

Relationship between total free Sugars Consumption and Incidence of Laryngopharyngeal Reflux in Adolescents

Audy Apriliani,¹ Yenny²

¹Undergraduate Program, Faculty of Medicine, Universitas Trisakti, Jakarta, Indonesia

²Department of Pharmacology & Pharmacy, Faculty of Medicine, Universitas Trisakti, Jakarta, Indonesia

Received: 09-10-2023 / Revised: 30-10-2023 / Accepted: 24-11-2023

DOI: <https://doi.org/10.32553/ijmbs.v7i11.2745>

Corresponding author: Yenny; yennyfarmako@trisakti.ac.id (ORCID 0000-0001-9390-5527)

Conflict of interest: No conflict of interest.

Abstract

Background: Up to date there are still few studies showing the relationship between laryngopharyngeal reflux (LPR) and free sugars consumption in adolescents. We consequently aimed to discover any association of free sugars consumption with LPR in Indonesian adolescents.

Methods: This cross-sectional study was conducted on 210 middle school students in Jakarta, Indonesia. Data on age and gender were collected using a questionnaire, while body mass index was determined by anthropometric measurement. Free sugars consumption and LPR were evaluated by means of Semi-Quantitative Food Frequency Questionnaire (SQ-FFQ) and Reflux Symptom Index (RSI), respectively. Data were analyzed using Mann-Whitney test at level of significance $p < 0.05$.

Results: Median age (min - max) was 16 (15 – 18) years, body mass index 19.8 (15.4 – 27.0) kg/m², and free sugars consumption 6.7 (1.5 – 70.6) g/day. The prevalence of LPR was 14.3%. There was a statistically significant difference in free sugars consumption of the LPR negative versus the LPR positive groups ($p < 0.049$).

Conclusion: Free sugars consumption was strongly related to laryngopharyngeal reflux incidence. There is a need for a policy on and monitoring of free sugars consumption to decrease its harmful impact on adolescent health.

Keywords: free sugars, laryngopharyngeal reflux, adolescents, Indonesia

Introduction

Laryngopharyngeal reflux (LPR) is a “syndrome caused by reflux of gastric contents into the pharynx or larynx, which leads to symptoms of throat clearing, hoarseness, pain, globus sensation, cough, excess mucus production in the throat, and dysphonia”,⁽¹⁾ and possibly raising the risk of laryngeal carcinoma.⁽²⁾ LPR incidence and prevalence are extremely variable due to the nonspecific symptoms and absence of a gold standard diagnostic test.⁽³⁾ The study conducted by Liu et al.⁽⁴⁾ found the LPR prevalence in 17 to 25-year-old Chinese college students to be 8.1%,

the LPR symptoms being linked to both emotional eating and depressive symptoms. Another study on Chinese college students conducted by Li et al.⁽⁵⁾ showed that the LPR prevalence was 8.11%, where higher free sugars consumption resulted in a 1.656-fold rise in the LPR risk after adjustment for multiple covariates. The study by Spantideas et al.⁽⁶⁾ reported that LPR prevalence was 18.8% in the Greek general population. LPR can be decreased by lifestyle interventions, such that in the prevention of LPR, determining its risk factors is essential.⁽⁷⁾ Other

factors that are linked to causative factors of LPR are among others age,^(5, 8, 9) BMI,⁽¹⁰⁾ sleep quality,⁽¹⁰⁾ alcohol consumption, smoking,⁽⁶⁾ and diet.⁽¹¹⁾

The World Health Organization (WHO) has coined the phrase “free sugars” to denote mono- and disaccharides that have been added to “foods and beverages by the manufacturer, cook, or consumer”. The phrase also comprises the “sugars naturally present in honey, syrups, fruit juices and fruit juice concentrates”.⁽¹²⁾ The study that was conducted by Rachmah *et al.*⁽¹³⁾ among Indonesian adolescents aged 15–17 years showed their total sugars intake to be 58.80 g/day. The total sugars consumption in Indonesian adolescents is therefore higher than that found in the *Survei Sosial Ekonomi Nasional (Susenas)* [Indonesian National Socio-Economic Survey], as well as the value of 22.5 g/d found in a study on Chinese adolescents aged 12-17 years.⁽¹⁴⁾ In this connection the *Susenas* also found the Indonesian “visible sugar” consumption to be 23.8 g in 2009.⁽¹⁵⁾ High free sugars consumption may cause an increase in dental caries, obesity,⁽¹⁶⁾ and greater daytime sleepiness in Chinese adolescents.⁽¹⁷⁾ In Lechien’s study, the intake of acid foods and beverages with a high fat content that are low in protein and high in sugar was linked to more frequent proximal reflux episodes.⁽¹¹⁾

The findings of our study may hopefully lead to the formulation of a policy on and the formation of a program for minimizing the impact of free sugars consumption in adolescents. In view of the high total free sugars consumption in adolescents, the still scarce evidence on the prevalence of LPR, and the connection of LPR with free sugars consumption, this study was performed to find the LPR prevalence in Indonesian adolescents and evaluate the connection of LPR with free sugars consumption.

Methods

Design and Subjects of study

This was an analytical observational cross-sectional study that was conducted at the 19th

State Islamic Senior High School (MAN 19), South Jakarta, from September to December 2022. The inclusion criteria were: i) male and female students aged 15 – 18 years; ii) belonging to classes X, XI, and XII; iii) agreeing to participate in this study by signing the informed consent sheet after receiving clarification about the study from the investigators. We excluded from this study students who consumed proton pump inhibitors, were smokers, had sleep apnea, consumed alcoholic beverages, or were diagnosed as having gastroesophageal reflux disease at the time of data collection. The study subjects were chosen by cluster random sampling from the list of students of each class.

Sample size estimation

For the sample size estimation, the investigators used the following formulas:

Infinite population formula:

$$n = \frac{Z\alpha^2 \times p \times q}{d^2}$$

Finite population formula:

$$n = \frac{n_0}{(1 + \frac{n_0}{N})}$$

The prevalence of LPR disorder in adolescents was assumed to be 18.8%,⁽⁶⁾ $Z\alpha$ at $\alpha 5\% = 1.96$, and measurement accuracy = 0.05. Because the finite population size in our research setting was 684 persons, the minimal sample size was calculated to be 209 persons.

Measurements

Direct face-to-face interviews were conducted to collect data on sociodemographic characteristics (age, gender) followed with measurement of weight and height to calculate the subject’s body mass index (BMI).

Body mass index

Height and weight were determined by competent personnel. A calibrated standard stadiometer was used to find the height of the barefoot subject at 0.1 cm accuracy. Digital scales were used to find the weight of the lightly clothed and barefoot subject at 0.1 kg accuracy.

The BMI is defined as the “weight in kilograms divided by the square of the height in meters”, and its categories are determined based on the WHO Asia-Pacific region criteria, namely BMI <18.5 kg/m² (“underweight”), BMI = $18.5 - 22.9$ kg/m² (“normal weight”), BMI = $23 - 24.9$ kg/m² (“overweight”), and BMI ≥ 25 kg/m² (“obesity”).⁽¹⁸⁾

Free Sugars Consumption

To measure free sugars consumption, we used the validated Indonesian version of the Semi Quantitative Food Frequency Questionnaire (SQ-FFQ) on sweetened beverages and foods to evaluate past daily free sugars intake.⁽¹³⁾ The adolescents were subdivided into 2 groups on the basis of daily free sugars intake. The categories of adolescents according to the American Heart Association were the low sugars group (women ≤ 25 g/day; men ≤ 36 g/day) and high sugars group (women > 25 g/day; and men > 25 g/day).⁽¹⁹⁾

Laryngopharyngeal reflux

Laryngopharyngeal reflux was determined using the validated Indonesian version of the Reflux Symptom Index (RSI) with Cronbach alpha = 0.81.⁽²⁰⁾ This index reflects the degree of extra-esophageal symptoms and is the commonest index for LPR. The RSI questionnaire comprises 9 items that include (1) hoarseness or vocal problems, (2) throat clearing, (3) excess mucus production in the throat or postnasal drip, (4) difficulty swallowing, (5) coughing after eating or lying down, (6) breathing difficulties or choking spells, (7) troublesome or annoying cough, (8) sensation of something sticking to the throat or of a lump in the throat, and (9) heartburn, chest pain, indigestion, or stomach

acid coming up. Each item is graded on a 0- to 5-point scale from asymptomatic to most severe. The sum of item scores ranges from 0 to 45 points, patients with scores ≥ 13 being considered LPR positive.

Data analysis

Prior to the data analysis, data cleaning was performed using consistency, range, and logical checks. To test for normally distributed data, the Kolmogorov-Smirnov test was performed for all numerical data. Non-normally distributed data were presented as median (min – max) and categorical data as frequency (%). The Mann-Whitney test was used to find differences in age, BMI, and free sugars consumption of the LPR positive versus the LPR negative groups at $p < 0.05$.

Ethical clearance

The study obtained approval for ethical clearance by the Research Ethics Commission, Faculty of Medicine, Universitas Trisakti, under number 140/KER-FK/VII/2022.

Results

Subject characteristics

This study comprised 210 students, the majority (70 students or 33.3%) being 15 - 16 years old. A total of 107 students (51.0%), was female, 114 (54.3%) had normal BMI, and 201 (95.7%) subjects had low free sugars consumption. The prevalence of subjects with positive LPR was 30 (14.3%) (Table 1).

Table 1 depicts the sociodemographic characteristics, body mass index, and free sugars consumption of the subjects.

Table 1: Distribution of sociodemographic characteristics, body mass index, free sugars consumption, and LPR status of study subjects (n=210)

Variable	Median (min – max)	Frequency (n)	Percentage (%)
Age (years)	16 (15 – 18)		
15		70	33.3
16		70	33.3
17		57	27.2
18		13	6.2
Gender			
Male		103	49
Female		107	51
Body mass index (kg/m²)	19.8 (15.4 – 27.0)		
Underweight		65	31
Normal weight		114	54.3
Overweight		30	14.3
Obesity		1	0.5
Free sugars consumption(g/day)	6.7 (1.5 – 70.6)		
Low		201	95.7
High		9	4.3
Laryngopharyngeal reflux	4 (0 – 37)		
Negative		180	85.7
Positive		30	14.3

Legend: Body mass index is categorized as “underweight” (<18.5 kg/m²), “normal weight” (18.5 – 22.9 kg/m²), “overweight” (23 – 24.9 kg/m²), and “obesity” (≥25 kg/m²); free sugars consumption is categorized as low (< 25 g/day) and high (≥ 25 g/day); LPR is categorized as negative (score < 13) and positive (score ≥ 13)

Comparison of age, body mass index, free sugars consumption, and LPR status of respondents

Table 2 presents a comparison of study subjects with and without LPR with regard to age, BMI, and level of free sugars consumption. No statistically significant differences were found in

age and body mass index between the groups of LPR negative and LPR positive subjects (p = 0.133 and p = 0.892). However, a statistically significant difference was found in free sugars consumption between the LPR negative and LPR positive groups (p< 0.049).

Table 2: Comparison of age, body mass index, and free sugars consumption in the LPR groups

Variable	Laryngopharyngeal reflux		P value
	Negative (n = 180)	Positive (n = 30)	
Age (years)			
<15	3 (0 – 12)	16 (13 – 20)	0.094
≥15	2 (0 – 12)	16 (16 – 37)	
Body mass index (kg/m²)			
Underweight - normal	3 (0 – 12)	16.5 (13 – 37)	0.892
Overweight - obesity	2 (0 – 12)	15 (14 – 20)	
Free sugars consumption(g/day)			
Low	3 (0 – 12)	16 (13 – 37)	0.049*
High	1 (0 – 12)	16 (13 – 20)	

Legend: Values are presented as median (min -max); classification of categorical data: body mass index: underweight - normal (BMI = < 22.9 kg/m²), overweight – obesity (BMI ≥23.0 kg/m²); free sugars consumption: low (< 25 g/day), high (≥ 25 g/day); LPR: negative (score < 13), positive (score ≥ 13); statistical analysis = Mann-Whitney test; *p<0.05 = statistically significant

Discussion

The LPR prevalence in the present study amounted to 14.3% in Indonesian adolescents, which is higher than the prevalence of 8.1% found in the Chinese adolescent studies.^(4, 5) The study of Spantideas *et al.*⁽⁶⁾ reported an LPR prevalence of 18.8% in the Greek general population, while a different study estimated the LPR prevalence in the general population to range from 5% to 90% (mean: 23.7%).⁽²¹⁾ The differences in LPR prevalence are extremely difficult to determine, because the symptoms are not specific and there is no gold standard diagnostic test.⁽³⁾ Although RSI is the most frequent measure used to evaluate LPR, the occurrence of variations in LPR prevalence in previous studies may be due to differences in the RSI thresholds that were used to establish the diagnosis of LPR. Our study used an RSI threshold of ≥ 13 , which is identical to that used by the studies of Spantideas *et al.*⁽⁶⁾ and Li *et al.*⁽⁵⁾, whereas Kamani *et al.*⁽²²⁾ used an RSI threshold of >10 .

The results of this study show that the median (min-max) free sugars consumption was 6.7 (1.5 – 70.6) g/day, while there were only 9 (4.3%) subjects in the category of high free sugars consumption. These study results differ from those of Li *et al.*⁽⁵⁾ who obtained a sugar consumption in adolescents of 53.14 ± 44.75 (g/day) as well as from the study results of Rachmah *et al.*⁽¹³⁾ among Indonesian adolescents whose total sugar intake was 58.80 g/day. The differences in the results of our study with those of the studies that have been conducted previously may have been caused by differences in local eating habits, parental socioeconomic status,⁽²³⁾ parental free sugars intake, knowledge, and attitude or behavior, guidance behavior associated with adolescent free sugars intake,⁽¹⁶⁾ and measuring and analytical methods of free sugars in different countries. In the study conducted by Li *et al.*,⁽⁵⁾ free sugars consumption was evaluated by a “food frequency questionnaire (FFQ) on sweetened drinks and foods” constructed based on two prior studies by

the Center for Disease Control and Prevention of China, while our study used the validated Indonesian version of SQ-FFQ.⁽¹³⁾ In addition, there were differences in the criteria that were used in determining the free sugars consumption in our study, based on the American Heart Association recommendations,⁽¹⁹⁾ whereas the study of Li *et al.*⁽⁵⁾ used criteria that were based on the WHO recommendations.⁽²⁴⁾

Our study results showed no statistically significant differences of age group versus LPR group ($p=0.133$), thus differing from the study results of Li *et al.*⁽⁵⁾ on adolescents aged 12 – 14 years. These investigators showed that older adolescents aged 13 years and 14 years had significant 3.03- and 2.65-fold risks, respectively, of suffering from LPR than had 12-year-old adolescents [(AOR = 3.03; 95%CI = 1.680 – 5.454; $p<0.001$) and AOR = 2.65; 95%CI = 1.400 – 5.023; $p= 0.003$]. Kakaje *et al.*⁽²⁵⁾ showed that the age group of <30 years had a significant 0.5-fold risk of suffering from LPR than did the older age groups (OR = 0.534; 95%CI = 0.325 – 0.877; $p= 0.012$). The study of Li *et al.*⁽⁸⁾ showed that the highest prevalence rate was in the 18 - 40 year age group in comparison with the age group older than 40 years. Chen *et al.*⁽⁹⁾ showed that in the Chinese general population the prevalence of LPR was low in the 10 - 19 year-olds, but peaked at 6.29% in the 30 - 39 year-olds. The study by Jeon *et al.*⁽²⁶⁾ found that older persons aged above 55 years with suspected LPR symptoms, who were under 24h HEMII-pH monitoring, had a significantly higher LPR diagnostic rate as compared to younger persons (73.5% vs. 60.8%, $p = 0.034$). Up to the present, the relationship between age and LPR is still controversial, because of the presumably age-dependent nonspecific LPR symptoms,⁽²⁷⁾ causing LPR incidence to increase with advancing age.⁽²⁸⁾ Because the nerve endings in the elderly do not function optimally, elderly with LPR may not have the typical LPR symptoms.⁽²⁸⁾ Some have argued that age apparently decreases the perception of LPR symptoms, because older

persons with LPR may obtain lower symptom scores or cure rates at the start of the study.⁽²⁷⁾

The relationship between BMI and LPR incidence is still debatable. Our study results indicated that 30 (14.3%) adolescents were overweight, 1 (0.5%) adolescent had obesity, and no significant association was found between BMI and LPR incidence ($p = 0.094$). Our study results differ from those of the study of Wang *et al.*⁽¹⁰⁾ showing that subjects with BMI >25 kg/m² had a 0.61-fold LPR risk than had subjects with BMI ≤ 20 kg/m² (OR= 0.61; 95% CI 0.39 - 0.95, $p = 0.054$). Obesity is known to be related to gastroesophageal reflux disease, in that visceral fat synthesizes various cytokines that may lead to esophageal inflammation and damage to the esophageal mucosal barrier through reflux-independent mechanisms, such that the esophageal mucosa becomes particularly susceptible to GERD-induced injury.⁽²⁹⁾ However, in this respect the results of LPR studies are conflicting.^(6, 10)

Our study results showed statistically significant differences in free sugars consumption between the LPR negative and positive groups ($p < 0.049$). Our results are identical to those of the study of Li *et al.*⁽⁵⁾ where free sugars consumption significantly increased the risk of LPR 1.656 times after adjustment for multiple covariates (AOR=1.656; 95%CI = 2.516 – 6.661, $p=0.003$). Free sugars consumption (particularly mono- and disaccharides) may increase the reflux of gastric contents as a result of the release of neurohormones, relaxation of the distal esophageal sphincter, and the occurrence of carbohydrate fermentation in the colon.⁽³⁰⁾

There are various recommendations for sugar intake. The WHO recommendation is that adults and children should lower the daily free sugars intake to less than 10% of total energy intake. For additional health benefits, people should reduce their free sugars intake to less than 5% or approximately 25 g/day (6 teaspoons).⁽³¹⁾ The Indonesian Ministry of Health is of the opinion that free sugars intake above 50 g/day is excessive, carrying the risk of non-

communicable disease such as diabetes mellitus.⁽³²⁾ In addition, a position paper of the European Society for Paediatric Gastroenterology, Hepatology and Nutrition Committee on Nutrition recommends that free sugars intake be decreased to $<5\%$ of energy intake in children and adolescents aged ≥ 2 to 18 years.⁽³³⁾

There are several limitations in our study. Firstly, we determined LPR using the validated Indonesian language version of the RSI questionnaire, but this was not confirmed by an objective method, such as measurement of pH, because the latter is not easily done in a field study, due to its invasiveness and high cost. Secondly, the SQ-FFQ used in our study was the validated Indonesian language version and the data collection was assisted by trained personnel, but several free sugars containing foods were not included because the SQ-FFQ free sugars-containing food items were extremely small in number. Thirdly, we could not identify any causal relationship due to the cross-sectional design of the study. Fourthly, in Indonesian adolescents the prevalence of anxiety is quite high.⁽³⁴⁾ LPR patients have more severe somatic anxiety symptoms, which might be a candidate cofactor associated with the LPR-related symptoms which in this study was not excluded.⁽³⁵⁾

Although the Indonesian Ministry of Health has issued regulations on the inclusion of information on sugars, fat, and salt contents on labels of manufactured and fast foods,⁽³²⁾ policies are still needed in connection with free sugars consumption in adolescents, such as education on the effects of free sugars consumption on adolescent health, food labels stating the composition of sugars, and the habit of reading the food label before consuming foods and beverages. There is still a need for studies of a better design to confirm the results of this study.

Conclusion

Free sugars consumption is validly related to incidence of LPR in adolescents.

Acknowledgement

The authors would like to thank the Head of MAN 19, Jakarta, Indonesia, the Dean and Vice-Deans of the Faculty of Medicine, Universitas Trisakti, and Richard Tjan DTMH (Mahidol) as proofreader.

References

1. Krause AJ, Walsh EH, Weissbrod PA, et al. An update on current treatment strategies for laryngopharyngeal reflux symptoms. *Annals of the New York Academy of Sciences*. 2022;1510(1):5-17.
2. Yin CY, Zhang SS, Zhong JT, et al. Pepsin and Laryngeal and Hypopharyngeal Carcinomas. *Clinical and experimental otorhinolaryngology*. 2021;14(2):159-68.
3. Lechien JR, Akst LM, Hamdan AL, et al. Evaluation and Management of Laryngopharyngeal Reflux Disease: State of the Art Review. *Otolaryngology--head and neck surgery : official journal of American Academy of Otolaryngology-Head and Neck Surgery*. 2019;160(5):762-82.
4. Liu H, Yang Q, Luo J, et al. Association between Emotional Eating, Depressive Symptoms and Laryngopharyngeal Reflux Symptoms in College Students: A Cross-Sectional Study in Hunan. *Nutrients*. 2020;12(6).
5. Li F, Lin Q, Yang Q, et al. The Association between Free Sugars Consumption and Laryngopharyngeal Reflux: A Cross-Sectional Study among Chinese Adolescents. *Nutrients*. 2021;13(9).
6. Spantideas N, Drosou E, Bougea A, et al. Laryngopharyngeal reflux disease in the Greek general population, prevalence and risk factors. *BMC ear, nose, and throat disorders*. 2015;15:7.
7. Lechien JR, Saussez S, Muls V, et al. Laryngopharyngeal Reflux: A State-of-the-Art Algorithm Management for Primary Care Physicians. *Journal of clinical medicine*. 2020;9(11).
8. Li CF, Zhang LH, Wang WL, et al. The prevalence and relationship between laryngopharyngeal reflux disease, anxiety and depression in otorhinolaryngology outpatients. *Chinese journal of otorhinolaryngology head and neck surgery*. 2020;55(3):241-8.
9. Chen XM, Li Y, Guo WL, et al. Prevalence of laryngopharyngeal reflux disease in Fuzhou region of China. *Zhonghua er bi yan hou tou jing wai ke za zhi = Chinese journal of otorhinolaryngology head and neck surgery*. 2016;51(12):909-13.
10. Wang M, Mo T, Tan J, et al. Risk Factor-Related Lifestyle Habits of Patients With Laryngopharyngeal Reflux. *Ear, nose, & throat journal*. 2022;1455613221078182.
11. Lechien JR, Bobin F, Muls V, et al. Patients with acid, high-fat and low-protein diet have higher laryngopharyngeal reflux episodes at the impedance-pH monitoring. *European archives of oto-rhino-laryngology : official journal of the European Federation of Oto-Rhino-Laryngological Societies (EUFOS) : affiliated with the German Society for Oto-Rhino-Laryngology - Head and Neck Surgery*. 2020;277(2):511-20.
12. World Health Organization. Diet, nutrition and the prevention of chronic diseases: report of a joint WHO. 2003.
13. Rachmah Q, Kriengsinyos W, Pongcharoen T. Development and Validity of Semi-Quantitative Food Frequency Questionnaire as a New Research Tool for Sugar Intake Assessment among Indonesian Adolescents. *Heliyon*. 2021;7:e07288.
14. Liu S, Yu D, Guo Q, et al. Consumption status and trend of added sugar containing food among Chinese from 2002 to 2012. *Journal of hygiene research*. 2016;45(3):398-401.
15. Herdiansyah. Analisis konsumsi lemak, gula dan garam penduduk Indonesia Gizi Indonesia. 2011;34(2):92 - 100.
16. Zhang R, Yang Q, Tang Q, et al. Is Adolescents' Free Sugar Intake Associated with the Free Sugar Intake of Their Parents? *Nutrients*. 2022;14(22).
17. Xi Y, Lin Q, Yang Q, et al. Association between Free Sugars Intake and Excessive

- Daytime Sleepiness among Chinese Adolescents. *Nutrients*. 2021;13(11).
18. World Health Organization. The Asia-Pacific perspective: redefining obesity and its treatment. 2000.
 19. American Heart Association. How much sugar is too much? 2019.
 20. Sugihartono T, Hidayat AA, Lusida MAP, et al. Validity and Reliability of the Reflux Symptoms Index Translated into Indonesian: The Role of Upper Endoscopy in Assessing Extra-Esophageal Gastroesophageal Reflux Disease Symptoms. *The Korean journal of gastroenterology = Taehan Sohwagi Hakhoe chi*. 2023;82(1):18-24.
 21. Lechien JR, Allen JE, Barillari MR, et al. Management of Laryngopharyngeal Reflux Around the World: An International Study. *The Laryngoscope*. 2021;131(5):E1589-e97.
 22. Kamani T, Penney S, Mitra I, et al. The prevalence of laryngopharyngeal reflux in the English population. *European archives of oto-rhino-laryngology : official journal of the European Federation of Oto-Rhino-Laryngological Societies (EUFOS) : affiliated with the German Society for Oto-Rhino-Laryngology - Head and Neck Surgery*. 2012;269(10):2219-25.
 23. Yang Q, Xi Y, Liu H, et al. Free Sugars Intake among Chinese Adolescents and Its Association with Dental Caries: A Cross-Sectional Study. *Nutrients*. 2021;13(3).
 24. World Health Organization. Guideline: sugars intake for adults and children: World Health Organization; 2015 [cited 2023 19 November]. Available from: <https://www.who.int/publications/i/item/9789241549028>.
 25. Kakaje A, Alhalabi MM, Alyousbashi A, et al. Laryngopharyngeal reflux in war-torn Syria and its association with smoking and other risks: an online cross-sectional population study. *BMJ open*. 2020;10(11):e041183.
 26. Jeon SY, Park JM, Lee YC, et al. Differences in Diagnostic Rates After Hypopharyngeal-esophageal Impedance-pH Monitoring of Laryngopharyngeal Reflux Patients by Age and Sex. *Journal of Voice*. 2022.
 27. Lechien JR, Finck C, Huet K, et al. Impact of age on laryngopharyngeal reflux disease presentation: a multi-center prospective study. *European archives of oto-rhino-laryngology : official journal of the European Federation of Oto-Rhino-Laryngological Societies (EUFOS) : affiliated with the German Society for Oto-Rhino-Laryngology - Head and Neck Surgery*. 2017;274(10):3687-96.
 28. Mendelsohn AH. The Effects of Reflux on the Elderly: The Problems with Medications and Interventions. *Otolaryngologic clinics of North America*. 2018;51(4):779-87.
 29. Paris S, Ekeanyanwu R, Jiang Y, et al. Obesity and its effects on the esophageal mucosal barrier. *American journal of physiology Gastrointestinal and liver physiology*. 2021;321(3):G335-g43.
 30. Piche T, des Varannes SB, Sacher-Huvelin S, et al. Colonic fermentation influences lower esophageal sphincter function in gastroesophageal reflux disease. *Gastroenterology*. 2003;124(4):894-902.
 31. World Health Organization. WHO calls on countries to reduce sugars intake among adults and children. [cited 2023 19 November]. Available from: <https://www.who.int/news/item/04-03-2015-who-calls-on-countries-to-reduce-sugars-intake-among-adults-and-children>.
 32. Peraturan Menteri Kesehatan Republik Indonesia No. 30 tahun 2013 tentang Pencantuman informasi kandungan gula, garam, dan lemak serta pesan kesehatan untuk pangan olahan dan pangan siap saji. [cited 203 19 November]. Available from: https://p2ptm.kemkes.go.id/uploads/VHcrbkVobjRzUDN3UCs4eUJ0dVBndz09/2018/10/Permenkes_No_30_Th_2013_Gula_Garam_Lemak.pdf.
 33. Fidler Mis N, Braegger C, Bronsky J, et al. Sugar in Infants, Children and Adolescents: A Position Paper of the European Society for Paediatric Gastroenterology, Hepatology and

- Nutrition Committee on Nutrition. Journal of pediatric gastroenterology and nutrition. 2017;65(6):681-96.
34. Akbar UM, Yenny Y. Anxiety and Its Associated Factors Among School-aged Adolescents in East Jakarta, Indonesia during the Coronavirus Disease-2019 Pandemic. Open Access Macedonian Journal of Medical Sciences. 2022;10(B):1122-8.
35. Kang JW, Lee MK, Lee YC, et al. Somatic anxiety in patients with laryngopharyngeal reflux. Laryngoscope Investigative Otolaryngology. 2023;8(5):1288-93.