BUKTI KORESPONDENSI

ARTIKEL JURNAL INTERNASIONAL BEREPUTASI

Judul : The effect of stress level on the therapeutic outcomes of type 2 diabetes mellitus at the regional public hospital of West Nusa Tenggara province

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No	Perihal	Tanggal
1.	Bukti penerimaan abstrak artikel untuk dipresentasikan secara oral pada **Scientific committee of Annual Conference on Pharmacy Practice and Pharmaceutical Sciences (ACPPPS) 2020**	17 Oktober 2020
2.	Bukti proofreading manuskrip	18 November 2020
3.	Bukti penerimaan manuskrip/full paper untuk dipublikasi pada ***Pharmacy Education Journal***	20 November 2020
4.	Bukti konfirmasi review dan hasil review manuskrip pertama	16 Februari 2021
5.	Bukti manuskrip yang diresubmit	17 Februari 2021
6.	Bukti konfirmasi pengecekan *galley* manuskrip	19 Juli 2021
7.	Bukti penerimaan publikasi	25 Juli 2021
8.	Bukti konfirmasi artikel *published online*	28 Juli 2021

1. Bukti penerimaan abstrak artikel untuk dipresentasikan secara oral pada Scientific committee of Annual Conference on Pharmacy Practice and Pharmaceutical Sciences (ACPPPS) 2020

(17 Oktober 2020)

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Letter of Acceptance PIT IAI 2020

1 message

Ikatan Apoteker Indonesia <billing@iai.id> Sat, Oct 17, 2020 at 3:44 PM
Reply-To: Ikatan Apoteker Indonesia <billing@iai.id>
To: Baiq Leny Nopitasari <baiqleny.nopitasari@gmail.com>
Cc: b4nch4@gmail.com

Dear **Baiq Leny Nopitasari**,
Abstract Code: **OP2020008**

Scientific committee of Annual Conference on Pharmacy Practice and Pharmaceutical Sciences (ACPPPS) 2020 would like to inform you that your abstract entitled **"The Effect of Stress Level on the Therapeutic Outcomes of Type 2 Diabetes Mellitus at The General Hospital of West Nusa Tenggara Province"**, has been accepted by the scientific committee of ACPPPS 2020 for Oral Presentation. We are pleased to invite you to participate in the event which will be held on November 5-7, 2020.

The final agenda of the presentation is currently being finalized and it will be announced on the website (link: www.iai.id/pit2020/presentationschedule).

Selected papers will be published in International Proceeding of Annual Conference in Pharmacy Practice and Pharmaceutical Sciences which indexed in ISI Web of Science/ Scopus (in progress). Please follow the guidance in the website (link: www.iai.id/pit2020/fullpaper) to submit your full paper manuscript. We will inform you about the additional cost for publishing.

For any update or further information, kindly do reach us through:
email: infopit2020@gmail.com
whatsapp: 0813-6534-0190 or 0811-314-411

We thank you once again for your cooperation, and we look forward to meeting you virtually.

With kindest regards

Christina Avanti, Ph.D
Scientific Committee

2. Bukti proofreading manuskrip

(18 November 2020)

Category: Clinical Pharmacy (CP)

The Effect of Stress Level on the Therapeutic Outcomes of Type 2 Diabetes Mellitus at ~~The~~ the ~~General Hospital~~Regional Public Hospital of West Nusa Tenggara Province

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Abstract

Diabetes Mellitus (DM) is a complex chronic disease ~~that~~ which requires ongoing medical care with a multifactorial risk reduction strategy beyond glycemic control. ~~Patient~~ Patients' self-management, education and support are very important to prevent acute complications and ~~reduce~~ to reduce the risk of long-term complications. Type 2 diabetes is a disease characterized by an ~~increase in~~ increase of blood glucose levels and cannot be cured. Stress levels ~~can~~ may affect Fasting Blood Glucose (FBG) and 2-hours Postprandial Blood Glucose (2HPPBG). Stress level consists of several levels ~~including~~ comprising of normal, mild, moderate, severe, and very heavy. ~~This study aims to~~ The objective of this study is to determine the effect of stress levels on the therapeutic outcomes of type 2 DM patients at ~~The~~ the ~~General Hospital~~Regional Public Hospital of West Nusa Tenggara Province. This research method ~~is~~ was an analytic observational with a sample of 37 patients using the Perceived Stress Scale (PSS) questionnaire. Data analysis ~~using~~ used linear regression test. The results showed that stress had a significant effect on Fasting Blood Glucose (FBG) with a significance value of p (0.038) ~~and~~, and ~~stress~~ it had a significant effect on blood sugar levels of 2-hours Postprandial Blood Glucose (2HPPBG) with a significance value of p (0.001).

Keywords: diabetes Mellitus; stress level; fasting blood glucose; 2-hours postprandial blood glucose; PSS

Introduction

Diabetes Mellitus (DM) is a disease in which glucose (simple sugar) levels in the blood are high because ~~the body~~ body cannot release or use insulin sufficiently. ~~Patient~~ Patients' self-management, education and support are very important to prevent acute complications and ~~reduce~~ to reduce the risk of long-term complications. There is a significant evidence ~~that~~ which supports various interventions to improve the outcome of therapy for DM patients [1]. According to the results ~~of the~~from Riset Kesehatan Data (Data Health Research) in 2018, the prevalence of non-communicable diseases has increased when compared to the previous year [2]. The prevalence of DM in Indonesia according to the consensus of the Indonesian Endocrinology Association based on doctor's diagnoses in populations aged <15 years ~~has increased~~ had increased from 2013, ~~namely~~ which was 0.15% ~~then~~, while in 2018 to 0.2% [3]. ~~Then the~~ Moreover, the prevalence of DM based on blood tests in people aged >15 years ~~has increased~~ had increased from 2013, ~~namely~~ which was 10.9% in 2018 [2].

The psychological impact of DM ~~began to be felt~~ has been felt by patients since the diagnosis of DM ~~and~~, and the disease had been going on for several months. The ~~patient~~ patients ~~begins~~ began to experience psychological disorder including stress related to the treatment ~~he/she is~~ they ~~taking~~ take [4]. According to Glover (2016), stress has been one of the factors ~~that arise~~ arising in diabetics. ~~According to him,~~He stated that stress greatly affects diabetes because it ~~will affect~~affects the control and level of blood glucose levels [5]. When a person is ~~faced~~ encountered with a stressful situation, the stress response can be in the form of ~~an increasing~~ a raising ~~the~~ hormone adrenaline which ~~can~~ eventually ~~convert~~ converts glycogen reserves in the liver into glucose. Continuously, high blood glucose levels ~~can lead~~ may lead to complications of diabetes.

Stress and Diabetes Mellitus have a very close relationship, especially in urban residents. Life pressures and unhealthy lifestyles accompanied by rapid technological advances and various illnesses ~~that are being~~ suffered in the same time have caused a person's condition to deteriorate, ~~thus triggering~~ which triggers stress. Diabetes Mellitus patients who experience stress ~~can cause~~ may cause problems in controlling blood glucose [6][7][8]. Measuring stress levels in DM patients ~~using~~ used the Perceived Stress Scale

(PSS) questionnaire to identify the respondent's stress description ~~which consists~~ comprising of 10 question items. The questionnaire used ~~is~~ was an instrument ~~that~~ which has been validated by Zaenal Arifin in 2011 with a validity and reliability value of 0.85 [9]. ~~Measurement~~ The measurement of diabetes stress has an important role in improving the quality of health and well-being of patients, especially at ~~The~~ the ~~General Hospital~~Regional Public Hospital of West Nusa Tenggara Province. The incidence of diabetes mellitus ~~is~~ was included in ~~the~~ 10 magnitude of the disease contained in the disease department at ~~The~~ the ~~General Hospital~~Regional Public Hospital of West Nusa Tenggara Province in 2018 with a total of 2,249 outpatients per year. The level of diabetes stress is very ~~important~~ essential to be examined at ~~The~~ the ~~General Hospital~~Regional Public Hospital of West Nusa Tenggara Province because Diabetes Mellitus is always included in ~~the~~ 10 magnitude of the disease.

~~The purpose of this study~~ The objective of this study is to determine the effect of stress on fasting blood glucose levels (FBG) and 2 hours after meals (2hPPG) in outpatients with type 2 diabetes mellitus at the~~The General Hospital~~Regional Public Hospital of West Nusa Tenggara Province.

Material and Method

This study used an analytical observational method with a cross sectional approach ~~to determine~~in determining the effect of stress on fasting blood glucose levels (FBG) and ~~2 hours~~2-hours after meals (2hPPG) in patients with type 2 diabetes mellitus at the Internal Medicine Department of the ~~General Hospital~~Regional Public Hospital of West Nusa Tenggara Province. The time of the study was performed for a period of 4 four months, ~~namely~~ which were February 2020- to May 2020. The inclusion criteria were T2DM patients with age ≥ 46 years ~~received~~ who had received oral antidiabetics at least 6 months with ICD code X E.11 before the stress measurements and were willing to sign the informed consent form. ~~Exclusion~~ The exclusion criteria ~~are~~ were deaf patient, illiterate and pregnant patient. Subjects who met the inclusion criteria were 37 T2DM patients. This study ~~has~~ had been approved by the ethics committee of ~~General Hospital~~Regional Public Hospital of West Nusa Tenggara Province, Indonesia with number 070.2/13/KEP/2020.

Questionnaire Perceived of Stress Scale (PSS) declared valid and usable by conducting direct observational interviews with patients using a questionnaire ~~that~~

consisting ofconsists of 10 question items whose validitywhich validity has had been tested by Zaenal Arifin (2011) with validity and reliability test results of 0.85 with a total item of the similar question which was same as the results declared valid and usable [9]. Data collection was done administered by an interview with PSS and medical records or patient patients' status which include includes name, age, gender, diagnosis, treatment, and laboratory data. PSS are valid and reliable scale covering both anxiety and depression, that which could beis used to measure the degree of individual's response to stressful situations. It has been mentioned specifically that the PSS is an effective scale to measure in measuring the relationship between stress appraisal and the risk for any disease [10][11].

Data The data were analyzed descriptively to describe patients' characteristics. To see the effect of stress levels on FBG and 2hPPG, SPSS 20.0 analysis was carried outperformed, then inputting input the research data using linear regression and seeing identified the significance value of each data. Linear regression is a statistical method used to formfor forming a model or relationship between one or more independent variables X and a response variable Y. Regression analysis with one independent variable X is called simple linear regression.

Results and Discussion

Subject characteristic

The characteristics of T2DM patients taken during the study including included gender, patient age, and and length of time the patient suffered from DM.

Table 1. Initial data Data on the characteristics Characteristics of subjectSubject

Characteristics		N	Percentage (%)
Gender	Men	21	56.75
	Women	16	43.25
Age	<50 years	3	8.10
	>50 years	34	91.90
	6 months	1	2.70

Long Suffering of Diabetes	>6 months	36	97.30

Based on table 1, ~~it shows~~ it is identified that more DM patients are male as many as 21 people (56.75%), and female as many as 16 people (43.24%). The results of this study are different from the research result conducted by Levine (2008), ~~which means~~ meaning that women have a tendency to experience diseases related to endocrine disorders such as diabetes mellitus and gestational diabetes mellitus (GDM) [12]. ~~In addition~~Furthermore, women ~~of~~ in productive age have a tendency to experience Polycystic Ovarian Syndrome (POS) with a frequency of 5-10%. In Polycystic Ovarian Syndrome (POS) ~~it~~, it can be ~~found~~ identified that there is a disruption in insulin secretion and insulin activity as well as a disturbance in blood pressure regulation ~~which is~~ whichi is as an early sign of ~~the risk of~~ cardiovascular disorders. POS is associated with insulin resistance~~, has~~ which has a risk for impaired glucose tolerance, diabetes and hypertension.

DM is a disease ~~whose~~ which prevalence continues to increase. T2DM is a disease that generally occurs in the middle of age and elderly. The prevalence and occurrence of T2DM ~~is~~ are ~~associated~~ associated with the increasing age. About 50% of T2DM are over 60 years old [13]. The results showed that for a total of 37 patients, ~~there were~~ 34 patients aged more than 50 years (91.89%) and 3 people aged less than 50 years old (8.10%), with an average patient age is 62 years old. ~~Thus~~ Hence, the current research ~~conducted~~ is the same as research conducted by Dunning (2009) which ~~states~~ explains that the prevalence of DM increases in the elderly, especially in developing countries and in developed countries ~~with an increase in prevalence~~ ranging from 10-20% at the age of 60-70 years [14]. The ~~Enhancement~~ enhancement in age ~~can~~ may cause a decrease in pancreatic beta cell function [15]. ~~According to~~ Pereira et al (2008~~),~~) emphasized that age is associated with the occurrence of insulin resistance and obesity in the elderly [16].

Based on table 1, it shows that patients ~~who suffer~~suffering from diabetes more than 6 months are 97.29%, while patients ~~who suffer~~ suffering less than 6 months are 2.70%. ~~This was~~It ~~also~~ was also conducted ~~done~~ by Safitri (2016) who ~~stated~~ discovered that 42.8% of patients ~~suffered~~ suffered from diabetes in the <5 years range [17]. Different things were found in ~~paper~~ the research conducted by American Diabetes Association

(2009) ~~that~~ which shows that 32.6% of respondents suffered from diabetes in the 5-10 year range [18].

The Effect of Stress on Blood Glucose Levels

Stress levels are associated with fasting blood glucose levels (FBG), ~~the~~ patients must be fasting for at least 10-12 hours first, then, the examination ~~is carried out~~ was administered ~~then~~ 2 hours after eating (2hPPG) ~~where~~ in which the examination ~~is carried out~~ was administered 2 hours after having meal~~, then~~ . Then, the blood glucose anytime which means that the test can be ~~done~~ conducted while fasting or not fasting, but in this study, blood glucose anytime was not ~~taken~~ performed because the tests could not be ~~done~~ completed simultaneously.

Random blood glucose test is a blood glucose check ~~that is~~ which is ~~carried out~~ performed every time, without any conditions of fasting and eating. This examination ~~is carried out~~ was administered ~~4~~ four times a day at the time before eating and before bed so that it can be ~~done~~ performed independently. ~~Examinations~~ The examinations of blood glucose levels at any time ~~not~~ did not ~~described~~ describe long-term DM control (blood glucose control for approximately 3 months). Thus, it ~~cannot~~ could not be used as a reference to see the relationship of stress with a patient's blood sugar levels. Normally, the results of the examination of blood glucose levels at any time~~, it ranges~~ range from 80--144 mg/dl. This random blood glucose examination ~~is carried out~~ was administered only to overcome problems ~~that may~~ which ~~arise~~ arose due to sudden changes in glucose levels [19].

Table 2. Linear regression analysis on the effect of stress levels on blood glucose levels

No	Domain	P-*value*	
		FBG	2hPPG
1.	Stress level	0,038	0,001

Note: *-P < 0,05 means there is a significant effect.

Table 3. Linear regression correlation effect of stress level on blood glucose levels

No	Domain	Correlation	
		FBG	2hPPG

1.	Stress level	0.295	0.508

The relationship between stressful experiences and controlling blood glucose level is very different ~~between~~ among individuals with type 2 diabetes. The mechanism of the influence of stress factors on blood glucose levels can be direct, which is stress ~~will affect~~ affects the neuroendocrine system, while ~~indirectly~~ the indirect influence is related to the duration of stress.

The effects of stress on the neuroendocrine system ~~include~~ consist of stimulation of the nervous system by activating the sympathetic-adrenal-medulla (SAM) system ~~which is then~~ followed by hypothalamic-pituitary-adrenal (HPA) activity. During stress, the sympathetic nervous system stimulates the adrenal glands of the medulla to secrete the ~~hormones~~ epinephrine and nor-epinephrine hormones into the blood circulation. The activity of the ~~hormones~~ epinephrine and nor-epinephrine hormones produces metabolic effects ~~that~~ which increase metabolic rate and increase blood glucose levels [20][21].

Stress causes ~~the~~ hypothalamus to secrete Corticotrophins Releasing Factor ~~which causes~~ causing adrenocorticotropin release and stimulates the adrenal cortex to secrete glucocorticoid hormones ~~such as~~ as cortisol ~~which causes~~ causing the increasing production of glucose by the liver and ~~reduces~~ reducing glucose uptake by tissues. Cortisol affects the breakdown of carbohydrates, proteins and fats through ~~the process of~~ gluconeogenesis process which produces glucose as an energy source and plays a significant role in influencing body functions during the resting period [22][23].

The results ~~showed~~ show that there was a significant relationship between stress levels and fasting blood glucose levels (FBG) in type 2 DM patients at the Regional Public Hospital of West Nusa Tenggara Province with a value of $p = 0.038$ ($p < 0.05$) and ($r = 0.295$)~~, and there~~. There ~~is~~ was also a significant relationship between stress levels and blood glucose levels 2 hours after eating (2hPPG) in type 2 DM patients at the Regional Public Hospital of West Nusa Tenggara Province with a value of $p = 0.001$ ($p < 0.05$) and ($r = 0.508$). Based on the research ~~that has been done~~conducted, it was found that the higher the stress level is, the higher ~~of~~ the fasting blood glucose level (FBG) will be~~, and conversely~~. Conversely, the lower the stress level is, the lower ~~of~~ the fasting blood glucose level (FBG) will be~~, which was~~ obtained with a p value <0.05. ~~Likewise~~Similarly,

with 2hPPG, the higher of stress level is, the higher ~~of~~ the blood glucose level 2 hours after eating (2hPPG) will be~~, and conversely~~. Conversely, the lower ~~of~~ the stress level is, the lower ~~of~~ the blood glucose level will be, 2 hours after eating (2hPPG) obtained with a p value <0,05.

The research was conducted in accordance with ~~the results of research~~ the research result conducted by Lustman et al (2005), which ~~showed~~ found a relationship between stress, low self-care and hyperglycemia (p = 0.05) and the relationship between stress and increased hemoglobin glycosylate (HbA1c) after controlling for body weight [24]. Stress in DM patients ~~can~~ may cause biochemical changes such as hyperglycemia, ~~activity of~~ the hypothalamus-pituitary-adrenal pathway activity (HPA-axis) and stress [25].

Meanwhile, ~~according to~~ Szoke (2008~~),)~~ stated that there is a significant relationship between stress and diabetes, especially in women aged 20-39 years, as well as in men, however, there is also a picture of more stress at a young age [26]. This difference, according to the researcher, ~~can be caused~~ is caused by differences in individual responses to stress and an even description of the stress of respondents as measured by the Perceived Stress Scale (PSS) instrument.

Furthermore, the correlation value obtained ~~is~~ was a positive correlation where the higher ~~of~~ the stress level is, the higher ~~of~~ the blood glucose levels obtained~~, which is~~ indicated by the higher the ~~of~~ correlation value, and contrary. ~~From~~ Based on the data above, it can be seen that the FBG correlation value is lower than 2hPPG. ~~This is because~~ It is because the significant value of FBG is higher than 2hPPG~~;~~, the lower ~~of~~ the significance value, the more significant ~~of~~ the relationship between stress levels and blood glucose levels in T2DM, the higher ~~of~~ the correlation value, and contrary.

When the study was conducted, the factor ~~that had~~ which had a big effect on the ~~increasing of stress~~stress increasing ~~when~~ measuring blood glucose levels 2 hours after eating (2hPPG) ~~is that~~ when the patient was in the hospital while waiting in a queue, ~~at the hospital the~~ long queue ~~caused the patient~~made the patient ~~to be~~ impatient to ~~get his/her~~ have the turn. ~~Examination~~The examination showed that it ~~, causing~~ caused the patient to feel emotional which resulted in increased ~~patient~~ patients' stress. ~~Furthermore~~Moreover, the limitation of the chairs where the ~~patient waits~~patients were waiting ~~which results in the patient being~~made them tired from standing for a long time which causes ~~the patient to be~~ emotional, thereby increasing the patient's stress. The

unsatisfactory service also causes patient stress to increase~~, such as~~ like less~~-~~friendly staff, and etc.

Conclusion

Based on the research ~~that has been done~~ conducted and from the discussion, ~~the conclusion~~it can be concluded thats ~~is~~ stress level has a significant effect on fasting blood glucose levels (FBG) with a value of ~~P~~ p = 0.038 (~~P~~p<0.05), and the stress levels have a significant effect on ~~2 hours~~2-hours postprandial glucose levels (2hPPG) with a ~~P~~p-value of 0.001 (~~P~~ p <0,05).

Acknowledgements

The authors ~~wish to~~ thank all the research participants for their cooperation ~~and~~ particularly to ~~this research was funded by a~~ University of Muhammadiyah Mataram, Indonesia who has funded this research.

Conflict of Interest

The authors declare no conflict of interest.

November 18, 2020

PROOFREADER STATEMENT
The information appearing herein has been read & evaluated in grammar & punctuation without changing the meaning & information from the original document by Center for International language & Cultural Studies of Islamic University of Indonesia CILACS UII
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PROOFREADER STATEMENT

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Name : Wahyu Tejo, S.S

Posotion : English Teacher and Translator of CILACS UII

as a proofreader of the document:

"THE EFFECT OF STRESS LEVEL ON THE THERAPEUTIC OUTCOMES OF TYPE 2 DIABETES MELLITUS AT THE REGIONAL PUBLIC HOSPITAL OF WEST NUSA TENGGARA PROVINCE"

explained that the aforementioned documents have been read and evaluated in grammar and punctuation without changing the meaning & information from the original document.

Yogyakarta, November 18, 2020

Proofreader

Wahyu Tejo, S.S

3. Bukti penerimaan manuskrip/full paper untuk dipublikasi pada *Pharmacy Education Journal*

(20 November 2020)

Kepada
Yth **apt. Baiq Leny Nopitasari, M.Farm**

Dengan hormat,

Bersama dengan ini kami sampaikan bahwa manuskrip dengan judul: **The Effect of Stress Level on the Therapeutic Outcomes of Type 2 Diabetes Mellitus at the Regional Public Hospital of West Nusa Tenggara Province**, kategori **Clinical Pharmacy, Pharmacy Education, and Regulation** sudah terima. Manuskrip akan dilakukan peer-review dan hasil review akan diinformasikan kepada penulis melalui email.
Atas perhatiannya, kami ucapkan terima kasih.

Panitia Ilmiah

PIT Virtual IAI 2020

Gmail

Baiq Leny Nopitasari <baiqleny.nopitasari@gmail.com>

Bukti Penerimaan Manuskrip PIT Virtual IAI 2020

1 message

rudi.hendra@lecturer.unri.ac.id <rudi.hendra@lecturer.unri.ac.id> Fri, Nov 20, 2020 at 8:34 PM
To: baiqleny.nopitasari@gmail.com

Kepada
Yth Bapak/Ibu Peserta PIT Virtual IAI 2020

Dengan hormat,

Bersama dengan ini kami sampaikan bahwa manuskrip bapak/ibu sudah kami terima (bukti terlampir). Manuskrip akan di peer-review dan hasilnya akan kami informasikan melalui email
Atas perhatiannya kami ucapkan terima kasih.

Panitia Ilmiah
PIT Virtual IAI 2020

Bukti Penerimaan Manuskrip apt. Baiq Leny Nopitasari, M.Farm.pdf
172K

4. Bukti konfirmasi review dan hasil review manuskrip pertama

(16 Februari 2021)

Gmail

Baiq Leny Nopitasari <baiqleny.nopitasari@gmail.com>

[PIT virtual IAI 2020] Decision on Manuscript the Effect of Stress Level on the Therapeutic Outcomes of Type 2 Diabetes Mellitus at the Regional Public Hospital of West Nusa Tenggara Province

1 message

Rudi Hendra <rhendra@iai.id> Tue, Feb 16, 2021 at 7:23 PM
To: baiqleny.nopitasari@gmail.com

Dear Baiq Leny Nopitasari

Your manuscript entitled “The Effect of Stress Level on the Therapeutic Outcomes of Type 2 Diabetes Mellitus at the Regional Public Hospital of West Nusa Tenggara Province" which you submitted to the Pharmacy Education Journal in collaboration with The Indonesian Pharmacists association (IAI), has been reviewed and the reviewer comments are attached.

The reviews are in general favourable and suggest that, subject to **minor correction**, your paper could be suitable for publication. Please consider these suggestions, and We look forward to receiving your revision.

When you revise your manuscript please highlight the changes you make in the manuscript by using the track changes mode in MS Word or by using bold or coloured text. To submit your revision, please click on the link below:

https://forms.gle/YtxXX7rpoo82Jk1q7

Due date: **March 2nd 2021**

Thank you

Sincerely

Scientific Committee
PIT Virtual IAI 2020

CHECK2_Manuscript_apt Baiq Leny Nopitasari M.Farm_Pharmacy Education_2020 - Baiq Leny Nopitasari.docx
57K

General comments

The topic of this paper has intrigued me. It is common to read that stress can jeopardize health. This paper has materialized such idea into evidence. Despite the interesting topic, this paper unfortunately was structured and written in poor compliance to the journal requirement. There is potential for publishing the paper if the authors have made significant revisions as the following:

Abstract

Please take a moment to understand the guideline for publication in the journal. Check the link https://pharmacyeducation.fip.org/pharmacyeducation/about/submissions for further details. As you may aware, the journal requires a structured version of abstract which should not exceed 150 words. This mean abstract consists of background, objective, methods, results and conclusion. The current version does not fit to this structure.

Introduction

Great introduction, love to read it. No issue

Methods

No concern

Results

Tables should be inserted on separate pages within the file and should be consecutively numbered with Roman numerals. Indicate in the margin where tables should be inserted.

I don't think that reporting additional information about random blood glucose is necessary in the results section. The authors might explore more about the results between fasting blood glucose and 2 hours pp

Discussion

No issue

Conclusion

No issue

References

No issue

The Effect of Stress Level on the Therapeutic Outcomes of Type 2 Diabetes Mellitus at the Regional Public Hospital of West Nusa Tenggara Province

Baiq Leny Nopitasari[1*], Baiq Nurbaety[2]

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Abstract

Diabetes Mellitus (DM) is a complex chronic disease which requires ongoing medical care with a multifactorial risk reduction strategy beyond glycemic control. Patients' self-management, education and support are very important to prevent acute complications and to reduce the risk of long-term complications. Type 2 diabetes is a disease characterized by an increase of blood glucose levels and cannot be cured. Stress levels may affect Fasting Blood Glucose (FBG) and 2-hours Postprandial Blood Glucose (2HPPBG). Stress level consists of several levels comprising of normal, mild, moderate, severe, and very heavy. The objective of this study is to determine the effect of stress levels on the therapeutic outcomes of type 2 DM patients at the Regional Public Hospital of West Nusa Tenggara Province. This research method was an analytic observational with a sample of 37 patients using the Perceived Stress Scale (PSS) questionnaire. Data analysis used linear regression test. The results showed that stress had a significant effect on FBG with a significance value of p (0.038), and it had a significant effect on blood sugar levels of 2HPPBG with a significance value of p (0.001).

Keywords: Diabetes Mellitus; Stress Level; FBG; 2HPPBG; PSS.

Introduction

Diabetes Mellitus (DM) is a disease in which glucose (simple sugar) level in the blood is high because body cannot release or use insulin sufficiently. Patients' self-management, education and support are very important to prevent acute complications and to reduce the risk of long-term complications. There is a significant evidence which supports various interventions to improve the outcome of therapy for DM patients (American Diabetes Association, 2020). According to the results from Riset Kesehatan Data (Data Health Research) in 2018, the prevalence of non-communicable diseases has increased when compared to the previous year (Data Health Research, 2018). The prevalence of DM in Indonesia according to the consensus of the Indonesian Endocrinology Association based on doctor's diagnoses in populations aged <15 years had increased from 2013, which was 0.15%, while in 2018 to 0.2% (Perkeni, 2015). Moreover, the prevalence of DM based on blood tests in people aged >15 years had increased from 2013, which was 10.9% in 2018 (Data Health Research, 2018).

The psychological impact of DM has been experienced by the patients since the early stage of the disease i.e diagnosis of DM and it may last over years given its chronic progress. The patients began to experience psychological disorder including stress related to the treatment they take (Avci & Kelleci, 2016). According to Glover (2016), stress has been one of the factors arising in diabetics. He stated that stress greatly affects diabetes because it affects the control and level of blood glucose levels (Glover *et al*., 2016). When a person is encountered with a stressful situation, the stress response can be in the form of a raising hormone adrenaline which eventually converts glycogen reserves in the liver into glucose. Continuously, high blood glucose levels may lead to complications of diabetes.

Stress and Diabetes Mellitus have a very close relationship, especially in urban residents. Life pressures and unhealthy lifestyles accompanied by rapid technological

advances and various illnesses suffered in the same time have caused a person's condition to deteriorate, which triggering stress. Diabetes Mellitus patients who experience stress may cause problems in controlling blood glucose (Golden *et al*., 2008; Knol *et al*., 2006; Richard *et al*., 2002). Measuring stress levels in DM patients used the Perceived Stress Scale (PSS) questionnaire to identify the respondent's stress description comprising of 10 question items. The questionnaire used was an instrument which has been validated by Zaenal Arifin in 2011 with a validity and reliability value of 0.85 (Arifin, 2011). The measurement of diabetes stress has an important role in improving the quality of health and well-being of patients, especially at the Regional Public Hospital of West Nusa Tenggara Province. The incidence of diabetes mellitus was included in 10 magnitude of the disease contained in the disease department at the Regional Public Hospital of West Nusa Tenggara Province in 2018 with a total of 2,249 outpatients per year. The level of diabetes stress is very essential to be examined at the Regional Public Hospital of West Nusa Tenggara Province because Diabetes Mellitus is always included in 10 magnitude of the disease.

The objective of this study is to determine the effect of stress on fasting blood glucose levels (FBG) and 2 hours after meals (2hPPG) in outpatients with type 2 diabetes mellitus at the Regional Public Hospital of West Nusa Tenggara Province.

Methods

This study used an analytical observational method with a cross sectional approach in determining the effect of stress on fasting blood glucose levels (FBG) and 2-hours after meals (2hPPG) in patients with type 2 diabetes mellitus at the Internal Medicine Department of the Regional Public Hospital of West Nusa Tenggara Province. The time of the study was performed for a period of four months from February 2020 to May 2020. The inclusion criteria were T2DM patients with age ≥46 years who had received oral antidiabetics at least 6

months with ICD code X E.11 before the stress measurements and were willing to sign the informed consent form. The exclusion criteria were deaf patient, illiterate and pregnant patient. Subjects who met the inclusion criteria were 37 T2DM patients. This study had been approved by the ethics committee of the Regional Public Hospital of West Nusa Tenggara Province, Indonesia number 070.2/13/KEP/2020.

Questionnaire Perceived of Stress Scale (PSS) declared valid and usable by conducting direct observational interviews with patients using a questionnaire consisting of 10 question items which validity had been tested by Arifin (2011) with validity and reliability test results of 0.85 with a total item of the similar question which was same as the results (Arifin, 2011). Data collection was administered by an interview with PSS and medical records or patients' status which includes name, age, gender, diagnosis, treatment, and laboratory data. PSS are valid and reliable scale covering both anxiety and depression, which is used to measure the degree of individual's response to stressful situations. It has been mentioned specifically that PSS is an effective scale in measuring the relationship between stress appraisal and the risk for any disease (Vasanth *et al*., 2017; Al Kalaldeh & Abu Shosha; 2012).

The data were analyzed descriptively to describe patients' characteristics. To see the effect of stress levels on FBG and 2hPPG, SPSS 20.0 analysis was performed, input the research data using linear regression and identified the significance value of each data. Linear regression is a statistical method used for forming a model or relationship between one or more independent variables X and a response variable Y. Regression analysis with one independent variable X is called simple linear regression.

Results

Subject characteristic

The characteristics of T2DM patients taken during the study included gender, patient age, and length of time the patient suffered from DM.

Table 1. Initial Data on the Characteristics of Subject

Characteristics		N	Percentage (%)
Gender	Men	21	56.75
	Women	16	43.25
Age	<50 years	3	8.10
	>50 years	34	91.90
Long Suffering of Diabetes	6 months	1	2.70
	>6 months	36	97.30

The Effect of Stress on Blood Glucose Levels

Stress levels are associated with fasting blood glucose levels (FBG), the patients must be fasting for at least 10-12 hours first, then the examination was administered 2 hours after eating (2hPPG) in which the examination was administered 2 hours after having meal. Then, the blood glucose anytime which means that the test can be conducted while fasting or not fasting, but in this study blood glucose anytime was not performed because the tests could not be completed simultaneously.

Random blood glucose test is a blood glucose check which is performed every time, without any conditions of fasting and eating. This examination was administered four times a day at the time before eating and before bed so that it can be performed independently. The examinations of blood glucose levels at any time did not describe long-term DM control (blood glucose control for approximately 3 months). Thus, it could not be used as a reference to see the relationship of stress with a patient's blood sugar levels. Normally, the results of the examination of blood glucose levels at any time, range from 80-144 mg/dl. This random blood glucose examination was administered only to overcome problems which arose due to sudden changes in glucose levels (Rachmawati, 2015).

Table 2. Linear Regression Analysis on the Effect of Stress Levels on Blood Glucose Levels

No	Domain	P-*value*

		FBG	2hPPG
1.	Stress level	0,038	0,001

Note:* P < 0,05 means there is a significant effect.

Table 3. Linear Regression Correlation Effect of Stress Level on Blood Glucose Levels

No	Domain	Correlation	
		FBG	2hPPG
1.	Stress level	0.295	0.508

Discussion

Based on table 1, it is identified that more DM patients are male as many as 21 people (56.75%), and female as many as 16 people (43.24%). The results of this study are different from the research result conducted by Levine (2008), meaning that women have a tendency to experience diseases related to endocrine disorders such as diabetes mellitus and gestational diabetes mellitus (GDM) (Levine, 2008). Furthermore, women in productive age have a tendency to experience Polycystic Ovarian Syndrome (POS) with a frequency of 5-10%. In Polycystic Ovarian Syndrome (POS), it can be identified that there is a disruption in insulin secretion and insulin activity as well as a disturbance in blood pressure regulation which is as an early sign of cardiovascular disorders. POS is associated with insulin resistance, which has a risk for impaired glucose tolerance, diabetes and hypertension.

DM is a disease which prevalence continues to increase. T2DM is a disease that generally occurs in the middle of age and elderly. The prevalence and occurrence of T2DM are associated with the increasing age. About 50% of T2DM are over 60 years old (Yakaryılmaz & Öztürk, 2017). The results showed that for a total of 37 patients, 34 patients aged more than 50 years (91.89%) and 3 people aged less than 50 years old (8.10%), with an average patient age is 62 years old. Hence, the current research is the same as research conducted by Dunning (2009) which explains that the prevalence of DM increases in the elderly, especially in developing countries and in developed countries ranging from 10-20%

at the age of 60-70 years (Dunning, 2009). The enhancement in age may cause a decrease in pancreatic beta cell function (Kalyani *et al.*, 2010). Pereira et al (2008), emphasized that age is associated with the occurrence of insulin resistance and obesity in the elderly (Pereira *et al*., 2008).

Based on table 1, it shows that patients suffering from diabetes more than 6 months are 97.29%, while patients suffering less than 6 months are 2.70%. It was also conducted by Safitri (2016) who discovered that 42.8% of patients suffered from diabetes in the <5 years range (Safitri, 2016). Different things were found in the research conducted by American Diabetes Association (2009) which shows that 32.6% of respondents suffered from diabetes in the 5-10 year range (American Diabetes Association, 2009).

The relationship between stressful experiences and controlling blood glucose level is very different among individuals with type 2 diabetes. The mechanism of the influence of stress factors on blood glucose levels can be direct, which is stress affects the neuroendocrine system, while the indirect influence is related to the duration of stress.

The effects of stress on the neuroendocrine system consist of stimulation of the nervous system by activating the sympathetic-adrenal-medulla (SAM) system followed by hypothalamic-pituitary-adrenal (HPA) activity. During stress, the sympathetic nervous system stimulates the adrenal glands of the medulla to secrete the epinephrine and nor-epinephrine hormones into the blood circulation. The activity of the epinephrine and nor-epinephrine hormones produces metabolic effects which increase metabolic rate and increase blood glucose levels (Lloyd *et al*., 2005; Champaneri *et al*., 2010).

Stress causes hypothalamus to secrete Corticotrophins Releasing Factor which causing adrenocorticotropin release and stimulates the adrenal cortex to secrete glucocorticoid hormones as cortisol causing the increasing production of glucose by the liver and reducing glucose uptake by tissues. Cortisol affects the breakdown of carbohydrates, proteins and fats

through gluconeogenesis process which produces glucose as an energy source and plays a significant role in influencing body functions during the resting period (Hasan *et al*., 2014; Cosgorve *et al*., 2012).

The results show that there was a significant relationship between stress levels and fasting blood glucose levels (FBG) in type 2 DM patients at the Regional Public Hospital of West Nusa Tenggara Province with a value of $p = 0.038$ ($p < 0.05$) and ($r = 0.295$). There was also a significant relationship between stress levels and blood glucose levels 2 hours after eating (2hPPG) in type 2 DM patients at the Regional Public Hospital of West Nusa Tenggara Province with a value of $p = 0.001$ ($p < 0.05$) and ($r = 0.508$). Based on the research conducted, it was found that the higher the stress level is, the higher the fasting blood glucose level (FBG) will be. Conversely, the lower the stress level is, the lower the fasting blood glucose level (FBG) will be, obtained with a p value <0.05. Similarly, with 2hPPG the higher of stress level is, the higher the blood glucose level 2 hours after eating (2hPPG) will be. Conversely, the lower the stress level is, the lower the blood glucose level will be, 2 hours after eating (2hPPG) obtained with a p value <0,05.

The research was conducted in accordance with the research result conducted by Lustman et al (2005), which found a relationship between stress, low self-care and hyperglycemia ($p = 0.05$) and the relationship between stress and increased hemoglobin glycosylate (HbA1c) after controlling for body weight (Lustman *et al*., 2005). Stress in DM patients may cause biochemical changes such as hyperglycemia, the hypothalamus-pituitary-adrenal pathway activity (HPA-axis) and stress (Llorente & Malphurs, 2007).

Meanwhile, Szoke (2008) stated that there is a significant relationship between stress and diabetes, especially in women aged 20-39 years, as well as in men, however, there is also a picture of more stress at a young age (Szoke *et al*., 2008). This difference, according to the

researcher, is caused by differences in individual responses to stress and an even description of the stress of respondents as measured by the Perceived Stress Scale (PSS) instrument.

Furthermore, the correlation value obtained was a positive correlation where the higher the stress level is, the higher the blood glucose levels obtained, indicated by the higher the correlation value, and contrary. Based on the data above, it can be seen that the FBG correlation value is lower than 2hPPG. It is because the significant value of FBG is higher than 2hPPG, the lower the significance value, the more significant the relationship between stress levels and blood glucose levels in T2DM, the higher the correlation value and contrary.

When the study was conducted, the factor which had a big effect on the stress increasing when measuring blood glucose levels 2 hours after eating (2hPPG) was when the patient was in the hospital while waiting in a queue, the long queue made the patient impatient to have the turn. The examination showed that it, caused the patient to feel emotional which resulted in increased patients' stress. Moreover, the limitation of the chairs where the patients were waiting made them tired from standing for a long time which causes emotional, thereby increasing the patient's stress. The unsatisfactory service also causes patient stress to increase, like less friendly staff, and etc.

Conclusion

Based on the research conducted and from the discussion, it can be concluded that stress level has a significant effect on fasting blood glucose levels (FBG) with a value of $p = 0.038$ ($p<0.05$) and the stress levels have a significant effect on 2-hours postprandial glucose levels (2hPPG) with a p-value of 0.001 ($p <0,05$).

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Conflict of Interest

The authors declare no conflict of interest.

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5. Bukti manuskrip yang diresubmit (17 Februari 2021)

The Effect of Stress Level on the Therapeutic Outcomes of Type 2 Diabetes Mellitus at the Regional Public Hospital of West Nusa Tenggara Province

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Abstract

Diabetes Mellitus (DM) is a complex chronic disease which requires ongoing medical care with a multifactorial risk reduction strategy beyond glycemic control. Patients' self-management, education and support are very important to prevent acute complications and to reduce the risk of long-term complications. Stress levels may affect fasting blood glucose (FBG) and 2-hours postprandial blood glucose (2HPPBG). The objective of this study is to determine the effect of stress levels on the therapeutic outcomes of type 2 DM patients at the Regional Public Hospital of West Nusa Tenggara Province. This research method was an analytic observational with a sample of 37 patients using the Perceived Stress Scale (PSS). Data analysis used linear regression test. The results showed that stress had a significant effect on FBG with a significance value of p (0.038), and it had a significant effect on blood sugar levels of 2HPPBG with a significance value of p (0.001).

Keywords: Diabetes Mellitus; Stress Level; FBG; 2HPPBG; PSS.

Introduction

Diabetes Mellitus (DM) is a disease in which glucose (simple sugar) level in the blood is high because body cannot release or use insulin sufficiently. Patients' self-management, education and support are very important to prevent acute complications and to reduce the risk of long-term complications. There is a significant evidence which supports various interventions to improve the outcome of therapy for DM patients (American Diabetes Association, 2020). According to the results from Riset Kesehatan Data (Data Health Research) in 2018, the prevalence of non-communicable diseases has increased when compared to the previous year (Data Health Research, 2018). The prevalence of DM in Indonesia according to the consensus of the Indonesian Endocrinology Association based on doctor's diagnoses in populations aged <15 years had increased from 2013, which was 0.15%, while in 2018 to 0.2% (Perkeni, 2015). Moreover, the prevalence of DM based on blood tests in people aged >15 years had increased from 2013, which was 10.9% in 2018 (Data Health Research, 2018).

The psychological impact of DM has been experienced by the patients since the early stage of the disease i.e diagnosis of DM and it may last over years given its chronic progress. The patients began to experience psychological disorder including stress related to the treatment they take (Avci & Kelleci, 2016). According to Glover (2016), stress has been one of the factors arising in diabetics. He stated that stress greatly affects diabetes because it affects the control and level of blood glucose levels (Glover *et al*., 2016). When a person is encountered with a stressful situation, the stress response can be in the form of a raising hormone adrenaline which eventually converts glycogen reserves in the liver into glucose. Continuously, high blood glucose levels may lead to complications of diabetes.

Stress and Diabetes Mellitus have a very close relationship, especially in urban residents. Life pressures and unhealthy lifestyles accompanied by rapid technological

advances and various illnesses suffered in the same time have caused a person's condition to deteriorate, which triggering stress. Diabetes Mellitus patients who experience stress may cause problems in controlling blood glucose (Golden *et al*., 2008; Knol *et al*., 2006; Richard *et al*., 2002). Measuring stress levels in DM patients used the Perceived Stress Scale (PSS) questionnaire to identify the respondent's stress description comprising of 10 question items. The questionnaire used was an instrument which has been validated by Zaenal Arifin in 2011 with a validity and reliability value of 0.85 (Arifin, 2011). The measurement of diabetes stress has an important role in improving the quality of health and well-being of patients, especially at the Regional Public Hospital of West Nusa Tenggara Province. The incidence of diabetes mellitus was included in 10 magnitude of the disease contained in the disease department at the Regional Public Hospital of West Nusa Tenggara Province in 2018 with a total of 2,249 outpatients per year. The level of diabetes stress is very essential to be examined at the Regional Public Hospital of West Nusa Tenggara Province because Diabetes Mellitus is always included in 10 magnitude of the disease.

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Results

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The characteristics of T2DM patients taken during the study included gender, patient age, and length of time the patient suffered from DM.

The Effect of Stress on Blood Glucose Levels

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Discussion

Based on table 1, it is identified that more DM patients are male as many as 21 people (56.75%), and female as many as 16 people (43.24%). The results of this study are different from the research result conducted by Levine (2008), meaning that women have a tendency to experience diseases related to endocrine disorders such as diabetes mellitus and gestational diabetes mellitus (GDM) (Levine, 2008). Furthermore, women in productive age have a

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Based on table 1, it shows that patients suffering from diabetes more than 6 months are 97.29%, while patients suffering less than 6 months are 2.70%. It was also conducted by Safitri (2016) who discovered that 42.8% of patients suffered from diabetes in the <5 years range (Safitri, 2016). Different things were found in the research conducted by American Diabetes Association (2009) which shows that 32.6% of respondents suffered from diabetes in the 5-10 year range (American Diabetes Association, 2009).

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stress factors on blood glucose levels can be direct, which is stress affects the neuroendocrine system, while the indirect influence is related to the duration of stress.

The effects of stress on the neuroendocrine system consist of stimulation of the nervous system by activating the sympathetic-adrenal-medulla (SAM) system followed by hypothalamic-pituitary-adrenal (HPA) activity. During stress, the sympathetic nervous system stimulates the adrenal glands of the medulla to secrete the epinephrine and nor-epinephrine hormones into the blood circulation. The activity of the epinephrine and nor-epinephrine hormones produces metabolic effects which increase metabolic rate and increase blood glucose levels (Lloyd *et al*., 2005; Champaneri *et al*., 2010).

Stress causes hypothalamus to secrete Corticotrophins Releasing Factor which causing adrenocorticotropin release and stimulates the adrenal cortex to secrete glucocorticoid hormones as cortisol causing the increasing production of glucose by the liver and reducing glucose uptake by tissues. Cortisol affects the breakdown of carbohydrates, proteins and fats through gluconeogenesis process which produces glucose as an energy source and plays a significant role in influencing body functions during the resting period (Hasan *et al*., 2014; Cosgorve *et al*., 2012).

The results show that there was a significant relationship between stress levels and fasting blood glucose levels (FBG) in type 2 DM patients at the Regional Public Hospital of West Nusa Tenggara Province with a value of $p = 0.038$ ($p < 0.05$) and ($r = 0.295$). There was also a significant relationship between stress levels and blood glucose levels 2 hours after eating (2hPPG) in type 2 DM patients at the Regional Public Hospital of West Nusa Tenggara Province with a value of $p = 0.001$ ($p < 0.05$) and ($r = 0.508$). Based on the research conducted, it was found that the higher the stress level is, the higher the fasting blood glucose level (FBG) will be. Conversely, the lower the stress level is, the lower the fasting blood glucose level (FBG) will be, obtained with a p value <0.05. Similarly, with 2hPPG the higher

of stress level is, the higher the blood glucose level 2 hours after eating (2hPPG) will be. Conversely, the lower the stress level is, the lower the blood glucose level will be, 2 hours after eating (2hPPG) obtained with a p value <0,05.

The research was conducted in accordance with the research result conducted by Lustman et al (2005), which found a relationship between stress, low self-care and hyperglycemia (p = 0.05) and the relationship between stress and increased hemoglobin glycosylate (HbA1c) after controlling for body weight (Lustman *et al*., 2005). Stress in DM patients may cause biochemical changes such as hyperglycemia, the hypothalamus-pituitary-adrenal pathway activity (HPA-axis) and stress (Llorente & Malphurs, 2007).

Meanwhile, Szoke (2008) stated that there is a significant relationship between stress and diabetes, especially in women aged 20-39 years, as well as in men, however, there is also a picture of more stress at a young age (Szoke *et al*., 2008). This difference, according to the researcher, is caused by differences in individual responses to stress and an even description of the stress of respondents as measured by the Perceived Stress Scale (PSS) instrument.

Furthermore, the correlation value obtained was a positive correlation where the higher the stress level is, the higher the blood glucose levels obtained, indicated by the higher the correlation value, and contrary. Based on the data above, it can be seen that the FBG correlation value is lower than 2hPPG. It is because the significant value of FBG is higher than 2hPPG, the lower the significance value, the more significant the relationship between stress levels and blood glucose levels in T2DM, the higher the correlation value and contrary.

When the study was conducted, the factor which had a big effect on the stress increasing when measuring blood glucose levels 2 hours after eating (2hPPG) was when the patient was in the hospital while waiting in a queue, the long queue made the patient impatient to have the turn. The examination showed that it, caused the patient to feel emotional which resulted in increased patients' stress. Moreover, the limitation of the chairs

where the patients were waiting made them tired from standing for a long time which causes emotional, thereby increasing the patient's stress. The unsatisfactory service also causes patient stress to increase, like less friendly staff, and etc.

Conclusion

Based on the research conducted and from the discussion, it can be concluded that stress level has a significant effect on fasting blood glucose levels (FBG) with a value of $p = 0.038$ ($p<0.05$) and the stress levels have a significant effect on 2-hours postprandial glucose levels (2hPPG) with a p-value of 0.001 ($p <0,05$).

Acknowledgements

The authors thank all the research participants for their cooperation particularly to University of Muhammadiyah Mataram, Indonesia who has funded this research.

Conflict of Interest

The authors declare no conflict of interest.

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Table I. Initial Data on the Characteristics of Subject

Characteristics		N	Percentage (%)
Gender	Men	21	56.75
	Women	16	43.25
Age	<50 years	3	8.10
	>50 years	34	91.90
Long Suffering of Diabetes	6 months	1	2.70
	>6 months	36	97.30

Table II. Linear Regression Analysis on the Effect of Stress Levels on Blood Glucose Levels

No	Domain	P-*value*	
		FBG	2hPPG
1.	Stress level	0,038	0,001

Note:* P < 0,05 means there is a significant effect.

Table III. Linear Regression Correlation Effect of Stress Level on Blood Glucose Levels

No	Domain	Correlation	
		FBG	2hPPG
1.	Stress level	0.295	0.508

6. Bukti konfirmasi pengecekan galley manuskrip (19 Juli 2021)

Gmail **Baiq Leny Nopitasari <baiqleny.nopitasari@gmail.com>**

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IAI CONFERENCE PROCEEDINGS

RESEARCH ARTICLE

The effect of stress level on the therapeutic outcomes of type 2 diabetes mellitus at the regional public hospital of West Nusa Tenggara province

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Keywords
Diabetes mellitus
Fasting blood glucose
2-hour postprandial blood glucose
Perceived stress scale
Stress level

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Abstract

Introduction: Diabetes Mellitus (DM) is a complex chronic disease that requires ongoing medical care with a multifactorial risk reduction strategy beyond glycemic control. Self-management, education, and support are essential to prevent acute complications and reduce the risk of long-term complications. Stress levels may affect fasting blood glucose (FBG) and 2-hours postprandial blood glucose (2HPPBG). **Objectives:** This study aims to determine the effect of stress levels on the therapeutic outcomes of type 2 DM patients at the regional public hospital of West Nusa Tenggara province. **Methods:** This observational, cross-sectinal research was carried out on a sample of 37 patients using the Perceived Stress Scale (PSS). Data analysis used a linear regression test. **Results:** The results showed that stress had a significant effect on FBG (p=0.038) and 2HPPBG (p=0.001) levels.

Introduction

Diabetes Mellitus (DM) is a disease in which blood glucose (simple sugar) levels are high because the body cannot release or use insulin sufficiently. Self-management, education, and support are essential to prevent acute complications and reduce the risk of long-term complications. A significant body of evidence supports various interventions to improve DM therapy outcomes (American Diabetes Association, 2020). According to Riset Kesehatan Data (Data Health Research), the prevalence of non-communicable diseases in 2018 has increased compared to previous years (Data Health Research, 2018). The prevalence consensus of the Indonesian Endocrinology Association reported that, in Indonesia, DM prevalence based on doctors' diagnoses in patients below 15 years has increased from 0.15% in 2013 to 0.2% in 2018 (Perkeni, 2015). In people above 15 years, and according to blood tests, it also increased between 2013 and 2018 (Data Health Research, 2018).

The psychological impact of DM, including treatment-related stress, is experienced by patients since the early stages of the disease and may last for years, given the chronic nature of the illness (Avci & Kelleci, 2016). Stress seems to highly influence diabetes because it affects the control and level of blood glucose levels (Glover *et al*., 2016). During a stressful situation, the body response can be in the form of increased adrenaline, which eventually converts glycogen reserves in the liver into glucose. Over time, high blood glucose levels may lead to complications of diabetes.

Stress and DM have a very close relationship, especially in urban residents. Life pressures and unhealthy lifestyles accompanied by rapid technological advances and various concomitant illnesses can cause a person's condition to deteriorate. DM patients who experience stress may have problems in controlling blood glucose (Golden *et al*., 2008; Knol *et al*., 2006; Richard *et al*., 2002). Stress levels in DM patients were measured using the Perceived Stress Scale (PSS), a 10-item questionnaire that identifies the respondent's stress description. This instrument was validated by Zaenal Arifin in 2011, with a validity and reliability value of 0.85 (Arifin, 2011). The measurement of diabetes stress plays an essential role in improving the quality of health and well-being of patients, especially at the regional public hospital of West Nusa Tenggara province, where the number of outpatients in 2018 reached 2.249 per year.

The objective of this study is to determine the effect of stress on fasting blood glucose levels (FBG) and 2 hours after meals (2hPPG) in outpatients with type 2 diabetes mellitus at the regional public hospital of West Nusa Tenggara province.

Methods

This study used an analytical observational method with a cross-sectional approach in determining the effect of stress on fasting blood glucose levels (FBG) and 2-hours after meals (2hPPG) in patients with type 2 diabetes mellitus (T2DM) at the Internal Medicine Department of the regional public hospital of West Nusa Tenggara province. It was performed from February 2020 to May 2020. The inclusion criteria were T2DM patients aged ≥46 years who had been taking oral antidiabetics for at least six months (with ICD code X E.11) before the stress measurements and were willing to sign the informed consent form. The exclusion criteria were deaf, illiterate, and pregnant patients. The final sample included 37 T2DM patients who met the inclusion criteria. This study had been approved by the ethics committee of the regional public hospital of West Nusa Tenggara province, Indonesia, number 070.2/13/KEP/2020.

The Perceived of Stress Scale (PSS) is a valid 10-item tool, covering both anxiety and depression, used to measure the response of individuals to stressful situations by direct observational interviews with patients (Arifin, 2011); validity and reliability test results were 0.85, similar to Arifin results (Arifin, 2011). It is an efficient scale to measure the relationship between stress appraisal and the risk for any disease (Vasanth *et al*., 2017; Al Kalaldeh & Abu Shosha; 2012). Data were collected through interviews and medical records or patients, which include name, age, gender, diagnosis, treatment, and laboratory data.

The data were analysed descriptively on SPSS 20.0 using patients' characteristics. Linear regression was performed to measure the effect of stress levels on FBG and 2hPPG.

Results

Subject characteristic

The characteristics of T2DM patients taken during the study included gender, patient age, and length of time the patient suffered from DM.

The effect of stress on blood glucose levels

Stress levels are associated with fasting blood glucose levels (FBG); the patients must be fasting for at least 10-12 hours, then blood glucose levels are measured 2 hours after eating (2hPPG) a meal. In this study, random blood glucose levels (measured at any time of the day without any conditions of fasting and eating) were not performed because the tests could not be completed simultaneously. This examination was administered four times a day: before eating and before bed to be performed independently. It did not describe long-term DM control (blood glucose control for approximately three months). Thus, it could not be used as a reference to see the relationship of stress with a patient's blood sugar levels. The normal range of random blood glucose levels is 80-144 mg/dl. This random blood glucose examination was administered only to overcome problems that arose due to sudden changes in glucose levels (Rachmawati, 2015).

Discussion

Our sample included more males (21 patients, 56.75%) than females (16 patients, 43.24%), different from the findings of Levine (2008), showing that women are more likely to experience endocrine-related diseases, such as diabetes mellitus and gestational diabetes mellitus (GDM) (Levine, 2008). Furthermore, 5-10% of women in productive age are prone to experience Polycystic Ovarian Syndrome (POS). This condition is associated with disrupted insulin secretion, insulin activity, and blood pressure regulation, an early sign of cardiovascular disorders.

T2DM generally occurs in middle-aged people and the elderly. Its prevalence and occurrence are associated with older age, with about 50% of T2DM patients being over 60 years old (Yakaryılmaz & Öztürk, 2017). In our

sample, 34 patients were more than 50 (91.89%), and 3 were less than 50 (8.10%), with an average patient age is 62 years old, consistent with the research conducted by Dunning (2009), explaining that the prevalence of DM increases with age, especially in developing and developed countries ranging from 10-20% at the age of 60-70 years (Dunning, 2009). Ageing may cause a decrease in pancreatic beta-cell function (Kalyani *et al.,* 2010). Pereira et al. (2008) emphasized that age is associated with insulin resistance and obesity in the elderly (Pereira *et al*., 2008).

Table I shows that 97.29% of patients had diabetes for more than six months. In a study conducted by Safitri (2016), 42.8% of patients had diabetes from less than five years (Safitri, 2016). The American Diabetes Association (2009) revealed that 32.6% of respondents had diabetes from 5-10 years (American Diabetes Association, 2009).

Table I: Initial data on the characteristics of the subject

Characteristics		n	Percentage (%)
Gender	Men	21	56.75
	Women	16	43.25
Age	<50 years	3	8.10
	>50 years	34	91.90
The long suffering of diabetes	6 months	1	2.70
	>6 months	36	97.30

The relationship between stressful experiences and controlling blood glucose levels is very different among individuals with T2DM. Stress can affect blood glucose levels directly (by acting on the neuroendocrine system) or indirectly (related to the duration of stress).

The effects of stress on the neuroendocrine system consist of stimulating the nervous system by activating the sympathetic-adrenal-medulla (SAM) followed by hypothalamic-pituitary-adrenal (HPA) activity. During stress, the sympathetic nervous system stimulates the adrenal glands of the medulla to secrete epinephrine and norepinephrine into the blood circulation. The activity of these hormones produces metabolic effects, i.e., increased metabolic rate and blood glucose levels (Lloyd *et al*., 2005; Champaneri *et al*., 2010).

Stress causes the hypothalamus to secrete Corticotrophins Releasing Factor, which releases adrenocorticotropin and stimulates the adrenal cortex to secrete glucocorticoid hormones, such as cortisol, thereby increasing the production of glucose by the liver and reducing its uptake by tissues. Cortisol affects the breakdown of carbohydrates, proteins, and fats through the gluconeogenesis process, which produces glucose as an energy source and plays a significant role in influencing body functions during the resting period (Hasan *et al*., 2014; Cosgorve *et al*., 2012).

The results of this study showed a significant relationship between stress levels and both FBG (p = 0.038 and r = 0.295) and 2hPPG (p = 0.001 and r = 0.508) in T2DM patients at the regional public hospital of West Nusa Tenggara province (Table II). This showed the higher the stress, the higher the FBG and with 2hPPG.

Table II: Linear regression analysis on the effect of stress levels on blood glucose levels

Domain	*r* and *p*-value	
	FBG	2hPPG
Stress level	r = 0.295	r = 0.508
	p = 0.038	p = 0.001

p < 0,05 means there is a significant effect.

The results are consistent with those of Lustman and the authors (2005), showing a relationship between stress, low self-care, and hyperglycemia (p=0.05) and between stress and increased haemoglobin glycosylate (HbA1c) after controlling for body weight (Lustman *et al*., 2005). Stress in T2DM patients may cause biochemical changes, such as hyperglycemia and the hypothalamus-pituitary-adrenal pathway activity (HPA-axis) (Llorente & Malphurs, 2007).

In 2008, Szoke reported a significant relationship between stress and diabetes, especially in women aged 20-39 years and men, showing more stress at a young age (Szoke *et al*., 2008). This difference could be due to differences in individual responses to stress and its description as measured by the PSS.

Furthermore, the correlation between stress and FBG and 2hPPG was positive, where the higher the stress, the higher the values. Also, the FBG correlation value was lower than that of 2hPPG.

When the study was conducted, measuring 2hPPG was a factor that had a considerable effect on stress. Indeed, waiting in a queue, tiredness from standing because of the limited number of chairs, and the unsatisfactory service at the hospital, made patients irritable and emotional and resulted in increased stress.

Conclusion

This study showed that higher stress significantly increases fasting blood glucose (FBG) and 2-hours postprandial glucose (2hPPG) levels.

Acknowledgements

The authors thank all the research participants for their cooperation, particularly to the University of Muhammadiyah Mataram, Indonesia, who has funded this research.

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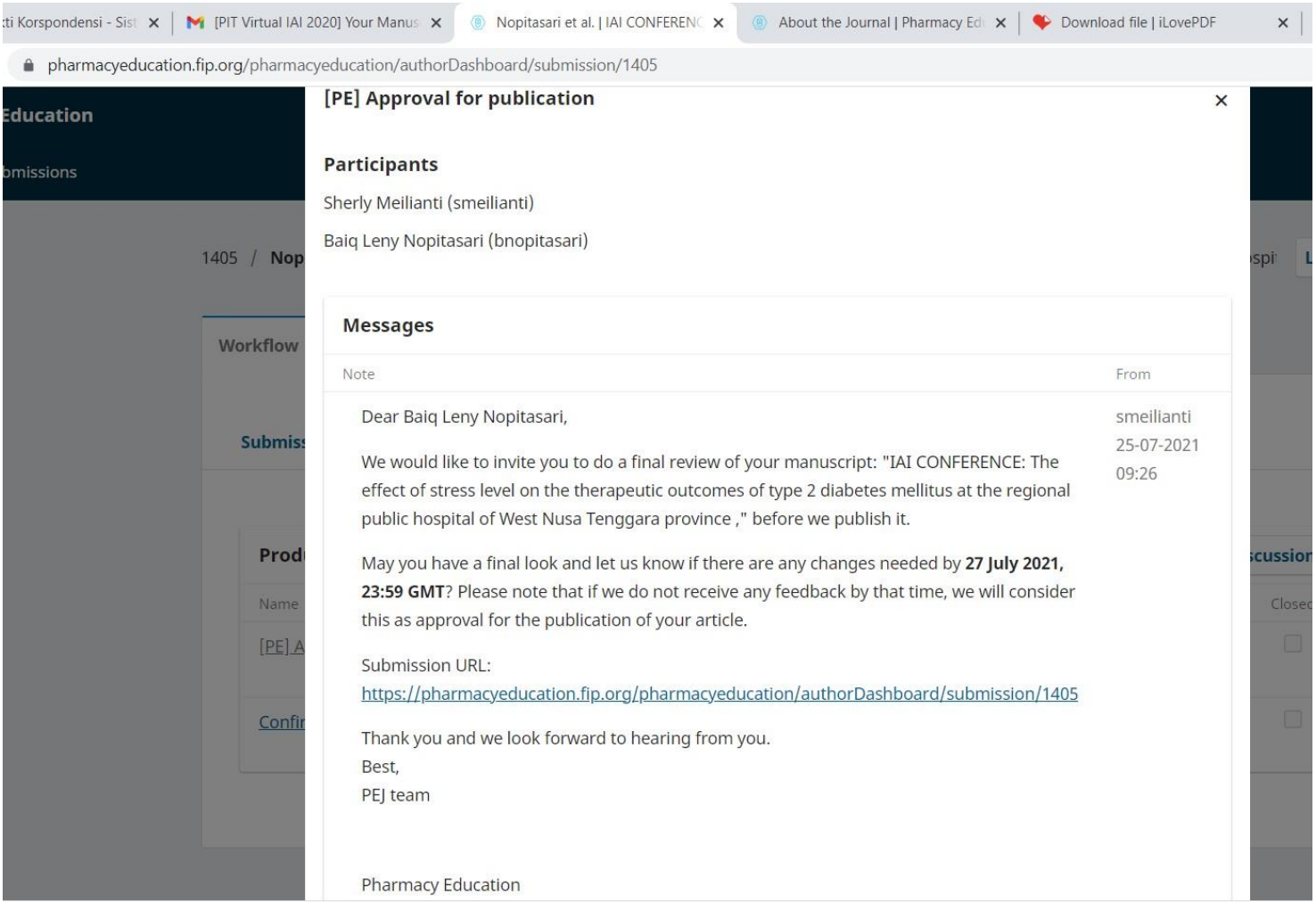
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May you have a final look and let us know if there are any changes needed by 27 July 2021, 23:59 GMT? Please note that if we do not receive any feedback by that time, we will consider this as approval for the publication of your article.
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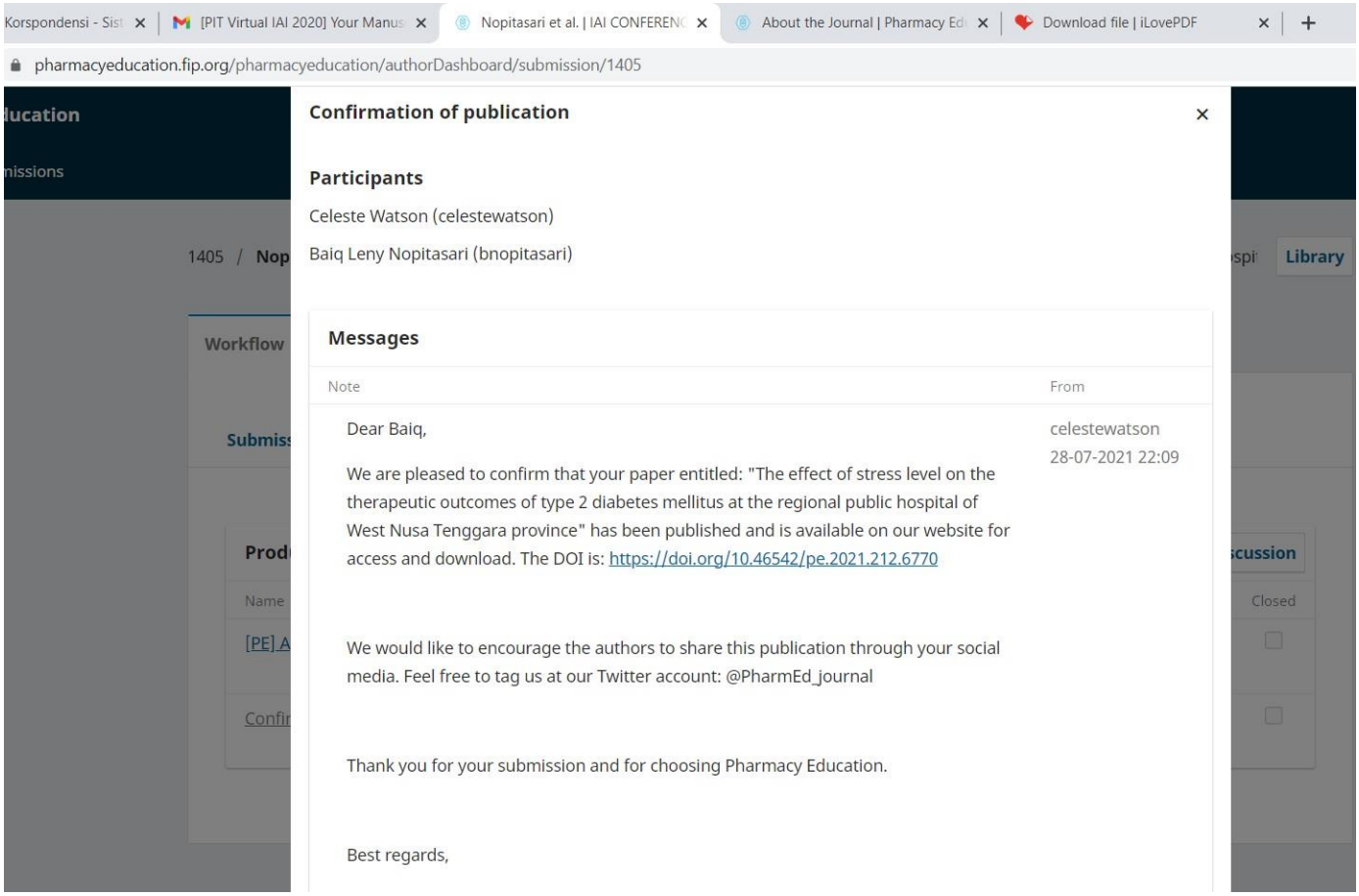
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Celeste Watson (celestewatson)
Baiq Leny Nopitasari (bnopitasari)
Messages
Note
From
Dear Baiq,
We are pleased to confirm that your paper entitled: "The effect of stress level on the therapeutic outcomes of type 2 diabetes mellitus at the regional public hospital of West Nusa Tenggara province" has been published and is available on our website for access and download. The DOI is: https://doi.org/10.46542/pe.2021.212.6770
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Gmail **Baiq Leny Nopitasari <baiqleny.nopitasari@gmail.com>**

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3 messages

Rudi Hendra <rhendra@iai.id> Thu, Jul 29, 2021 at 7:12 AM
To: adin.hakim@poltekkesjkt2.ac.id, afifah unjani <afifah@lecture.unjani.ac.id>, alvikusuma99@gmail.com, andi hermansyah <andi-h@ff.unair.ac.id>, Amal Fadholah <a.fadholah15@gmail.com>, annapradiningsih@gmail.com, asti rindarwati <asti.rindarwati@gmail.com>, ayukhariadini@ub.ac.id, baiqleny.nopitasari@gmail.com, Cyntiya Rahmawati <cyntiya.apt@gmail.com>, devioctavia1987@gmail.com, dewi@usd.ac.id, serlahwaty2@gmail.com, dimasdanangindriatmoko@gmail.com, Dina Christin Ayuning Putri <dinachristin@usd.ac.id>, Dolih Gozali <dolihgozali@gmail.com>, Erizal Zaini <erizal.ffua@gmail.com>, evanurinda@gmail.com, Fikri Alatas <fikrifaza@yahoo.co.id>, firmangustaman23@gmail.com, Fransiska Christianty <fransiska.farmasi@unej.ac.id>, fransiskussamuelrenaldi@gmail.com, helmina wati <republik.mina@gmail.com>, Husnul66@unlidrive.com, gekrai@angligan.com, ikanorcahyanti.unej@gmail.com, Ika Purwidyaningrum <ika_pur@setiabudi.ac.id>, Ika Puspitasari <ika.puspitasari@gmail.com>, ike.dhiah@staff.ubaya.ac.id, keni ida <keni.ida1992@gmail.com>, ledianasari@stfi.ac.id, lestyowulandari@unej.ac.id, Lusi Indriani <lusi.apoteker@gmail.com>, "Dr. apt. Lutfi Chabib, M.Sc." <lutfi.chabib@uii.ac.id>, noviayu.pharm@gmail.com, nuqi.gra@gmail.com, purwaniati@bku.ac.id, abielppump@gmail.com, felandj87@gmail.com, raharnis@yahoo.com, reynelda juliani sagala <reynelda.juliani@atmajaya.ac.id>, sinta.rachmawati@unej.ac.id, Nur Rahayuningsih <nur.rahayuridwan@gmail.com>, wahyuning setyani <wahyuningsetyani@gmail.com>, woro_yaning@yahoo.com, "Yulianto, S.Farm, Apt., M.P.H." <yulianto@uii.ac.id>, Yustina Sri Hartini <yustinahartini@usd.ac.id>, Zainul Islam <zainul_islam@uhamka.ac.id>
Cc: Sherly Meilianti <sherly@fip.org>

Dear Author,

We are pleased to notify you that your manuscript has now been **published online** at https://pharmacyeducation.fip.org/pharmacyeducation/issue/view/67, along with the following Digital Object Identifier (DOI): #.

Sincerely yours,
PIT Virtual IAI 2020
Scientific Committee

Alvi Kusuma <alvi.kusuma99@gmail.com> Thu, Jul 29, 2021 at 7:26 AM
To: Rudi Hendra <rhendra@iai.id>
Cc: Amal Fadholah <a.fadholah15@gmail.com>, Cyntiya Rahmawati <cyntiya.apt@gmail.com>, Dina Christin Ayuning Putri <dinachristin@usd.ac.id>, Dolih Gozali <dolihgozali@gmail.com>, "Dr. apt. Lutfi Chabib, M.Sc." <lutfi.chabib@uii.ac.id>, Erizal Zaini <erizal.ffua@gmail.com>, Fikri Alatas <fikrifaza@yahoo.co.id>, Fransiska Christianty <fransiska.farmasi@unej.ac.id>, Husnul66@unlidrive.com, Ika Purwidyaningrum <ika_pur@setiabudi.ac.id>, Ika Puspitasari <ika.puspitasari@gmail.com>, Lusi Indriani <lusi.apoteker@gmail.com>, Nur Rahayuningsih <nur.rahayuridwan@gmail.com>, Sherly Meilianti <sherly@fip.org>, "Yulianto, S.Farm, Apt., M.P.H." <yulianto@uii.ac.id>, Yustina Sri Hartini <yustinahartini@usd.ac.id>, Zainul Islam <zainul_islam@uhamka.ac.id>, abielppump@gmail.com, adin.hakim@poltekkesjkt2.ac.id, afifah unjani <afifah@lecture.unjani.ac.id>, andi hermansyah <andi-h@ff.unair.ac.id>, annapradiningsih@gmail.com, asti rindarwati <asti.rindarwati@gmail.com>, ayukhariadini@ub.ac.id, baiqleny.nopitasari@gmail.com, devioctavia1987@gmail.com, dewi@usd.ac.id, dimasdanangindriatmoko@gmail.com, evanurinda@gmail.com, felandj87@gmail.com, firmangustaman23@gmail.com, fransiskussamuelrenaldi@gmail.com, gekrai@angligan.com, helmina wati <republik.mina@gmail.com>, ikanorcahyanti.unej@gmail.com, ike.dhiah@staff.ubaya.ac.id, keni ida <keni.ida1992@gmail.com>, ledianasari@stfi.ac.id, lestyowulandari@unej.ac.id, noviayu.pharm@gmail.com, nuqi.gra@gmail.com, purwaniati@bku.ac.id, raharnis@yahoo.com, reynelda juliani sagala <reynelda.juliani@atmajaya.ac.id>, serlahwaty2@gmail.com, sinta.rachmawati@unej.ac.id, wahyuning setyani <wahyuningsetyani@gmail.com>, woro_yaning@yahoo.com

Thanks a lot.
[Quoted text hidden]

I Gusti Ayu Rai Widowati <gekrai@angligan.com> Thu, Jul 29, 2021 at 8:23 AM
To: Alvi Kusuma <alvi.kusuma99@gmail.com>

Cc: Rudi Hendra <rhendra@iai.id>, Amal Fadholah <a.fadholah15@gmail.com>, Cyntiya Rahmawati <cyntiya.apt@gmail.com>, Dina Christin Ayuning Putri <dinachristin@usd.ac.id>, Dolih Gozali <dolihgozali@gmail.com>, "Dr. apt. Lutfi Chabib, M.Sc." <lutfi.chabib@uii.ac.id>, Erizal Zaini <erizal.ffua@gmail.com>, Fikri Alatas <fikrifaza@yahoo.co.id>, Fransiska Christianty <fransiska.farmasi@unej.ac.id>, husnul66@unlidrive.com, Ika Purwidyaningrum <ika_pur@setiabudi.ac.id>, Ika Puspitasari <ika.puspitasari@gmail.com>, Lusi Indriani <lusi.apoteker@gmail.com>, Nur Rahayuningsih <nur.rahayuridwan@gmail.com>, Sherly Meilianti <sherly@fip.org>, "Yulianto, S.Farm, Apt., M.P.H." <yulianto@uii.ac.id>, Yustina Sri Hartini <yustinahartini@usd.ac.id>, Zainul Islam <zainul_islam@uhamka.ac.id>, abielppump@gmail.com, adin.hakim@poltekkesjkt2.ac.id, afifah unjani <afifah@lecture.unjani.ac.id>, andi hermansyah <andi-h@ff.unair.ac.id>, annapradiningsih@gmail.com, asti rindarwati <asti.rindarwati@gmail.com>, ayukhariadini@ub.ac.id, baiqleny.nopitasari@gmail.com, devioctavia1987@gmail.com, dewi@usd.ac.id, dimasdanangindriatmoko@gmail.com, evanurinda@gmail.com, felanDJ87@gmail.com, firmangustaman23@gmail.com, fransiskussamuelrenaldi@gmail.com, helmina wati <republik.mina@gmail.com>, ikanorcahyanti.unej@gmail.com, ike.dhiah@staff.ubaya.ac.id, keni ida <keni.ida1992@gmail.com>, ledianasari@stfi.ac.id, lestyowulandari@unej.ac.id, noviayu.pharm@gmail.com, nuqi.gra@gmail.com, purwaniati@bku.ac.id, raharnis@yahoo.com, reynelda juliani sagala <reynelda.juliani@atmajaya.ac.id>, serlahwaty2@gmail.com, sinta.rachmawati@unej.ac.id, wahyuning setyani <wahyuningsetyani@gmail.com>, woro_yaning@yahoo.com

Dear committee,

Thank you very much.
Stay safe and healthy.

Best regards,
Rai

On 29 Jul 2021, at 07.26, Alvi Kusuma <alvi.kusuma99@gmail.com> wrote:

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