Journal of the Medical Sciences
(Berkala Ilmu Kedokteran)

Volume 51, Number 1, 2019; 44-53
http://dx.doi.org/10.19106/JMedSci005101201906

Effects of resistant starch of mixed tubers snacks on glucose metabolism, leptin, visceral fat and body mass index in type 2 diabetes mellitus (T2DM)

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Submited: 2018-02-13
Accepted : 2019-03-09

ABSTRACT

Resistant starch could lower blood glucose, decrease adipocyte in adipose tissue and affect satiety hormones such as leptin. Tubers and pumpkin have high content of resistant starch, but their effectiveness to type 2 diabetes mellitus (T2DM) has not been known clearly. This research was conducted to determine the effectiveness of snack consumption made from tubers and pumpkins to BMI, visceral fat, glucose and leptin levels in the blood of T2DM patients and the correlation between the variables. The research method was pre-post clinical trial. Sixteen T2DM patients were in treatment (RS) and control groups. Subjects in RS group were given snack twice daily for 4 weeks. After following wash out process for 4 weeks, the same subjects was continued as subjects' control. Paired t-test and/or Wilcoxon-test was used to analyze the differences between values before and after treatment in the group and between groups. Pearson test was used to analyze the correlation of BMI, visceral fat, glucose and leptin level. The visceral fat was increased in RS group (p=0.04) after 4 weeks consuming snack but decrease in control group (p=0.04) without significant change of BMI. Leptin level was decreased (p=0.00) in RS group. Blood glucose significantly decreased (p=0.01) and leptin level increased slightly in control group. Comparing the RS and control group at the end of study, there were significantly different in the variation of visceral fat in the female groups (p=0.05) and leptin (p=0.05). Visceral fat correlated with BMI in the RS and control group. In conclusion, the mixed tubers and pumpkin snack decreased the leptin level but increased visceral fat.

ABSTRAK

Pati resisten dapat menurunkan glukosa darah, dan cadangan lemak pada jaringan adiposa serta mempengaruhi hormon yang berkaitan dengan rasa kenyang, salah satunya adalah leptin. Umbi-umbian dan labu kuning memiliki kandungan pati resisten yang cukup tinggi tetapi belum banyak penelitian mengenai efektivitas umbi-umbian dan labu kuning terhadap penderita diabetes melitus tipe 2 (DMT2). Penelitian ini dilakukan untuk mengetahui efektivitas konsumsi keripik berbahan baku umbi-umbian dan labu kuning terhadap indeks massa tubuh, lemak viseral, kadar glukosa, kadar leptin dalam darah penderita DMT2 serta korelasi antar variabel penelitian. Metode penelitian yang digunakan adalah *pre-post clinical trial* pada 16 subjek penderita DMT2 dalam kelompok perlakuan (RS) dan kelompok kontrol. Subjek dalam kelompok perlakukan diberi konsumsi makanan ringan dua bungkus sehari selama 4 minggu kemudian subjek yang sama menjadi subjek kelompok kontrol setelah jeda 4 minggu. Uji t berpasangan dan/atau uji Wilcoxon digunakan untuk menganalisa perbedaan pada awal dan akhir penelitian dalam satu kelompok dan antar kelompok. Uji korelasi Pearson digunakan untuk menganalisa korelasi BMI, lemak viseral, glukosa dan leptin. Hasil penelitian menunjukkan peningkatan lemak viseral pada kelompok RS (p=0,04) setelah mengonsumsi makanan ringan selama 4 minggu kebalikan dengan kelompok kontrol (p=0.04) tanpa perubahan berarti pada BMI. Kadar leptin menurun pada kelompok RS (p=0.00). Kelompok kontrol menunjukkan penurunan bermakna pada kadar glukosa darah (p=0.01) dan sedikit peningkatan dari leptin. Pada akhir penelitian, perbandingan antara kelompok RS dan kontrol menunjukkan perbedaan bermakna lemak viseral pada perempuan (p=0.05) dan leptin (p= 0.05). Uji korelasi menunjukkan adanya korelasi antara BMI dan lemak viseral baik pada kelompok RS maupun kontrol. Dapat disimpulkan makanan ringan berbahan umbi dan labu kuning dapat menurunkan kadar leptin dalam darah tetapi meningkatkan lemak viseral.

Keywords:
resistant starch
T2DM
leptin
visceral fat
diet

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INTRODUCTION

Type 2 diabetes mellitus (T2DM) is metabolic disorders characterized by hyperglycemia due to insufficient of insulin secretion, insulin action, or both.[1] This chronic hyperglycemia disorder causes severe or even fatal complications.[2] The prevalence of diabetes mellitus (DM) were 285 million adults in 2010 (6.4%), and is estimated to be 439 million adults (7.7%) in 2030.[3] During 20 years (2010-2030), DM in developing and developed countries could increase by 69 and 29%, respectively.[3] Approximately 90% of the cases are T2DM.[4] Countries with the largest numbers of diabetes cases are India, China, USA, Indonesia and Japan.[5]

The increased of T2DM prevalence is caused by various factors. Etiology of T2DM are multiple genetic factors, which are related to insufficient secretion of insulin and its resistance, along with environmental factors such as obesity, overeating, lack of physical activity and stress, as well as aging.[6,7] The T2DM patients are usually middle aged or older, but incident in young people, including children have been increasing.[7] Sigal *et al.* reported that diet and physical activity could reduce progressivity of impaired glucose tolerance (IGT) to diabetes effectively.[8]

Life style management, including medical nutrition therapy and physical activity has been proven to reduce risk factor of DM.[9] Replacement of starch in foods with resistant starch, which has a recommended minimum of 6 g/meal, might lead to lower postpandrial of blood glucose level since it has low glycemic index.[10] Animal studies have consistently shown that resistant starch increases insulin secretion and glucose metabolism.[11] The goal of diabetes management is to achieve and to maintain an HbAlc level of <7% or fasting blood glucose (FBG) < 100 mg/dL.[12] Resistant starch reduces postprandial insulinemia, increase fat oxidation, lower fat storage in adipocytes and increase satiety signaling including ghrelin, leptin, peptide tyrosine tyrosine (PYY), glucagon-like peptide-1 (GLP-1), gastric inhibitory peptide (GIP) and adiponectin.[13]

Several studies have shown that tubers contain high resistant starch.[14,15] Modification processing of tubers can increase their resistant starch content.[14] Indonesia as tropical country has many tubers plantation. East Indonesian population use tubers as their staple food. Effect of resistant starch of tubers for T2DM has not been widely known. This study aimed to evaluate the affectivity of mixed tubers snack in reducing blood glucose level, body mass index (BMI) and plasma leptin of T2DM subjects. Furthermore, the correlations between variables were also evaluated.

MATERIALS AND METHODS

Subjects recruitment

This was cross over study design involving T2DM patients who met inclusion and exclusion criteria were recruited in this study. The inclusion criteria were diagnosed as T2DM ≥ 1 year, age between 40 – 60 years, and level fasting blood glucose ≥ 126 mg/dL. The exclusion criteria were smoking, pregnant, lactating, and severe T2DM. Patients were studied on two occasions (two groups) separated by 4 weeks of wash out period. The 1st group was given mixed-tubers snack (RS group). The 2nd group was given mixed-tubers snack (control group). Blood samples were taken and analyzed two times, before and after the study. The study was approved by the Medical and Health Research Ethic Committee, Faculty of Medicine, Public Health and Nursing, Universitas Gadjah Mada, Yogyakarta. Informed consent was obtained from all individuals after a clearly explanation was given to the subjects.

Body weight (BW) and body height

(BH) were measured without shoes after taken fasting blood in the morning, and body mass index (BMI) was computed as weight in kg divided by height in meters squared (m^2). Visceral fat was measured by Bioelectrical Impedance Analysis (BIA). Fasting venous blood (10 mL) was taken out of each subject after 12 h fast and immediately divided into 3 labeled EDTA containing tubes. The tubes were centrifuged for 15 min at 2500-3000×g. The plasma od each sample was separated and immediately kept at −20°C until analysis. Plasma glucose was determined immediately after centrifugation.

Snack

Snack which given to subject was made by mixed tubers which is easily found in Indonesia. Indonesian people tend to enjoy eating crackers as snack, so in this study, tubers mixed snack were given to T2DM subjects. The process to produce the snack were: 1). *Cucurbita moschata* and *Dioscorea esculenta* L. were steamed until cooked then crushed well. 2). Steamed starch of *C. moschata, D. esculenta* L. and *Maranta arundinacea* were blended with tapioca and seasonings and put them in tube mold. 3). Steam the dough in tube mold until it was cooked. 4). Freeze the dough 24 h then cut and sun dried. 5). Fry the dry pieces in medium heat then spined. 6). The snack was ready to be consumed. The composition and total calories of the snack can be seen in TABLE 1. Total calories of one pack of snack was 75 kcal (16 g) and consumed twice daily in 4 weeks. Resistant starch in 32 g of snack is 4.25 g. Food record was used to monitor the subject's diet.

TABLE 1. Composition and total calories of 100 g tubers snack

Nutrition	Weight (g)	Calories (kcal)
Lipid	18.23	164.07
Protein	3.02	12.08
Carbohydrate	59.03	236.12
Soluble fiber	4.81	9.62
Unsoluble fiber	14.91	29.82
Total calories		451.71

Glucose blood level

Fasting glucose blood level was analyzed by enzymatic photometric GOD-FS glucose kit (DiaSys Diagnostic Systems). The procedure was performed according to the kit manual instructions.

Leptin

Leptin was analyzed by ELISA kit Leptin (*human)(sandwich*) 96 *wells* DRG with catalog number EIA2395. The procedure was done in accordance with the manual instructions of leptin kit.

Calculations and statistical analyses

Data were presented as mean ± standard deviation (SD). Statistical analyses were carried out using SPSS. The normal data were analyzed using paired t-test, whereas no normal data were analyzed using Wilcoxon test. The Pearson correlation coefficient was calculated to assess potential relationships. For this correlation, the change in percentage after hospital consumption was compared to the control. A p value < 0.05 was considered significant.

RESULTS

Characteristic od subjects

Subjects for this study were T2DM volunteers, consist of 7 male and 9 female. The mean of age was 52.75 ± 2.24 years, with BMI of 28.23 ± 3.39 kg/m^2 (TABLE 2). The visceral fat BMI and leptin of participants did not differ between the hospital and the control group at the start of the study, but the glucose levels of control group were higher than the RS group before treatment even though the study subjects were the same in both groups, after 4 weeks of washing.

TABLE 2. Baseline participants characteristic

Variable	RS (n=16)	Control (n=16)	p
BMI (kg/m^2)	28.23 ± 3.39	28.37 ± 2.89	0.551
Visceral fat (rating)	11.97 ± 0.31	12.53 ± 0.49	0.163
Leptin (ng/mL)	7.93 ± 2.22	8.08 ± 1.99	0.760
Glucose (mg/dL)	152.38 ± 1.29	183.35 ± 1.47	0.007

Noted: All body composition measurements were obtained after fasting for 12h between group differences determined by paired t test; Data presented as mean ± SD; RS: resistant starch

The TABLE 3 shows the after effect of consuming snack for 4 weeks. There was no significant change in BMI from baseline in all RS groups.

TABLE 3. BMI, visceral fat, glucose and leptin level before and after treatment in resistant starch (RS) group.

Variable	Before treatment	After treatment	Δ mean ± SD	p
BMI (mean ± kg/m^2)	28.32 ± 3.69	28.30 ± 2.94	0.02 ± 0.75	0.92
• Male	28.18 ± 3.03	28.12 ± 2.52	0.06 ± 0.80	0.86
• Female	28.27 ± 3.84	28.45 ± 3.38	-0.18 ± 0.46	0.70
Visceral fat [mean±SD rating]	12.31 ± 4.06	13.06 ± 4.06	-0.75 ± 1.29	0.04
• Male	14.43 ± 4.54	15.14 ± 3.93	-0.71 ± 1.11	0.14
• Female	10.67 ± 2.92	11.44 ± 3.54	-0.78 ± 1.48	0.15
• Glucose [mean ± mg/dL)	151.36 ± 1.29	147.91 ± 1.51	3.45 ± 0.22	0.30
• Male	137.59 ± 1.27	145.02 ± 1.65	0.95 ± 1.49	0.30
• Female	165.53 ± 1.28	147.91 ± 1.42	1.12 ± 1.22	0.13
Leptin [mean ± SD mg/dL]	7.94 ± 2.21	6.71 ± 2.16	1.18 ± 1.22	0.00
• Male	4.11 ± 1.45	3.55 ± 1.50	0.06 ± 1.22	0.07
• Female	13.22 ± 1.92	11.05 ± 1.81	1.20 ± 1.25	0.045

Note: data presented as mean ± SD; all data measurements were obtained after fasting for 12h

Control groups without mixed tuber snacks treatment is show in TABLE 4. Compared to the BMI of control group at the end of treatment, BMI in RS groups was slightly lower, although it was not significantly different (p=0.86).

TABLE 4. BMI, visceral fat, glucose and leptin level before and after study in control group

Variable	Before treatment	After treatment	Δ mean ± SD	p
BMI (mean ± kg/m^2)	28.37 ± 2.89	28.33 ± 3.12	0.04 ± 0.75	0.81
• Male	28.19 ± 2.58	28.19 ± 2.56	0.00 ± 0.02	0.40
• Female	28.51 ± 3.26	28.44 ± 3.64	0.07 ± 0.73	0.78
Visceral fat [mean±SD rating]	13.00 ± 5.54	12.25 ± 4.99	0.75 ± 1.29	0.04
• Male	15.57 ± 6.50	14.71 ± 5.62	0.86 ± 1.35	0.14
• Female	11.00 ± 3.94	10.33 ± 3.67	0.67 ± 1.32	0.17
Glucose [mean ± mg/dL)	183.35 ± 1.47	145.64 ± 1.48	1.26 ± 1.35	0.01
• Male	159.54 ± 1.40	146.46 ± 1.53	1.09 ± 1.22	0.30
• Female	203.65 ± 1.49	145.29 ± 1.47	1.40 ± 1.39	0.02
Leptin [mean ± SD mg/dL]	8.10 ± 1.99	8.55 ± 1.98	0.95 ± 1.43	0.56
• Male	4.83 ± 1.40	5.13 ± 1.28	0.94 ± 1.68	0.77
• Female	12.05 ± 1.86	12.75 ± 1.91	0.95 ± 1.23	0.44

Note: data presented as mean ± SD; all data measurements were obtained after fasting for 12h

The BMI in the female of RS group (TABLE 5) was higher than control group but it was not also significantly different (p=0.97).

TABLE 5. Comparison mean of BMI, visceral fat, glucose and leptin level between RS group and control group at the end of treatment

Variable	Δ mean ± SD	p
BMI (mean ± kg/m^2)	-0.03 ± 0.6	0.86
• Male	-0.07 ± 0.5	0.72
• Female	0.01 ± 0.69	0.97
Visceral fat [mean±SD rating]	0.81 ± 1.87	1.10
• Male	0.43 ± 2.37	0.65
• Female	1.11 ± 1.45	0.05
Glucose [mean ± mg/dL)	1.01 ± 1.41	0.95
• Male	0.99 ± 1.22	0.90
• Female	1.02 ± 1.56	0.91
Leptin [mean ± SD mg/dL]	0.78 ± 1.58	0.05
• Male	0.69 ± 1.83	0.16
• Female	0.87 ± 1.37	0.21

Note: data presented as mean ± SD; all data measurements were obtained after fasting for 12h

Visceral Fat

Consuming mixed tubers snack for 4 weeks significantly changed the visceral fat in the RS (TABLE3) and control groups (TABLE 4), although there were no significantly different between the RS and control group at the end of the treatment (TABLE 5). A significantly increase of visceral fat occurred in the RS group (p=0.02) but decreased in the control group (p=0.03) after 4 week. The mean of female visceral fat between RS and control groups at the end of study were significantly different (p=0.005) as shown in TABLE 5. At the end of the study, all of the visceral fat in the RS group increased as well as in both male and female groups, but the increase between genders was not significant (TABLE 3). Contrary to the RS group, in the control group, visceral fat decreased at the end of study, although it was not statistically significant except between female RS group and control group (TABLE 5).

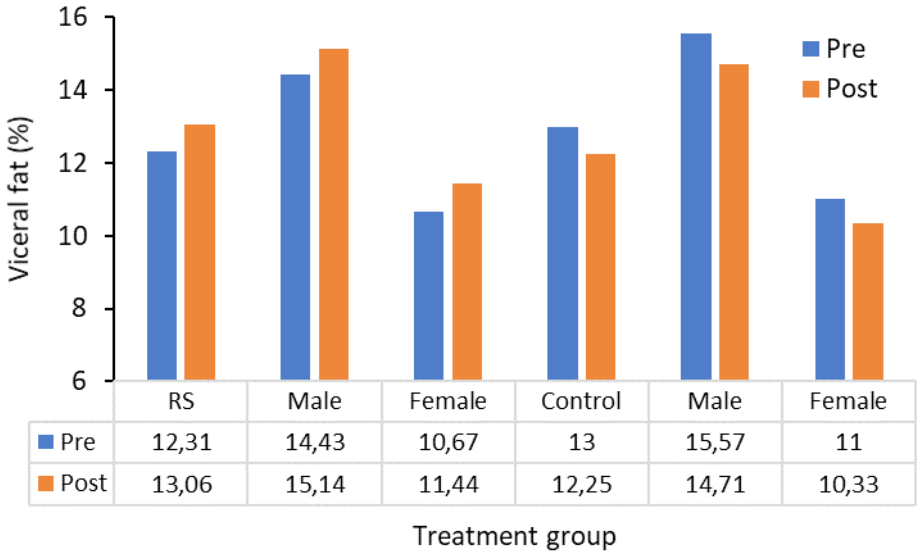

FIGURE 1. Visceral fat values before (pre) and after 4 weeks treatment (post) in RS and control groups

Glucose

Changes from baseline to week 4 for the plasma glucose in RS group are shown in TABLE 3. The decreased of glucose was not significantly different (p=0.30) but it was significant in control group (p=0.01) as shown in TABLE 4. Notable decrease of glucose from baseline to week 4 occurred in female control group (p= 0.02) (TABLE 4). FIGURE 2 shows line chart of glucose mean in all group.

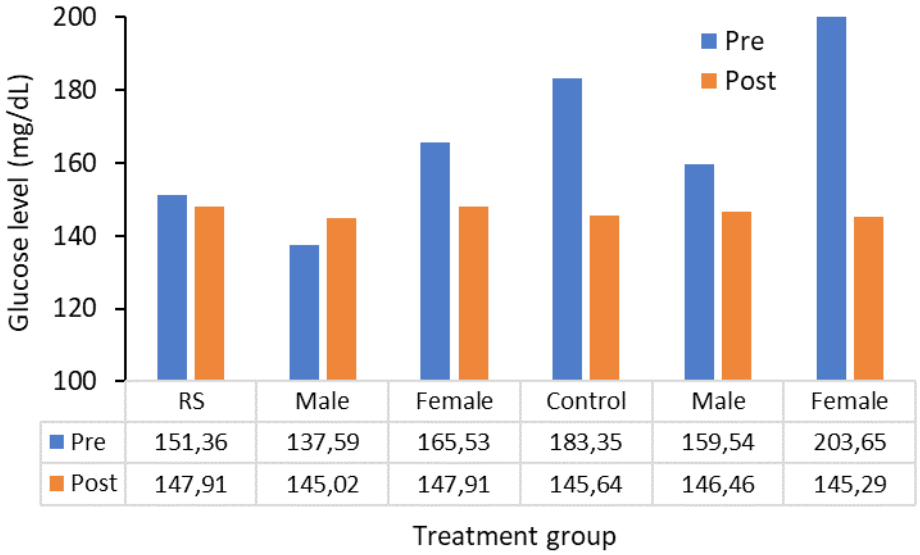

FIGURE 2. Mean of glucose level before (pre) and after 4 weeks treatment (post) in RS and control groups

Leptin

Consuming mixed tuber snack for 4 weeks significantly decrease the leptin in all RS group as well as in both male and female RS groups (TABLE 3). The change in leptin level at the end of week 4 were considerably different between RS group and control group (p=0.05) as shown in TABLE 5. FIGURE 3 shows line chart of leptin mean in all group.

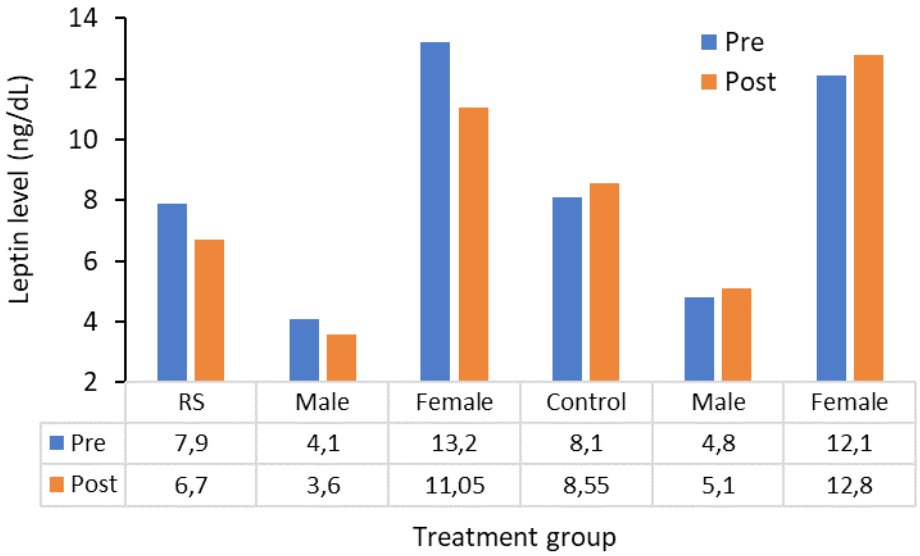

FIGURE 3. Mean of leptin before (pre) and after 4 weeks treatment (post) in RS and control groups

Relationship between body mass index and visceral fat

Pearson correlation between the mean of BMI and visceral fat was statistically significant in the beginning of study and at the end week 4 in all groups, both male and female. The mean of BMI has a pronounced strong correlation to the visceral fat at the end of study in RS group (r=0.79; p =0.000) and control group (r = 0.746; p = 0.001). The correlation between BMI and visceral fat was stronger in male RS group (r= 0.92; p=0.003) and female RS group (r= 0.956; p=0.000). There was no correlation between glucose and leptin.

DISCUSSION

Blood glucose level decreased in all groups but significantly in control group in accordance with a decrease in plasma glucose in the female control group. Plasma glucose in female control group increased sharply after the wash out period and 4 weeks later, plasma glucose decreased close to the level after 4 weeks of treatment. We assumed that the wash out period made female subjects feel unrestricted to eat since there was not food any recording, but the BMI did not change significantly.

Hyperglycemia is the result of impaired potential hepatic glucose phosphorylation and muscle glucose transport. Resistant starch consumption can improve insulin sensitivity, recover hepatic glucose phosphorylation capacity, restore hepatic gluconeogenesis and increase muscle glucose transportation.[16] The study showed there was a decrease in blood glucose level but it was still above normal glucose level. This may be due to a shorter 4-week treatment of bulb mixed snack foods compared to other RS studies. Without a change of habitual diet, exercise and the quantity of RS in tuber mixed snack, it is slightly below the recommended minimum level.

There was no significantly different in BMI in all groups at the end of the study. Similarly to some researchers, in this study, consuming 4 weeks of snack did not has effect on the BMI of T2DM patients. Due to their study, the feeding duration (4-12 weeks) of RS had no impact on the BMI.[13] Pearson correlation showed body mass index had strong correlation with visceral fat in all groups. Visceral fat increased considerably in RS groups, and decreased significantly in control groups. Resistant starch consumption shift hepatic fuel from lipid to carbohydrate utilization and improve insulin sensitivity.[16] Increase of BW and the accumulation of visceral fat could occur from the improvement of insulin sensitivity.[17]

Plasma leptin significantly decreased in RS group in accordance with a significant decreased in plasma leptin in female RS group. Leptin is a hormone synthesized by adipocytes and its level in the blood is related to adipocyte size and body fat percentage.[18] Resistant starch rendered adipocyte size smaller.[13] Subcutaneous adipose tissue greatly express and secrete leptin, more so than visceral adipose tissue.[19] Females have higher leptin levels than males, this may be due to hormonal differences and adipose distribution.[20]

CONCLUSION

Consuming mixed tubers snack for 4 weeks could lower leptin levels and increase visceral fat significantly. Increasing the RS in the mixed tubers snack composition may improve glucose levels in T2DM patients.

ACKNOWLEDGEMENTS

We would like to thanks all the parties who contribute to this study. We also would like to thank Ethics Commission of Medical and Health Research Faculty of Medicine, Public Health and Nursing,

Universitas Gadjah Mada, Yogyakarta for the permission of this study.

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