

# Gastroesophageal Reflux Disease among Elderly Type 2 Diabetes Mellitus in a Rural Area of Central Sulawesi: A Cross-sectional Study

**Kemas R. Notariza<sup>1</sup>, Nurcholis<sup>1</sup>, Hafiz Yusaryahya<sup>1</sup>, Nanda S. Karimah<sup>1</sup>, Ahmad Y. Mansur<sup>1</sup>, Gunawan Adhiguna<sup>1</sup>, Tri J. E. Tarigan<sup>2</sup>**

<sup>1</sup> Public Health Center (Puskesmas) of Beteleme, Subdistrict of Lembo, North Morowali Regency, Central Sulawesi, Indonesia.

<sup>2</sup> Division of Metabolic and Endocrinology, Department of Internal Medicine, Faculty of Medicine Universitas Indonesia - Cipto Mangunkusumo Hospital, Jakarta, Indonesia.

## Corresponding Author:

Tri Juli Edi Tarigan, MD. Ph.D. Division of Metabolic and Endocrinology, Department of Internal Medicine, Faculty of Medicine Universitas Indonesia - Cipto Mangunkusumo Hospital. Jl. Diponegoro no. 71, Jakarta 10430, Indonesia. email: tje\_tar@yahoo.com; kemasnotariza@yahoo.com.

## ABSTRAK

**Latar belakang:** diabetes melitus tipe 2 (DMT2) dan penyakit refluks gastroesofageal (gastroesophageal reflux disease [GERD]) sering dijumpai pada populasi lanjut usia (lansia). Studi ini bertujuan untuk menginvestigasi prevalensi, faktor-faktor risiko, dan insidens gejala-gejala alarm GERD pada pasien lansia dengan DMT2 di daerah pedesaan Sulawesi Tengah. **Metode:** studi potong-lintang ini dilakukan dari bulan Juli—September 2019 di Pusat Kesehatan Masyarakat (Puskesmas) Beteleme, Sulawesi Tengah. Pasien berusia  $\geq 60$  tahun, baru atau telah didiagnosis DMT2 berdasarkan kriteria American Diabetes Association (ADA) 2019 atau kriteria Perkumpulan Endokrinologi Indonesia (PERKENI) 2015, dipilih secara konsekutif. Kami mengeksklusi pasien yang sedang dalam terapi penghambat pompa-proton atau antagonis reseptor- $H_2$  atau memiliki riwayat pembedahan lambung atau esofagus. GERD didiagnosis pada pasien dengan skor  $\geq 8$  berdasarkan evaluasi dengan kuesioner GERD (GERD-Q) berbahasa Indonesia. **Hasil:** dari 60 pasien lansia dengan DMT2, 28,3% (interval kepercayaan [IK] 95%, 16,9-39,7) mengalami GERD. Analisis statistik memperlihatkan asosiasi signifikan antara frekuensi konsumsi teh ( $p=0,019$ ) dan kopi ( $p=0,015$ ) dengan GERD. Tidak ada hubungan bermakna yang ditemukan antara jenis kelamin ( $p=0,562$ ), obesitas ( $p=0,803$ ), ketercapaian pengendalian kadar glukosa darah ( $p=0,478$ ), durasi DMT2 ( $p=0,304$ ), dan jenis obat antihiperqlikemia ( $p=0,202$ ) dengan GERD. Penurunan berat badan merupakan gejala alarm dengan insidens tersering (47,1%; 95%CI, 23,4-70,8) pada kelompok GERD. **Kesimpulan:** prevalensi GERD cukup tinggi pada pasien lansia dengan DMT2. Konsumsi teh atau kopi berhubungan signifikan dengan GERD. Gejala-gejala alarm memerlukan evaluasi lebih lanjut untuk menyaring penyulit GERD.

**Kata kunci:** daerah pedesaan, diabetes melitus tipe 2, penyakit refluks gastroesofageal, usia lanjut.

## ABSTRACT

**Background:** type 2 diabetes mellitus (T2DM) and gastroesophageal reflux disease (GERD) are commonly seen in the geriatric population. This study aimed to investigate the prevalence, risk factors, and alarm-symptoms incidence of GERD among elderly patients with T2DM in a rural area of Central Sulawesi. **Methods:** this cross-sectional study was conducted from July—September 2019 in Public Health Center of Beteleme, Central Sulawesi. Patients aged  $\geq 60$  years old, newly or previously diagnosed with T2DM according to the 2019 American

*Diabetes Association (ADA) criteria or to the 2015 Indonesian Society of Endocrinology (PERKENI) criteria, were consecutively recruited. We excluded patients being on proton-pump inhibitor or H<sub>2</sub>-receptor antagonist therapy or having a history of gastric or esophageal surgery. GERD was diagnosed in patients with the score of  $\geq 8$  based on the Indonesian version of GERD questionnaire (GERD-Q). **Results:** among 60 elders with T2DM, 28.3% (95% confidence interval [CI], 16.9-39.7) had GERD. Statistical analysis showed that GERD was significantly associated with consumption frequency of tea ( $p=0.019$ ) and coffee ( $p=0.015$ ). No significant relationship was found between gender ( $p=0.562$ ), obesity ( $p=0.803$ ), achievement of blood glucose-level control ( $p=0.478$ ), duration of T2DM ( $p=0.304$ ), and type of antihyperglycemic drugs ( $p=0.202$ ) with GERD. Unintentional weight loss was the leading alarm symptom (47.1%; 95%CI, 23.4%-70.8%) found across the GERD group. **Conclusion:** GERD was prevalent among elderly patients with diabetes. Frequent consumption of either tea or coffee was associated with GERD. Alarm symptoms need further evaluation to screen for complications.*

**Keywords:** elderly, gastroesophageal reflux disease, rural area, type 2 diabetes mellitus.

## INTRODUCTION

Type 2 diabetes mellitus (T2DM) is a group of metabolic diseases characterized by hyperglycemia due to disorders in insulin secretion, insulin action, or both.<sup>1,2</sup> In Indonesia, the national prevalence of T2DM among people aged  $\geq 15$  years was 10.9% (95% confidence interval [CI], 10.5%-11.2 %) based on the Basic Health Research (Riskesdas) 2018.<sup>3</sup> The prevalence of T2DM among adults in rural sites was 1.4% (95% CI, 1.4%-1.5%). Central Sulawesi was one of the 12 provinces in Indonesia with a T2DM prevalence in adult population greater than the national one (2.2 [95% CI, 1.9-2.5] vs. 2.0 [95% CI, 2.0-2.1]).<sup>3</sup> T2DM is a common disease found in the aging population. In 2017, the global prevalence of T2DM among people aged 65-99 years was 18.8%, while Indonesia globally ranked 7th with most people older than 65 with T2DM (5.4 million).<sup>4</sup>

Gastroesophageal reflux disease (GERD) is a pathologic condition with troublesome symptoms and complications related to the reflux of stomach contents into the esophagus, oral cavity, and/or lung.<sup>5</sup> The prevalence of GERD in Indonesia reached 49.0% among adults with dyspepsia symptom who were sent to a primary-level referral hospital.<sup>6</sup> GERD is a malady commonly seen in the older population. The global prevalence of GERD in people aged  $\geq 50$  years was greater than people under 50 years (17.3% [95% CI, 13.3%-21.7%] vs. 14.0% [95% CI, 9.9%-18.7%]).<sup>7</sup> Esophageal acid clearance

is impaired in the elderly due to changes in esophageal motility and saliva production, hence the elders are more susceptible to suffer from GERD. Frequency of heartburn and regurgitation tends to decrease with advancing age, but on the contrary, elderly population has more atypical symptoms of GERD, such as dysphagia and odynophagia.<sup>8</sup> Older patients with GERD, compared with younger patients, are also at higher risk of developing serious complications of GERD, such as Barrett's esophagus, severe esophagitis, ulceration, stricture, and esophageal cancer.<sup>8,9</sup>

In the clinical practice, more than 70% of diabetic patients reported gastrointestinal symptoms. GERD was the most frequent gastrointestinal problem found among T2DM patients, with the prevalence of 60%.<sup>10</sup> However, preceding studies about the relationship between T2DM and GERD showed conflicting results, ranging from a solid association to no significant one.<sup>11-14</sup>

The prevalence of GERD among diabetic adults in a rural area of Indonesia was 29.7%.<sup>15</sup> However, up to now there is still no study which specifically investigate the prevalence of GERD among older population with T2DM. A research on this and its related risk-factors has never been conducted at any rural area settings in Indonesia, including in Central Sulawesi, where the primary health care facilities are the spearhead and the only center for managing T2DM and GERD in rural communities. This study aimed to investigate the prevalence, risk

factors, and alarm-symptoms incidence of GERD among elderly patients with T2DM in a rural area of Central Sulawesi.

## METHODS

This cross-sectional study was conducted from July – September 2019 in Public Health Center (Puskesmas) of Beteleme, Subdistrict of Lembo, North Morowali Regency, Central Sulawesi. Patients aged 60 years or older, newly or previously diagnosed with T2DM according to the 2019 American Diabetes Association (ADA) criteria or to the 2015 Indonesian Society of Endocrinology (PERKENI) criteria, were consecutively recruited. The exclusion criteria were ongoing therapy with proton-pump inhibitor or H2-receptor antagonist, or history of either gastric or esophageal surgery. Assuming the proportion of GERD in adult patients with T2DM in rural area of Indonesia to be 29.7%<sup>15</sup>, a minimum of 52 participants were required to determine the prevalence with a significance level ( $\alpha$ ) of 0.05 and the expected absolute precision of 0.125. The study protocol was designed in accordance with the ethical principles in the Declaration of Helsinki and was approved by the Head of Puskesmas Beteleme (No. 445/441.a/SK/PKM-BTL/VII/2019).

After giving written informed consent, eligible subjects were asked to fill in a questionnaire about subjects' characteristics, including demographic information (age, gender, ethnic, education background, occupation), history of T2DM diagnosis, medication history, dietary pattern (daily meal frequency, consumption frequency of tea, coffee, chocolate, orange, tomato, spicy foods, gassy foods/drinks, alcohol), smoking habit (Brinkman's index), and alarm symptoms of GERD (persistent dysphagia, persistent odynophagia, upper gastrointestinal bleeding, unintentional weight loss). Participants were also asked to complete the validated Indonesian-language GERD questionnaire (GERD-Q). This instrument was chosen because they included patients aged 18 years old or more, without excluding those aged older than 60 years.<sup>16</sup> GERD was diagnosed in patients with the score

of  $\geq 8$  on the evaluation of GERD-Q.<sup>17</sup>

Physical examination was performed to measure subjects' height, weight, and body mass index (BMI). Obesity was defined based on the BMI classification in adult Asians by WHO Western Pacific Region.<sup>18</sup> The achievement of blood glucose-level control was assessed based on the 2-hour postprandial capillary blood glucose-level or the most recent fasting capillary blood glucose-level in the last 3 months.<sup>2</sup>

Data analysis used the Statistical Package for the Statistical Package for the Social Sciences (SPSS) software (IBM Corp. Released 2011. IBM SPSS Statistics for Windows, Version 20.0. Armonk, NY: IBM Corp.). Statistical analysis for the independent and dependent variables which were dichotomous unpaired categorical data used Chi-Square test, with the requirements of no cell with zero frequency and no cell with expected frequency  $<5$ . Otherwise, the Fisher test was used. For the independent variables with polychotomous nominal-scaled unpaired categorical data and the dependent variables with dichotomous nominal-scaled categorical data, the Chi-Square test was used if the requirements were met. Otherwise, the Mann-Whitney test was used. For the independent variables with unpaired numeric data and the dependent variables with nominal-scaled categorical data, we used the independent T-test if the data distribution was normal. Otherwise, the Mann-Whitney test was used.

## RESULTS

Of the 64 diabetic older adults recruited in this study, 2 patients were excluded because they were already taking ranitidine. Two others were excluded because they were on omeprazole therapy. Thus, there were 60 subjects eligible for this study. Thirty-seven (61.7%) of them were female and the median age was 66 (60-82) years. Mori was the commonest ethnicity (76.6%). Subjects' educational background was predominantly (26.7%) high school. Nearly half (48.3%) of the patients were retired civil servants (**Table 1**).

**Table 1.** Demographic characteristics of subjects (n=60)

Variables	Values
Age (years), median (min-max)	66 (60-82)
Gender, n (%)	
- Female	37 (61.7)
- Male	23 (38.3)
Ethnicity, n (%)	
- Mori	46 (76.6)
- Bugis	3 (5.0)
- Javanese	3 (5.0)
- Pamona	3 (5.0)
- Toraja	3 (5.0)
- Balinese	1 (1.7)
- Talaud	1 (1.7)
Educational background, n (%)	
- Elementary school	15 (25.0)
- Junior high school	8 (13.3)
- Senior high school	16 (26.7)
- Diploma	6 (10.0)
- Undergraduate	14 (23.3)
- Postgraduate	1 (1.7)
Occupation, n (%)	
- Retired civil servant	29 (48.3)
- Entrepreneur	6 (10.0)
- Farmer	12 (20.0)
- Housewife	12 (20.0)
- Others	1 (1.7)

**Table 2.** Prevalence of GERD among older patients with T2DM

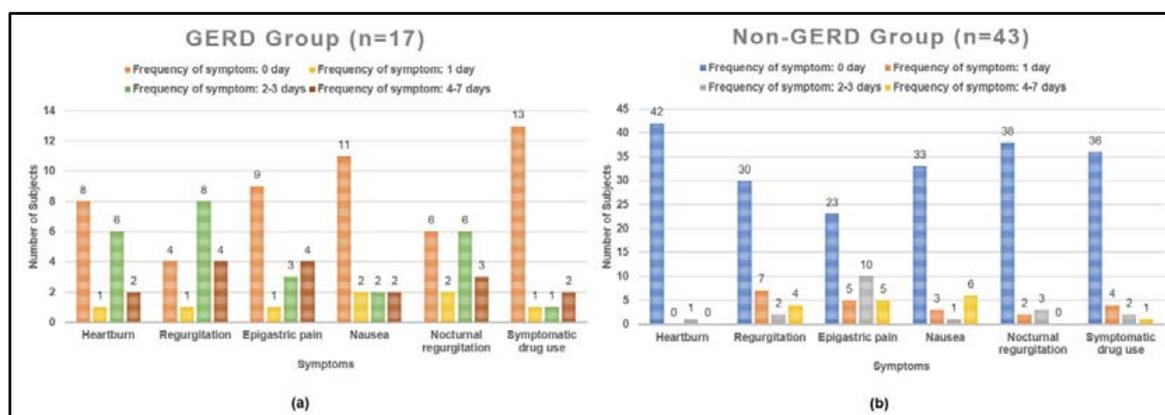
GERD Status	n (%)	95%CI
Positive (GERD-Q score ≥8)	17 (28,3)	16,9-39,7
Negative (GERD-Q score <8)	43 (71,7)	60,3-83,1
Total	60 (100,0)	

GERD-Q: *gastroesophageal reflux disease questionnaire*; 95%CI: 95% confidence interval

The prevalence of GERD among elderly patients with T2DM was 28.3% (95% CI, 16.9%-39.7%) (Table 2). In the GERD group (n=17), regurgitation was the most prevailing symptoms (76.5%). Heartburn was reported by less subjects (52.9%). Eleven (64.7%) subjects reported nocturnal regurgitation. Symptomatic drug was taken by 4 (23.5%) subjects. In the non-GERD group (n=43), epigastric pain was the commonest reported symptoms (46.5%) (Figure 1).

Obesity was found on 46.7% of the subjects. Metformin monotherapy was the commonest antihyperglycemic drugs being taken by the subjects (48.3%), but target of blood glucose-level control was only achieved by 33.3%. The proportion of subjects with daily meal frequency of 1-3 times was 88.3%. The median duration of T2DM was 36 (1-312) months. The median Brinkman’s index, which represented the subjects’ smoking habit, was 0 (0-1836). The consumption frequency of tea, coffee, chocolate, orange, spicy foods, gassy foods/ drinks, and alcohol had the same median, which was 0 (0-7) day. The median consumption frequency of tomato was 7 (0-7) days.

No significant relationship was found between gender (p=0.562), obesity (p=0.803), achievement of blood glucose-level control (p=0.478), type of antihyperglycemic drugs (p=0.202), daily meal frequency (p=0.309), duration of T2DM (p=0.304), and smoking habit (p=0.875) with GERD (Table 3). The consumption frequency of either tea (p=0.019) or coffee (p=0.015) was significantly associated with GERD. The consumption frequency of chocolate (p=0.924), orange (p=0.276), tomato



**Figure 1.** Frequency of GERD symptoms during the previous week among (a) the GERD group and (b) the non-GERD group.

( $p=0.607$ ), spicy foods ( $p=0.231$ ), gassy foods/drinks ( $p=0.268$ ), or alcohol ( $p=0.268$ ) was not associated with GERD (**Table 4**). Unintentional

weight loss was the leading alarm symptom found across the GERD group (**Table 5**).

**Table 3.** Association between Variables and GERD.

Variables	GERD Status (n [%])		p-Value
	GERD (n=17)	Non-GERD (n=43)	
<b>Gender</b>			0.562
- Female	9 (52.9)	28 (65.1)	
- Male	8 (47.1)	15 (34.9)	
<b>Obesity</b>			0.803
- Obese	7 (41.2)	21 (48.8)	
- Non-obese	10 (58.8)	22 (51.2)	
<b>Achievement of blood glucose-level control</b>			0.478
- Unachieved	13 (76.5)	27 (62.8)	
- Achieved	4 (23.5)	16 (37.2)	
<b>Type of antihyperglycemic drugs</b>			0.202
- No medication	2 (11.8)	5 (11.6)	
- Metformin	7 (41.2)	22 (51.2)	
- Sulfonylurea	0 (0.0)	7 (16.3)	
- Insulin	3 (17.6)	6 (13.9)	
- Metformin and sulfonylurea	3 (17.6)	3 (7.0)	
- Insulin and oral antihyperglycemic agent	2 (11.8)	0 (0.0)	
<b>Daily meal frequency</b>			0.309
- 1-3 times	14 (82.4)	39 (90.7)	
- > 3 times	3 (17.6)	4 (9.3)	
Duration of T2DM (month), median (min-max)	60 (3-288)	36 (1-312)	0.304
Smoking habit (Brinkman's index), median (min-max)	0 (0-200)	0 (0-1836)	0.875

**Table 4.** Association between Consumption Frequency of Gastric Acid Inducing Food/Drink and GERD.

Variables	GERD (n=17)	Non-GERD (n=43)	p-Value
Consumption frequency of tea (days in a week), median (min-max)	2 (0-7)	0 (0-7)	0.019
Consumption frequency of coffee (days in a week), median (min-max)	2 (0-7)	0 (0-7)	0.015
Consumption frequency of chocolate (days in a week), median (min-max)	0 (0-7)	0 (0-2)	0.924
Consumption frequency of orange (days in a week), median (min-max)	0 (0-7)	0 (0-7)	0.276
Consumption frequency of tomato (days in a week), median (min-max)	7 (0-7)	7 (0-7)	0.607
Consumption frequency of spicy foods (days in a week), median (min-max)	3 (0-7)	0 (0-7)	0.231
Consumption frequency of gassy foods/drinks (days in a week), median (min-max)	0 (0-7)	0 (0-7)	0.268
Consumption frequency of alcohol (days in a week), median (min-max)	0 (0-7)	0 (0-7)	0.268

**Table 5.** Incidence of Alarm Symptoms of GERD.

Alarm Symptoms	Incidence (%)	95%CI
Persistent odynophagia	2 out of 17 (11.8)	0--27.1
Persistent dysphagia	3 out of 17 (17.6)	0--35.7
Gastrointestinal bleeding	1 out of 17 (5.9)	0--17.1
Unintentional weight loss	8 out of 17 (47.1)	23.4-70.8

95%CI: 95% confidence interval

## DISCUSSION

The present study revealed that the prevalence of GERD among elderly patients with T2DM was 28.3% (95% CI, 16.9%-39.7%). This finding was comparable with that among diabetic adults in another rural area of Indonesia (29.7%).<sup>15</sup> It might be caused by the mean age of the population in that study which was only quite younger than the median age of the population in our study (54.2 [SD 9.7] vs. 66 [60-82] years).

The prevalence of GERD found in this study was far higher than that was reported from an urban population. A study with 278 healthy subjects in Depok, Indonesia found that the prevalence of GERD was 9.35%.<sup>19</sup> He et al.<sup>20</sup> in their study in China also found that adults living at rural area had a higher risk of suffering GERD than those at urban area. The difference in GERD prevalence between rural and urban populations might be due to different educational background and economic status, which were found significantly associated with GERD.<sup>19</sup>

The proportions of patients in the GERD group experiencing regurgitation and heartburn during the previous week were 76.5% and 52.9%, respectively. This finding was supported by earlier studies which reported that older patients had lower sensitivity to heartburn.<sup>21,22</sup>

Gender was not associated with GERD ( $p=0.562$ ). Sun et al.<sup>23</sup> and Spantideas et al.<sup>24</sup> revealed a similar finding. In contrary, Suwita et al.<sup>15</sup> found that female gender was associated with GERD in diabetic adult population ( $p=0.048$ ). A relatively higher proportion of female subjects (71%) observed in that study<sup>15</sup> compared with others may be the contributor to the opposite result.

Obesity was found in 41.2% of GERD patients and in 48.8% of non-GERD patients, hence obesity was not significantly associated with GERD ( $p=0.803$ ). This finding was similar to the result of previous study in rural area of Indonesia<sup>15</sup> reporting the proportion of obesity was 37% in the GERD group and 38% in the non-GERD group, thus no association was observed between obesity and GERD ( $p=0.897$ ). Obese patients had lower heartburn severity, pain sensation, and nausea.<sup>21</sup> This might suggest that less symptoms of GERD were reported by

obese patients. On the contrary, a meta-analysis of 9 cross-sectional studies showed that obesity, compared to normal BMI, was significantly associated with a greater risk of both GERD symptoms and complications (i.e. erosive esophagitis, esophageal adenocarcinoma).<sup>25</sup> The pathologic mechanisms by which obesity causes reflux disease included mechanical and humoral factors, as well as motility disorders.<sup>26,27</sup>

There was no association between achievement of blood glucose-level control and GERD ( $p=0.478$ ). Uncontrolled diabetes status was not different between the GERD group and the non-GERD group among T2DM patients ( $p=0.421$ ).<sup>15</sup> Ha et al.<sup>28</sup> reported no difference in HbA1c levels between T2DM patients with GERD and without GERD (7.1% [SD 0.1%] vs. 7.6% [SD 0.4%],  $p=0.358$ ).

No difference was observed between GERD group and non-GERD group with respect to type of antihyperglycemic drugs ( $p=0.202$ ). Metformin monotherapy was the most used among the GERD group (41.2%) and the non-GERD group (51.2%). According to Ha et al.<sup>28</sup>, the percentage of individual treatment drugs was not different between T2DM patients with GERD and without GERD. In opposition, T2DM patients using oral hypoglycemic agents (OHAs) had a higher risk (odds ratio [OR] 2.203; 95% CI, 1.056–4.598) of developing GERD compared to T2DM patients treated with diet modification only.<sup>29</sup> However, any specific drugs that caused GERD could not be identified because many subjects in that study<sup>29</sup> were on multiple OHAs.<sup>30</sup>

Daily meal frequency was not different between two groups ( $p=0.309$ ). Another study also showed no significant relationship between number of meals per day and GERD symptoms ( $p=0.497$ ), but most symptoms occurred in the postprandial period.<sup>31</sup> The reflux could possibly be more influenced by the food type and volume.

Duration of T2DM was not associated with GERD ( $p=0.304$ ). Suwita et al.<sup>15</sup> found no association too between duration of T2DM and GERD ( $p=0.976$ ). These results could be influenced by the relatively shorter duration of T2DM among the participants, which the median was 36 (1-312) months in our study and was 2 (0-19) years in Suwita et al.<sup>15</sup> There was no

difference between T2DM patients with GERD and T2DM patients without GERD in respect of T2DM duration (8.7 [SD 0.8] vs. 8.5 [SD 0.5] months,  $p=0.808$ ).<sup>28</sup>

Diabetic patients with GERD had longer duration of diabetes compared to diabetic patients without GERD (113.5 [SD 8.7] vs. 94.0 [SD 10.6] months,  $p<0.05$ ).<sup>32</sup> This might suggest that the difference in GERD prevalence would be more prominent among T2DM patients whose disease duration has been around 10 years. Therefore, it is noteworthy to consider the mean or median duration of T2DM in interpreting the study result.

Smoking habit was not associated with GERD ( $p=0.875$ ). In other studies, smoking was reported as an associated factor in GERD.<sup>33,34</sup> It was related to the effect of nicotine, which mediates the release of nitric oxide at the LES, decreasing the distal esophageal peristalsis and the sphincter pressure and thus resulting in reflux.<sup>35</sup> Lack of smoking subjects in this study might be the cause of the opposite finding.

The consumption frequency of tea was significantly associated with GERD ( $p=0.019$ ). Tea could trigger GERD by decreasing LES pressure.<sup>36-38</sup> Theophylline in tea was the contributor to the LES relaxation and thereby increasing esophageal acid reflux.<sup>36</sup> However, a meta-analysis of 23 studies found no relationship between tea consumption and the risk of GERD overall. In subgroup analysis based on geographical region, tea drinking significantly increased the risk of GERD in East Asia (OR 1.27; 95% CI, 1.07–1.51).<sup>37</sup> Tea consumption was greater among populations in Asian countries, e.g. China and Japan,<sup>39</sup> and it might lead to the more prominent result in East Asia.<sup>37</sup> The variance in the quantity and quality of tea in each population-based study could be the reason of the conflicting results.

There was a significant association between consumption frequency of coffee and GERD ( $p=0.015$ ). Coffee ingestion could decrease LES tone.<sup>33,40</sup> Despite that transient effect, a meta-analysis of 15 case-control studies found no association between coffee intake and GERD. However, through subgroup analyses in which the groups were subdivided according to the

definition of GERD (diagnosed by endoscopy or by symptoms alone), the endoscopy group showed a significantly higher OR (1.17 [95% CI, 1.08–1.26] vs. 0.99 [95% CI, 0.84–1.16]).<sup>41</sup> It could be influenced by the variability of questionnaires used in each study.

There was no association between consumption-frequency of orange and GERD ( $p=0.276$ ). This result was opposite to Feldman et al.<sup>42</sup> who demonstrated that orange juice triggered frequent heartburn in 32.5% subjects. The heartburn score of orange juice was significantly higher than water (1.05 vs. 0.22,  $p<0.001$ ). Low consumption-frequency of orange in this study could interfere with the analysis of this association.

The consumption frequency of chocolate or spicy foods was not associated with GERD ( $p=0.924$ ; 0.231, respectively). Chocolate or spicy foods was found to have a significant association with GERD.<sup>31</sup> Chocolate induced gastric acid reflux and increased lower esophageal exposure to acid. Capsaicin in spicy foods could enhance noxious postprandial heartburn through direct effects on sensory neurons.<sup>43</sup> The lack of consumption frequency of chocolate or spicy foods might contribute to the contrary result.

No association was identified between the consumption frequency of tomato and GERD ( $p=0.607$ ). Conversely, Alkhatthamia et al.<sup>31</sup> reported that tomato consumption was associated with GERD. However, although tomato could induce GERD symptoms because of its low acidity, the symptom induction could be influenced by other factors since there were incongruencies in relationship between food acidity and GERD symptoms.<sup>40</sup>

There was no association between consumption frequency of gassy foods/drinks and GERD ( $p=0.268$ ). It was consistent with a systematic review of 17 studies. Carbonation could induce decline in intra-esophageal pH and LES basal pressure, but those changes were transient and have not been associated with GERD.<sup>44</sup>

No difference in the median frequency of alcohol consumption was identified between the GERD group and the non-GERD group (0 [0-7] vs. 0 [0-7] day,  $p=0.268$ ). It was comparable

with that was reported by Ha et al.<sup>28</sup> and Sun et al.<sup>23</sup> In contrary, Bujanda et al.<sup>45</sup> revealed that alcohol consumption could facilitate GERD development by lowering the pressure of the LES and esophageal motility, increasing gastrin level and acid secretion, and delaying gastric-emptying. Low consumption frequency of alcohol might be the reason why alcohol drinking was not significantly associated with GERD in this study.

The commonest alarm symptom in the GERD group was unintentional weight loss (47.1%; 95% CI, 23.4%-70.8%). Incidence of persistent odynophagia, persistent dysphagia, and gastrointestinal bleeding was not statistically significant due to the wide confidence interval, but their presence was still clinically important. Incidence of alarm symptoms found in this study was higher than that of Eisendrath et al.<sup>46</sup> (10.5%) whose mean age of participants was 47.37 (SD 16.23) years. The older age of patients and T2DM could be the major factors in the higher rates of alarm symptoms. We suggest future studies to include larger subjects to reduce the standard of error in the calculation of confidence interval and obtain narrower confidence interval.

Our study had some limitations. The time constraint made us only had 60 eligible subjects, but this number still exceeded the minimum sample size needed. Other factors that could influence GERD occurrence, including medications which affected gastric acid secretion and history of *Helicobacter pylori* infection, were not checked. Moreover, this study did not use any specific tool to test cognitive function objectively, but all subjects who took part in this study were fully conscious, were able to give informed consent, and found no problems in answering the questions on the questionnaire.

This study also had some merits. We used a validated questionnaire for the establishment of GERD diagnosis. Without compromising the reliability of the results, it made this study still possible to conduct despite limited resources in rural area. To the best of our knowledge, it was the first study in Indonesia that evaluated GERD among elderly patients with T2DM in a rural area.

## CONCLUSION

Among elderly diabetic patients, GERD was prevalent and often presented with regurgitation. Frequent consumption of either tea or coffee was associated with GERD. Early identification of alarm symptoms could be essential for general practitioners' decision to timely refer patients for endoscopy and further investigations. Studies with greater number of subjects and examination of *Helicobacter pylori* are needed to confirm which factors are related to GERD in geriatric patients with T2DM.

## STATEMENT OF PRIOR PRESENTATION

This study was presented in the form of scientific poster at the 28th Jakarta Diabetes Meeting (JDM), November 16-17, 2019 in Jakarta, Indonesia.

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## REFERENCES

1. American Diabetes Association. Diagnosis and classification of diabetes mellitus. *Diabetes Care*. 2014;37:S81-90.
2. Soelistijo SA, Novida H, Rudijanto A, et al. Konsensus pengelolaan dan pencegahan diabetes mellitus tipe 2 di Indonesia 2015. Jakarta: Pengurus Besar Perhimpunan Endokronologi Indonesia; 2015.
3. Badan Penelitian dan Pembangunan Kesehatan Kementerian Kesehatan Republik Indonesia. Laporan nasional Riset Kesehatan Dasar (Riskesdas) 2018. Jakarta: Sekretariat Badan Litbang Kesehatan Kementerian Kesehatan Republik Indonesia; 2018.
4. International Diabetes Federation. *IDF diabetes atlas*. 8th ed. Brussels: IDF; 2017.
5. Katz PO, Gerson LB, Vela MF. Guidelines for the diagnosis and management of gastroesophageal reflux disease. *Am J Gastroenterol*. 2013;108:308-28.
6. Darnindro N, Manurung A, Mulyana E, Harahap A. Prevalence of gastroesophageal reflux disease (GERD) in dyspepsia patients in primary referral hospital. *Indones J Gastroenterol Hepatol Dig Endosc*. 2018;19:91-6.
7. Eusebi LH, Ratnakumaran R, Yuan Y, Solaymani-Dodaran M, Bazzoli F, Ford AC. Global prevalence of, and risk factors for, gastro-oesophageal reflux symptoms: a meta-analysis. *Gut*. 2018;67:430-40.

8. Chait MM. Gastroesophageal reflux disease: important considerations for the older patients. *World J Gastrointest Endosc.* 2010;2:388.
9. Poh CH, Navarro-Rodriguez T, Fass R. Review: treatment of gastroesophageal reflux disease in the elderly. *Am J Med.* 2010;123:496–501.
10. Du YT, Rayner CK, Jones KL, Talley NJ, Horowitz M. Gastrointestinal symptoms in diabetes: prevalence, assessment, pathogenesis, and management. *Diabetes Care.* 2018;41:627–37.
11. Sun XM, Tan J-C, Zhu Y, Lin L. Association between diabetes mellitus and gastroesophageal reflux disease: a meta-analysis. *World J Gastroenterol.* 2015;21:3085–92.
12. Punjabi P, Hira A, Prasad S, Wang X, Chokhavatia S. Review of gastroesophageal reflux disease (GERD) in the diabetic patient. *J Diabetes.* 2015;7:599–609.
13. Nandyal S, Suria S, Chogtu B, Bhattacharjee D. Risk of GERD with diabetes mellitus, hypertension and bronchial asthma -- a hospital based retrospective cohort study. *J Clin Diagnostic Res.* 2017;11:OC25-29.
14. Lee SD, Keum B, Chun HJ, Bak Y-T. Gastroesophageal reflux disease in type II diabetes mellitus with or without peripheral neuropathy. *J Neurogastroenterol Motil.* 2011;17:274–8.
15. Suwita CS, Benny, Mulyono DR, et al. Gastroesophageal reflux disease among type-2 diabetes mellitus patients in a rural area. *Med J Indones.* 2015;24:43–9.
16. Simadibrata M, Rani A, Adi P, Djumhana A, Abdullah M. The gastro-esophageal reflux disease questionnaire using Indonesian language: a language validation survey. *Med J Indones.* 2011;20:125–30.
17. Jones R, Junghard O, Dent J, et al. Development of the GerdQ, a tool for the diagnosis and management of gastro-oesophageal reflux disease in primary care. *Aliment Pharmacol Ther.* 2009;30:1030–8.
18. World Health Organization Western Pacific Region. The Asia-Pacific perspective: redefining obesity and its treatment. Australia: Health Communications Australia Pty; 2000.
19. Abdullah M, Makmun D, Syam AF, et al. Prevalence, risk factors and socio-epidemiological study of gastroesophageal reflux disease: an urban population based study in Indonesia. *Asian J Epidemiol.* 2016;9:18–23.
20. He J, Ma X, Zhao Y, et al. A population-based survey of the epidemiology of symptom-defined gastroesophageal reflux disease: the Systematic Investigation of Gastrointestinal Diseases in China. *BMC Gastroenterol.* 2010;10:94–103.
21. Lopez-Alvarenga JC, Vargas JA, Lopez LH, et al. Effect of body weight and esophageal damage on the severity of gastroesophageal reflux symptoms: Mexican GERD Working Group. *Arch Med Res.* 2009;40:576–81.
22. Johnson DA, Fennerty MB. Heartburn severity underestimates erosive esophagitis severity in elderly patients with gastroesophageal reflux disease. *Gastroenterology.* 2004;126:660–4.
23. Sun H, Yi L, Wu P, Li Y, Luo B, Xu S. Prevalence of gastroesophageal reflux disease in type II diabetes mellitus. *Gastroenterol Res Pract.* 2014;2014:10–3.
24. Spantideas N, Drosou E, Bougea A, Assimakopoulos D. Gastroesophageal reflux disease symptoms in the Greek general population: Prevalence and risk factors. *Clin Exp Gastroenterol.* 2016;9:143–9.
25. Hampel H, Abraham NS, El-Serag HB. Meta-analysis: obesity and the risk for gastroesophageal reflux disease and its complications. *Ann Intern Med.* 2005;143:389–90.
26. Emerenziani S, Rescio MP, Guarino MPL, Cicala M. Gastro-esophageal reflux disease and obesity, where is the link? *World J Gastroenterol.* 2013;19:6536–9.
27. Chang P, Friedenberg F. Obesity and GERD. *Gastroenterol Clin North Am.* 2014;43:161–73.
28. Ha JO, Lee TH, Lee CW, et al. Prevalence and risk factors of gastroesophageal reflux disease in patients with type 2 diabetes mellitus. *Diabetes Metab J.* 2016;40:297–307.
29. Nishida T, Tsuji S, Tsujii M, et al. Gastroesophageal reflux disease related to diabetes: analysis of 241 cases with type 2 diabetes mellitus. *J Gastroenterol Hepatol.* 2004;19:258–65.
30. Punjabi P, Hira A, Prasad S, Wang X, Chokhavatia S. Review of gastroesophageal reflux disease (GERD) in the diabetic patient. *J Diabetes.* 2015;7:599–609.
31. Alkhatamia AM, Alzahrana AA, Alzhrania MA, Alsuwata OB, Mahfouza MEM. Risk factors for gastroesophageal reflux disease in Saudi Arabia. *Gastroenterol Res.* 2017;10:294–300.
32. Kase H, Hattori Y, Sato N, Banba N, Kasai K. Symptoms of gastroesophageal reflux in diabetes patients. *Diabetes Res Clin Pract.* 2008;79:e6–7.
33. Zhang Y, Chen SH. Effect of coffee on gastroesophageal reflux disease. *Food Sci Technol Res.* 2013;19:1–6.
34. Kahrilas PJ, Gupta RR. Mechanisms of acid reflux associated with cigarette smoking. *Gut.* 1990;31:4–10.
35. Thomas GAO, Rhodes J, Ingram JR. Mechanisms of disease: nicotine - a review of its actions in the context of gastrointestinal disease. *Nat Clin Pract Gastroenterol Hepatol.* 2005;2:536–44.
36. Berquist WE, Rachelefsky GS, Kadden M, Siegel SC, Katz RM, Mickey MR, et al. Effect of theophylline on gastroesophageal reflux in normal adults. *J Allergy Clin Immunol.* 1981;67:407–11.
37. Cao H, Huang X, Zhi X, Han C, Li L, Li Y. Association between tea consumption and gastroesophageal reflux disease A meta-analysis. *Med (United States).* 2019;98:1–10.
38. Chang CH, Wu CP, Wang J Der, et al. Alcohol and tea consumption are associated with asymptomatic erosive esophagitis in Taiwanese men. *PLoS One.* 2017;12:1–14.

39. Chang K, FAO Intergovernmental Group on Tea A Subsidiary Body of the FAO Committee on Commodity Problems (CCP). World tea production and trade: current and future development. Rome; 2015.
40. Newberry C, Lynch K. The role of diet in the development and management of gastroesophageal reflux disease: why we feel the burn. *J Thorac Dis.* 2019;11:S1594–601.
41. Kim J, Oh SW, Myung SK, et al. Association between coffee intake and gastroesophageal reflux disease: A meta-analysis. *Dis Esophagus.* 2014;27:311–7.
42. Feldman M, Barnett C. Relationships between the acidity and osmolality of popular beverages and reported postprandial heartburn. *Gastroenterology.* 1995;108:125–31.
43. Rodriguez-Stanley S, Collings KL, Robinson M, Owen W, Miner PB. The effects of capsaicin on reflux, gastric emptying and dyspepsia. *Aliment Pharmacol Ther.* 2000;14:129–34.
44. Johnson T, Gerson L, Hershovici T, Stave C, Fass R. Systematic review: the effects of carbonated beverages on gastro-oesophageal reflux disease. *Aliment Pharmacol Ther.* 2010;31:607–14.
45. Bujanda L. The effects of alcohol consumption upon the gastrointestinal tract. *Am J Gastroenterol.* 2000;95:3374–82.
46. Eisendrath P, Tack J, Devière J. Diagnosis of gastroesophageal reflux disease in general practice: A Belgian national survey. *Endoscopy.* 2002;34:998–1003.