seluruh provinsi Papua pada seleksi Persipura U-21 Januari 2016. Data performa terdiri atas indeks massa tubuh (IMT), lemak bawah kulit, ketahanan jantung paru, kapasitas anaerobik, daya tahan otot, kelentukan, daya ledak, kekuatan, keseimbangan, kecepatan reaksi, serta tingkat konsentrasi. Hasil penelitian menunjukkan bahwa seluruh subjek berada dalam kondisi sehat dan sebagian besar subjek (85%) memiliki IMT yang normal. Karakteristik fisik lemak bawah kulit menunjukkan sebagian besar subjek adalah kurang pada bagian trisep (83%) dan suprailiaka (58%). Kemampuan fisik dasar untuk sepak bola berada pada kategori baik, sedangkan kemampuan kognitif dalam kategori kurang. Simpulan penelitian menunjukkan perlu perbaikan komponen fisik dasar atlet melalui perencanaan latihan yang terukur dan terprogram dengan baik, serta pembinaan mental dan kognitif untuk peningkatan performa atlet.

**Kata kunci:** Karakteristik, performa, remaja akhir, sepak bola

Received: 8 September 2017; Revised: 31 July 2018; Accepted: 1 August 2018; Published: 30 August 2018

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## Introduction

The skills of playing soccer and the basic ability of a soccer athlete are closely related to the physical, tactical, and mental characteristics of the athlete. Basic skills are important elements to master and learn from the beginning of the training in order to develop the quality of the game that determines the performance of the teams in the game. Improved football achievement determined by many factors such as infrastructure, quality of trainers, basic conditions and talent of players, and measurable training. Factors that play an important role in a football athlete is the physical ability and basic techniques of football and the ability of teamwork when playing.<sup>1,2</sup>

A well-scaled and programmed physical exercise can start from an early age or the start of the athlete into the training program. Improved physical conditions obtained through the provision of exercise, among others strength training, flexibility, speed, agility, and endurance. These aspects of the exercise are useful for knowing and leveraging the conditions of every soccer athlete. A trainer providing training to athletes will then provide an evaluation of the results of the training provided as the planning capital of the next training program or as a threshold to determine the eligibility of his or her athlete in a match.<sup>1,3</sup>

The evaluation of the physical condition should include everything that affects the performance of a football athlete. The good physical condition of a football athlete can sustain technical skills, tactics, and strategies in a football game for 2 × 45 minutes. Physical conditions influenced by internal factors such as gender, age, and race, as well as external factors such as nutrition, weather, and biophysical conditions. Many also know that Papua has human resources, including children or adolescents who naturally have a physical condition that meets the standards to become a football athlete. Physical conditions owned by Papuan children and adolescents may be influenced by both internal and external. The enthusiasm of Papuan children and teenagers to become football athletes were very high. Evidence came from the many participants who follow every event on Persipura players selection every year such as the selection of U-21 football athletes (age 21 years and under).<sup>3,4</sup>

This paper analyzes the profile of the late adolescence performance of Papua at the selection of Persipura U-21 football athletes.

The result can serve as a strategic evaluation material in improving the ability, performance, and achievement of football in Papua.

## Methods

Subjects in this study are 97 late adolescents (ages 16–21 years) men who came from all provinces of Papua to follow the selection of football Persipura U-21 athletes conducted in January 2016. This research was a descriptive study with a cross-sectional design. All subjects have undergone physical assessment, with blood pressure tests were performed using a sphygmomanometer and lung function using a respirometry. A physician conducted all the tests to ensure all subjects were healthy and fit to follow all performance tests. After examination, it is checked to obtain performance data of athletes in the form of body mass index (BMI) based on WHO criteria for Asia-Pacific, under skin fat using skin calipers, pulmonary heart resistance through 2.4 km run test, anaerobic capacity through a 50 m run test. Endurance component examination is measured based on muscle endurance through push-up and sit-up movement, flexibility using the flexometer tool, explosive power through vertical jump activity and opera medicine ball. Strength components are measured using hand grip, hand dynamometer, back dynamometer, and leg dynamometer, while balance through balance test. Also, subjects assessed for reaction speed through color and sound stimuli at various sound frequencies and concentration levels using a grid concentration test. All measurements conducted in Abepura, Jayapura. The research was approved by the Health Research Ethics Committee, Faculty of Medicine, Universitas Padjadjaran, Bandung number: 827/UN6.C1.3.2/KEPK/PN/2015.

All data categorized based on the provisions of Perhimpunan Ahli Ilmu Faal Olahraga Indonesia (PAIFORI). Data processing is done using Microsoft Excel 360.<sup>10</sup>

## Results

All subjects who followed the assessment were 21 years old and under with normal blood pressure and lung function. BMI description and criteria is in Table 1. Most subjects (85%) had normal BMI, while the rest were abnormal, either deficient or overweight.

The results of the assessment of the physical characteristics of the subcutaneous fat listed

**Table 1 Body Mass Index**

Body Mass Index	Total Subject	
	n=97	%
Underweight	6	6
Normal	82	85
Overweight	8	8
Obese I	1	1

**Table 2 Physical Characteristic of Subcutaneous Fat**

Component	Subcutaneous Fat		
	Low	Normal	Over
Tricep	81 (83%)	16 (17%)	0 (0%)
Subscapula	20 (21%)	72 (74%)	5 (5%)
Suprailiac	56 (58%)	35 (36%)	6 (6%)

in Table 2 show that most subjects had low subcutaneous fat in triceps (83%) and supraciliary (58%), whereas in the subscapular part the subjects had normal subcutaneous fat.

Table 3 shows a collection of physical performance components. The component was chosen based on the characteristics of the activities performed during the football game.

The reaction speed seen in Table 4 reflects

**Table 4 Reaction Speed Performance**

Component	Reaction Speed		
	Low	Enough	Good
Colour	0 (0%)	54 (56%)	43 (44%)
Sound			
500 Hz	0 (0%)	66 (68%)	31 (32%)
1 KHz	0 (0%)	65 (67%)	32 (33%)
3 KHz	0 (0%)	55 (57%)	42 (43%)

the subject's ability to respond to the dynamics that occur in a football game such as the speed at which the feed-pass, penalty, or response takes place during off-side.

## Discussion

The description of the body mass index held by prospective football athletes in the U-21 show that most (85%) are at a reasonable level as shown in Table 1. Reflecting the balance of nutrients as physical structural is essential in conducting training programs. Nevertheless, there are still 9% of athlete candidates who have excess BMI so that adjustment of exercise in order to decrease body fat is recommended to be a program in conditioning exercises. 6% are still on the underweight criteria, so the attention to the fulfillment of the nutritional aspect to reach the

**Table 3 Characteristic of Basic Physical Ability**

Component	Basic Physical Ability				
	Very Low	Low	Enough	Good	Very Good
2.4 km run	1 (1%)	5 (5%)	22 (22%)	50 (52%)	19 (20%)
50 m run	45 (46%)	15 (16%)	26 (27%)	7 (7%)	4 (4%)
Endurance					
Arm	0 (0%)	0 (0%)	4 (4%)	24 (25%)	69 (71%)
Abdomen	0 (0%)	0 (0%)	40 (41%)	55 (57%)	2 (2%)
Flexibility	0 (0%)	27 (28%)	33 (34%)	22 (23%)	15 (15%)
Strength					
Arm	0 (0%)	2 (2%)	15 (15%)	46 (48%)	34 (35%)
Back	0 (0%)	3 (3%)	21 (22%)	44 (45%)	29 (30%)
Leg	0 (0%)	36 (37%)	31 (32%)	27 (28%)	3 (3%)
Power					
Arm	0 (0%)	44 (45%)	26 (27%)	20 (21%)	7 (7%)
Leg	0 (0%)	44 (45%)	1 (1%)	4 (4%)	48 (50%)
Balance	0 (0%)	1 (1%)	6 (6%)	8 (8%)	82 (85%)
Concentration	34 (35%)	49 (51%)	13 (13%)	1 (1%)	0 (0%)

proportional BMI through high carbohydrate diet with a simple type of sugar is necessary. Simple sugar is chosen as a BMI enhancement strategy because the majority of Papuans have a habit of consuming tubers and papeda which are a simple type of glucose.<sup>1,4</sup>

The regulation of nutrient intake in sports must follow balanced nutrition. Macronutrient balance such as carbohydrates, fats, and proteins should be done individually according to the needs of each athlete. The macronutrients required by the athlete must be in proportion to their performance. The macronutrient balance shows from the body fat composition. Increased body fat will decrease agility and has an impact on the athlete's performance. Based on the characteristics of subcutaneous fat in the supraciliary area 58% and triceps 83% as seen in Table 2 indicate that the subject can move agile because of slight obstacles of the underlying subcutaneous fat. However, the fat under the skin also has a function as a major energy reserve after glucose runs out and insulation of body temperature. Insulation of body temperature is needed in the adjustment of cold environmental conditions when attending training and when competing. Body fat also serves as a protection against concussion so expect a proportionate body fat can minimize injury to the athlete. Therefore, it is necessary to have the intake of high-calorie nutrition that aims to increase the fat under the skin so that the function of energy reserves, isolation, and protection maintained.<sup>5,6</sup>

In addition to nutritional intake requirements, physical ability is also required to support the performance of athletes for aerobics and anaerobic. Aerobic ability required to support the stamina as seen from cardiopulmonary resistance, while the anaerobic ability needed to support the dexterity seen from the speed, muscle strength, and power.<sup>1,6</sup>

The 50-meter run test results showed that almost half of the athlete candidates had deficient speed (46%) (see Table 3). This situation requires adjustment to future training programs by increasing the type of exercise that improves the capacity of exercise in the anaerobic energy system. Most of the activities when doing football require running speed at such short distances and time as when chasing the ball from the opponent. Such activities fall within the anaerobic predominant category.<sup>3,6</sup>

Another physical capability that needs to be improved is the leg muscle strength which in the

measurement results is 1/3 the number is in a low category. Leg muscle strength is the capital to obtain optimal limb activity performance. Components of muscle strength that are not well prepared will increase the injury and skill training process and football techniques less than optimal.<sup>1,3,7</sup>

In addition to muscle strength, football also requires a good limb power. Football activities such as dribbling and kicking the ball require significant power, on the other hand, power requires mostly in the form of good leg muscle strength. Therefore, the strength and power of the muscles of the legs should train in synergy. Limb power component at prospective athletes Persipura U-21 is proportional to the strength of the legs. The results showed that 45% of participants had low limb power.<sup>1,4</sup>

Achievement is a combination of good physical component quality, proper technique and strategy, and excellent mental (cognitive) ability. The link between cognition and exercise explained in a study of the increase in brain-derived neurotrophic factors (BDNF) at a time when exercise has a positive relationship with cognitive function. One of the mental abilities (cognitive) is the ability of concentration. The results of this study indicate that the concentration of prospective candidate athletes mostly located in the category below enough (low 51%, deficient 35%). Concentration is required when going to a match because it is related to the response speed during a match. The concentration assessed only reflects the state of one's concentration when it is measured. Therefore, attempts to improve concentration just before the game can be made to escalate the athlete's ability to act on field conditions.<sup>8-11</sup>

## Conclusion

Physical characteristics of prospective football Persipura U-21 athletes are in a good category. However, the specific physical components need to improve through improvement and well-programmed exercise plans.

## Conflict of Interest

The authors declare no conflict of interests.

## Acknowledgement

Our gratitude goes to the team from Perhimpunan

Ahli Ilmu Faal Olahraga Indonesia (PAIFORI) and the KONI Science of Jayapura city who has assisted in licensing and data collection.

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## RESEARCH ARTICLE

## Differences of Vital Lung Capacity and FEV<sub>1</sub>/FVC Ratio on Children in Urban and Rural

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### Abstract

Urban areas are places with high levels of air pollutant. This air pollution causes decreased lung function and obstruction in the respiratory tract. The absorption of dust particles and pollution is inhaled into the lungs through the respiratory mechanism. The entry of toxic material will react with the cells causing free radicals that will damage cells, especially in the respiratory system. This study was aimed to knowing the differences vital lung capacity and forced expiration volume in 1 second/forced vital capacity (FEV<sub>1</sub>/FVC) ratio in children in urban areas with high level pollution and in rural areas not exposed to pollution. This study was an observational analytic study, implemented in September–December 2016 with a total sample of 70 children consisting of 35 children in Palembang city and 35 children in Musi Rawas area. Data analysis to determine the differences of lung vital capacity and FEV<sub>1</sub>/FVC ratio in children in rural and urban with independent t test. The result showed that the average value of urban vital lung capacity in urban (1,205 mL) was lower than the mean value of vital lung capacity of children in rural (1,493 mL) and there was significant difference in the value of vital lung capacity in rural children and urban (p=0.004). The ratio of FEV<sub>1</sub>/FVC for children in urban areas (91.05%) was lower than the ratio of FEV<sub>1</sub>/FVC for children in rural (93.96%) as well as a significant difference in the ratio of FEV<sub>1</sub>/FVC in rural and urban children (p=0.001). In conclusion, the mean value of lung vital capacity and the ratio of FEV<sub>1</sub>/FVC of children in urban areas is lower than mean value of vital lung capacity of children in rural areas.

**Keywords:** FEV<sub>1</sub>, FVC, spirometry, vital lung capacity

## Perbedaan Kapasitas Vital Paru dan Rasio FEV<sub>1</sub>/FVC pada Anak di Perkotaan dan Pedesaan

### Abstrak

Perkotaan merupakan tempat dengan tingkat paparan polusi udara yang tinggi. Polusi udara ini menyebabkan penurunan fungsi paru-paru dan obstruksi pada saluran pernapasan. Absorpsi partikel debu dan polusi terhirup masuk paru-paru melalui mekanisme pernapasan. Masuknya bahan toksik ini akan bereaksi dengan sel sehingga menimbulkan radikal bebas yang akan merusak sel terutama pada sistem pernapasan. Tujuan penelitian ini adalah mengetahui perbedaan kapasitas vital paru dan rasio *forced expiration volume in 1 second/forced vital capacity* (FEV<sub>1</sub>/FVC) pada anak di perkotaan dengan tingkat polusi yang cukup tinggi dibanding dengan pedesaan yang tidak terpapar polusi. Penelitian merupakan penelitian observasional analitik dilaksanakan pada bulan September–Desember 2016 dengan jumlah sampel 60 orang terdiri atas 30 orang anak di Kota Palembang dan 30 anak di daerah Musi Rawas. Analisis data untuk mengetahui perbedaan kapasitas vital paru dan rasio FEV<sub>1</sub>/FVC pada anak di pedesaan dan perkotaan menggunakan uji T tidak berpasangan. Hasil penelitian didapatkan nilai rerata kapasitas vital paru anak di perkotaan (1.205 mL) lebih rendah daripada nilai rerata kapasitas vital paru anak di pedesaan (1.493 mL) dan didapatkan perbedaan bermakna nilai kapasitas vital paru antara anak di perkotaan dan pedesaan (p=0,004). Nilai rasio FEV<sub>1</sub>/FVC anak di perkotaan (91,05%) lebih rendah daripada rasio FEV<sub>1</sub>/FVC anak di pedesaan (93,96%) yang berbeda bermakna (p=0,001). Simpulan, nilai rerata kapasitas vital paru dan rasio FEV<sub>1</sub>/FVC anak di daerah perkotaan lebih rendah daripada nilai rerata kapasitas vital paru anak di daerah pedesaan.

**Kata kunci:** FEV<sub>1</sub>, FVC, kapasitas vital paru, spirometri

Received: 9 September 2017; Revised: 31 July 2018; Accepted: 25 August 2018; Published: 30 August 2018

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## Introduction

Many developing countries are faced with air pollution problems. Air pollution is an entry or mixing of harmful elements into the atmosphere so that it can lead to environmental damage that can reduce the quality of the environment. Air pollution is important study material because of the existence of chemical substances, biological materials, and particles that harm people, which humans can't avoid breathing or breathing air.<sup>1</sup>

In general, there are two sources of air pollution, ie pollution due to natural sources, such as volcanic eruptions, and those derived from human activities, such as those originating from transportation, plant emissions, forest burning, and others. In the world, there are six major types of air pollutants derived from human activities: carbon monoxide (CO), sulfur oxide (SO<sub>x</sub>), nitrogen oxide (NO<sub>x</sub>), particulates, hydrocarbons (HC), and photochemical oxides, including ozone. In Indonesia, approximately 70% of air pollution caused by motor vehicle emissions. Motor vehicles release hazardous substances that can have negative impacts, both on human health and on the environment, such as lead (Pb), nitrogen oxide (NO<sub>x</sub>), hydrocarbons (HC), carbon monoxide (CO), and photochemical oxides (Ox). Motor vehicles contribute nearly 100% of lead, 13–44% of suspended particulate matter (SPM), 71–89% of hydrocarbons, 34–73% NO<sub>x</sub>, and almost all carbon monoxide (CO). The main source of dust comes from burning household waste, which includes 41% of the dust source.<sup>2</sup>

Air pollution usually occurs in large industrial density cities as well as biomass burning areas that produce gases that contain substances above the limits of reasonableness. The narrowness of green land or trees in an area can also worsen the air quality in the place. More and more motor vehicles and industrial tools that emit gas that pollute the environment will get worse also air pollution that occurs.<sup>3</sup>

Air pollution contains ultrafine particles of combustion emissions, PAH compounds, carbon organic, inorganic elements (metal) and compounds contained in biomass burning ultrafine smoke particles such as benzo pyrene (BaP), CO, and Pb, when the compound enters the cell will produce radical compounds such as O<sub>2</sub> (superoxide radical), OH (hydroxyl radical) and H<sub>2</sub>O<sub>2</sub> (hydrogen peroxide). These substances can react directly with extracellular and intercellular

elements such as proteins, lipids, carbohydrates and DNA.<sup>2</sup>

Toxic materials in the form of organic gases and ultrafine particles can enter the alveolus of the lungs through the respiratory system and can enter into circulatory system and transferred to other organs. The entry of these toxic substances will react with the cells causing reactive oxygen species (ROS). When the radical compound reacts with the cell, it will cause lipid peroxidation, membrane protein damage and DNA damage. Lipid peroxidation results in a decrease in membrane fluidity in the membrane barrier function resulting in the destruction of even cell death.<sup>4</sup>

Ultrafine particles can cause respiratory effects, namely pulmonary inflammation, allergic response, and decreased lung function. Based on research by Masrurroh et al.<sup>5</sup> the exposure of particles concentrated in the air in the short term, can induce the occurrence of rat inflammation of pulmo such as emphysema, defined as a widening of the alveoli, alveoli ducts and loss of the boundary membrane between of alveoli and alveoli ducts. The loss of the boundary between the alveoli and subsequent alveoli widening is due to cell death or cell apoptosis in the alveoli membrane.<sup>5,6</sup>

Pulmonary inflammation, allergic response, and pulmonary emphysema as a result of exposure to forest fire haze are expected to affect the results of lung spirometry examination. Exposure to air pollution will generally cause obstruction in the respiratory tract as indicated by a decrease in FEV<sub>1</sub>/FVC ratio. Children are vulnerable ages to be affected by the effects of air pollution on health that can inhibit the growth and intellectual development of children.<sup>7</sup>

This study aims to determine differences in vital lung capacity and FEV<sub>1</sub>/FVC ratios of urban children exposed to air pollution and rural children not exposed to air pollution.

## Methods

This study was a comparative descriptive study to see differences in lung function in children in urban and rural. This research was conducted in September–December 2016 on two places, namely in one elementary school in the city of Palembang and in one of the primary schools in the area of Musi Rawas aren't exposed to air pollution. This research has received a certificate of ethics number: 07/X/2016 from Research Ethics

Committee, Unit of Bioethics, Humanities and Islamic Medicine (UBHKI), Faculty of Medicine, Universitas Muhammadiyah Palembang. The variables studied were pulmonary vital capacity and ratio of FEV<sub>1</sub>/FVC in children in urban and rural areas.

Data analysis using primary data from the result of measurement directly both variable in two group of the sample by using spirometry tool. Procedure examination with the tool, steps as follows: sample asked to stand by inserting mouthpiece spirometry into the mouth and nose covered with nose clamp tool, then asked to breathe as for five times and ends with maximum inspiration and expiration maximally. The experiment was repeated three times, taking the highest value. After that, the data were analyzed by unpaired t test and presented in the tabular and narrative form.

## Results

The study was conducted on elementary school children in urban and rural areas with a total samples of 70 people. Each group consisted of 35 samples who met inclusion criteria and didn't meet the exclusion criteria. Sampling was done by stratified random sampling technique in 4<sup>th</sup>, 5<sup>th</sup> and 6<sup>th</sup> grade elementary school children.

The average result of vital capacity of lungs in urban children was 1,205 mL, smaller than the lung's vital capacity for rural children of 1,493 mL. After normality test data obtained all data was normally distributed. Then after data analysis using unpaired t test, got value  $p=0.010$  ( $p<0.05$ ) so it can be concluded that there was significant difference of vital capacity of lung in children in urban and in rural (Table).

The average FEV<sub>1</sub>/FVC ratio for children in urban areas was 91.05%, greater than the ratio of FEV<sub>1</sub>/FVC for rural children of 93.06%. After

the normality test data obtained all data was normally distributed. Then after data analysis using unpaired t test, got value  $p=0.030$  ( $p<0.05$ ) so it can be concluded that there was significant difference of ratio of FEV<sub>1</sub>/FVC between children in urban and in rural (Table).

## Discussion

From the results obtained value of vital lung capacity in children in urban lower than children in rural areas. This is consistent with Sandra<sup>8</sup> research on the Indonesian human lung capacity survey which results in differences in vital pulmonary capacity for each different population.

Forced vital capacity (FVC) is defined as the volume of air exhaled with maximal effort from a maximum inspiration. Vital capacity is similar to the FVC. Many factors that affect a person's vital lung capacity include age, sex, physical activity, nutritional status, history of disease and environment. Urban environments have high smoke exposure that can affect lung function. In addition, low physical activity in children in urban areas causes vital lung capacity to be lower than children in rural areas.<sup>9</sup>

By performing regular physical activity, vital capacity of a person's lung increases. Theoretically, the muscles can contract maximally so that chest cavity widened, it causes the amount of O<sub>2</sub> entering the bloodstream in the lung increases as well as the increase of pulmonary blood flow. Thus total amount of O<sub>2</sub> entering the blood also increases during physical activity, otherwise amount of CO<sub>2</sub> released will also increase.<sup>10</sup>

From the results of this study, obtained the value of the ratio of FEV<sub>1</sub>/FVC in children in urban lower than children in rural. This is consistent with the research of Barros et al.<sup>11</sup> explains that the ratio of FEV<sub>1</sub>/FVC can detect the presence of airway obstruction in many individuals such

**Table Vital Lung Capacity Value and Ratio Value FEV<sub>1</sub>/FVC**

	Mean (mL)	Standard Deviation	p'	p''
Vital lung capacity				
Urban	1,205	0.63800	0.8979	0.010
Rural	1,493	0.36028	0.9764	
Rasio FEV <sub>1</sub> /FVC				
Urban	91.05	4.47372	0.7885	0.030
Rural	93.96	7.29595	0.8790	

p': test data normality, p'': unpaired t test

as the ratio of FEV<sub>1</sub>/SVC so reliable to detect the presence of later lung obstructive disease. Sandra9 study also obtained traffic police staf who had restriction lung function status of 8 people (38.1%) more than police staf had restriction lung function status of 2 people (9.5%). This is in line with the decline in air quality characterized by high levels of NO<sub>2</sub>, SO<sub>2</sub> and dust from air pollution and motor vehicle fumes.

Pollution from vehicle fumes contains ultrafine particles that have a very small size ( $\leq 0.1 \mu\text{m}$ ) that can be inhaled up to alveoli. Ultrafine particles (UFPs) cause the mucociliary and alveolar clearance functions to be exceeded, allowing the ultrafine particles to persist in the alveolus and causing immediate reaction with epithelial cells and causing cell damage to alveoli. UFP can cause effects on the respiratory system, namely increased pneumonia, allergic response, and decreased lung function. The exposure of particles concentrated in the air in the short term, may induce lung inflammation such as emphysema, defined as a widening of the alveoli, alveoli ducts and loss of the boundary membrane between alveoli and alveoli ducts. The loss of the boundary between alveoli and subsequent alveoli widening is due to cell death or cell apoptosis in the alveoli membrane. While the destruction of the alveolar septum is a damage to alveolar membrane which occurs damage to elastin protein and collagen epithelial membrane. Exposure to urban air pollution in general will cause obstruction in the respiratory tract as indicated by a decrease in the ratio of FEV<sub>1</sub>/FVC.<sup>4-6</sup>

Trissekti et al.<sup>12</sup> research about the average FEV<sub>1</sub> value of basement parking attendant is greater than the average FEV<sub>1</sub> value of open space parking practitioners, because basement parking has a good exhaust fan working system so as to minimize the pollution caused by motor vehicle fume effectively and quickly so that not cause respiratory tract disturbance.

### Conclusion

The mean value of lung vital capacity and the ratio of FEV<sub>1</sub>/FVC of children in urban areas is lower than mean value of vital lung capacity of children in rural areas.

### Conflict of Interest

The authors declare that they have no conflict of interest.

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## RESEARCH ARTICLE

## Influence of A Clear Vision on Nurse Performance at Al Islam Hospital Bandung

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### Abstract

Nurses have to work as a team to be able to perform their job effectively. One of the factors that play roles in building good teamwork is a clear vision. This study aimed to review the influence of a clear vision towards nurse performance at Al Islam Hospital Bandung in 2017. This study was a cross-sectional verification quantitative case study on a population of 212 nurses working at the inpatient unit of Al Islam Hospital Bandung. A sample of 147 nurses participated in the survey after the proportional stratified random sampling was applied based on the inpatient room and the length of the work period. Data collected by distributing questionnaires to nurses and head nurses. The statistical analysis was then performed using simple linear regression analysis. Pearson correlation coefficient formula was used to discover the correlation between two variables, followed by the determination coefficient analysis to explain the strength of the influence the X variable has on the Y variable. Results showed that a clear vision gave 56.6% influence on the quantity of nurse performance, 57.9% influence on the quality of nurse performance, and 76.5% influence on both quantity and quality of nurse performance. In conclusion, a clear vision gives a positive impact towards nurse performance both quantitatively and qualitatively. Hence, clearer vision means better nurse performance.

**Keywords:** Nurse, performance, vision

## Pengaruh Visi yang Jelas terhadap Kinerja Perawat di Rumah Sakit Al Islam Bandung

### Abstrak

Perawat harus bekerja sama dalam satu tim agar memiliki kinerja yang tinggi. Salah satu yang berperan untuk membentuk kerja sama tim yang baik adalah visi yang jelas. Penelitian ini bertujuan mengkaji pengaruh visi yang jelas terhadap kinerja perawat di Rumah Sakit Al Islam Bandung pada tahun 2017. Metode penelitian yang digunakan adalah studi kasus dengan jenis penelitian analisis kuantitatif yang menggunakan rancangan *cross sectional* dan verifikatif. Populasi penelitian ini adalah perawat yang bekerja di Unit Rawat Inap Rumah Sakit Al Islam Bandung sebanyak 212 orang. Sampel diambil menggunakan *proportional stratified random sampling* berdasar atas ruang rawat inap dan masa kerja perawat, yaitu sebanyak 147 orang. Teknik pengumpulan data dilakukan dengan membagikan kuesioner kepada perawat dan kepala perawat. Data dianalisis dengan analisis regresi linear sederhana. Untuk mengetahui korelasi kedua variabel digunakan rumus koefisien korelasi Pearson, kemudian analisis koefisien determinasi untuk menjelaskan seberapa besar perubahan nilai pada variabel Y dapat diprediksi oleh perubahan variabel X. Hasil analisis data menunjukkan bahwa visi yang jelas memberikan pengaruh sebesar 56,6% terhadap kuantitas kinerja perawat, 57,9% terhadap kualitas kinerja perawat, dan 76,5% terhadap kuantitas dan kualitas kinerja perawat. Simpulan, visi yang jelas memberikan pengaruh positif terhadap kinerja perawat baik secara kuantitas maupun kualitas, semakin tinggi atau kuat visi yang jelas maka semakin meningkat kinerja perawat.

**Kata kunci:** Kinerja, perawat, visi

Received: 12 July 2017; Revised: 13 February 2018; Accepted: 17 April 2018; Published: 30 August 2018

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## Introduction

Hospital nurses working in a team should have a clear vision for the future.<sup>1</sup> A clearly defined vision is essential to make sure that everyone understands the vision.<sup>2</sup>

Schwirian<sup>3</sup> defines performance as the effectiveness and productivity of nurses in playing their roles and assuming their responsibilities related to providing direct patient care. Performance, as defined by Schwirian, is considered as a classical definition in nursing, and many academicians have reviewed the meaning, the first definition of performance to mention nursing specifically. Therefore, the description of nurse performance from Schwirian used in this study.

The Schwirian's model of nurse performance is considered to be the basis of nurse performance. This model involves six domains as illustrated below.<sup>3</sup> The first domain is the leadership domain that deals with actions that nurses can do in performing their leadership functions. Leadership is defined as an activity to praise, mobilize, and inspire others enthusiastically towards achievement through giving advice, guidance, and teaching regardless of the specific area of an individual. Leadership involves items such as the ability to guide other health team members and delegate effectively. The second domain is teaching or collaboration. Education or cooperation relates to the behaviors adopted by a nurse when he or she provides instructions to patients and family members and other health professionals who contribute to the welfare of patients through the methodology, knowledge, and other solutions. Teaching or collaboration involves items such as teaching preventive health measures and encouraging families to participate in patient care. The third domain is planning or evaluation. Planning or assessment is a behavior that involves the ability to identify and evaluate patient care services dynamically and holistically. The fourth domain is the interpersonal relationship or communication. Interpersonal relationship or disclosure relates to the behavior of a nurse and the scope of interpersonal relationship or connection between the nurse and the patients as well as other health staff. Interpersonal relationship and communication involve items such as helping patients to communicate with others and contributing to productive work relationships with other health team members. The fifth domain is professional

development. Professional development refers to high performance and responsible behavior towards professional growth, knowledge updates, and expertise in professional nursing activities and majors. Professional development describes the characteristics of professionalism, such as using learning opportunities for personal and professional growth. The five performance domains in Schwirian's nurse performance model are vital factors when nurses have to work well to achieve the organizational and job goals. It is clear that performance has been defined based on the behaviors and motivation of individuals to work. Schwirian indicates that the model can be used in a range of performance assessments and, specifically, on nurse performance evaluation.<sup>4-8</sup>

According to Nursing and Midwifery Office, New South Wales Department of Health,<sup>1</sup> a clear vision is one of the foundations to build teamwork in a nursing team. The collaboration will result in high performance within an organization, reduce errors, produce quality services, and improve productivity and patient satisfaction.<sup>9</sup>

An unclear vision may hamper the teamwork of a nursing team. As a result, the time required to provide health services is longer than it should be. This condition indicates that the performance is sub-optimal, preventing the team to provide optimum health services thus will influence the patients satisfaction level.<sup>10</sup>

The purpose of this study was to examine the influence of clear vision on the performance of nurses at Al Islam Hospital Bandung.

## Methods

This study applied the case study method. A cross-sectional quantitative analytical study that was also a verification study aimed to determine the influence of nurses' teamwork on the nurse performance at the Inpatient Unit of Al Islam Hospital Bandung in 2017.

The population of this study consisted of 212 nurses who worked in the Inpatient Unit of Al Islam Hospital Bandung. Sampling for this study was performed using proportional stratified random sampling method based on the inpatient room and nurse's work period. The sample size to achieve was 147 people.

The inclusion criteria of this study were the working period of at least one year, education of at least Diploma in Nursing, and working at the Inpatient Unit of Al Islam Hospital Bandung. The exclusion criteria in this study were on leave,

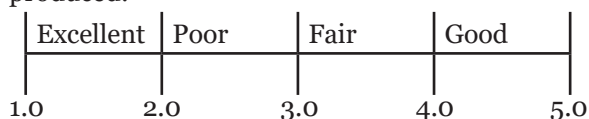


assigned in an ongoing education program, and working in the Intensive Care Unit or ICU.

Data on a clear vision and nurse performance collected by distributing questionnaires that tested for validity and reliability to the nurses and head nurses at the Inpatient Unit of Al Islam Hospital Bandung.

After data were collected, analysis of respondent characteristics was conducted to understand the background of respondents. The result of this analysis was subsequently used as an input to clarify the study data. Data on characteristics of respondents consisted of gender, age, education, and employment. A descriptive analysis was used to describe respondent's opinion on each statement in the questionnaire in the form of scale. The scales used were excellent, good, fair, and poor with the following scoring criteria: maximum index value = highest scale = 4, minimum index value = lowest scale = 1, interval distance = (maximum value-minimum value):  $4 = (4-1) / 4 = 0.75$ .

Thus, the following continuous line was produced:



The analysis technique used in this study was

simple linear regression analysis to determine the influence of clear vision variable (X) on nurse performance variable (Y).

To understand the correlation between the two variables, the Pearson Correlation Coefficient formula was used with the following criteria of correlation values: coefficient interval of 0.00–0.199 represents a very weak correlation; coefficient interval of 0.20–0.399 represents a weak correlation; coefficient interval of 0.40–0.599 represents a moderate correlation; coefficient interval of 0.60–0.799 represents a strong correlation; and coefficient interval of 0.80–1.000 represents a very strong correlation.<sup>10</sup>

The analysis of the coefficient of determination was then performed to explain the extent of the changes in variable Y could be predicted by changes in variable X. The results of the analysis were then interpreted using the following rules: R<sup>2</sup> of 0.00–19.99 represents very low influence; R<sup>2</sup> of 20.00–39.99 represents low influence; the value of R<sup>2</sup> 40.00–59.99 represents medium influence; R<sup>2</sup> of 60.00–79.99 represents a high influence; and R<sup>2</sup> of 80.00–100 represents a very high influence.<sup>12</sup>

## Results

Table 1 describes the characteristics of the

**Table 1 Respondent Characteristics**

Variables	n=147		%
	Head Nurse (n=9)	Nurse (n=138)	
Gender			
Male	0	25	17.0
Female	9	113	83.0
Age (years)			
<20	0	42	28.6
20–25	0	58	39.5
26–30	0	16	10.9
31–35	8	14	15.0
36–40	1	0	0.7
41–45	0	4	2.7
>45			
Education level			
Diploma in nursing	9	138	100.0
Length of working period (year)			
<1	0	34	15.6
1–3	0	59	23.2
3–10	0	11	40.1
10–15	2	7	8.8
15–20	7	4	9.5
>20	0		2.8

**Table 2 Score for Clear Vision**

Question	Head Nurses' Mean	Nurses' Mean
1 Explanation on the team vision by the head nurse is described with....	3.20	3.30
2 Implementation of value of vision among nurses....	3.10	3.29
3 Explanation on the unity of instruction is described by the head nurse to all nurse with....	3.16	3.29
Mean	3.15	3.29

**Table 3 Score for Nurse Performance Quantity**

Question	Head Nurses' Mean	Nurses' Mean
1 Give praise for achievement to those under his/her direction....	2.93	3.27
2 Give recognition for achievement to those under his/her direction....	3.13	3.32
3 Delegate responsibility for care based on assessment of priorities of nursing care....	3.10	3.54
4 Delegate responsibility for care based on ability....	3.18	3.60
5 Delegate responsibility for care based on limitation of health care personnel....	3.14	3.32
6 Guide other health team members in planning for nursing care....	3.17	3.46
7 Accept responsibility for the level of care under his/her direction....	3.37	3.55
8 Remain open to the suggestions of those under his/her direction....	3.37	3.61
9 Use suggestions of those under his/her direction when appropriate....	3.27	3.42
10 Teach a patient's family members about the patient's needs....	3.54	3.66
11 Teach preventive health measure to patients and their families....	3.59	3.66
12 Identify and use community resources in developing a plan of care for a patient and his/her family....	2.84	3.23
13 Identify and use community resources in developing a plan of care for a patient and his/her family....	2.84	3.19
14 Encourage the family to participant in the care of the patient....	3.65	3.82
15 Identify resources within the health care agency....	2.92	3.19
16 Use resources within the health care agency....	2.93	3.20
17 Develop a plan of care for a patient and his/her family....	3.48	3.67
18 Communicate facts to patients and their families....	3.60	3.57
19 Communicate ideas to patients and their families....	3.31	3.51
20 Plan for the integration of patient needs with family needs....	3.39	3.50
21 Coordinate the plan of nursing care with the medical plan of care....	3.50	3.71
22 Identify and include in nursing care plans anticipated changes in patient's conditions....	3.46	3.61
23 Evaluate results of nursing care....	3.82	3.78
24 Communicate a feeling of acceptance of each patient and a concern for the patient's welfare....	3.11	3.54
25 Seek assistance when necessary....	3.69	3.69
26 Help patients communicate with others....	3.37	3.58

27	Verbally communicate facts, ideas, and feelings to other health care team members....	3.40	3.52
28	Promote the patients' rights to privacy....	3.63	3.70
29	Contribute to an atmosphere of mutual trust, acceptance, and respect among other health team members....	3.37	3.67
30	Explain nursing procedures to a patient prior to performing them....	3.81	3.80
31	Use nursing procedures as opportunities for interaction with patients....	3.65	3.77
32	Contribute to productive working relationships with other health team members....	3.37	3.65
33	Help a patient meet his/her emotional needs....	3.18	3.50
34	Use opportunities for patient teaching when they arise....	3.41	3.59
	Mean	3.34	3.54

respondents. Most of the nurses at the Inpatient Unit of Al Islam Hospital Bandung were female nurses in various ages; however, the majority were in the productive age, had a Diploma in Nursing degree, and had been working for more than three years.

Respondents' scoring for clear vision (X) was the combined scoring of the nurses and the head nurses for clear vision, which is listed in Table 2.

Table 2 shows that the head nurses' mean score for this dimension (X) was 3.15 and the nurses' mean score for the clear vision dimension (X) was 3.29.

The respondents' scoring for nurse performance (Y) was divided into the nurses' and head nurses' scores for performance quantity, performance quality, and combined performance quantity and quality (Y).

Table 3 presents that the mean scores for nurse performance quantity (Y) given by head nurses and nurses were 3.34 and 3.54, respectively.

Table 4 shows that the mean score for the head nurses' response to nurse performance quality (Y) was 2.94 and the mean score for the nurses' response to nurse performance quality (Y) was 2.95.

The influence of their clear vision on nurse performance analyze using simple linear regression analysis performed by SPSS software 18. The result of  $Y = 1.485 + 0.607 X$ .

The constant value implied that when the clear vision (X) was zero or the nurse performance quantity (Y) was not influenced by the clear view, the mean nurse quantitative performance was 1.485. Meanwhile, the regression coefficient b implied that if the explicit vision variable (X) increased by one unit, the nurse performance

quantity (Y) would increase by 0.607. When the regression coefficient was positive, the meaning was that the clear vision brought a positive influence to the nurse performance quantity; hence, the higher or stronger the clear vision was, the higher the increase in the nurse performance quantity.

To determine the relationship between clear vision and nurse performance quantity, Pearson Correlation analysis used. Based on the processing results of the SPSS software 18, the correlation coefficient (r) of the correlation between clear vision and nurse performance quantity was 0.752, meaning that there was a strong relationship between clear vision and the nurse performance. The amount of the influence of the clear vision towards the quantity of nurse performance seen by the coefficient of determination that is calculated using the following formula:  $KD = r^2 \times 100\% = (0.752)^2 \times 100\% = 56.6\%$ . The ratio of determination of 56.6% resulted from this formula showed that the clear vision brought 56.6% influence on nurse performance quantity with the remaining 43.4% of the nurse performance quantity could be explained by other variables that not examined in this study.

The influence of clear vision on nurse performance quantity analyze using simple linear regression analysis performed by SPSS software 18. The result of  $Y = 1.485 + 0.607 X$ .

The constant value A implied that when the clear vision (X) was zero or the nurse performance quantity (Y) was not influenced by the clear vision, and the mean nurse quantitative performance was 0.810. Meanwhile, the regression coefficient b implied that if the clear vision variable (X)

**Table 4 Score for Nurse Performance Quality**

<b>Question</b>	<b>Head Nurses' Mean</b>	<b>Nurses' Mean</b>
1 Give praise for achievement to those under his/her direction....	2.75	2.77
2 Give recognition for achievement to those under his/her direction....	2.86	2.75
3 Delegate responsibility for care based on assessment of priorities of nursing care....	2.86	2.78
4 Delegate responsibility for care based on ability....	2.93	2.89
5 Delegate responsibility for care based on limitation of health care personnel....	2.86	2.91
6 Guide other health team members in planning for nursing care....	2.89	2.92
7 Accept responsibility for the level of care under his/her direction....	2.91	2.89
8 Remain open to the suggestions of those under his/her direction....	3.01	2.98
9 Use suggestions of those under his/her direction when appropriate....	2.95	2.87
10 Teach a patient's family members about the patient's needs....	3.05	3.10
11 Teach preventive health measure to patients and their families....	3.03	2.97
12 Identify and use community resources in developing a plan of care for a patient and his/her family....	2.47	2.80
13 Identify and use community resources in developing a plan of care for a patient and his/her family....	2.52	2.72
14 Encourage the family to participant in the care of the patient....	3.06	3.01
15 Identify resources within the health care agency....	2.68	2.76
16 Use resources within the health care agency....	2.70	2.88
17 Develop a plan of care for a patient and his/her family....	3.03	2.97
18 Communicate facts to patients and their families....	3.03	2.95
19 Communicate ideas to patients and their families....	2.93	2.87
20 Plan for the integration of patient needs with family needs....	2.93	2.95
21 Coordinate the plan of nursing care with the medical plan of care....	2.95	2.97
22 Identify and include in nursing care plans anticipated changes in patient's conditions....	2.97	2.94
23 Evaluate results of nursing care....	3.08	3.02
24 Communicate a feeling of acceptance of each patient and a concern for the patient's welfare....	2.87	2.93
25 Seek assistance when necessary....	3.12	3.07
26 Help patients communicate with others....	3.01	3.02
27 Verbally communicate facts, ideas, and feelings to other health care team members....	2.92	2.90
28 Promote the patients' rights to privacy....	3.09	3.05
29 Contribute to an atmosphere of mutual trust, acceptance, and respect among other health team members....	2.90	3.01
30 Explain nursing procedures to a patient prior to performing them....	3.14	3.20
31 Use nursing procedures as opportunities for interaction with patients....	3.03	3.03
32 Contribute to productive working relationships with other health team members....	2.96	2.97
33 Help a patient meet his/her emotional needs....	2.94	2.89

34 Use opportunities for patient teaching when they arise....	2.97	3.03
35 Use learning opportunities for ongoing personal and professional growth....	3.02	3.11
36 Demonstrate a knowledge of the legal boundaries of nursing....	3.05	2.96
37 Demonstrate knowledge in the ethics of nursing....	3.03	3.13
38 Accept and use constructive criticism....	3.07	3.24
Mean	2.94	2.95

increased by one unit, the nurse performance quantity (Y) would increase by 0.662. When the regression coefficient was positive, the meaning was that the clear vision brought a positive influence to the nurse performance quantity; hence, the higher or stronger the clear vision was, the higher the increase in the nurse performance quantity.

The relationship between clear vision and nurse performance quality analyzed using Pearson correlation analysis. Based on the results the correlation coefficient (r) of the correlation between clear vision and nurse performance quality was 0.761, meaning that there was a strong relationship between clear vision and nurse performance quality.

The amount of the influence that the clear vision brought to the quality of nurse performance seen by the coefficient of determination, which was calculated using the following formula:  $KD = r^2 \times 100\% = (0.761)^2 \times 100\% = 57.9\%$ . The coefficient of a determination result of 57.9% showed that clear vision brought 57.9% influence on the quality of nurse performance, while the remaining 42.1% of the nurse performance quality explained by other variables not examined in this study. Simple linear regression analysis was performed using SPSS software 18 with the following result:  $Y = 1.179 + 0.625 X$ .

## Discussion

This study presents that, based on the assessment of nurses and head nurses, a clear vision brings the positive influence on nurse performance, both quantitatively and qualitatively; hence, the higher or stronger the clear vision is, the more increase seen in the nurse performance increased. This phenomenon explained as follows.

Nursalam<sup>13</sup> stated that a vision is simple and carries utmost importance because a vision can affect the views of other people. This vision drafted, concisely, easily understood, and

implemented by everyone.

Nurses working in a unit must have a clear vision for the future and shared values that should be displayed and reviewed frequently. Individual team goals should be agreed from the beginning of a shift to ensure that everyone is heading towards the same direction.<sup>1</sup>

Clearly defined vision is essential so that everyone can understand the concept. A clear vision helps the nurse as the team member to know where the team is going and helps the team to understand when success achieved by determining what the team is doing and what the team wants to accomplish in details. The members to work together efficiently and tend to make the success.<sup>2</sup>

A clear vision creates a sense of belonging. With this, the nurse as a team member manages to feel that he or she "has" goals and work towards achieving those goals. Also, the sense of belonging will last a long time if members consider that other members support the same vision.<sup>2</sup>

A clear vision helps to develop team unity while obscuring vision extends confusion or, sometimes, individualism. If the nurse as the team member does not agree about the meaning of the vision of the team, he or she will work individually to achieve their interpretation of the vision. He or she may also try to protect his or her own goals, even if it is at the expense of the team.<sup>2</sup>

A clear vision is a critical component to ensure that members of the team are leading towards the same goal. A lot of time, money, and energy, not to mention motivation and enthusiasm, are lost when each member of the team does not aim for the same results.<sup>2</sup>

## Conclusion

A clear vision brings a positive influence to nurse performance, both quantitatively and qualitatively. The higher or stronger the clear vision is, the higher the increase is seen in the



nurse performance increased.

### Conflict of Interest

The authors declare no conflict of interests.

### Acknowledgment

We would like to extend our gratitude to the Director of Al Islam Hospital Bandung and all head nurses and nurses at the Inpatient Unit of Al Islam Hospital Bandung.

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## RESEARCH ARTICLE

## Factors Affecting the Incidence of Filariasis in Welamosa Village Ende District East Nusa Tenggara

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### Abstract

Filariasis is a chronic communicable disease caused by filarial worms, which consists of three species: *Wucherria bancrofti*, *Brugaria malayi*, and *Brugaria timori*. This disease is transmitted through mosquito bites, infects lymph tissue (lymph) and causes swelling of the legs, breasts, arms and genital organs. Welamosa village, Ende district, located in East Nusa Tenggara (NTT) province is reported as one of the highest cases of 40 cases in 2015. This research aims to analyze the influence of social factor of demography and socio-cultural environment factor to elephantiasis incident in Welamosa village, Ende district. The study was conducted in July–September 2016 in Welamosa village and Wolowaru sub-district, Ende district. The type of research was observational analytic with case-control with 49 people as sampling. The research instrument used questionnaire and check list. The data analysis used statistical test of SPSS program with backward regression logistic test. The results showed five variables as risk factors of elephantiasis occurrence, age (OR=42.518), education (OR=38.248), occupation (OR=8.404), outdoor activity at night (OR=5.097) and sex (OR=0.193). In conclusion, social demographic factors (age, gender, occupation, and education) and environmental and social-cultural factors of attitude (outdoor activities at night) are risk factors for filariasis incidence in Welamosa village, Ende district.

**Keywords:** Filariasis, Ende district, Welamosa

## Faktor yang Memengaruhi Kejadian Penyakit Filariasis di Desa Welamosa Kabupaten Ende Nusa Tenggara Timur

### Abstrak

Filariasis adalah penyakit menular menahun yang disebabkan oleh parasit berupa cacing filaria yang terdiri atas tiga spesies, yaitu *Wucherria bancrofti*, *Brugaria malayi*, dan *Brugaria timori*. Penyakit ini menginfeksi jaringan limfe (getah bening) dan menular melalui gigitan nyamuk, serta menyebabkan pembengkakan kaki, tungkai, payudara, lengan, dan organ genital. Desa Welamosa, Kabupaten Ende terletak di Provinsi Nusa Tenggara Timur (NTT) dilaporkan sebagai salah satu kecamatan dengan kasus filariasis tertinggi, yakni 40 kasus pada tahun 2015. Tujuan penelitian adalah menganalisis pengaruh faktor sosial demografi dan faktor lingkungan sosial budaya terhadap kejadian filariasis di Desa Welamosa, Kabupaten Ende. Penelitian dilaksanakan pada bulan Juli–September 2016 di Desa Welamosa dan Kecamatan Wolowaru, Kabupaten Ende. Jenis penelitian merupakan analitik observasional dan pengambilan sampel menggunakan *case control* sebanyak 49 orang. Instrumen penelitian menggunakan kuesioner dan ceklis. Analisis data menggunakan uji statistik program SPSS dengan *backward regression logistic test*. Hasil penelitian menunjukkan lima variabel yang merupakan faktor risiko kejadian filariasis, yaitu usia (OR=42,518), pendidikan (OR=38,248), pekerjaan (OR=8,404), aktivitas di luar rumah pada malam hari (OR=5,097), dan jenis kelamin (OR=0,193). Simpulan, faktor sosial demografi (usia, jenis kelamin, pekerjaan, dan pendidikan) serta faktor lingkungan sosial budaya sikap (aktivitas di luar rumah pada malam hari) merupakan faktor risiko terhadap kejadian filariasis di Desa Welamosa, Kabupaten Ende.

**Kata kunci:** Filariasis, Kabupaten Ende, Welamosa

Received: 18 November 2017; Revised: 4 August 2018; Accepted: 27 August 2018; Published: 30 August 2018

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## Introduction

Filariasis is a contagious disease caused by infections of filarial worms transmitted through the bite of various types of mosquitoes. Filariasis worms consist of 3 species: *Wucherria bancrofti*, *Brugaria malayi*, and *Brugaria timori*. All of these species can be found in Indonesia, but more than 70% of filariasis cases in Indonesia are caused by *Brugaria malayi*.<sup>1</sup>

In 2014, filariasis cases affect 632 million (57%) of the population living in Southeast Asia (9 endemic countries) and 410 million (37%) of the population live in Africa (35 endemic countries). While the rest (6%) suffered by residents living in the Americas (4 endemic countries), the Eastern Mediterranean (3 endemic countries) and the western Pacific (22 endemic countries). Since 2000, USD 5.6 million fund has been granted worldwide to eradicate filariasis. In an attempt to eliminate filariasis by 2020, WHO has established a global agreement (The Global Goal of Elimination of Lymphatic Filariasis as a Public Health Problem by The Year 2020).<sup>2</sup>

In Indonesia filariasis was firstly reported by Haga and Van Eecke in 1889. Among the three types filaria worms, *Brugaria malayi* has the most widespread effect in Indonesia. *Brugaria timori* is found only in Timor island, Flores, Rote, Alor and several small islands in East Nusa Tenggara (NTT).<sup>1</sup>

The five provinces with the highest filariasis chronic cases in 2016 were NTT (2,864), Aceh (2,372), West Papua (1,244), Papua (1,184), and West Java (955). With 4.7% of the average prevalence of microfilariae in 2015. In case of the transmission of filariasis in endemic areas is not handled then the number of elephantiasis disease patient will increase from 13,032 to 4,807,148 infected people.<sup>1</sup>

From 2002–2014 the cumulative cases of filariasis in chronic disability in NTT were 3,175 cases.<sup>1</sup> In 2015, there were 68 new filariasis cases occurring in Belu, Ende, Ngada, West Sumba, and Rote Ndao regencies with the highest infected areas being Rote Ndao, Central Sumba, Ngada, East Sumba, Kupang, and Ende.<sup>3</sup>

Ende district ranks the sixth in chronic cases in 2015, with the number of cases as many as 348 cases.<sup>3</sup> Most cases were found in Welamosa village, in which there were 40 cases, Detusoko 38 cases and Kota Baru with 37 cases with over 95% of over 15 years old patients.<sup>4</sup>

Filariasis can cause lifelong disability and

social stigma in the form of exclusion, disrupted social activities, and discomfort for the patient and his family when it has caused swelling of the hands, feet, breasts and scrotum. Another impact is the economic burden of medical expenses, productive days lost due to illness, and household members who takes care for the sick.<sup>5</sup>

Based on the data showing the high filariasis cases in Ende district, it is necessary to do a handling so that the number of cases does not become higher. The first step to do the handling is to identify the factors that influence the incidence of filariasis.

Environmental factors are the triggers of filariasis incidence. Environmental factors at home include the physical environment of houses that do not meet the criteria of healthy homes, such as ceiling construction and wall house, lighting, and humidity, are also to trigger the incidence of filariasis.<sup>6,7</sup> Meanwhile, the external environmental factors in question are those associated with mosquito breeding sites as vectors of the disease. These factors include stagnant water, rice fields, swamps, aquatic plants, shrubs, and animal reservoirs.<sup>7</sup> The next risk factor is the habit of going out at night and the habit of not using mosquito nets while sleeping.<sup>8,9</sup> Moreover, knowledge of filariasis that will increase individual awareness of the risk factors to be considered.<sup>9</sup> Gender, occupation, and age are also risk factors for this disease.

Faridah et al.<sup>6</sup> in different research about *Aedes aegypti* control in Cibeusi and Cikeruh village Jatinangor sub-district, concluded that high dengue fever case is also influenced by host factor (age, sex, mobility, immunological status, and virus serotype infecting), environmental factor home density and mosquitoes, mosquito breeding and resting places, larvae free numbers, and rainfall), and behavioral factors (sleep patterns and vector control efforts).

The purpose of this study was to analyze the influence of demographic social factors such as age, sex, occupation, and education as well as to analyze the influence of socio-cultural environmental factors such as knowledge, attitude, prevention and place of misery to the occurrence of filariasis disease in Ende district.

## Methods

This study was analytic observational by using case-control design. The population was all cases of both acute and chronic filariasis found

in the district with the highest case in Welamosa with 49 cases. The case samples were filariasis patients registered in the Welamosa Public Health Center and diagnosed with filariasis. The control sample was 49 healthy individuals who were not registered as filariasis sufferers at the Wolowaru Public Health Center as a community health center with low cases and had similar characteristics. The sampling technique used the total sample based on cases recorded in the public health center book. The study was conducted in July–September 2016.

The data in this study include primary data and secondary data. Secondary data were cases obtained from Ende District Health Office and public health center at the research location, while primary data were collected directly through interview, questionnaire. Moreover, the data regarding the environmental condition were obtained through direct observation by using observation sheet.

The data collection process was conducted at each of the respondents' houses, within 14 days. The respondents were given questions about filariasis, actions and attitudes toward the incidence of filariasis disease. Adding to this, the observation data includes livestock ownership, the use of mosquito nets and the use of wire netting.

The data from the interview with the respondents and environmental observation were

processed by using the Microsoft Excel program for a univariate variable, while statistic test was analyzed by using SPSS program with backward logistic regression test.

The study has been registered with the Medical Research Ethics Commission of the Faculty of Medicine, Universitas Nusa Cendana, Kupang and has been granted a research ethic license with decision sheet number: 107/UN 15.16/KEPK/2016 and registration number UN16080115. All respondents in this study were asked for approval and have signed the informed consent.

## Results

This study was conducted on 49 samples who meet the criteria as research subjects. The frequency distribution of social demographic characteristics is illustrated in Table 1.

Table 1 shows that in case of groups; the proportion of sex, there were more female than male respondents. Regarding age of respondents, 90% of them were mostly over 50 years. In terms of education, 86% of the respondents only completed primary school or they do not attend school. Most of the respondents were farmers (84%). The number of family members who live in the house was mostly 4 people and more (78%).

In the control group, it was found that most of the respondents were male (57%). The age

**Table 1 Characteristics of Social Demographics of Case and Control Groups**

Variable	Control		Case		Total	
	Numbers	%	Numbers	%	Numbers	%
Gender						
Woman	21	43	31	63	52	53
Male	28	57	18	37	46	47
Age (years)						
≤50	38	78	5	10	43	44
>50	11	22	44	90	55	56
Education						
SMP/SMA/PT	33	67	7	14	40	41
SD/no school	16	33	42	86	58	59
Work						
Non-farmers	22	45	8	16	30	31
Farmers	27	55	41	84	68	69
Family members (persons)						
1–4	26	53	11	22	37	38
>4	23	47	38	78	61	62

SMP: *sekolah menengah pertama* (junior high school), SMA: *sekolah menengah atas* (high school), PT: *perguruan tinggi* (college), SD: *sekolah dasar* (elementary school)

**Table 2 Characteristics of Socio-Cultural Factors of Cases of Control Groups**

Variable	Control		Case		Total	
	Numbers	%	Numbers	%	Numbers	%
Knowledge						
Good	30	61	17	35	47	48
Enough/less	19	39	32	65	51	52
Attitude						
Good	32	65	31	63	63	64
Enough/less	17	35	18	37	35	36
Action						
Good	33	67	16	33	49	50
Fair/less	16	33	33	67	49	50
Source of information						
District health	42	86	37	75	79	81
Not district health	7	14	12	25	19	19
Livestock						
None	27	55	11	22	38	39
There are	22	45	38	78	60	61
Outdoor activity						
Not exit	35	72	25	51	60	61
Exit	14	29	24	49	38	39
Mosquito nets						
Yes	36	73	27	55	63	64
No	13	27	22	45	35	36
Wire gauze						
Yes	18	37	7	14	25	26
No	31	63	42	86	73	74

of respondents was less than 50 years (78%). Regarding education, the majority of respondents had completed junior high school, senior high school and university (67%). The occupation was not very different between farmers (55%) and non-farmers (45%). The number of family members who live in the house was mostly 1–4 people or less than 4 people (53%).

The frequency distribution of socio-cultural factors is described in Table 2. Table 2 shows that

among the case group, most respondents had sufficient/less knowledge about filariasis (65%). The attitude of respondents was mostly good (63%). Respondent's action is mostly enough/less (67%). The majority of information about filariasis came from health worker (75%). Based on ownership of livestock and livestock farm, it can be seen that the majority had livestock barn (78%). Furthermore, 51% of the respondents had outdoor activities at night. 55% of the respondents

**Table 3 Results of Multivariate Analysis Variable Research on Case and Control of Filariasis Events in Ende District**

Variables in the Equation	B	S.E.	Wald	Df	Sig.	Exp (B)	95% CI
Gender	-1.646	0.790	4.339	1	0.037	0.193	0.041–0.907
Job	2.129	0.855	6.198	1	0.013	8.404	1.573–44.905
Age	3.750	0.854	19.271	1	0.000	42.518	7.970–226.819
Education	3.644	0.907	16.146	1	0.000	38.248	6.466–226.239
Outdoor activity	1.841	0.841	3.754	1	0.053	5.097	0.981–26.480
Constant	-5.650	1.328	18.112	1	0.000	0.004	



used mosquito nets during night sleep but most of them did not use netting wire (86%).

In the control group can be seen that most respondents had good knowledge (61%). The respondents' attitude was mostly good (65%) and the action of the majority of respondents is good as well (67%). Based on sources of information about filariasis, most of the respondents got information from health workers (86%). Most of the respondents do not have livestock and livestock enclosure (55%). Most of the respondents did not have outdoor activity at night (71%). Most respondents used mosquito net (73%) but did not have wire screen for the window (63%).

Based on the results of analysis by using backward logistic regression test, there were five variables influencing filariasis incidents in Ende district namely gender, occupation of the respondent, age, education and outdoor activity.

As illustrated in Table 3, the prediction model of filariasis occurrence with the prediction ability of 89% and the remaining 11% is influenced by factors outside the model, with the following equation:  $Y = 5.650 - 1.646 \text{ sex} + 2.129 \text{ work} + 3.750 \text{ age} + 3.644 \text{ education} + 1.841 \text{ outdoor activities at night}$ .

Male respondents were 0.193 times more prone to filariasis than women. Respondents working as farmers were at greater risk of filariasis than those who did not work as farmers (8.404 times). Respondents aged over 50 years had the greatest risk of filarial infection by 42.5 times compared with those who were 50 years. Respondents with low education (elementary/uneducated) had 38 times higher risk of filariasis infection than those with higher education. Respondents who had outdoor activity at night had 5.097 times more vulnerable to be infected by filariasis than those who stay at home.

## Discussion

The number of women in the case group is slightly higher than that of men, whereas in the control group the number of male respondents is higher. Based on logistic regression test, sex influenced filariasis incidence with OR 0.193 value, which means that women have a higher risk to be infected by filariasis compared with men. The study found that 63% of women in the case group had filariasis. This result is similar to Garjito et al.<sup>7</sup> research in 2013, that women also have a risk of contracting filariasis while helping their husbands working in the field. Regarding

night outdoor activity, filarial mosquitoes do not only bite outside but also bite inside the house.<sup>7</sup>

The results of this study is in accordance with Riftiana and Soeyoko<sup>8</sup> research in 2010 conducted in Pekalongan Regency with obtained value OR=1.680 and p=0.310. This means that men are expected to have higher risk of filariasis infection by 1.607 times greater, but this was not statistically significant. Sex variables is not significantly related to filariasis incidence in Pekalongan regency because both men and women have the same risk to be infected by filaria.

Similarly, Afra et al.<sup>9</sup> also concluded that male respondents are at higher risk with 19% filariasis incidence, whereas among respondents with no risk (women) there was as many as 81% who experienced filariasis. Based on the results of the chi-square test, p=0.482, which means that there is no significant relationship between sex and filariasis incidence. Filariasis events can occur to both men and women.

The results of this study differ from those of Santoso et al.<sup>10</sup> that men have a greater risk of contact with filariasis transmitting mosquitoes due to their outdoor activities during the night. Although men in some endemic locations have more frequent frequency bites when working outdoors, women also have the risk of contact with mosquitoes inside the house.

There is no research claiming that genetically men are more susceptible to contracting filariasis than women. Transmission of filariasis occurs when there are 3 elements namely a source of transmission, the presence of vectors, and humans who are susceptible to filariasis.

In general, filariasis vector mosquitoes such as *Anopheles*, *Culex* and *Mansonia* are more likely to bite at night. This makes filariasis incidence in men is higher than in women. This is caused by the fact that generally men are more often to have contact with vectors because of their work and other outdoor activities until late at night, like as chatting with neighbors and watching TV together. Thus, men are more exposed to vectors with exophilic and exophagic nature where it will be easier for mosquitoes to bite.<sup>11</sup>

Based on age group it was found that among the case group, there were high occurrences of filariasis to those who are over 50 years old (90%). Then, based on logistic regression test, those who are over 50 years old are 42.518 times more risky compared to under 50 years old group. Although filarial infection can occur in all age groups, adults are more likely to be infected by filariasis

due to contact with their workplace vectors and risky behaviors such as more outdoor activities.<sup>11</sup>

Santoso et al.<sup>10</sup> stated that people who are more than 47 years old has higher potential to be infected by filariasis (28%) in comparison with the other age group. In other words, the older a person the more possible for him to have filariasis disease. This is illustrated by the percentage climbing from 5.5% (0–5 years) to 27% (31–46 years).

Afra et al.<sup>9</sup> states that there are a significant relation between age and filariasis incidence. It was found that 14% of the younger respondents (25–45 years) had filariasis while among the group at risk (<25 years or >45 years), 86% of them had filariasis.

In contrast, a study conducted by Riftiana and Soeyoko<sup>8</sup> also stated that there was no significant relationship between age and filariasis incidence. Riftiana and Soeyoko<sup>8</sup> found the magnitude of risk for age variables as seen in the value of OR=1.607, meaning that people who have a productive age are estimated to have filariasis disease 1.607 times greater than people who are not productive. However, this is not statistically significant with the value of  $p=0.331$  at  $\alpha=0.05$ .

Despite the insignificant relation between age and filariasis occurrence, there may be other factors like internal factors (congenital) attached to the individual. Although the age of each individual is the same, different intelligence, perception, emotions, and motivation will result in different behavior. Likewise, although individuals with older ages have more experience than younger ones, it cannot be guaranteed that they have good behavior, because essentially each individual will respond differently towards though the similar object or concept. This is caused by the peculiar nature of the individual himself. Therefore, age differences do not cause differences in activity in the prevention of filariasis.<sup>9</sup>

Types of respondents' occupation in this study are grouped by farmers and non-farmers because the majority of the population in the case and control groups works as farmers who own rice fields and plantations. Employment as a farmer in this study is a risk factor for filariasis with OR=8.804, which means that respondents who work as farmers have a risk to be exposed to filariasis 8.804 times greater than the non-farmers. This is possible because in addition to their low education where 86% of them only finished primary school, they also work

as farmers. This type of work is one of the risk factors for workers experiencing multiple bites of filariasis transmitting vectors.<sup>5</sup> The results of this study found that most of the filariasis patients work as farmers (84%) and a few number of non-farmers (16%). Some previous research results indicate that work at risk relates to filariasis events.

Riftiana and Soeyoko<sup>8</sup> categorizes work at risk in Pekalongan regency as farmers and other jobs done at night namely trader, laborer or artisan. The result of this research is OR=3.519,  $p=0.014$  at  $\alpha=0.05$ . In terms of biological significance, this means that the night jobs other than farmers will increase the risk of filariasis as much as 3.519 times compared to people who work during the day and this is statistically significant.

The rice field environment is suitable as a breeding ground for filariasis mosquitoes because the water is stagnant and directly related to the rice fields. Moreover, filariasis transmitting mosquitoes live at the roots of aquatic plants in the swamp. Therefore, working closely to mosquito breeding places has a great tendency to have contact with filariasis transmitting mosquitoes.<sup>11</sup>

Environmental conditions such as forest, rice fields, swamps that are often overgrown with water plants and sewage and trenches are one of the best habitats for breeding and resting of vector mosquitoes of certain species. There are 2 kinds of *Filariasis bancrofti*. First, the urban bancrofti filariasis with its main vector *Culex fatigans* that live in house, breeding on the dirty water around the house. Second, rural *Filariasis bancrofti* with its vector mosquito *Aedes*, *Anopheles* and *Mansoni*. *B. malayi* and *B. timori* only exist in rural areas, because the vectors cannot breed in urban areas. *B. timori* is usually located in the rice fields in accordance with the vector (*An. barbirostris*) breeding place. *B. malayi* can be found in humans and animals usually located on the beach or stream with swamps.<sup>9</sup>

Welamosa village, Wewaria sub-district, Ende district is one of the villages with the geographical condition of the mountains and the rice fields. Annual rainfall is quite high, so it is an area of breeding places. This is one of the factors causing the high spread of mosquito carrying filaria worm. Almost 70% of Welamosa area consists of the plantation, rice fields and shrubs which are the mosquitoes breeding places as well as transit for the mosquitoes that can transmit filariasis disease. Unprotected environmental sanitation conditions can be a breeding ground

for mosquitoes. Puddles, ditches or sewers can also be breeding ground for mosquitoes.

Formal education measured in this research is the education level of junior/senior high school/university and level of uneducated/elementary school. The higher level of education will affect the level of knowledge and attitudes in preventing the incidence of certain diseases. In this study, 86% of the cases are not educated or finished primary school but only 14% of them have completed high school or university. On the contrary, 67% of the control groups have finished high school and higher education the other 33% did not attend school or finished primary school. The statistical test of logistic regression results showed that education level has  $OR=38.248$ , meaning that low educated respondents have 38.248 times higher risk to be infected by filariasis compared with the highly educated person. In this study, the level of knowledge is fair/less common in the case group compared to the control group. This has an impact on the low attitudes and actions to prevent filariasis.

Amelia<sup>12</sup> concluded that there is a correlation between the level of knowledge about filariasis and filariasis incidence in Kertoharjo village, Pekalongan regency. The value of  $OR=10.714$  indicates that respondents whose level of knowledge about filariasis is low have a risk of 10.714 times higher than respondents whose level of knowledge about filariasis is high. Knowledge of filariasis disease is very important to support filariasis disease eradication. Prevention efforts were undertaken by increasing the knowledge of the community through simple and applicative extension activities such as avoiding contact with vector filariasis disease mosquitoes, including using mosquito nets, closing house ventilation with wire screen, and using mosquito repellent.<sup>13</sup>

The outdoor activities at night is a risk factor for the filariasis incident in Ende district with  $OR=5.097$ , meaning that people who have outdoor activity at night have a risk of 5.097 times higher than those who do stay at home all day. The habit of outdoor activity at night is related to the intensity of contact with the filariasis transmitting vector. Although sucking blood from pets, mammals, and poultry, filariasis transmitting mosquitoes prefer human blood. Female *Cx. quinuefasciatus* mosquito sucks human and animal blood throughout the night from until morning, both inside and outside the home.<sup>11</sup>

In this study it is found that 49% of the case group had outdoor activity outside at night

compared to the control group which was only 29%. If you see patients who have a habit of going out at night with jobs at risk, then all patients who often out of the house at night have a risk for exposure to mosquito bites causing filariasis.

Garjito et al.<sup>7</sup> also concluded that the out-of-home habit factor was significantly related to filariasis in Pangku Tolole village, Ampibabo, Central Sulawesi. Likewise, the research from Windiastuti et al.<sup>14</sup> stated that respondents who have a habit of being outdoors at night have 9.034 times greater risk of filariasis compared to respondents who do not have a habit of being outdoors at night. The habit of respondents to go out at night when mosquito *Cx. quinquefasciatus* bite will increase the risk of filariasis incidence. These factors are closely related to the existing mosquito species. Based on research that has been done, the peak density of mosquitoes bite occurred at 20.00–21.00 pm. High overnight activities during the night will give greater opportunities for contact with mosquitoes, *Cx. quinquefasciatus* thus at risk of filariasis.

Based on bionomic mosquitoes related to blood-seeking activities, communities in Ende district are at risk for activities outside the home during the night so that the habit of people out of the house at night has a high tendency to have contact with filariasis transmitting mosquitoes.<sup>7</sup>

However, a study by Uloli et al.<sup>15</sup> suggested that out-of-home behavior at night was not associated with filariasis. Uloli et al used a case-control study design. When viewed from the percentage of patients and controls, most of the respondents had a habit of outdoors activity at night. That is equal to 87% and 78 % with a value of  $p=0.103$ .<sup>15</sup>

## Conclusions

Social demographic factors (age, gender, occupation, and education) and environmental and social-cultural factors of attitude (outdoor activities at night) are risk factors for filariasis incidence in Welamosa Village, Ende District.

## Conflict of Interest

The authors declare no conflict of interests.

## Acknowledgment

The authors would like to express gratitude towards the Head of East Nusa Tenggara Provincial Health Office, the Head of Ende District

Health Office and the Head of Ende General Hospital, who have given permission and paid attention during the implementation of research activities. The authors also thank the Head of the Welamosa Public Health Center and the Head of Wolowaru Public Health Center for their support and participation in the survey and interview with the population during the research.

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## RESEARCH ARTICLE

**Acute Toxicity Test of Unripe Papaya (*Carica papaya* L.) Aqueous Extract (UPAE) on The Blood Urea and Creatinine Concentration**Yuktiana Kharisma,<sup>1</sup> Yuke Andriane,<sup>1</sup> Titik Respati<sup>2</sup><sup>1</sup>Department of Pharmacology, <sup>2</sup>Department of Public Health,  
Faculty of Medicine, Universitas Islam Bandung, Bandung, Indonesia**Abstract**

Unripe papaya aqueous extract (UPAE) widely used as lactation stimulator, antidiabetes, antibacterial, and anti-inflammatory. The utilization of papaya is not known for its safety yet, so it is necessary to research its toxicity. The purpose of this study was to investigate the acute toxicity of UPAE on renal function through measurement of blood urea and creatinine levels. This study was conducted in July 2017 in Laboratory of Medical Biology, Faculty of Medicine, Universitas Islam Bandung. This study used pure in vivo experimental design on 11 Swiss Webster mice using the dose of acute toxicity determination based on new recommended methods of 0; 50; 200; 400; 800; 1,000; 1,500; 2,000; 3,000; 4,000; and 5,000 mg/kgBW. After 24 hours, 1 mL blood drawn through the tail examined for blood urea and creatinine levels. The measurement of urea content using kinetic method point and creatinine level using modified Jaffe method. Provision of UPAE at doses of 0, 50, 200, 400, 800, and 1,000 mg/kgBW resulted on blood urea equal to 39, 35, 48, 49, 48, and 32 mg/dL respectively. Blood urea level 23, 22, 28, 34, and 35 mg/dL was obtained at 1,500 UPAE doses; 2,000; 3,000; 4,000; and 5,000 mg/kgBW dosages respectively. After 24 hours of UPAE administration, the creatinine level in various doses using new recommended method of (0–5,000 mg/kgBW) were 0.75, 0.54, 0.53, 0.50, 0.60, 0.54, 0.52, 0.55, 0.42, 0.51, and 0.40 mg/dL. In conclusion, UPAE do not cause acute toxicity on renal function through measurement of blood urea and creatinine levels.

**Keywords:** Acute toxicity, unripe papaya aqueous extract**Toksistas Akut Ekstrak Air Buah Pepaya (*Carica papaya* L.) terhadap Kadar Ureum dan Kreatinin Darah****Abstrak**

Ekstrak air buah pepaya muda (EABPM) digunakan secara empiris sebagai laktagogum, antidiabetes, antibakteri, dan antiinflamasi. Tingkat keamanannya belum banyak diketahui sehingga perlu dilakukan penelitian uji toksistas akut. Tujuan penelitian ini adalah mengetahui toksistas akut EABPM terhadap fungsi ginjal melalui pengukuran kadar ureum dan kreatinin plasma. Penelitian ini dilaksanakan pada bulan Juli 2018 di Laboratorium Biologi Medis, Fakultas Kedokteran, Universitas Islam Bandung. Penelitian ini menggunakan desain eksperimental murni *in vivo* terhadap 11 ekor mencit betina galur Swiss Webster dengan penentuan dosis sesuai dengan *new recommended method*: 0, 50, 200, 400, 800, 1.000, 1.500, 2.000, 3.000, 4.000, dan 5.000 mg/kgBB. Setelah 24 jam, diambil darah melalui ekor mencit sebanyak 1 mL untuk diperiksa kadar ureum dan kreatinin plasma. Pengukuran kadar ureum menggunakan *point kinetic method* dan kadar kreatinin menggunakan metode Jaffe yang dimodifikasi. Pemberian EABPM pada dosis 0, 50, 200, 400, 800, dan 1.000 mg/kgBB didapatkan kadar ureum plasma 39, 35, 48, 49, 48, dan 32 mg/dL secara berurutan. Kadar ureum plasma 23, 22, 28, 34, dan 35 mg/dL didapatkan pada pemberian dosis EABPM sebanyak 1.500, 2.000, 3.000, 4.000, dan 5.000 mg/kgBB. Kadar kreatinin plasma dalam berbagai dosis (0–5.000 mg/kgBB) adalah 0,75; 0,54; 0,53; 0,50; 0,60; 0,54; 0,52; 0,55; 0,42; 0,51; dan 0,40 mg/dL. Simpulan, EABPM tidak menimbulkan tanda toksistas akut pada fungsi ginjal melalui pengukuran kadar ureum dan kreatinin plasma.

**Kata kunci:** Ekstrak air buah pepaya muda, toksistas akut

Received: 30 May 2018; Revised: 31 July 2018; Accepted: 27 August 2018; Published: 30 August 2018

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## Introduction

Indonesia is a country rich in natural materials, especially medicinal plants (herbs), with approximately 25,000 to 30,000 plant species found. The community uses a total of 7,000 plant species in Indonesia as medicine, and only 283 species registered with the Food and Drug Administration (BPOM).<sup>1</sup> The use of herbal medicine through the utilization of natural materials has become a tradition for generations. Research on medicinal plants has increased rapidly along with the growing use of medicinal plants in the treatment effort in the community, especially the traditional community.<sup>2,3</sup>

Medicinal plants are used empirically and are considered safe for consumption because they come from nature. However, the use of traditional medicines should have a scientific basis for their safety and effectiveness by identifying active substances. Ethno-pharmacology/ethno-pharmaceutical that performing pre-clinical tests of plant extracts on experimental animal models is essential.<sup>4</sup>

Papaya (*Carica papaya* L.), *Carica* clan *Caricaceae* is a plant that is widely studied today. Papaya has a wide range of medicinal benefits due to their abundant and active compounds such as papain enzymes, carotenoids, alkaloids, monoterpenoids, flavonoids, minerals, vitamins, glucosinolates, and carposides. Benefits of papaya in medicine include anticancer, antioxidant, antidiabetic, antifertility, anti-inflammatory, antihelminthic, antibacterial, antimalarial, anti-dengue, and wound healing.<sup>5</sup>

Active compounds in papaya can provide several benefits if used in the appropriate dosage. Examples of papaya active compounds are alkaloids, saponins, and flavonoids which have antibacterial, antioxidant, anti-inflammatory effects, as well as lactation stimulant (lactagogue). However, if the utilization of the papaya is not suitable for its use, it can have adverse effects. Such adverse effects will result in functional impairment of organs and cells.<sup>6</sup> Thus, toxicity and safety testing of herbal products and natural ingredients is an important thing to do. The World Health Organization (WHO) puts the issue of traditional drug safety into one of the essential steps in Traditional Drug Development Strategy of 2014–2023.<sup>7</sup>

Toxicity can cause damage to several organs of the body. Toxicity tests are needed to assess the

safety of a drug, as well as substances recognized as supplements or foods. This test can protect the public against the adverse effects of a drug preparation. One such toxicity test is an acute toxicity test, a test to identify undesirable effects at the first 24-hour interval after administration of one/several substances. One of the initial screening assessments of acute toxicity of test preparation is the calculation of lethal dose 50 (LD50).<sup>8,9</sup>

Based on research that has been done using Karber method it is known that unripe papaya aqueous extract (UPAE) LD50 (*Carica papaya* L.) acute toxicity test is 2,520 mg/kgBW.<sup>10</sup> In research conducted by Nadiyah et al.<sup>11</sup> LD50 from papaya fruit extract (*Carica papaya* L.) found to be >5,000 mg/kgBW. Acute toxicity of unripe papaya fruit juice extract has also performed on erythrocyte morphology. This study states that UPAE does not result in erythrocyte morphological changes in microscopic examination of a peripheral blood smear.<sup>6</sup>

The kidneys are vital organs that are essential for the body and perform various functions. They include the excretion function of metabolism and foreign substances that the body does not need, the water balance and electrolyte arrangement. Also involves in the regulation of the osmolarity of the body fluids and the electrolyte concentration, the acid-base balance arrangement, the arterial pressure, hormone secretion and gluconeogenesis.<sup>12</sup> Measurement of blood urea and creatinine levels is one of the markers on renal function evaluation. The increase in serum levels of the enzyme indicates the occurrence of renal injury.<sup>13</sup>

The purpose of this study was to investigate the acute toxicity of UPAE on renal function through measurement of blood urea and creatinine levels.

## Methods

This study used purely in vivo experimental design on eleven Swiss Webster mice aged 6–8 weeks weighing 25–30 grams. Research subjects were divided into four 77.4 cm<sup>2</sup> by 12.7 cm plastic tubs with woven wire cover. The room set to a temperature of about 19–25°C, freed from predator and sanitation maintained. Mice went to adaptation period of seven days.

The research material is 2.5–3 months old unpeeled papaya fruit (including seed) from plantation in Leles sub-district, Garut regency,

West Java. The selected papaya is unripe fruit with dark green skin, smooth, no defect, white flesh and seed, picked from healthy plants. This experimental laboratory study conducted at the Laboratory of Medical Biology, Faculty of Medicine, Universitas Islam Bandung (Unisba) in July 2018. The proposed (new) recommended method selected for use in this toxicity test study were 0; 50; 200; 400; 800; 1,000; 1,500; 2,000; 3,000; 4,000; and 5,000 mg/kgBW. After 24 hours, 1 mL blood was collected through the tail to check blood urea and creatinine levels. At the end of the study, research subjects sacrificed through decapitation. This study have obtained ethical clearance from Health Research Ethics Committee, Faculty of Medicine, Unisba number: 095/Komite Etik FK/III/2017.

## Results

Phytochemical screening results of UPAE is obtained from secondary metabolite in the form of saponin, alkaloid, flavonoid, triterpenoid, quinone, and tannin.

In this study, blood urea content of the research subjects without UPAE (control) was 39 mg/dL. Provision of UPAE at dose 50, 200, 400, 800, and 1,000 mg/kgBW showed the result of blood urea of 35, 48, 49, 48, and 32 mg/dL respectively. The plasma urea content with value 23, 22, 28, 34, and 35 mg/dL was obtained on the subject of the study by UPAE dosages of 1,500; 2,000; 3,000; 4,000; and 5,000 mg/kgBW.

Plasma creatinine level after 24 hours of

**Table 2 Blood Urea and Creatinine Measurement**

Dosages (mg/kgBW)	Blood Urea (mg/dL)	Creatinine (mg/dL)
0	39	0.75
50	35	0.54
200	48	0.53
400	49	0.50
800	48	0.60
1,000	32	0.54
1,500	23	0.52
2,000	22	0.55
3,000	28	0.42
4,000	34	0.51
5,000	35	0.40

UPAE in various doses using new recommended method (0–5,000 mg/kgBW) were 0.75, 0.54, 0.53, 0.50, 0.60, 0.54, 0.52, 0.55, 0.42, 0.51, and 0.40 mg/dL.

## Discussion

The kidney is a vital organ that keeps the body homeostatically by regulating water and electrolyte balance, regulating acid-base balance, and regulating the osmolarity of body fluids and electrolytes. The kidneys selectively excrete solutes and water and throw out the rest of the metabolism. Kidney damage can be caused by toxins or medications that damage nephron epithelial cells.<sup>15</sup>

The measurement of the biochemical parameters of urea and creatinine levels was performed as an initial stage of evaluation of renal function that was used as one of the benchmarks of acute organ damage. Urea and creatinine are also indicators of glomerular filtration rate (GFR) which is a marker of kidney function.<sup>13</sup> Impaired kidney function leads to decreased renal filtration rate, accompanied by accumulation of metabolic (urea and creatinine) residues in the blood so that the levels of these two substances in this blood can be used as an indicator of the degree of kidney health.<sup>16</sup>

Urea is a major metabolite derived from protein intake as well as breakdown of tissue proteins while creatinine is a product of muscle creatin catabolism. The range of urea values is

**Table 1 Phytochemical Screening of Unripe Papaya Aqueous Extract**

Secondary Metabolite	Reaction	Result
Saponin	Sample + HCl (shaken)	+
Alkaloid	Sample + Dragendorff reagent + CHCl <sub>3</sub> +HCl	+
Flavonoid	Sample + Mg + HCl + amyl alcohol	+
Terpenoid	Sample + ether + H <sub>2</sub> SO <sub>4</sub> + acetic acid glacial	+
Quinone	Sample + NaOH	+
Tannin	Sample + Stiasny reagent	+

quite wide due to normal variation due to protein intake, endogenous protein catabolism, hydration state, hepatic urea synthesis, and renal urea excretion.<sup>17,18</sup> Increased urea levels can be caused by an increase in the catabolism of tissue proteins accompanied by negative nitrogen balance, an excessive protein-breaking process occurs in cases of leukemia in which leukocyte protein leaks, presence of urea-erythrocyte disorder, due to prerenal, renal or postrenal disorder or due to high protein consumption.<sup>13</sup>

Creatinine is a type of amino acid that is a waste product in the blood and excreted through the kidneys into the urine. Generally, creatinine stores in muscles as energy reserves in the form of a creatinine-phosphate source of adenosine triphosphate (ATP). Another place that produces creatinine is in the liver, pancreas, and kidneys. High creatinine levels are thought to be due to severe muscle activity (hard exercise) or due to impaired kidney discharge systems. Creatinine levels are relatively stable because protein does not influence them from the diet.<sup>18</sup>

Measurement of urea and creatinine levels in this study showed different values when compared with controls. However, this is not an indicator of renal impairment because the parameters of renal impairment are indicated by an increase in blood creatinine levels doubled from the normal range and occurring for more than two weeks.<sup>19,20</sup> This may be due to a decline in kidney function as part of the physiological dynamics. The fluctuations occurring in the study subjects did not indicate renal impairment because they are not accompanied by a doubling of urea levels in the range of control values (average) and not followed by a parallel increase in creatinine.<sup>19,21</sup>

Further research is needed on UPAE toxicity through sub-chronic and chronic toxicity tests to complement the safety data in the form of morphological, functional, and life-long changes in the subject.

## Conclusion

Provision of unripe papaya fruit extract by using a dose of acute toxicity determination based on new recommended method did not affect renal function.

## Conflict of Interest

All authors state whether there was not a conflict

of interest in this article.

## Acknowledgement

We would also like to show our gratitude to the Clinical Pathology and all the staff of Cicalengka Hospital for sharing their pearls of wisdom with us during this research. We are also immensely grateful to all the staff of Medical Biology Laboratory of Universitas Islam Bandung (UNISBA) for the contributions and cooperation a long this research process.

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## RESEARCH ARTICLE

## High ESAT-6 Expression in Granuloma Necrosis Type of Tuberculous Lymphadenitis

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### Abstract

A granuloma is one of host cellular immune response form to intracellular and persistent pathogens, and result in the aggregation of several activated immune cells. Intracellular pathogens manipulate host immune responses to avoid immune reactions. *M. tuberculosis* is the intracellular and persister pathogen, which can stimulate granuloma formation. The formation this granulomas still have different opinions, whether it is the host's way to isolate *M. tuberculosis*, or how these pathogens are to escape immune responses. Early secretory antigenic target (ESAT)-6 is a typical secretory protein produced by the locus of the gene region of difference (RD)-1 *M. tuberculosis*. ESAT-6 plays a role in the immunopathogenesis of tuberculosis. This study aims to compare ESAT-6 antigen expression from *M. tuberculosis* between granulomas with necrosis and granulomas without necrosis. This study was an analytic observation study with a cross-sectional design. Forty-six lymph node paraffin blocks from tuberculous lymphadenitis patients in Department of Anatomical Pathology, Dr. Hasan Sadikin General Hospital, Bandung in 2017 were made in preparations and stained by hematoxylin eosin to assess the presence of necrosis in granulomas, immunohistochemical using ESAT-6 antibodies, then it was quantified using histoscore. Histoscore for ESAT-6 not normally distributed, so it uses Mann-Whitney test used. The results showed that there were 31 granulomas with necrosis (histoscore mean=27.6%) and 15 granulomas without necrosis (histoscore mean=15.1%), there was a significant difference with  $p < 0.05$  ( $p = 0.03$ ). The conclusion of this study there is a high histoscore ESAT-6 expression in granuloma type of necrosis tuberculous lymphadenitis.

**Keywords:** ESAT-6, granuloma, necrosis

## Ekspresi ESAT-6 Tinggi pada Granuloma Limfadenitis Tuberkulosis Tipe Nekrosis

### Abstrak

Granuloma merupakan salah satu bentuk respons imun seluler pejamu terhadap patogen intraseluler. Patogen intraseluler memanipulasi respons imun pejamu untuk menghindari reaksi imun. *M. tuberculosis* adalah patogen intraseluler dan persisten yang dapat menstimulasi pembentukan granuloma. Terbentuknya granuloma masih memberikan pendapat yang berbeda, apakah merupakan cara tubuh untuk mengisolasi *M. tuberculosis* atau cara patogen ini untuk menghindari respons imun. *Early secretory antigenic target* (ESAT)-6 adalah protein sekretori khas yang dihasilkan oleh lokus gen *region of difference* (RD)-1 *M. tuberculosis*. ESAT-6 berperan dalam imunopatogenesis tuberkulosis. Penelitian ini bertujuan menganalisis perbedaan ekspresi antigen ESAT-6 *M. tuberculosis* antara granuloma dengan nekrosis dan granuloma tanpa nekrosis. Penelitian ini merupakan penelitian observasi analitik dengan desain *cross sectional*. Blok parafin kelenjar getah bening didapat dari pasien yang didiagnosis limfadenitis tuberkulosis di Departemen Patologi Anatomi, RSUP Dr. Hasan Sadikin Bandung pada tahun 2017. Blok parafin tersebut dibuat blangko preparat dan diwarnai dengan hematoksin eosin untuk menilai nekrosis pada granuloma serta imunohistokimia menggunakan antibodi ESAT-6. Kemudian, sediaan preparat imunohistokimia tersebut dikuantifikasi menggunakan metode *histoscore* sehingga didapatkan data berupa nilai skor dari pewarnaan ESAT-6. Selanjutnya, dilakukan uji beda antara *histoscore* granuloma dengan nekrosis dan granuloma tanpa nekrosis tersebut dianalisis karena nilai skor ESAT-6 berdistribusi tidak normal sehingga menggunakan uji Mann-Whitney. Hasil penelitian menunjukkan terdapat 31 granuloma dengan nekrosis (*histoscore* rerata=27,6%) dan 15 granuloma tanpa nekrosis (*histoscore* rerata=15,1%), serta terdapat perbedaan signifikan dengan  $p < 0,05$  ( $p = 0,03$ ). Simpulan, ekspresi ESAT-6 tinggi pada granuloma limfadenitis tuberkulosis dengan nekrosis.

**Kata kunci:** ESAT-6, granuloma, nekrosis

Received: 24 August 2018; Revised: 28 August 2018; Accepted: 28 August 2018; Published: 30 August 2018

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## Introduction

Tuberculosis is still a high burden of disease in the world and in Indonesia.<sup>1</sup> Several factors influence this disease to have the impact on the treatment and prevention program.<sup>2,3</sup> Tuberculosis has several types with extrapulmonary tuberculosis incidence is about 20% of all tuberculosis. Lymphadenitis is the most extrapulmonary tuberculosis.<sup>1</sup>

A granuloma is one of host cellular immune response form to intracellular and persistent pathogens, and result in the aggregation of several activated immune cells. There are differences on the host's cellular immune response to different mycobacterium species, depending on their respective virulence. *Mycobacterium bovis* can modulate miR-155 expression in macrophages, through toll-like receptor 2 (TLR2) and NF- $\kappa$ B signals. The transduction signal will activate the apoptosis event of macrophage cells, as one of the pathways for cell death to eliminate intracellular *M. tuberculosis*. *M. tuberculosis* also induces the expression of miR-155 but differs in the final results of mycobacterium elimination. *M. tuberculosis* tends to be more resistant to macrophage apoptosis for the elimination of intracellular mycobacterium, compared to *M. bovis*. The host immune response to *M. smegmatis* is the same as that of *M. bovis*. *M. bovis* and *M. smegmatis* are less virulent compared to *M. tuberculosis*. This phenomenon shows that *M. tuberculosis* causes failure of the innate immune response to eliminate *M. tuberculosis*, so it is more likely to progress to adaptive immune response.<sup>3,4</sup>

Adaptive immune response to *M. tuberculosis* different from another mycobacterium, through induction of T helper two cells (Th2). The infection becomes more progressive and can cause reactivation. Reactivation occurs through the destruction of a stable granuloma so that localized *M. tuberculosis* can come out of the granuloma confinement and become outside the cell. The extracellular *M. tuberculosis* induces the host's immune response. The results of *M. tuberculosis* reaction with the host's immune response cause the clinical condition of the infectious disease. *M. tuberculosis*, which is already outside the cell and granuloma, infects the tissue more widely and can spread through lymphogens and hematogenous.<sup>5</sup>

The cell population of granulomas consisting of giant Langerhans cells (GLCs) and epithelioid cell (EC) shows the host's immune response

ability to infectious agents, in other words, the infectious agent is not too aggressive. Conversely, the picture of necrosis shows the aggressiveness of infectious agents.<sup>6</sup> Necrosis is one of the pathways of macrophage cell death, and shows the failure of macrophages to eliminate *M. tuberculosis*.<sup>7-9</sup> Necrosis is also a mechanism for cellular or slow-type hypersensitivity response, to eliminate intracellular bacteria.<sup>10,11</sup>

*M. tuberculosis* has an early secretory antigenic target-6 (ESAT-6) antigens. *M. bovis* BCG and *M. avium* do not own the antigen. Early secretory antigenic target-6 is secreted by *M. tuberculosis* so that it can be detected in the blood or granuloma tissue of active pulmonary tuberculosis patients.<sup>1-3</sup> ESAT-6 can be detected in tuberculous granuloma lymphadenitis, and immunohistochemical staining for ESAT-6 antigen has been shown to provide 88.6% sensitivity.<sup>4</sup>

ESAT-6 plays a role in the immunopathogenesis of tuberculosis.<sup>2,5</sup> Several studies have proven that ESAT-6 plays a role in the immune response to mycobacterium, including its influence on the expression of IL-6, IL-8, TNF- $\alpha$  by macrophages.<sup>3,6-8</sup> Studies in vitro on macrophage cell cultures proven that ESAT-6 can modulate the expression of microRNA-155 through receptors TLR1 or TLR6.<sup>5</sup> MicroRNA-155 through IL-6 can increase MMP-1, which contributes to granuloma rupture and causes necrosis. Based on the framework, this study aims to analyze the role of ESAT-6 in granulomas in tuberculous lymphadenitis.

## Methods

The material used in this study is stored lymph nodes paraffin blocks from tuberculous lymphadenitis patients diagnosed histopathologically in Anatomical Pathology Department, Dr. Hasan Sadikin General Hospital Bandung in 2017. The inclusion criteria were as follows; paraffin block stored less than four years, and tissue volume was sufficient for research and archives. The exclusion criteria are paraffin blocks derived from patients diagnosed with diabetes mellitus, positive HIV, and immunodeficiency.

Paraffin blocks that are suitable for the inclusion and exclusion criteria were sliced using microtomes and preparations were made and stained using ESAT-6 immunohistochemistry and hematoxylin eosin. The preparation observed under a light microscope and ESAT-6

quantification used histoscore. The histoscore value was the result of the multiplication between the intensity of the brown color and the color distribution. Brown intensity consists of 3 scores: 1 for low intensity, 2 for moderate intensity and 3 for high intensity. The brown color distribution scores consists of; score 1 (0–20%), score 2 (>20–50%), score 3 (>50–80%), and 4 (>80–100%).

Type of granuloma, the presence of granuloma and necrosis area observed from the preparations stained with hematoxylin eosin. Determination of histoscore and histopathology conducted by three observers, consisting of the anatomical pathologist and two researchers. Statistical

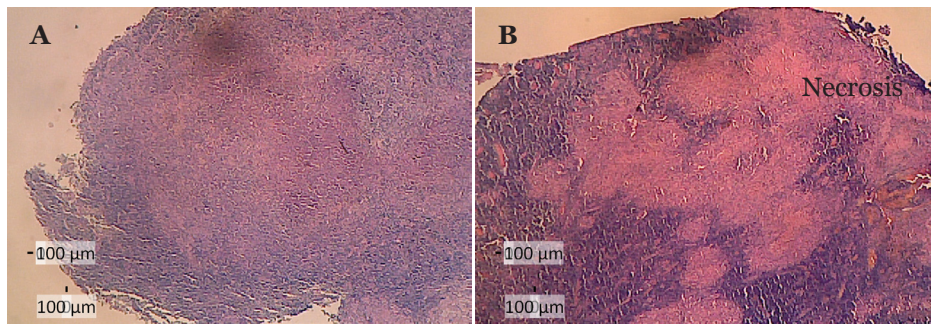
analysis was done using Mann-Whitney test.

This study has approved by Health Research Ethics Committee, Faculty of Medicine, Universitas Padjadjaran, Bandung number: 1050/UN6.C10/PN/2017.

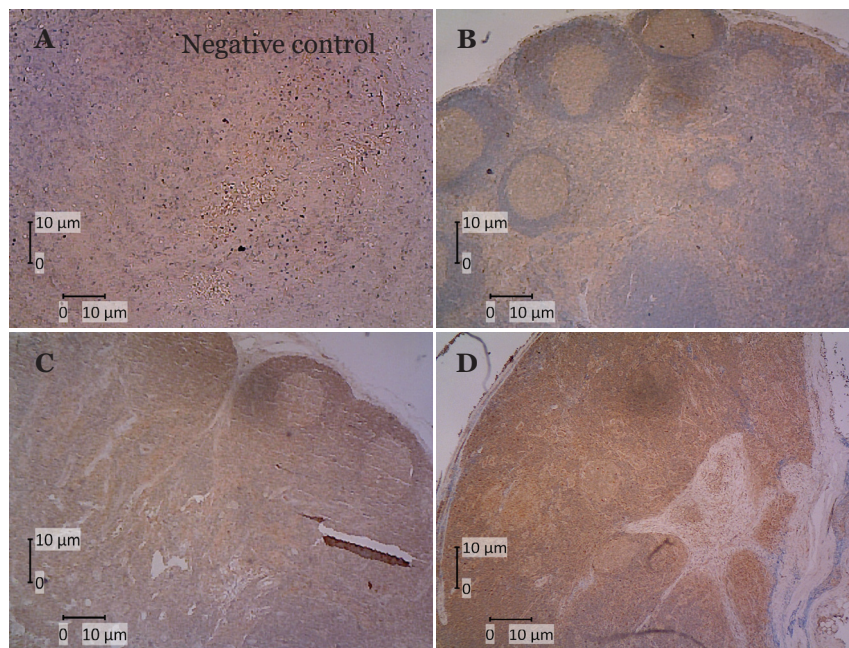
**Results**

Assessment of granuloma necrosis stained by hematoxylin eosin, in Figure 1A shows granulomas without necrosis, while Figure 1B shows granulomas with necrosis.

ESAT-6 appears as shown in Figure 2. The average ESAT-6 histoscore values for each group



**Figure 1 Hematoxylin Eosin Staining**  
 A. Granuloma without necrosis (40×); B. Granuloma with necrosis (40×)



**Figure 2 Early Secretory Antigenic Target (ESAT)-6 Staining**  
 A. (100×) as a negative control, in granulomatous lymphadenitis shows negative ESAT-6 given a score of 0, low intensity; B. (100×) image scored 1; C. (100×) medium intensity image is given a score of 2, high intensity; and D. (100×) images, given a score of 3

**Table Average ESAT-6 Histoscore**

Necrosis	Average ESAT-6 Score	Sig*
Negative	15.1 (15)	0.03
Positive	27.6 (31)	
Total	100 (46)	

\*Mann Whitney test ( $p < 0.05$ , significant different)

seen in Table.

## Discussion

A granuloma is an aggregation of some inflammatory cells, especially mature macrophages which form aggregates in response to an antigen. The antigens come from a bacterium, fungus, foreign body, and immune complex.<sup>9</sup> The purpose of forming a granuloma is to isolate the antigen from the host and facilitate eradication of the antigen. This essential immune reaction provides the body with protection from antigen recognition, very important in cases of mycobacterial infection. Immune disorders cause granuloma to form accompanied by necrosis. Granuloma occurs in TNF- $\alpha$  deficiency, interleukin-12 (IL-12), or interferon-gamma (IFN- $\gamma$ ).<sup>10</sup>

Assessment of cell populations against granulomas consisting of GLCs and EC shows the host's immune response ability to infectious agents, in other words, infectious agents are not too aggressive. On the other hand, the picture of necrosis shows the aggressiveness of the infectious agent.<sup>1,12</sup> Necrosis is one of the pathways of macrophage cell death and shows the failure of macrophages to eliminate *M. tuberculosis*.<sup>5,7</sup> Necrosis is also one of the mechanisms of slow cellular type or hypersensitivity response, to eliminate intracellular bacteria.<sup>10,11</sup> In this study granuloma assessment based on the presence of necrosis, without assessing other cellular components.

Histoscore ESAT-6 was higher in granulomas with features of necrosis, compared with granulomas without necrosis, caused by the high expression of ESAT-6 by *M. tuberculosis* or a large number of *M. tuberculosis*. Early secretory antigenic target-6 is a typical secretory protein produced by the locus of the gene region of difference-1 (RD-1) *M. tuberculosis* virulent isolate H37Rv.<sup>12</sup>

Early secretory antigenic target-6 usually

found as a complex with culture filtrate protein (CFP)-10, has a molecular weight of 27 kDa and is composed of two mycobacterial proteins namely ESAT-6 (Rv3875 or EsxA) with a molecular weight of 6 kDa and CFP-10 (Rv3874 or 2-4EsxB) with a molecular weight of 10 kDa.<sup>12</sup>

*M. tuberculosis* has 22 pairs of genes from 11 genomic loci in the region of difference (RD)-1 4.5 which codes the ESAT-6/CFP-10 antigen family.<sup>7</sup> ESAT-6 secretion is carried out actively, using energy from adenosine triphosphate (ATP) with the help of gene groups such as the ATPase Rv3977 and Rv3871 membrane complexes and the Rv3877 transmembrane protein. The functional structure of this complex in the secretion process is the CarmCFP-10 which will bind to the ATPase membrane complex and will be carried through the cytoplasmic membrane by transmembrane proteins so that the ESAT-6/CFP-10 complex will be secreted by *M. tuberculosis*.<sup>13</sup>

Early secretory antigenic target-6 in granuloma lymphadenitis is one evidence of *M. tuberculosis* and plays a role in the formation of necrosis in granulomas.

## Conclusion

High histoscore ESAT-6 expression in granuloma type necrosis tuberculous lymphadenitis, the presence of necrosis in granulomas indicates a diagnosis for lymphadenitis caused by *M. tuberculosis*.

## Conflict of Interest

There was not a conflict of interest in this article.

## Acknowledgement

This research could be carried out with full support from the Education and Research Department and the Department of Anatomical Pathology, Dr. Hasan Sadikin General Hospital, Bandung. Research funding supports comes from the doctoral grant from Ministry of Research, Technology and Higher Education of the Republic of Indonesia, contract number: 156/B.04/Rek/III/2018.

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## RESEARCH ARTICLE

## Evaluation on the Implementation of Rural-Based Program for Undergraduate Medical Student

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### Abstract

Evaluation of a program is needed to determine whether the program could be implemented and generate inputs to improve the program. The objective of this study was to evaluate the implementation of community-based programs for medical clerkship students in rural areas. This research was a qualitative study using interpretivism paradigm and case study approach. Data collection method was focus group discussions with the head of the public health center (puskesmas) and preceptor. Data were analyzed through transcription, coding, categorization, and generating theme. The study was conducted from August 2015 to November 2016 in Sukabumi and Cianjur, West Java. Triangulation method and member check were conducted to elicit valid and reliable data. Two focus group discussions were conducted with 11 informants comprises 5 heads of puskesmas and 6 preceptors. There were 7 themes generated from the discussion. The themes were socialized and disseminate the information; collaboration and local government involvement; integration of education and service; encourage lifelong learning; encourage the improvement of performance; skill enhancement; and sustainability. Implementation of community-based medical education curriculum in rural areas has been implemented. Sustainability of the curriculum is needed to contribute to the improvement of community health status.

**Keywords:** Community, medical education, rural, undergraduate

## Evaluasi Implementasi Program Ilmu Kesehatan Masyarakat di Daerah Pedesaan untuk Program Profesi Dokter

### Abstrak

Evaluasi sebuah program dibutuhkan untuk mengetahui apakah program tersebut dapat dilaksanakan dan mendapatkan masukan yang akan digunakan dalam rangka memperbaiki program. Tujuan penelitian ini adalah melakukan evaluasi pelaksanaan program pendidikan kedokteran berbasis daerah pedesaan untuk mahasiswa profesi dokter. Penelitian ini merupakan penelitian kualitatif dengan paradigma *interpretivism* dan pendekatan studi kasus. Pengumpulan data dilakukan dengan diskusi kelompok terarah kepada kepala puskesmas dan preceptor lapangan. Pengambilan data dilakukan pada bulan Agustus 2015 sampai November 2016 di Sukabumi dan Cianjur, Jawa Barat. Analisis data hasil wawancara dilakukan melalui proses transkripsi, koding, kategorisasi, dan penyusunan tema. Triangulasi dan *member check* dilakukan untuk mendapatkan data yang valid dan reliabel. Dua diskusi kelompok terarah dilakukan kepada 11 informan yang terdiri atas 5 orang kepala puskesmas dan 6 orang preceptor. Berdasar atas hasil diskusi didapatkan 7 tema dalam evaluasi kurikulum pendidikan, yaitu sosialisasi dan diseminasi informasi; kolaborasi dan keterlibatan pemerintah setempat; integrasi pendidikan dan pelayanan; mendorong pembelajaran sepanjang hayat; mendorong peningkatan kinerja staf; pemahaman keterampilan; serta keberlanjutan. Pelaksanaan kurikulum pendidikan kedokteran berbasis komunitas di daerah pedesaan telah dilakukan dengan baik, hal ini terlihat dari beberapa manfaat yang dikemukakan oleh informan. Agar implementasi kurikulum ini memberikan hasil yang lebih baik untuk masyarakat dibutuhkan keberlanjutan program.

**Kata kunci:** Komunitas, pedesaan, pendidikan kedokteran, profesi dokter

Received: 12 September 2017; Revised: 26 September 2018; Accepted: 26 September 2018; Published: 27 September 2018

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## Introduction

The ideal doctor according to the results of the ASEAN medical council meeting has several characteristics such as professional, ethical, having managerial and leadership skills.<sup>1</sup> This is a challenge for medical education institutions to produce qualified graduates as expected. Medical education in Indonesia is carried out by following international standards recommended by the World Federation for Medical Education (WFME). WFME encourages strategy in medical education to achieve self-directed learning and lifelong learner.<sup>2</sup> This global standard is translated into a competency-based curriculum with an integrated approach (horizontally and vertically), individual, family, and community-oriented health care in the context of primary health services.<sup>1</sup> Medical education is directed to produce graduates who meet the needs of the community and the education process is more emphasis on health promotion, disease prevention, and community assessment.<sup>2</sup>

In order to produce graduates that meet the needs of the community, an educational curriculum is required to encourage the achievement of competencies, focus on interdisciplinary learning, community-based and health service oriented.<sup>3</sup> The curriculum must be able to equip students with management skills, leadership, cross-cultural communication, procedural skills and emergency.<sup>4</sup> Most medical institution do not create the curriculum that encourages students to work in community.<sup>5</sup>

The Faculty of Medicine of Universitas Padjadjaran has implemented a community-based curriculum since 2005. Students are placed in the public health center (puskesmas) in urban areas of West Java. This curriculum aims to provide the environment for students to learn the management of the puskesmas and manage public health problems.<sup>6</sup> In 2014, Faculty of Medicine, Universitas Padjadjaran developed community-based education for rural areas by placing students in the southern part of West Java province. This program has been running for 2 years and has not been evaluated for its success.

Evaluation of a program is needed to find out whether objective is of the program are met and identify feedback for improvement.<sup>7,8</sup> This evaluation should be conducted continuously and regularly involving not only relevant stakeholders but also students.<sup>9</sup> The objective of this study was

to evaluate the implementation of community-based programs for medical clerkship students in rural areas.

## Methods

This research was a qualitative research using a case study approach. This study uses the paradigm of interpretivism to elicit the perspective of people who are directly involved in the implementation of the program. Sampling was conducted purposively in accordance with the research objectives. Two focus group discussions were performed to collect data. The informants involved were the heads of the puskesmas and preceptors from 5 health centers in Sukabumi and Cianjur districts, West Java. There were 5 heads of the puskesmas and 6 preceptors who were involved in this study. Informants were chosen because they involved actively in the implementation of the program.

Focus group discussions were conducted using interview guidelines, aimed to (1) explore the need for integration of educational and service to strengthen health systems; (2) assess the implementation of the program using the Logic Model theory; and (3) exploring benefits and obstacles in implement the program. The need for integration of educational and service to strengthen health systems was explored from the perspective of informants. The program evaluation is assessed based on input, process, outcomes and environmental factors. The interviews were conducted using the recording device and interview guideline. All informants signed the informed consent. Data analysis was performed through the process of transcription, coding, categorization and theme compilation. Triangulation method and member check were performed to have valid and reliable data. The study was conducted from August 2015 to November 2016 and has been approved by the Health Research Ethics Committee of Faculty of Medicine Universitas Padjadjaran with registration number 033/UN6.C1.3.2/KEPK/PN/2015.

The curriculum of community-based programs for medical clerkship students in rural areas is explained in Table.

Students were placed in the puskesmas for 4 weeks, divided into several groups consisting of 5–10 people. The supervisor who was later called the field preceptor was a functional doctor at the

**Table Curriculum of Community-Based Programs for Medical Clerkship Students in Rural Area**

<b>The Components</b>	<b>Definition</b>
Competency	Able to manage individual, family or community health problems in a comprehensive, holistic, continuous, coordinated & collaborative manner in the context of public health center.
Objectives	<ol style="list-style-type: none"> <li>1. Explain how to manage information systems at the public health center.</li> <li>2. Understand and implement methods to identify the conditions and problems of puskesmas' management and health problems as well as local community resources for solving the problems.</li> <li>3. Exploring data related to health determinants which include environmental, behavior, heredity and health services both in health care, families and communities.</li> <li>4. Plan, implement and evaluate group and community health education program.</li> </ol>
Delivery methods	<ol style="list-style-type: none"> <li>1. Community health teaching with field preceptor.</li> <li>2. Case report session with internal preceptor.</li> <li>3. Clinical science session with internal preceptor.</li> <li>4. Expert session.</li> <li>5. Home visit, community empowerment.</li> </ol>
Evaluation	Written examination, group mini project. Mini CEX.

puskesmas who had followed the standardization of clinical and community teaching assessment.

*understand the activities and what can be done by the us (puskesmas)...."*

## Results

Focus group discussions were conducted on 11 informants consisting of 5 heads of the puskesmas and 6 preceptors. There were 7 themes: socialize and disseminate the information; collaboration and local government involvement; integration of education and service; encourage lifelong learning; encourage the improvement of performance; skill enhancement; and sustainability.

Socialize and disseminate the information: before the implementation of the program, socialization and information dissemination was very important. This can be seen from the statement of informants.

*"It is very good to do in the beginning, because we know what activities...."*

*"....with this kind of socialization, we really*

Socialization and information dissemination will assist the preceptor and head of the puskesmas to understand the purpose and process of learning.

Collaboration and involvement of the community and local government: the success of implementing community-based education programs must be supported by collaboration and involvement of local government and communities. The collaboration made local government responsible for the presence of students and the success of the program. This is as revealed by the informant.

*"So we are responsible for the existence of students here because they will live and stay with local people...so we have to know what kind of place to prepare."*

Integration of education and services: the

placement of students in the community provided benefits for the puskesmas. This was revealed during focus group discussions.

*"In the learning process, the preceptors will be responsible...this program is good enough...help to run the program in the puskesmas...."*

*"...the students are very creative, so the staff is very happy because the students assist them to implement the health service program...and being taught new things...especially for programmers."*

Students are required to performed one intervention in the community according to the priority of health problems. This activity is one form of integration between education and health service.

*"...my suggestion is students should not identify new health problems but they can assist the puskesmas to solve current health problems...mmhmm...because the puskesmas has targets to be achieved."*

*"There has been no health education in the village for a long time because lack of staff, but with this program, several activities in the community can be carried out."*

In selecting the priority of the health problems is not only based on current data, but could be based on the priority program of the puskesmas.

*"...in our puskesmas...the selection of health problems are based on input from the head of the puskesmas...."*

Encourage lifelong learning: this program provides an opportunity for field preceptors to recall the theory of management in puskesmas and learn the latest issues in public health.

*"The material provided is aspects that we have forgotten for a long time, for example thinking about problem analysis, we only know how to practice but not for theory...so this really helps us to recall the theory...."*

The benefits perceived by the field preceptors are this program bring new insights and knowledge for them. Being the field receptor

makes the preceptors feel proud because they have the experience of being an educator.

*"Happy to be a preceptor...new experience...new insights...learning again...interesting...."*

Encourage the improvement of staff performance: the program can improve staff capacity in terms of management skill. In the learning process, students observe and interview staff to obtain data and perform situation analysis. This activity triggered the staff to provide comprehensive data and improve the recording and reporting process in the puskesmas.

*"...the staffs are trying to tidy up their records...usually they reluctant to provide data...but because the students ask...finally staff provides data and encourage them to tidy up the data...."*

*"There are so many staffs who are difficult to provide data when the student ask...mmhhhh they are afraid, especially those who manage the program at the puskesmas. It's difficult for students to intervene...but finally, the data are given."*

*"Staffs are taught to make good graphics on the computer...so that data can be read easily...creative students...."*

Skill improvement: specific skills related to the data collection process must be learned by students before being placed in the community.

*"The method of data collection is more emphasized, how to retrieve data...because students are confused and need to know how to retrieve data, including how to analyze it...in the puskesmas they should do that."*

This program provides opportunities for students to apply the knowledge and skills. Before the students are placed, students should be equipped with adequate skills including cultural competence.

*"...the discipline of students is good, but they don't make good relationship with staff and local people...it's like...there is a gap with the staff...maybe because of the language barrier...ewuh pakewuh-lah."*

Sustainability: based on the FGDs, the sustainability of the program is necessary to integrate education and services which in turn it will help to solve local health problems.

*"It is better if the program is continued...because it will be very helpful for puskesmas...so that the activities can be evaluated continuously."*

The head of puskesmas expected the community interventions conducted regularly and evaluated continuously.

*"...when the activities are continuous...it can be evaluated for its success...for example disease prevention..."*

*"...hopefully in the future there will be better cooperation...there are doctors who can be placed in Sukabumi because we really need it..."*

## Discussion

This study was a case study to evaluate community-based medical education programs in rural areas. This program had been implemented in several rural areas in West Java. The study found that the success of a program implementation requires several support systems and influenced by several factors.

The socialization of the program will influence the success of the program. At this stage, detail explanation about the objectives of the program, learning methods, and supporting resources was introduced. This effort helps related stakeholders understand the benefits of the program.<sup>8</sup>

The results of this study found that the implementation of the program will run optimally if related stakeholders such as the community and local government are involved from the beginning of the program. This study supports other research that collaboration between related stakeholders greatly determines the success of the program so that the program can be developed in a wider scope.<sup>10,11</sup> Community and local government support will help implement the program continuously.<sup>12-14</sup> Through community involvement, community members are actively involved in fostering students and contributing to their educational experience.<sup>13</sup>

This study showed that the implementation of this program not only encourages the learning process but also the improvement of health services at puskesmas. Previous research stated

that placing students in the community will help in identifying health-related problems that ultimately help people improve health.<sup>15</sup> Other research stated that participating directly in the community can provide experience to students to manage problems in the community.<sup>3</sup> This integration is a concrete implementation of the learning principles such as student-centered, student-teacher, and student-community/health service relationship.<sup>13</sup>

The involvement of doctors at the puskesmas as preceptor provides benefits for them in enhancing management skills and updating related knowledge. There is also an opportunity for them to become a medical educator.<sup>16</sup> One systematic study stated that doctors in practice setting are the main key to the success of medical education.<sup>4</sup>

The implementation of this program has provided benefits for increasing staff motivation at the puskesmas. Community-based education can be a strategy to improve the performance of medical personnel in rural and remote areas.<sup>17</sup> Regular evaluations will encourage human resources to improve performance.<sup>18</sup>

Programs that involving students will provide direct experience in managing real problems in the community, enhance critical thinking and innovation. Through this program, students can more easily relate theory to practice.<sup>13,19</sup> Students practice to communicate and effectively managing community health problems.<sup>4,8</sup> The early involvement of students should be accompanied by equipping students with the related skills.<sup>11,20</sup>

Sustainability is one of the expected outcomes of program implementation. Program objectives can be assessed if the program can be carried out continuously with regular and periodic evaluations.<sup>21,22</sup>

This study has a limitation because the data obtained does not reflect the overall program implementation. The analysis is needed from the perspective of students as an actor of the program.

## Conclusion

The community-based medical education in rural areas has been implemented as planned. Sustainability of the curriculum is needed to contribute to the improvement of community health status.

### Conflict of Interest

The authors declare that they have no conflict of interest.

### Acknowledgement

The authors would like to thank the Faculty of Medicine Universitas Padjadjaran for supporting this study.

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The Editor would like to thank you for the effort and expertise of all reviewers, without which it would be impossible to maintain the high standards of peer-reviewed journals.

**Prof. Dr. Budi Setiabudiawan, dr., Sp.A.(K.), M.Kes.**

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**Dr. Yani Triyani, dr., Sp.P.K., M.Kes.**

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p-ISSN 2301-9123



9 772301 912306

e-ISSN 2460-5441



9 772460 544103