World Nutrition Journal
Volume 5, Issue 02, February 2022

eISSN 2580-7013

Published by

INDONESIAN NUTRITION ASSOCIATION

World Nutrition Journal Editorial Office

Wisma Nugraha Building, Suite 510, 5th Floor
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Cover design by. Harryarts / Freepik

Aim and Scope

World Nutrition Journal (abbreviated: W Nutr J) is an international, English language, peer-reviewed, and open access journal upholding recent evidence related to nutrition sciences. The journal accepts manuscripts in terms of original paper, case report, editorial, and letter to editor.

About

World Nutrition Journal was founded in 2016 as the official journal of Indonesian Nutrition Association. It aims to publish high quality articles in the field of community, clinical, and critical care aspects of nutrition sciences

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eISSN 2580 - 7013

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World Nutrition Journal |eISSN 2580-7013

EDITORIAL

In memoriam – Prof. Dr. dr. Saptawati Bardosono, MSc

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Received 26 February 2022
Accepted 26 February 2022
Published: 28 February 2022

Link to DOI:
10.25220/WNJ.V05.i2.0001

Abstract

The editorial is dedicated to honor the passing of Prof. Saptawati Bardosono on October 15th, 2021

Keywords in memoriam; saptawati bardosono; world nutrition journal

Citation: Pansawira P, Sutanto LB. In memoriam-Prof. Dr. dr. Saptawati Bartdosono, MSc. World Nutrition Journal.2022 Feb 28, 5(2):i-ii.

Website : http://www.worldnutrijournal.org

In memoriam

The passing of Prof. Saptawati Bardosono on October 15th last year was a great sadness and loss for the entire scientific community, especially nutrition-related. It was also an immeasurable grief for us, the editorial team of World Nutrition Journal.

Her passion in nutrition began when she served as a physician in a remote village of Papua, back in the early '80s. Afterward, Prof. Saptawati Bardosono dedicated her whole life researching and educating both medical professionals and society in relation to nutritional knowledge and promotion of living healthier. She was particularly devoted to child's nutrition to prevent stunting.

She had done numerous research which included studies in nutrition for pregnant and lactating women, infants, toddlers, pre-school children, and adults; both clinical and community-related. She spoke in numerous seminars and established many workshops, not to mention writing and publishing many books, modules, and articles. She was also acting as the secretary of Indonesian Nutrition Association (*Perhimpunan Nutri Indonesia*).

In 2016, she founded the World Nutrition Journal, the official journal of Indonesian Nutrition Association, as an open access journal for the expansion of nutrition-related knowledge and acts as a media, both for medical students and experts, to publish their researches, in which she acted as the editor-in-chief.[1]

No words can describe how dedicated and brilliant her ideas were. We will cherish not only for her memory, education, advices, and creativities, but also her warmth, generosity, and kindness. She was the irreplaceable mentor, our teacher, and our mother-figure with a hearty laugh and caring personality. As her students, colleagues, and friends, let us continue our duty to never quit in pursuing knowledge for the advancement of nutrition science.

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References

1. Bardosono S. The Importance of Nutrition Journal Publication. World Nutrition Journal. 2017 Sep 6;1(1):i-i.

World Nutrition Journal |eISSN 2580-7013

ORIGINAL PAPER

The relation of Brinkman index and body mass index with spirometry result of chronic obstructive pulmonary disease (COPD) outpatients in the pulmonology and respiratory medicine department of Zainoel Abidin general hospital

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Received 4 May 2021
Accepted 4 January 2022
Published: 28 February 2022

Link to DOI:
10.25220/WNJ.V05.i2.0002

Citation: Muzlifa R, Mulyadi, Husnah. The relation of Brinkman index and body mass index with spirometry result of chronic obstructive pulmonary disease (COPD) outpatients in the pulmonology and respiratory medicine department of Zainoel Abidin general hospital. World Nutrition Journal.2022 Feb 28, 5(2): 1-7.

Website : http://www.worldnutrijournal.org/

Abstract

Background: chronic obstructive pulmonary disease (COPD) is one of the major health problems worldwide. Smoking is the main risk factor of the COPD development. Not only COPD has clinical manifestations in the lungs, it also manifest outside lungs called systemic effects.One of systemic effects found in COPD patients is weight loss leading to declining lung function. This study aims to determine the relation of Brinkman Index and Body Mass Index (BMI) with spirometry result of COPD outpatients in RSUDZA.

Methods: The study was held in lung outpatients department in RSUDZA Banda Aceh on December 5th until 28th with cross sectional design The sampling method is nonprobability sampling with accidental sampling technique. Respondents consisted of 30 patients who had agreed to informed consent given. Medical record used to obtain Brinkman index, BMI, and spirometry result of the patients.

Results: The results of analysis shows majority of respondents are male (83,3%), dominated by 56-65 years age range (40,0%) and had moderate Brinkman Index (46,7%). The majority of respondents (53,3%) had an abnormal BMI (severe underweight (13,3%), underweight (6,7%), overweight (23,3%), and obese (10,0%)) and severe spirometry result (53,3%). The data was analyzed by the Spearman Correlation. With the Spearman Correlation, there was no association between Brinkman Index and spirometry result with p value 0,412 (p value >0,05). Meanwhile, there was an association between the BMI and spirometry result with p value 0,006 (p < 0,05). The strength of the correlation is moderate (rs =-0,488).

Conclusion: The lower the BMI, the more severe the spirometry result.

Keywords: Brinkman index, body mass index, spirometry result, lung function, FEV_1, COPD

Introduction

Chronic obstructive pulmonary disease (COPD) is one of a major problem in the health sector worldwide. Its prevalence and mortality increases every year. COPD is the fourth leading cause of death in the world and is expected to be the third cause by 2020. This is related to the lack of intervention in risk factors, especially smoking and exposure to fuel fumes and air pollution. COPD not only manifests in the lungs, but also manifests outside the lungs called systemic effects. One of the systemic effects found in COPD patients is weight loss.[1-3]

Smoking is the main risk factor for the development of COPD. The World Health Organization (WHO) shows 84% (1.09 billion

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people) of all smokers in the world are in developing countries. (4) In Indonesia, data obtained from 10-year follow-up interviews with residents show the prevalence of smokers in 2013 was 29.3 %.The province with the highest prevalence of smokers is Riau (30.7%). The prevalence of smokers in Aceh is 29.3%.[5]

The Global Burden of Disease (GBD) estimates that the approximate number of COPD patients in the world is 328 million people. The prevalence of men is higher (168 million), while women are 160 million.[1] Studies conducted in the European population for 40 years showed that the prevalence of COPD varies between 15-20% and is found to be higher in men than women.[2] Based on Riset Kesehatan Dasar (RISKESDAS) 2013, the prevalence of COPD in Indonesia was 3.7%. The province with the highest prevalence was Nusa Tenggara Barat at 10.0%. The prevalence of COPD in Aceh was 4.3%.[3]

COPD patients often show significant weight loss as the disease progresses.[8] It is well known that 25-40% of all COPD patients losing weight. Body Mass Index (BMI) is an important predictor of mortality and morbidity of COPD patients.[9] Results of the study by Guo et al.[8] showed that underweight COPD patients increase the risk of mortality by 40%. Underweight patients are more likely experience a faster decrease in pulmonary function.[6] Assal and Kamal.[7] showed a positive relationship between BMI and prediction of forced expiratory volume in 1 second (VEP_1).[9]

Spirometry is a gold standard examination for the diagnosis of COPD and is objective in measuring airflow resistance.[7] Spirometry is performed to assess the mechanical function of the lungs, chest wall, and respiratory muscles by measuring the amount of air exhaled from total lung capacity to residual volume.[8] Mitra et al.[1] study showed an association between BMI and the severity of COPD patients' airway obstruction as measured by spirometry. Patients with low BMI tend to have a greater risk of accelerating disease severity.[9]

Study on the relation of the Brinkman index and body mass index with the results of spirometry of COPD patients has never been done in Aceh. In fact, patients' nutritional status is very important to be considered by health workers to prevent worsening of the disease. Based on the facts described above, the researchers wanted to conduct a study on the relationship between Brinkman index and body mass index with spirometry results of patients with chronic obstructive pulmonary disease (COPD) in the Pulmonology and Respiratory Medicine Department of Zainoel Abidin Regional Hospital.

Methods

This is an analytic observational study with cross-sectional design. The study was conducted in the Pulmonology and Respiratory Medicine Department of Zainoel Abidin Regional Hospital in Banda Aceh. The data were collected on 5th to 28th December 2018. The study population includes all COPD outpatients who had fulfilled the inclusion and exclusion criteria. The sampling method used is non probability sampling with accidental sampling technique. The total sample is obtained based on a preliminary study and in accordance with the context of the research conducted. The minimum sample needed is 30 samples. The instrument used in this study is a questionnaire to assess the degree of smoking based on the Brinkman index and medical records to obtain body mass index and spirometry results of COPD patients. An ordinal measuring scale is used for the Brinkman index, body mass index, and spirometry results.

Results

Research was conducted in the Pulmonology and Respiratory Medicine Department of Zainoel Abidin Regional Hospital in Banda Aceh on 05 to 28 December 2018. The study sample was 30 respondents who met the inclusion criteria.

Characteristics of respondents include the distribution of gender, age, education history, and smoking history. The following will present the distribution data of the characteristics of the respondents in **Table 1**.

Results in **Table 1** show that the majority of respondents were male as many as 25 (83.3%). The female respondents numbered 5 (16.7%). The results

of this study are in line with the study of Muthmainnah, et al.[12] on COPD patients in the Lung Department of Arifin Achmad Hospital in Riau showed the number of male COPD patients are higher as many as 57 respondents (80.28%) and 14 women respondents (19.71%). Smoking is a major risk factor for COPD. Men are at greater risk of developing COPD because there are more male smokers than women. This is related to the influence of association and the existence of norms in society in Aceh, which is the negative perception of women who smoke.[10,11]

Table 1. Characteristics

Characteristics of Respondents	Frequency	Percentage (%)
Gender		
Male	25	83,3
Female	5	16,7
Age		
17-25 years	1	3,3
26-35 years	4	13,3
36-45 years	2	6,7
46-55 years	7	23,3
56-65 years	12	40,0
>65 years	4	13,3
Educational Background		
Uneducated	1	3,3
Elementary School	3	10,0
Junior High School	10	33,3
Senior High School	10	33,3
College	6	20,0
Smoking History		
Yes	23	76,7
No	7	23,3
Total	**30**	**100**

In this study, the respondent's age range was 18-70 years. The majority of respondents are at the age of 56-65 years with a total of 12 respondents (40.0%). This result is in line with the study of Rohmah (2018) on COPD patients in the Physiotherapy Pediatric Clinic of the Surakarta Lung Health Center shows the majority of respondents were at age 55-65 years as many as 8 respondents (66.70%).[12]

The results of the study showed that the education of respondents was dominated by secondary schools (junior high school and senior high school) as many as 10 respondents (33,3%), college 6 respondents (20.0%), elementary school 3 respondents (10.0%), and the lowest was uneducated 1 respondent (3.3%).

This result is in line with the study of Sidabutar et al.[15] on COPD patients in Adam Malik General Hospital Medan showed that the highest education was junior high school students 68 respondents (61.8%) and senior high school 17 respondents (15.5%).[13] The result is possible because there is an influence on the level of education of knowledge about the danger of smoking for health. Individuals who have good education know the adverse effects of smoking on health so that they can avoid it. The education level of COPD patients is also closely related to the ability to utilize health services available in the surrounding environment.[14,15]

The results showed that as many as 23 respondents had a smoking history (76.7%), 7 people had not smoked (23.3%). This result is in line with the study of Laode, et al.[25] on COPD patients in Kendari showed that the majority of respondents had a smoking history as many as 32 (68.1%). The results supported by the literature showed the most important COPD risk factors were smoking.[16]

Table 2. Brinkman Index

Brinkman Index	Frequency	Percentage (%)
Mild	7	23,3
Moderate	14	46,7
Severe	9	30,0
Total	**30**	**100,0**

The results from **Table 2** showed the majority of respondents have a moderate Brinkman index as many as 14 people (46.7%).

Table 3. Body Mass Index

Body Mass Index	Frequency	Percentage (%)
Severe underweight	4	13,3
Underweight	2	6,7
Normal	14	46,7
Overweight	7	23,3
Obese	3	10,0
Total	**30**	**100,0**

The results of **Table 3** showed the majority of respondents had abnormal body mass index as many as 16 people (53.3%) (severe underweight 4 respondents (13.3%), underweight 2 respondents (6.7%), overweight 7 respondents (23.3%) and obese 3 respondents (10.0%).

Table 4. Spirometry Result

Spirometry Result	Frequency	Percentage
Mild	2	6,7
Moderate	6	20,0
Severe	16	53,3
Very Severe	6	20,0
Total	30	100,0

The results of **Table 4** show the majority of respondents had a severe spirometry as many as 16 (53.3%).

Based on the results of **Table 5**, respondents with a mild Brinkman index as many as 3 respondents (42.9%) had severe spirometry result. Respondents with a severe Brinkman index as many as 2 respondents (22.2%) had mild spirometry result. The results of the statistical test with the Spearman correlation showed a p value of 0.412 (p value> 0.05) which means that there is no relationship.

The results of this study are not in accordance with several studies which state that the Brinkman index has a significant effect on lung function in COPD patients. Naser, et al.[18] conducted a study of COPD patients in the Pulmonary Department of M. Djamil General Hospital showed that there is a relationship between the Brinkman index with severity of COPD with p value = 0.025.[17]

Chronic obstructive pulmonary disease (COPD) is an irreversible respiratory disease that can generally be prevented and treated which is characterized by obstructed air flow and persistent respiratory symptoms due to abnormalities that occur in the airway or alveoli or both.[18] Smoking is a risk factor and the main cause of COPD. The possibility for an individual to suffer from COPD depends on the smoking dose, the number of cigarettes smoked in one day, and the duration of smoking that can be measured using the Brinkman index. The Brinkman Index can be calculated by multiplying the number of cigarettes smoked per day with the duration of smoking in the year.[19]

Based on the results in **Table 6**, respondents with severe underweight BMI tend to be more dominant in patients with severe spirometry results as many as 3 respondents (75%) and very severe as many as 1 respondent (25.0%). Respondents with underweight BMI had 1 respondent (50%) with severe spirometry result and 1 respondent (50%) with very severe spirometry result. Respondents with normal BMI had moderate spirometry results as many as 3 respondents (21.4%), severe 7 respondents (50.0%), and very severe as many as 4 respondents (28.6%). Respondents with obese BMI had mild spirometry results as many as 1 respondent (14.3%), moderate as many as 2 respondents (28.6%), and severe as many as 4 respondents (57.1%). Respondents with overweight BMI had mild spirometry results of 1 respondent (33.3%), moderate as many as 1 respondent (33,3%), and severe as many as 1 respondent (33.3%). Respondents with overweight and obese BMI were not found in patients who had very severe spirometry results. The results of the statistical test using the Spearman Correlation test shows p value of 0.006 (p value <0.05), which means that there is a relationship between the two variables. The value of the Coefficient Correlation (rs) is -0.448 which indicates a moderate correlation, and the direction of the relationship is negative (-), which means that the lower the BMI the worse the results of the spirometry.

The results of this study are in line with the research of Assal and Kamal.[7] of 154 COPD patients in Cairo, Egypt, showing that there was a relationship between BMI and VEP1 values (r =

Table 5. The Relation Between Brinkman Index and Spirometry Result

Brinkman Index	Spirometry Result										r_s	P *Value*
	Mild		Moderate		Severe		Very Severe		Total			
	n	%	n	%	n	%	n	%	n	%		
Mild	0	0	3	42,9	3	42,9	1	14,3	7	100	0,155	0,412
Moderate	0	0	3	21,4	9	64,3	2	14,3	14	100		
Severe	2	22,2	0	0	4	44,4	3	33,3	9	100		

Table 6. The Relation between Body Mass Index and Spirometry Result

Body Mass Index	Spirometry Result										r_s	P *Value*
	Mild		Moderate		Severe		Very Severe		Total			
	n	%	n	%	n	%	n	%	n	%		
Severe underweight	0	0	0	0	3	75,0	1	25,0	4	100	-0,488	0,006
Underweight	0	0	0	0	1	50,0	1	50,0	2	100		
Normal	0	0	3	21,4	7	50,0	4	28,6	14	100		
Overweight	1	14,3	2	28,6	4	57,1	0	0	7	100		
Obese	1	33,3	1	33,3	1	33,3	0	0	3	100		

Table 7. GOLD Classifications of Spirometry Result

Category	FEV1
Mild	$FEV_1 \geq 80\%$ prediction
Moderate	$50\% \leq FEV_1 < 80\%$ pediction
Severe	$30\% \leq FEV_1 < 50\%$ prediction
Very Severe	$FEV_1 < 30\%$ prediction

Table 8. Classifications of Brinkman Index

Category	Value
Mild	0-200
Moderate	200-600
Severe	>600

0.295, P <0.05). Nadifah.[20] conducted a study of 34 respondents of COPD patients in Tugurejo Hospital Semarang showed that there was a relationship between BMI and VEP1 values of COPD patients

Table 9. Classifications of Body Mass Index

Category	IMT (kg/m^2)
Severe Underweight	< 17,0
Underweight	17,0 - 18,4
Normal	18,5 - 25,0
Overweight	25,1 - 27,0
Obese	> 27,0

with p value 0.044 with a correlation coefficient of 0.348 indicating a weak relationship.

One important management of COPD patients is adequate nutrition since COPD patients generally will experience weight loss so that lung function decreases due to decreased ventilation capacity and strength of respiratory muscles.[21] Changes in physiological aspects that characterize in patients with COPD it is suspected that this is a cause of weight loss experienced by patients so that patients experience malnutrition.

Conclusion

The majority of respondents have moderate Brinkman index as many as 14 people (46.7%). For body mass index, The majority of respondents had abnormal body mass index as many as 16 people (53.3%), severe underweight 4 respondents (13.3%), underweight 2 respondents (6.7%), overweight 7 respondents (23.3%), and obese 3 respondents (10.0%). For the spirometry result, the majority of respondents had severe spirometry as many as 16 (53.3%). Respondents with a mild Brinkman index as many as 3 respondents (42.9%) had severe spirometry result. Respondents with a severe Brinkman index as many as 2 respondents(22.2%) had mild spirometry result. In conclusion, there was no relation between body mass index and spirometry result with a p value of 0.412 (p value> 0.05). However, respondents with severe underweight BMI tend to be more dominant in patients with severe spirometry results as many as 3 respondents (75%) and very severe as many as 1 respondent (25.0%). In conclusion, there was a correlation between body mass index and spirometry result with p value 0,006 (p value <0.05), which means that there is a relationship between the two variable.

Conflict of Interest

Authors declared no conflict of interest regarding this article.

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References

1. Saha A, Barma P, Biswas A, Ghosh S, Malik T, Mitra M, et al. A Study of Correlation Between Body Mass Index and GOLD Staging Of Chronic Obstructive Pulmonary Disease Patients. J Assoc Chest Physicians [Internet]. 2013;1(2):58. Available from: http://www.jacpjournal.org/text.asp?2013/1/2/58/123217
2. Fitriana P, Susanti E. Influence of Smoking on Chronic Obstructive Pulmonary Disease (Copd). J Major. 2015;4(5):67–75.
3. Badan Penelitian dan Pengembangan Kesehatan. Riset Kesehatan Dasar (RISKESDAS) 2013. Lap Nas 2013. 2013;1–384.
4. Lõpez-Campos JL, Tan W, Soriano JB. Global burden of COPD. Respirology. 2016;21(1):14–23.
5. Terzikhan N, Verhamme KMC, Hofman A, Stricker BH, Brusselle GG, Lahousse L. Prevalence and Incidence Of COPD in Smokers And Non-Smokers: The Rotterdam Study. Eur J Epidemiol. 2016;31(8):785–92.
6. Shimray A, Singh W, Ningshen K, Kanan W, Devi A, Laishram R. Association Body Mass Index And Spirometric Lung Function In Chronic Obstructive Pulmonary Disease (Copd) Patients Attending Rims Hospital, Manipur. J Med Soc [Internet]. 2014;28(3):157. Available from: http://www.jmedsoc.org/text.asp?2014/28/3/157/148498
7. Assal H, Kamal E. Body Mass Index and Its Relation to GOLD Stage In Chronic Obstructive Pulmonary Disease Patients. Egypt J Chest Dis Tuberc [Internet]. 2016;65(2):411–4. Available from: http://linkinghub.elsevier.com/retrieve/pii/S0422763815301382
8. Guo Y, Tianyi Z, Wang Z, Feifei Y, Qin X, Wei G, et al. Body Mass Index and Mortality in Chronic Obstructive Pulmonary Disease: A Meta-Analysis. PLoS One. 2012;7(8):8.
9. Roberts C. Michael, Lopez-Campos JL, Pozo-Rodriguez F, Hartl S. European hospital adherence to GOLD recommendations for chronic obstructive pulmonary disease (COPD) exacerbation admissions. Thorax. 2013;68(12):1169–71.
10. ZN AU, Amin Z, Thufeilsyah F. Spirometri. Ina J Chest Crit Emerg Med. 2014;1(1):35–8.
11. Niagara H. Gambaran Faktor Faktor yang Mempengaruhi Terjadinya Penyakit Paru Obstruksi Kronis (PPOK) Dunia (WHO) dalam panduan Global Initiatif for Chronic Obstructive Lung Disease (GOLD) tahun 2012 , Chronic Obstructive Pulmonary Disease (COPD) atau Penyaki. 2013;26.
12. Al muthmainnah et. al. Gambaran Kualitas Hidup Pasien Ppok Stabil Di Poli Paru RSUD Arifin Achmad Provinsi Riau Dengan Menggunakan Kuesioner Sgrq. Jom Fk. 2015;2(2):1–20.
13. Fajrin O, Yovi I, Burhanuddin L. Gambaran Status Gizi Dan Fungsi Paru Pada Pasien Penyakit Paru Obstruktif Kronik Stabil Di Poli Paru Rsud Arifin Achmad. Jom FK. 2015;2(2).
14. Rohmah IN. Pengaruh Pemberian Taping pada Punggung Atas Terhadap Arus Puncak Respirasi

Penderita Penyakit Paru Obstruksi Kronis (PPOK). 2018;
15. Sidabutar P, Rasmaliah, Hiswani. Karakteristik Penderita Penyakit Paru Obstruktif Kronik (PPOK) yang Dirawat Inap di RSUP H. Adam Malik Medan Tahun 2012. 2012;
16. PDPI. Pedoman Diagnosis dan Penatalaksanaan di Indonesia. Jakarta: Perhimpunan Dokter Paru Indonesia; 2011.
17. Vogelmeier CF, Criner GJ, Martinez FJ, Anzueto A, Barnes PJ, Bourbeau J, et al. Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Lung Disease 2017 Report: GOLD Executive Summary. Eur Respir J [Internet]. 2017;49(3):1700214. Available from: http://erj.ersjournals.com/lookup/doi/10.1183/13993003.00214-2017
18. Djamil PRM, Naser F, Medison I. Artikel Penelitian Gambaran Derajat Merokok Pada Penderita PPOK di Bagian. 2013;5(2):306–11.
19. Nugraha I. Hubungan Derajat Berat Merokok Berdasarkan Indeks Brinkman Dengan Derajat Berat PPOK. 2013;53(9):1689–99.
20. Nadifah C. Hubungan antara Indeks Massa Tubuh (IMT) dengan Volume Ekspirasi Paksa dalam Detik (VEP1) pada Pasien PPOK. 2017;
21. Enderina D. Gambaran Status Gizi Pada Pasien Penyakit Paru Obstruktif Kronik (Ppok) Di Rawat Inap Rsud Arifin Achmad Pekanbaru. Jom Fk. 2016;3(2):1–9.
22. Permatasari N, Saad A, Christianto E. Gambaran Status Gizi pada Pasien PPOK yang menjalani Rawat Jalan di RSUD Arifin Achmad Pekanbaru. 2016;12.
23. Enderina D. Gambaran Status Gizi Pada Pasien Penyakit Paru Obstruktif Kronik (Ppok) Di Rawat Inap Rsud Arifin Achmad Pekanbaru. Jom Fk. 2016;3(2):1–9.
24. Permatasari N, Saad A, Christianto E. Gambaran Status Gizi pada Pasien PPOK yang menjalani Rawat Jalan di RSUD Arifin Achmad Pekanbaru. 2016;12.
25. Ismail L, Sahrudin S, Ibrahim K. *Analisis faktor risiko kejadian penyakit paru obtruktif kronik (PPOK) di wilayah kerja Puskesmas Lepo-Lepo Kota Kendari tahun 2017* (Doctoral dissertation, Haluoleo University).

World Nutrition Journal |eISSN 2580-7013

ORIGINAL PAPER

Flavonoid intake and its correlation to malondialdehyde serum among reproductive-aged women with obesity

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Received 28 December 2021
Accepted 14 February 2022
Published: 28 February 2022

Link to DOI:
10.25220/WNJ.V05.i2.0003

Citation: Nasruddin NI, Hardiany NS, Lestari W. Flavonoid intake and its correlation to malondialdehyde serum among reproductive-aged women with obesity. World Nutrition Journal.2022 Feb 28, 5(2): 8-17.

Website :
http://www.worldnutrijournal.org/

Abstract

Background: Obesity modulates oxidative stress and can be detected by examining malondialdehyde (MDA) serum levels. Flavonoids are natural bioactive ingredients that can be found in various types of vegetables and fruits that function as antioxidants to suppress that oxidative stress.

Objective: This study aimed to determine the correlation between flavonoid intake and MDA serum levels in obese women of reproductive age.

Methods: This cross-sectional study was conducted in Kendari, Indonesia from April to October 2021. The purposive sampling method was used to obtain 88 subjects who met the research criteria. Data were collected through interviews covering flavonoids intake using validated SQ-FFQ. Anthropometric measurements were performed to assess nutritional status, and laboratory tests were applied to determine MDA serum levels.

Results: The average intake of flavonoids in the subjects was 142,26 ± 56,53 mg per day. Meanwhile, the average MDA serum level in the subjects was 2.16 mol/L, ranging from 1.09 nmol/ml to 6.71 nmol/ml. There was no significant correlation between total flavonoid intake and MDA serum levels in obese women of reproductive age (r=0,188, p=0,079). However, there was a weak correlation between the intake of flavonoid subclasses, namely flavan-3-ols/flavanols and MDA serum levels (r=0.325, p=0.002).

Conclusion: We conclude that there was no correlation between total flavonoid intake and MDA serum levels. However, there was a correlation between flavan-3-ols/flavanols and MDA serum levels in the subjects.

Keywords: flavonoid intake, malondialdehyde, oxidative stress, obesity, women of reproductive age

Introduction

Obesity has become one of the triple burdens of malnutrition, with the number of its cases increasing three times since 1975 to 2016. In 2017 alone, it is associated with 4.7 million deaths worldwide.[1] The prevalence of obesity in women is 15% or considerably higher than men with around 11% of 650 million people in the world.[2] The increase in cases also occurred in Indonesia from 14.8% in 2013 to 21.8% in 2018.[3] In Kendari, the prevalence of obesity in the population aged over than 18 years is 22.3% in 2017 (25.71% for women, 13.09% for men), or relatively higher compared to the national average. While it is predicted that the prevalence will continue to rise since there is still no obesity prevention program in the city.[3,4]

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Obesity can cause a permanent oxidative stress due to reactive oxygen species (ROS). It also decreases endogenous antioxidants, triggering various non-communicable diseases such as coronary heart disease, diabetes mellitus, hypertension, malignancy, as well as female reproductive system disorders and the intergenerational transmission of obesity from mother to foetus.[5–7] Modulation of oxidative stress affects all reproductive phases of a woman's life. For instance, it can cause, among others, infertility, premature delivery, intrauterine growth restriction (IUGR) and fetal death.[8,9]

Oxidative stress in obese women can be detected by examining malondialdehyde (MDA) levels in plasma, serum, or urine. It can be measured accurately using various methods and is relatively inexpensive[10]. As it is stable in isolated body fluid samples, it is also not affected by diurnal variations and dietary fat content, which is a specific product of fat peroxidation.[10]

Consumption of fruits and vegetables has been shown to reduce oxidative damage but, nationally, consumption of vegetables and fruits in Indonesia is still below the recommended level.[3] Apriyanti et al.[11] found that risky food consumption behaviours, including the habit of consuming sweet, salty, fatty, preserved, caffeinated, and flavoured foods/drinks were mostly exhibited by obese women of productive age in Kendari.

Dietary intervention with natural bioactive foods such as polyphenols has become an alternative approach in overcoming obesity and metabolic diseases. It is a novel way since it can modulate physiological and molecular pathways, that performing in energy metabolism, stimulating the beta oxidation, inhibiting adipocyte differentiation and counteracting oxidative stress.[12] Flavonoid is the most polyphenol subclass consumed by humans and it has antioxidant, anti-inflammatory and anti-carcinogenic effects.[13] However, the epidemiological evidence is limited and usually inconsistent. Most of the studies on flavonoid intake and MDA were also intervention trials.[12] For the examples, a study conducted by Hirano found the effects of green tea consumption can lower MDA levels in human.[14] Meanwhile, Gonzalez et al.[15] in 2013 found an inverse relationship between flavonoid intake and MDA levels. Ultimately, Alipour et al.[16] showed that flavonoid intake was not significantly associated with MDA levels.

Such inconsistency in research on flavonoid intake and MDA serum levels as parameters of oxidative stress shows a gap to fill in this area. Moreover, similar studies, especially in women of reproductive age with obesity, have never been conducted in Indonesia. To our knowledge, this is the first study about flavonoid intake and oxidative stress in obese women in Indonesia. In addition, it can be a reference for a further study on food consumption or antioxidants sources to overcome oxidative damage and reduce the risk of various diseases. Thus, this study was conducted to determine flavonoid intake and its correlation with MDA serum levels in obese women of reproductive age in Kendari, Indonesia.

Methods

Subjects and study design

This cross-sectional study was carried out during the Covid-19 pandemic in Kendari, Southeast Sulawesi, Indonesia. Purposive sampling was used to obtain samples. The inclusion criteria for this study were women aged 19-45 years old with body mass index (BMI) ≥25 kg/m^2 who voluntarily agreed to take part in the study by signing informed consent. Those who were pregnant, smoker (active or passive), on diet and/or exercised for weight loss program, had chronic diseases (i.e. heart diseases, diabetes mellitus and hypertension) used multivitamin and/or herbal and/or on medication, consumed alcohol, and reached menopause, were exempted from this study. Sample size was determined based on correlation analysis (α=0.05; β=0.20; r=0.3), and the sum of samples was 85 subjects. However, out of 105 subjects who signed the informed consent, 17 subjects did not meet the criteria, therefore only 88 samples were further analysed.

Data collection

Data collection was conducted from April to October 2021 after it was submitted and approved by the Ethics Committee of Faculty of Medicine, University of Indonesia – Cipto Mangunkusumo Hospital (No. 593/UN2.F1/ETIK/PPM.00.02/2021, protocol number 21-06-0601). There were 3 enumerators with an education background in nutrition assisted in this study. Data obtained through the interview process, physical examination and laboratory examination.

Characteristic data

Subject's characteristic data including age, education, occupation and income were obtained through interviews. Education was categorised into high (graduated from diploma and above), moderate (graduated from junior or high school) and low (graduated from elementary school and below). Occupation was categorised into employee and not employee. Income was categorised into two groups, more than, and less than or equal to the value of minimum wage (UMK) in Kendari (Rp 2,768,592).[17] The participants of this study are those who are considered obese by the Nutritional status based on the BMI in kg/m^2 according to WHO Asia-Pacific criteria. Those who have BMI 25 - 29.9 kg/m^2 were assigned to Group of Obese 1. Meanwhile, the rest of participants (BMI ≥ 30 kg/m^2) were assigned to Group of Obese 2.

Flavonoid intake assessment

The assessment of flavonoid intake was done through an interview by 3 enumerators using a validated semi-quantitative food frequency questionnaire (SQ-FFQ), food model and food photo book. Subjects were asked to recall the food consumed in the last 6 months based on the list in SQ-FFQ. First, the quantity of food consumed was assessed by household size (URT) which is compared with the food photo book guide for individual food consumption surveys (SKMI 2014)[18] of the Ministry of Health of the Republic of Indonesia. Second, the data was processed using Nutrisurvey 2007. Based on the USDA Database for the Flavonoid Content of Selected Foods, we find that total flavonoid intake comprised six flavonoid subclasses, namely flavonols, flavones, flavanones, flavan-3-ol, anthocyanidins, and isoflavonoids.[12]

Using the USDA database as a reference, we then calculated participants' flavonoid levels. The total flavonoid intake was measured by the number of flavonoid subclass intakes in mg/day. The intake of the flavonoid subclass (mg/day) was obtained from the weight of the food (gr) divided by 100 multiplied the flavonoid content (mg) minus retention (0.85 for antosianidin and 0.5 for other subclasses).[12] If the raw weight was the same as the cooked weight, the flavonoid intake was calculated without retention.

Data analysis

Data were analyzed using SPSS version 20.0. Normality of the data distribution was determined by Kolmogorov Smirnof test. Data distribution was considered normal when p value ≥ 0,05. Data are presented in the form of mean ± standard deviation (SD) if normally distributed ($p \geq 0.05$), and in the form of median (minimum-maximum) if not normally distributed ($p < 0.05$). Categorical data were presented in the form of frequency distribution (n,%). Continuous data were presented in the form of median (minimum-maximum). The correlation between two variables was analyzed using the Pearson correlation test if the data distribution was normal, or the Spearman Rank correlation test if the data distribution was not normal. The possible range of values for the correlation coefficient (r) is -1 to 1. A correlation of -1 indicates a perfect negative correlation, and a correlation of 1 indicates a perfect positive correlation. Value 0,8 to 1 indicate very strong correlation, 0,6 to 0,8 indicate strong correlation, 0,4 to 0,6 indicate moderate correlation, 0,2 to 0,4 indicate weak correlation, and < 0,2 indicate very weak correlation. If the correlation coefficient is greater than zero, it is a positive relationship. Conversely, if the value is less than zero, it is a negative relationship. The correlations were considered significant if the p value < 0,05. Nutrisurvey 2007 was used to perform analysis of zinc intake.

Anthropometric measurement

Anthropometric measurements were performed to obtain data of heights and weights. Heights were measured using Microtoise Staturmeter 200 cm (with 0.1 cm accuracy). Weight measurement was done by using GEA SMIC ZT120. Both anthropometric measurements were performed twice, and then were used for body mass index (BMI) calculations. Nutritional status assessments were based on the BMI in kg/m^2 according to WHO Asia-Pacific criteria.

Laboratory examination

The blood tests were conducted as a screening process to determine the levels of fasting blood glucose, high density lipoprotein-cholesterol (HDL-C) and triglyceride. Those tests were also to determine the level of malondialdehyde (MDA) serum as an oxidative stress marker. The blood tests were performed in collaboration with Maxima Kendari Laboratory, while the examination of oxidative stress level was carried out at the Biochemistry Laboratory, Faculty of Medicine, University of Indonesia in Jakarta.

Five ml of blood samples were taken from the cubital vein, which was then centrifuged at 3000 rpm for 10 minutes to obtain the serum. The samples were examined using the Automated Clinical Analyser TMS 1024i to assess fasting blood glucose, HDL-C and triglyceride levels. Blood samples that passed the screening were afterward sent to the Biochemistry Laboratory of the Faculty of Medicine, University of Indonesia in Jakarta, for MDA serum level examination. The MDA level analysis was done using the TBA method. A total of 2 ml of serum was mixed with 1 ml of 20% TCA, followed by adding 2 ml of 0.67% TBA. The mixture was then allowed to stand for 10 minutes in a boiling water bath. It is then cooled using an ice-cold water bath. It was subsequently centrifuged at 6000 rpm for 30 seconds and its absorbance was read at 530 nm using a spectrophotometer.

Statistical Analysis

Data were analysed by using IBM SPSS version 26.0. Normality test was done by using Kolmogorov Smirnov. The data distribution was considered normal when the p value > 0.05. Continuous data were presented as mean ± SD or median (minimum-maximum). Categorical data were presented as a frequency distribution (n, %). Descriptive statistics of total flavonoid intake were expressed as mean ± SD and flavonoid subclasses as median (min-max). Additional analysis Independent T-Test and Mann-Whitney Test were done to determine the flavonoid intake difference and the MDA serum levels between the group of obese 1 and obese 2. MDA serum levels were expressed as mean ± SD or median (min-max). Spearman's correlation was used to determine whether there was a relationship between flavonoid intake and MDA serum levels. The level of significance was set at $p<0.05$.

Result

Among 105 subjects who were willing to take part in the study, there were 17 subjects who did not meet the criteria, so that the remaining 88 subjects were further analysed **(Figure 1).** The median age of 88 subjects was 28 (19-45) years old. The majority of subjects were employees with low income (below the UMK) and most of them were assigned to Group of Obese 1. Therefore, the BMI median value of all the subjects was 27.58 (25.02-39.20) kg/m^2. Subject's characteristics data is shown as **Table 1.**

The average total flavonoid intake in the subjects was 142,26 ± 56,53 mg per day. Total flavonoid intake in the Group of Obese 2 was higher than the Group of Obese 1. After performing the Independent T-Test analysis ($p > 0.05$), we found that there was no significant difference in total flavonoid between both groups. The result can be seen in **Table 2**. In addition, we found that the median value of MDA serum levels was 2.16 (1.09-6.71) nmol/ml. Furthermore, after taking the Mann-Whitney Test ($p > 0.05$) based on the subjects' obesity status, there was no significant difference in MDA serum levels in both groups, as seen in **Table 3.**

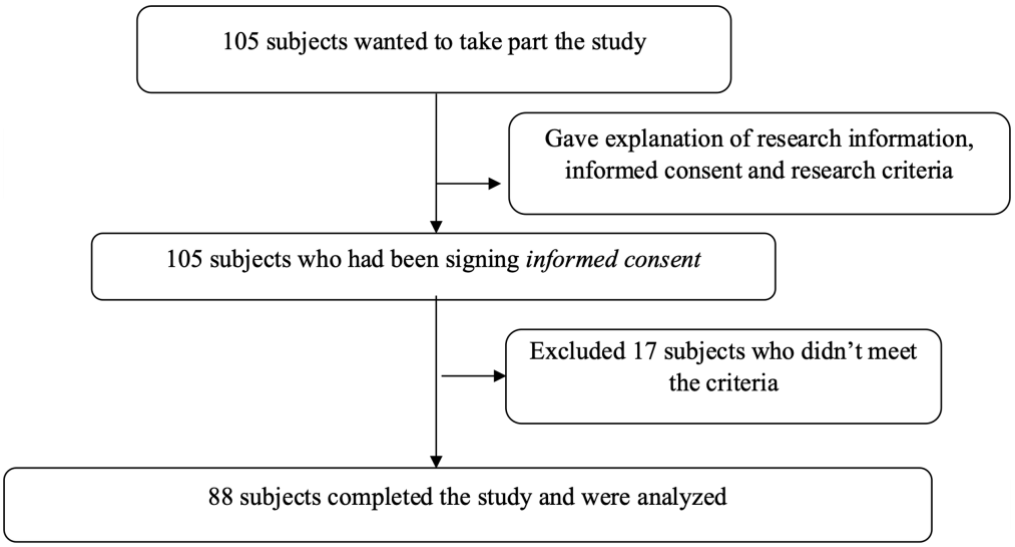

Figure 1. Subjects selection procedure

Table 1. Subjects' characteristics

Variabel	**Hasil**
Age (years)	28 (19-45)**
Education level, n (%)	
Low	-
Moderate	44 (50)
High	44 (50)
Occupation, n (%)	
Employee	49 (55.7)
Unemployee	39 (44.3)
Income, n (%)	
≤ UMK	75 (85.2)
> UMK	13 (14.8)
Antropometry	
Weight, (kg)	64.4 (55.00-99.25)**
Height, (cm)	153 (145-170)**
Body Mass Index, (kg/m^2)	27.58 (25.02-39.20)**
Nutritional status, n (%)	
Obese 1	70 (79.5)
Obese 2	18 (20.5)
Fasting blood glucose (mg/dl)	81,5 (44-144)**
High Density Lipoprotein (mg/dl)	50.16 ±10.08*
Triglyseride (mg/dl)	93 (34-473)**

*Mean ± SD
**Median (minimum-maximum)

Table 2. Subject's flavonoid intake

Variables	All n=88 (Mean±SD/ Median(min-maks))	Obese 1 n=70 (Mean±SD/ Median(min-maks))	Obese 2 n=18 (Mean±SD/ Median(min-maks))	*p*
Flavonoid	142,26 ± 56,53	137,06 ± 51,9	162,49 ± 69,82	0,089*
Flavonol	20,22 (1,65-71,79)	19,61 (1,65-60,34)	28,73 ± 17,12	0,118**
Flavon	1,46 (0,13-22,77)	1,46 (0,13-22,7)	1,26 (0,43-22,77)	0,84**
Flavanon	5,68 (0,00-53,92)	5,68 (0-53,92)	5,95 (0,01-49,59)	0,918**
Flavan-3-Ol	27,66 (0,02-94,79)	29,63 ± 22,71	33,75 ± 24,01	0,5*
Antosianidin	0,63 (0,00-13,51)	0,38 (0-13,51)	1,57 (0-4,59)	0,228**
Isoflavonoid	55,53 (2,67-213,43)	55,52 (2,67-213,43)	79,48 ± 50,85	0,066**

**Independent T-Test*
***Mann-Whitney Test*

Table 3. Subject's malondialdehyde serum levels

Variable	All n=88 (Mean±SD/ Median(min-maks))	Obese 1 n=70 (Mean±SD/ Median(min-maks))	Obese 2 n=18 (Mean±SD/ Median(min-maks))	*p*
MDA serum levels (nmol/ml)	2,16 (1,09-6,71)	2,17 (1,2-6,7)	2,28 ± 0,77	0,466*

**Mann Whitney Test*

Table 4. Correlation between flavonoid intake and malondialdehyde serum level

Variables	Malondialdehyde serum levels					
	All n=88		Obese 1 n=70		Obese 2 n=18	
	r	P[b]	r	P[b]	r	p
Total flavonoid intake	0,188	0,079	0,172	0,155	0,390	0,110[a]
Flavonol	-0,074	0,492	-0,046	0,706	-0,139	0,582[a]
Flavon	-0,097	0,370	-0,136	0,262	0,056	0,826[b]
Flavanon	-0,095	0,377	-0,099	0,413	-0,065	0,797[b]
Flavan-3-Ol	0,325	0,002†	0,305	0,010†	0,585	0,011[a]†
Antosianidin	-0,029	0,789	-0,046	0,705	0,053	0,834[b]
Isoflavonoid	0,094	0,383	0,063	0,604	0,422	0,081[a]

[a]*Pearson*
[b]*Spearman*
†: statistically significant

This study found no correlation between flavonoid intake and MDA serum levels in all subjects (r=0.188, p=0.079), both in the Group of Obese 1 (r=0.172, p=0.155) and Group of Obese 2 (r=0.39, p=0.11). However, there was a positive correlation between flavan-3-ols intake and MDA serum levels in all subjects (r=0.325, p=0.002), both in the Group of Obese 1 (r=0.305, p=0.01) and Group of Obese 2 (r=0.585, p=0.011). Data are summarised in **Table 4.**

Discussion

This study found no correlation between flavonoid intake and MDA serum levels in obese women of reproductive age in Kendari (p>0.05). The therapeutic effect of flavonoids is 250-400 mg per day.[19] Meanwhile, the intake of flavonoids in the subject is only 142.26 ± 56.53 mg per day. The result is in line with the study by Alipour et al.[16] which showed no association between flavonoid intake and MDA levels (p > 0.05) in 170 healthy women aged 20-48 years in Iran. In contrast, a study on 159 elderly people in Spain using the SQ-FFQ to estimate flavonoid intake and its association with plasma MDA conducted by Gonzalez et al.[15] showed a negative relationship between flavonoid intake and MDA through multiple regression analysis.

The anti-obesity potential associated with flavonoids is quite relevant and their regulatory effects have been observed in reducing food intake and nutrient absorption, modulating adipogenesis and adipocyte life cycle, triggering thermogenesis and energy consumptions, and regulating the gut microbiota.[20] A study by Kim et al.[21] showed that the high intake of flavonoids was associated with a decrease in obesity prevalence among women. It is similar to a study conducted by Jennings, which showed a relationship between the high intake of flavonoids and the low fat mass.[22]

Flavonoids have shown promising health-enhancing effects in human cell culture, experimental animals, and clinical studies in humans. The majority of studies linking flavonoid intake to MDA levels as a biomarker of oxidative stress resulted from intervention trials.[19] Hirano[14] for instance, has looked at the effect of tea consumption which has been shown to lower MDA. Gonzalez et al.[15] found an inverse relationship between flavonoid intake and MDA. Contrarily, Alipour et al.[16] showed a different result in which flavonoid intake was not significantly associated with MDA.

The variation in the body's response to flavonoids such as differences in the composition of the gut microbiota and the food matrix can affect the metabolism and effectiveness of flavonoids. The mechanism of the antioxidant effect of flavonoids is still not clearly understood. One possible explanation for this effect is through direct reaction with reactive oxidants or the influence of the non-enzymatic antioxidant capacity on plasma. Another mechanism of flavonoids is as an antioxidant. The flavonoids' compound has the ability to donate a hydrogen atom (as a reducing agent) to free radicals. After giving away the hydrogen atom, flavonoids is then transformed into a stabilized radical phenolic compound, so that it is not easy to participate in other radical reactions.[16]

Interestingly, this study found a significant positive correlation between the intake of one of the flavonoid subclasses, namely flavan-3-ol/flavanol (r=0,325, p=0,002) and MDA serum levels. This flavonoid subclass is mostly found in tea, apples, fruit juices, chocolate, etc.[21] The result shows that an increase in MDA levels is correlated with the increasing intake of flavan-3-ol/flavanol. However, the correlation in the Group of Obese 2 (r=0.585, p=0.011) was higher than the Group of Obese 1 (r=0.305, p=0.010). The subjects' most consumed sources of flavan-3-ol were tea, bananas and apples.

An experimental study conducted by Monreal et al.[22] on the green tea consumption of obese subjects' (rich of 3 ol flavans) demonstrates a decrease in MDA levels after drinking 4 glasses of green tea per day or supplementing with 2 green tea capsules per day for 8 weeks. Another study conducted by Majo et al.[23] reveals that low concentrated flavan-3-ols have a potential to be strong antioxidants that can perform as free radical scavengers. Nevertheless, the study also shows that flavan-3-ols can go through the auto-oxidation at higher concentrations, thereby reducing their potential as antioxidants.

Several popular antioxidants have been reported to have prooxidant behaviors. There are at least three factors that can affect the function of antioxidants, converting them to prooxidants. These factors include the presence of metal ions, the concentration of antioxidants in the matrix environment and their redox potentials.[24] The prooxidant effect may also be beneficial, in which mild levels of oxidative stress generate the increase of antioxidant defense levels and biotransformation enzymes, leading to overall cytoprotection. The prooxidant activity is considered to be directly proportional to the total number of hydroxyl groups in the flavonoid molecule. The extent to which flavonoids are able to act as anti-prooxidants in vivo is still poorly understood and requires further study.[25]

Although several studies have shown the ability of flavonoids to overcome lipid peroxidation, it turns out that flavonoids have an oxidation potential that can bring the antioxidant or pro-oxidant properties under different conditions. For instance, in high doses or when the metal ions are present, flavonoids are able to reduce Cu(II) to Cu(I) and thus initiate the formation of free radicals. In another condition, the high concentrations of phenolic compounds can turn into pro-oxidants.[24,25]

This study has not been able to prove a correlation between flavonoid intake and MDA levels in obese women of reproductive age in Kendari. Several things that could cause insignificant results, among others, are the sample size was not sufficient, especially to compare the two groups of obesity. In addition, the analysis of flavonoids intake in food used food databases from other countries, where the levels of flavonoids can be different with this study due to differences in soil type, temperature, pH, season, etc.

The database of food sources of flavonoids in Indonesia is also still very limited. One of those that is quite comprehensive is provided by a study by Sefrina et al.[12] which is used in this study. However, that research still also used information from the USDA food database. Due to the diverse variations and types of food, in determining the flavonoid level in food sources, it is necessary to carry out a more specific examination, not only by relying on existing data from other countries.

This study also relies heavily on the honesty of respondents in reporting the intake and providing information related to the exclusion criteria. Screening examinations are very limited, considering the time and funds. Therefore, no other examinations, such as endogenous antioxidant levels affecting MDA levels, were administered in this study.

Furthermore, the absence of a correlation between total flavonoids and MDA levels in this study could be due to the fact that the intake of the subjects was not sufficient to provide the desired effects. It is known that the therapeutic effect of flavonoids is 250-400 mg per day.[19] This value has not been achieved by the subjects in this study.

The limitations of this study is that it uses SQ-FFQ to assess the flavonoid intake which is very dependent on the subject's memory, so that recall bias can occur, and it is difficult to get accurate intake information. This method can also lead to underestimation or overestimation from the participants. There are also several elements causing variation of participants' food intakes such as type of food consumed in different climates and various regional zones, certain seasons that affect the phytochemical content, food processing methods, temperature and processing time. It is acknowledged that respondents did not correctly inform the amount of food they consumed because of the flat slope syndrome, and hence, it is more or less than the actual amount. This limitation was prevented by providing an explanation of the importance of food intake reports to assess the health condition of research subjects in the informed consent. To minimize this recall bias and make it easier for the subject to recall the food they consumed, food models and photos were also utilized.

This study also did not examine other factors that can affect MDA serum levels such as endogenous and exogenous antioxidant levels. The examination was not carried out due to time and funding constraints. Since this study used a cross-sectional design, we could not monitor changes in flavonoid intake and MDA levels in subjects and were unable to observe the association and causal relationship between those two variables. This study also did not distinguish between physical activity and stress

factors from the subjects affecting food selection and total energy intake, hence it is prone to bias.

However, this research is the first study to assess flavonoid intake in Kendari. Further research needs to be undertaken using a larger sample size, especially to compare the two obese groups. Other research using other designs such as case control or cohorts can also be considered. This study leaves a room to explore, especially in the field of flavonoid intake. For instance, by examining other factors which were not carried out in this study such as endogenous antioxidants, oxidative stress markers and MDA comparison. Another potential approach is conducting a validation test of sq ffq intake of flavonoids, utilizing a variety of foods that are more representative of the population. It is also necessary to conduct further studies on the foods containing flavonoids database in Indonesia, since by far, there is still limited information and similar studies to date. The future studies can therefore produce a more valid database.

Conclusion

This study found no correlation between total flavonoid intake and MDA serum levels but there was a positive correlation between one of the flavonoid subclasses, namely flavan-3-ol/flavanol. This result may be due to low intake of flavonoids that reduce the effectiveness of flavonoids as antioxidants. The findings of this study are expected to be used as a basic data for further research on the benefits and impacts of flavonoids, and factors that affect flavonoids as antioxidants, especially in reproductive age women with obesity.

Conflict of Interest

Authors declared no conflict of interest regarding this article.

Acknowledgment

We would like to convey our gratitude to all those who helped in the course of this study, including to Halu Oleo University for the scholarships provided, the study subjects, enumerators, teachers, and parents for giving us the opportunity to conduct the research.

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References

1. Ritchie H, Roser M. Obesity [Internet]. Our World in Data. 2017 [cited 2020 Aug 6]. Available from: https://ourworldindata.org/obesity. [Google Scholar]
2. WHO. Prevalence of obesity among adults, BMI >= 30 (age-standardized estimate) (%) [Internet]. 2020 [cited 2020 Dec 18]. Available from: https://www.who.int/data/gho/data/indicators/indicator-details/GHO/prevalence-of-obesity-among-adults-bmi-=-30-(age-standardized-estimate)-(-). [Google Scholar]
3. Indonesian Ministry of Health. RISKESDAS 2018. Kemenkes, Jakarta. https://www.kemkes.go.id/resources/download/infoterkini/hasil-riskesdas-2018.pdf
4. Dinas Kesehatan Provinsi Sulawesi Tenggara. Profil Kesehatan Provinsi Sulawesi Tenggara. 2017.
5. Harahap H, Irfannuddin I, Murti K. Pengaruh Diet Ketogenik terhadap Ekspresi Ki-67, Caspase-3, dan MDA pada Jaringan Hati. JMJ 2018; 6(2):185-194. [Google Scholar]
6. Tauqeer Z, Gomez G, Stanford FC. Obesity in Women: Insights for the Clinician. J Women's Health. 2018;27(4):444–57. [Google Scholar]
7. Savini I, Gasperi V, Catani MV. Oxidative Stress and Obesity. In: Ahmad SI, Imam SK, editors. Obesity [Internet]. Cham: Springer International Publishing; 2016 [cited 2020 Aug 6]. p. 65–86. Available from: http://link.springer.com/10.1007/978-3-319-19821-7_6. [Google Scholar]
8. Lu J, Wang Z, Cao J, Chen Y, Dong Y. A novel and compact review on the role of oxidative stress in female reproduction. Reprod Biol Endocrinol. 2018;16:80. [Google Scholar]
9. Agarwal A, Gupta S, Sharma RK. Role of oxidative stress in female reproduction. Reprod Biol Endocrinol. 2005;3:28. [Google Scholar]

10. Mulianto N. Malondialdehid sebagai Penanda Stres Oksidatif pada Berbagai Penyakit Kulit. Cermin Dunia Kedokteran. 2020;47(1):39-44. [Google Scholar]
11. Yanti A. Faktor – Faktor Yang Berhubungan Kejadian Obesitas Pada Wanita Usia Subur (Wus) Di Wilayah Kerja Puskesmas Lepo – Lepo. Midwifery Journal: Jurnal Kebidanan UM Mataram. 2020 Feb 6;5:5.
12. Sefrina LR, Briawan D, Sinaga T, Permaesih D. Flavonoid Database Based on Indonesian Foods. J Nutr Sci Vitaminol (Tokyo). 2020;66(Supplement):S251–5. [Google Scholar]
13. Sefrina LR, Rahmatunisa R. Estimasi Asupan Total Flavonoid Pada Mahasiswa Kesehatan Dan Non-Kesehatan Di Karawang. Jurnal Gizi Kerja dan Produktivitas. 2020 Sep 28;1(2):18–24. [Google Scholar]
14. Hirano-Ohmori R, Takahashi R, Momiyama Y, Taniguchi H, Yonemura A, Tamai S, et al. Green Tea Consumption and Serum Malondialdehyde-Modified LDL Concentrations in Healthy Subjects. J Am Coll Nutr. 2005;24(5):342–346. [Google Scholar]
15. González S, Cuervo A, Lasheras C. Polyphenol Intake in Elderly People Is Associated with Lipid Oxidative Damage. J Am Coll Nutr. 2013;32(6):384–390. [Google Scholar]
16. Alipour B, Rashidkhani B, Edalati S. Dietary flavonoid intake, total antioxidant capacity and lipid oxidative damage: A cross-sectional study of Iranian women. Nutrition. 2016;32(5):566–72. [Google Scholar]
17. UMK Kendari Rp 2,76 Juta – Kendari Pos [Internet]. [cited 2021 Mar 23]. Available from: https://kendaripos.co.id/2020/11/umk-kendari-rp-276-juta/
18. Sirajuddin, Surmita, Astuti T. Survei Konsumsi Pangan [Internet]. Pusat Pendidikan Sumber Daya Manusia Kesehatan Badan Pengembangan dan Pemberdayaan Sumber Daya Manusia Kesehatan Kementerian Kesehatan RI; 2018. Available from: http://bppsdmk.kemkes.go.id/pusdiksdmk/wpcontent/uploads/2018/09
19. Escobar-Cévoli R, Castro-Espín C, Béraud V, Buckland G, Zamora-Ros R, Béraud, GBV. An Overview of Global Flavonoid Intake and its Food Sources, Flavonoids-From Biosynthesis to Human Health, Intech: London, UK, 2017. DOI: 10.5772/67655. Available from: https://www.intechopen.com/chapters/54289. [Google Scholar]
20. García-Barrado MJ, Iglesias-Osma MC, Pérez-García E, Carrero S, Blanco, EJ, Carretero-Hernández M, et al. Role of Flavonoids in The Interactions among Obesity, Inflammation, and Autophagy. Pharmaceuticals. 2020;13(11):342. [Google Scholar]
21. Kim S-A, Kim J, Jun S, Wie G-A, Shin S, Joung H. Association between dietary flavonoid intake and obesity among adults in Korea. Appl Physiol Nutr Metab. 2020;45(2):203–212. [Google Scholar]
22. Jennings A, MacGregor A, Spector T, Cassidy A. Higher dietary flavonoid intakes are associated with lower objectively measured body composition in women: evidence from discordant monozygotic twins. Am. J. Clin. Nutr. 2017;105(3):626–634. [Google Scholar]
23. Di Majo D, La Guardia M, Leto G, Crescimanno M, Flandina C, Giammanco M. Flavonols and flavan-3-ols as modulators of xanthine oxidase and manganese superoxide dismutase activity. Int J Food Sci Nutr. 2014;65(7):886–892. [Google Scholar]
24. Wardani MN, Bafirman B, Indika PM. Pengaruh Pemberian Vitamin E Terhadap Kadar Malondialdehid (MDA) Pelari Jarak Jauh Sumatera Barat. Jurnal Stamina. 2018;1(1), 99-105. [Google Scholar]
25. Sotler R, Poljšak B, Dahmane R, et al. Prooxidant Activities Of Antioxidants And Their Impact On Health. Acta Clin Croat. 2019;58(4):726-736. [Google Scholar]

World Nutrition Journal |eISSN 2580-7013

LITERATURE REVIEW

Mother's coping strategies toward food insecurity during COVID-19 pandemic : a review article

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Received 24 June 2021
Accepted 4 January 2022
Published: 28 February 2022

Link to DOI:
10.25220/WNJ.V05.i2.0004

Citation: Vantono SA, Bardosono S, Wiradnyani LAA. Mother's coping strategies toward food insecurity during COVID-19 pandemic: a review article. World Nutrition Journal.2022 Feb 28, 5(2):18-22.

Website : http://www.worldnutrijournal.org/

Abstract

The COVID-19 pandemic has impacted many aspects of the country, including the economy and health care. Food insecurity is increasing, causing harm to children's nutrition and development. As a result, mother must deal with food insecurity to providing a balanced diet for her children aged 6 to 23 months. This study aims to review the possible mother's coping strategies used toward food insecurity to maintain child nutrition during the COVID-19 pandemic. To review the literature, the researcher utilized search engine such as PubMed, ScienceDirect, Oxford journal, and British Medical Journal. "COVID-19", "Coping Strategies", "Food Security", and "Child" were among the keywords chosen by the researcher. After filtering with the several criteria, the 17 articles were reviewed. Based on this paper review, we know that during the COVID19 pandemic, there is a coping strategy that assist mother to maintain their child nutrition. To address the problem of food insecurity, the possible mother's coping strategy used are adaptive coping strategies such as home-cooked meals, financial support, and receiving food assistance.

Keywords: COVID-19, coping strategies, food security, child

Introduction

COVID-19, a worldwide pandemic has been spreading. The economy was impacted, resulting in employment losses across the country.[1,2] Furthermore, due to poor families, employment losses have exacerbated food insecurity.[3] According to the data, household food insecurity has increased by one-third since COVID-19 with 35.5% of food insecure households classed as newly food insecure.[4] The household food insecurity is a risk factor for malnutrition among all groups, especially children.[5–7] Furthermore, the 6-23 month period is the golden age of growth and development for children, as well as the time when they need to eat nutritious complementary foods in addition to breastmilk.[8] In Indonesia, infant and young child feeding/IYCF practices is not optimal, in which only 40% of children aged 6-23 months received foods meeting the criteria of the minimum acceptable diet based on the 2017 Indonesia Demographic and Health Survey Data.[9,10] These numbers can be worsened during the pandemic because the food insecurity is increasing.[8,11] In addition, food insecurity has been linked to several long-term

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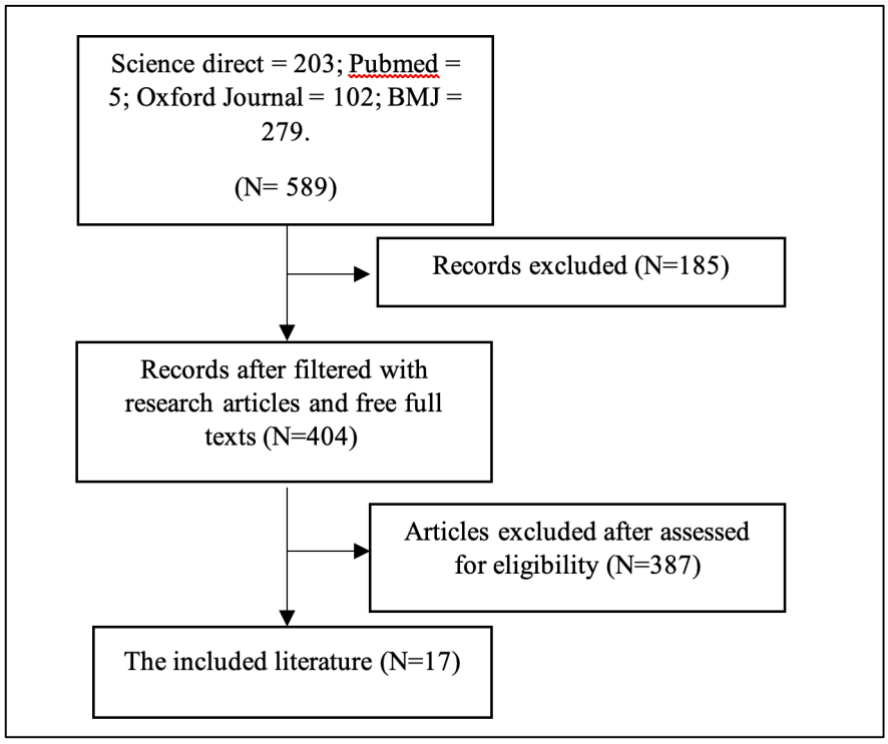

Figure. 1 Flow diagram of the article selection

health consequences, including an increased risk of chronic illness, cognitive and functional deficits, and depression in mothers.[12] As a result, the mother must deal with food insecurity during the pandemic with coping strategy. Coping strategy are not a unidimensional behavior but are attained by many behaviors, cognitions, and perceptions that form remedial actions undertaken by people with survival and livelihood are compromised or threatened.[13,14] It was practiced to increase the accessibility of food in their households to maintain the nutrition of the household member.[15] To the best our knowledge, there are few studies on mother's coping strategies in maintaining the adequate dietary intake of their children aged 6-23 months. The purpose of this paper is to conduct a review of the literature on the possible mother's coping strategies used toward food insecurity during the COVID-19 pandemic.

Methods

PubMed, ScienceDirect, Oxford Journal, and BMJ (British Medical Journal) were among the search engines utilized by the researcher. The keywords used in the article searching were the combinations of the terms including "COVID-19", "Coping Strategies", "Food Security", and "Child", The articles searching was carried out in two stage, that September 2020 – December 2020 and May – December 2021. In the first stage the researchers conducted a review of coping strategies toward food insecurity in general and during COVID-19, while in the second stage the researchers searched for updated article related COVID-19 context. The articles reviewed included in this study are those written in english, research articles, full text available, and eligible by critical appraisal.[16] Researchers have confirmed that no selected articles are doubled. The management of articles were conducted with named of each articles with order of author, year, and title of the article which saved in one folder on Zotero. Systematic review and retrospective studies with quantitative and qualitative study were included **(Figure 1)**.

Findings

A total 17 articles were reviewed by the researchers. Based on the literature review, people's coping strategy differ based on their location, community, social group, family, and cultural context. In addition, people's coping strategy are impacted by their past experiences. In Nansanga, Central Zambia, they were able to demonstrate, that socioeconomic differences influenced the coping strategy. For example, the low wealth class did seasonal jobs, the middle wealth class sold land to miners and trees, the high wealth class was selling alcohol and local brew.[17] Formal and informal work have influenced coping strategies in Sub-Saharan Africa. Food intake is lower in informally employed households, and coping strategy are used more frequently.[18] In the study that covering 62 countries such as Africa, Asia, Europe, Oceania and the Americas found that several reports highlighted that the financial impacts were tend to be higher for urban households than rural.[11] In Myanmar, people living in rural areas used loans more often than those living in urban.[19] In Bangladesh, people who live in rural areas were mild to moderate food insecure adopted either financial or both financial and food compromised coping strategies. But people who live in urban area with mild to moderate food insecure mostly applied both forms of coping strategies. Besides that, in severely food insecure household, most of them adopted both forms of coping strategies to survive.[7]

There are examples of household coping strategies such as farming, saving, loans, foraging of crisis food (roots, berries), sale of household assets, migration, sales of relief goods, child labor, prostitution, theft, violence.[13] Food insecure households in the United States have reported using coping strategy such as buying a limited variety of foods, relying on low-cost options, cooking in bulk, sharing food, shopping on promotions, using coupons, and making trade-offs between food and other family costs. They were also skipping meals at the end of the month.[12]

Coping Strategy during Pandemic COVID-19

During pandemic COVID-19, several studies found that coping strategies has differ by gender. Women have more financial impacts rather than men.[11] Several women have been laid off as a result of the COVID-19 pandemic. In Egypt, the fisher wives who having the children transient from housewifes into fish vendor while the fishermen tend to seek another gainful employment elsewhere.[20] Apart from that, in Indonesia, men began online marketing or adapted their motorcycles into motor taxis, even though their earnings were not much higher than their previous job's salary. Borrowing money from friends or loan sharks is a frequent household coping strategies. There is a voluntary contribution that rises during the pandemic in some areas.[21]

An overview of coping strategies in food-insecure households is provided in response to a pandemic or crisis that may raise the likelihood of food insecurity. During the pandemic of COVID-19 in the United Kingdom, food insecurity was linked to consumption of high-energy-density foods, overeating, overweight/obesity, decreased intake of fruits and vegetables, and an increase in home-prepared consumption in adults.[22] The study from eighty-two countries survey, there were 14.5% Children were reported to be having difficulty obtaining appropriate food.[23] Children and women in Bangladesh have been affected by the quality and amount of food available, putting them at risk of acute malnutrition due to a lack of nutritional variety. To deal with food insecurity, the majority of individuals borrowed money or food.[7] In Pakistan, the people who rely on government assistance by financial support have improved their food security during the COVID-19 pandemic.[24] Most of the households who experiencing food insecurity were more likely to engage in food-related coping strategies such as reduce the quality and quantity of food by relied on less preferred foods, reduced portion sizes, number of meals during COVID-19 pandemic, and borrowing money to buy food.[23,25] Based on the other study, It was found the food assistance program were one of the strategy to helped the household facing food insecurity during COVID-19 pandemic.[26]

Aside from that, there are many types of coping strategy, such as adaptive and maladaptive coping strategies. Behavioural disengagement, self-blame, and poor acceptance were among the maladaptive coping methods. Before lockdown, they were linked to emotional and uncontrollable eating, which worsened as stress increased. Increased consumption of fruits and vegetables, as well as home-cooked meals, was associated with reduced food insecurity and more adaptive coping strategies. Exercising and getting enough sleep are both elements of adaptive and problem-focused coping techniques.[22]

Conclusion

To the best our knowledge, we conclude that all mothers were encouraged to learn about an adaptive coping strategies. Early detection of at-risk children in food-insecure households must be reactivated by community nutrition and health workers to combat the risk of increasing undernourished.[27] The food assistance program would be good idea to assist mothers in coping with food insecurity during COVID-19 pandemic. Furthermore, for a better living, all sectors, including government, health, and social services, should act collaboratively.

Conflict of Interest

Authors declared no conflict of interest regarding this article.

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References

1. Nieuwenhuijsen MJ. COVID19 and the city; from the short term to the long term. Environ Res. 2020;191:1–3. DOI: 10.1016/j.envres.2020.110066
2. ILO. ILO Monitor: COVID-19 and the World of Work, Seven Edition. [Internet]. 2021 p. 1–12. Available from: https://www.ilo.org/wcmsp5/groups/public/@dgreports/@dcomm/documents/briefingnote/wcms_767028.pdf
3. Milovanska-Farrington S. Job Loss and Food Insecurity during the COVID-19 Pandemic. IZA Inst Labor Econ. 2020;14273:1–27. Available from: http://ftp.iza.org/dp14273.pdf
4. Niles MT, Bertmann F, Belarmino EH, Wentworth T, Biehl E, Neff R. The early food insecurity impacts of COVID-19. Nutrients. 2020;12(2096):1–19. DOI: 10.3390/nu12072096
5. Ali D, Saha KK, Nguyen PH, Diressie MT, Ruel MT, Menon P, et al. Household Food Insecurity Is Associated with Higher Child Undernutrition in Bangladesh, Ethiopia, and Vietnam, but the Effect Is Not Mediated by Child Dietary Diversity. J Nutr. 2013 Dec 1;143(12):2015–21. DOI: https://doi.org/10.3945/jn.113.175182
6. Grammatikopoulou MG, Gkiouras K, Theodoridis X, Markaki AG, Chourdakis M, Goulis DG. Food insecurity increases the risk of malnutrition among community-dwelling older adults. 2019;119:8–13. DOI: 10.1016/j.maturitas.2018.10.009
7. Das S, Rasul MdG, Hossain MS, Khan A-R, Alam MA, Ahmed T, et al. Acute food insecurity and short-term coping strategies of urban and rural households of Bangladesh during the lockdown period of COVID-19 pandemic of 2020: report of a cross-sectional survey. BMJ Open. 2020;10:1–12. DOI: 10.1136/bmjopen-2020-043365
8. Akseer N, Kandru G, Keats EC, Bhutta ZA. COVID-19 pandemic and mitigation strategies: implications for maternal and child health and nutrition. Am J Clin Nutr. 2020 Aug;112(2):251–6. DOI: https://doi.org/10.1093/ajcn/nqaa171
9. Puspitasari MD, Gayatri M. Indonesia Infant and Young Child Feeding Practice: The Role of Women's Empowerment in Household Domain. Glob J Health Sci. 2020;12(9):1–16. DOI:10.5539/gjhs.v12n9p129
10. National Population and Family Planning Board, Statistics Indonesia, Ministry of Health, The DHS Program ICF. Indonesia Demographic and Health Survey 2017. Jakarta: National Population and Family Planning Board; 2018 p. 186–8. Available from: https://dhsprogram.com/pubs/pdf/FR342/FR342.pdf
11. Bene C, Bakker D, Chavarro MJ, Even B, Melo J, Sonneveld A. Global assessment of the impacts of COVID-19 on food security. Elsevier. 2021;31. DOI:https://doi.org/10.1016/j.gfs.2021.100575

12. Kinsey EW, Oberle M, Dupuis R, Cannuscio CC, Hillier A. Food and financial coping strategies during the monthly Supplemental Nutrition Assistance Program cycle. Elsevier. 2019;7(100393):1–8. DOI: 10.1016/j.ssmph.2019.100393
13. WHO/EHA. Emergency health training programme for Africa. Panafrican Emergency Training Centre; 1998. Available from: https://www.academia.edu/28013985/EMERGENCY_HEALTH_TRAINING_PROGRAMME_FOR_AFRICA
14. Skinner EA, Edge K, Altman J, Sherwood H. Searching for the structure of coping: A review and critique of category systems for classifying ways of coping. Psychol Bull. 2003;129(2):216–69. DOI: 10.1037/0033-2909.129.2.216
15. Sulaiman N, Yeatman H, Russell J, Law LS. A Food Insecurity Systematic Review: Experience from Malaysia. Nutrients. 2021;13(945):1–39. Available from: https://doi.org/10.3390/nu13030945
16. Umesh G, Karippacheril JG, Magazine R. Critical appraisal of published literature. Wolters Kluwer. 2016;60(9):1–4. DOI: 10.4103/0019-5049.190624
17. Chilombo A, Van Der Horst D. Livelihoods and coping strategies of local communities on previous customary land in limbo of commercial agricultural development: Lessons from the farm block program in Zambia. Land Use Policy. 2021 May;104:105385. DOI: 10.1016/j.landusepol.2021.105385
18. Blekking J, Waldman K, Tuholske C, Evans T. Formal/informal employment and urban food security in Sub-Saharan Africa. Appl Geogr. 2020 Jan;114:102131. DOI: 10.1016/j.apgeog.2019.102131
19. Headey D, Goudet S, Lambrecht I, Oo TZ, Maffioli EM, Toth R. Poverty and Food Insecurity during COVID-19. Strategy Support Program. 2020;03:1–18. DOI: https://doi.org/10.2499/p15738coll2.134013
20. Barsoum G. From Fisher wives to fish vendors: Gendered livelihood transitions in a fishing village in Egypt. Elsevier. 2021;88:117–25. DOI: https://doi.org/10.1016/j.jrurstud.2021.10.012
21. Indonesia Rapid Gender Assessment in Response to COVID-19 – CARE | Evaluations [Internet]. [cited 2020 Aug 23]. Available from: http://www.careevaluations.org/evaluation/indonesia-rapid-gender-assessment-in-response-to-covid-19/
22. Coulthard H, Sharps M, Cunliffe L, van den Tol A. Eating in the lockdown during the Covid 19 pandemic; self-reported changes in eating behaviour, and associations with BMI, eating style, coping and health anxiety. Appetite. 2021 Jun;161:105082. DOI: 10.1016/j.appet.2020.105082
23. Jafri A, Mathe N, Aglago EK, Konyole SO, Ouedraogo M, Audain K, et al. Food availability, accessibility and dietary practices during the COVID-19 pandemic: a multi-country survey. Camb Univ Press. 2021;24(7):1798–805. doi:10.1017/S1368980021000987
24. Shahzad MA, Qing P, Rizwan M, Razzaq A, Faisal M. COVID-19 Pandemic, Determinants of Food Insecurity, and Household Mitigation Measures: A Case Study of Punjab, Pakistan. Healthcare. 2021;9(621):1–17. DOI: https://doi.org/10.3390/healthcare9060621
25. Nguyen PH, Kachwaha S, Pant A, Tran LM, Ghosh S, et al. Impact of COVID-19 on household food insecurity and interlinkages with child feeding practices and coping strategies in Uttar Pradesh, India: a longitudinal community-based study. BMJ Open. 2021;11:1–10. DOI: 10.1136/bmjopen-2021-048738
26. Lewis EC, Col on-Ramos U an, Gittelsohn J, Clay L. Food-Seeking Behaviors and Food Insecurity Risk During the Coronavirus Disease 2019 Pandemic. Journal of Nutrition Education and Behavior. 2021;0(0):1–13. DOI: 10.1016/j.jneb.2021.05.002
27. Ntambara J, Chu M. The risk to child nutrition during and after COVID-19 pandemic: what to expect and how to respond. Camb Univ Press. 2021;1–18. DOI: DOI: 10.1017/S1368980021001610

World Nutrition Journal |eISSN 2580-7013

ORIGINAL PAPER

Correlation of zinc intake with hair zinc levels and appetite in children aged 2-3 years in Jakarta

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Received 28 July 2021
Accepted 20 September 2021
Published: 28 February 2022

Link to DOI:
10.25220/WNJ.V05.i2.0005

Citation: Rosa AI, Sunardi D, Hardiany NS. Correlation of zinc intake with hair zinc levels and appetite in children aged 2-3 years in Jakarta. World Nutrition Journal.2022 Feb 28, 5(2):23-31.

Website : http://www.worldnutrijournal.org/

Abstract

Background: Children under five years experience rapid growth and development, so that adequate nutritional intake is very important. Zinc is essential for child development and growth. Children's zinc requirements are fulfilled from daily food intake that might be affected by Covid-19 pandemic. The aim of this study is to determine the correlation between zinc intake with hair zinc level and appetite in children aged 2-3 years in Jakarta.

Methods: This cross-sectional study was carried out from September to October 2020 in Kampung Melayu, Jakarta. Seventy children aged 2-3 years were taken using total population sampling method. Interviews were conducted to obtain characteristic data and zinc intake using semi quantitative-food frequency questionnaire (SQ-FFQ). Appetite were assessed using VAS appetite questionnaire. Hair samples were collected to check level of hair zinc. Spearman correlation was performed using SPSS.

Results: Median of zinc intake was 6 (1,2-22,5) mg/day, with 20% of the subjects had insufficient zinc intake. The median hair zinc value was 132 (30-451) µg/g, with 17,1% subjects zinc insufficient. The median of VAS appetite score was 54,5 mm. There were no significant correlation between zinc intake and hair zinc level (r = -0.077, p = 0.528). A weak positive correlation was found between appetite and hair zinc levels (r = 0,247, p = 0,039).

Conclusion: Zinc intake in children aged 2-3 years had no significant correlation with hair zinc level, and appetite had a weak positive correlation with hair zinc level.

Keywords: children aged 2-3 years, hair zinc, zinc intake, VAS appetite

Introduction

Children under five years experience rapid growth and development, so that adequate nutritional intake is very important. In a study of preschool-aged children in Jakarta, the prevalence of eating difficulties was 33.6%.[1] This problem makes nutritional needs unfulfilled, which can lead to malnutrition and growth disorders.[2] Feeding problems are more important among preschoolers who have high energy needs especially in children under five years of age.[2] Two years of age is a period of weaning from breast milk and complementary feeding, since then children are expected to have eaten similar food as their family, both in type and composition, age 2 to 3 years old is a very important transition period to pursue growth after the golden period. Therefore, it is important to pay attention to zinc intake at this age bracket to support optimal child growth.

Micronutrients that are important during growth are vitamins A, C, D, E, B, selenium and zinc. Unlike other minerals, zinc does not have large

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storage that can keep or release zinc according to variations in food intake, therefore adequacy of zinc is important. Research by Chao et al.[3] showed that zinc supplementation in malnourished children could increase appetite and growth.

The global prevalence of zinc deficiency is 31% with a range of 4% to 73%. The highest prevalence is found in Southeast and South Asia (34%-73%).[4] Zinc deficiency is more likely to occur during childhood, when daily zinc requirements are higher. Zinc deficiency can cause loss of appetite, which can have an impact on nutritional status and growth. Hair zinc levels can describe chronic zinc status, is more stable and is not affected by rapid fluctuations from diurnal and dietary variations, and is also more suitable for use in children because it is less invasive than plasma or serum zinc.

Hair zinc examination is a marker that can show a person's zinc status. The concentration of zinc in hair is the second largest concentration after zinc in teeth, which is 200 mg/kg by weight. The zinc concentration in hair is more stable and is not affected by rapid fluctuations associated with diurnal variations, diet, etc. Another advantage is that there is no trauma due to the sampling, it does not require preservatives or a certain temperature.[5]

The body needs more zinc during periods of rapid growth such as pregnancy, infancy, childhood and adolescence. The need for zinc for Indonesian children varies according to their age. At the age of 1-3 years, the need is 3 mg/day.[6] Foods rich in zinc are seafood, meat, whole grains, nuts, and dairy products. The difference between zinc intake and absorption must be considered, because even if zinc intake is adequate, levels of inhibitors (fiber and phytate) in the diet can prevent zinc from being absorbed adequately.[7]

Visual analog scale (VAS) questionnaire is widely used in nutrition research to assess appetite and food intake. VAS is correlated with energy intake, and can predict eating motivation in subjects who eat a normal diet in a normal environment.[8] Several studies have used the VAS in children and adolescents to assess hunger and satiety.[9] Subjects were asked to answer questions by marking on a 100 mm line with the left end meaning “not at all” and the right end meaning “extremely”. Variations of VAS are in the form of 10-point Likert scale, bipolar and unipolar scale, 150 mm horizontal line, and 7-point scale with qualitative labels at the same distance. However, a 100 mm horizontal line without markings except for labels at both ends is the most widely used form of VAS.[9] Several studies of appetite in children had used VAS with assessment by parents. Research conducted in the Philippines and Taiwan used VAS questionnaire for parents to assess their child's appetite.[10,11] The VAS is filled at set times, usually just before and after one feeding episode and periodically at intervals between meals (usually 1 hour). In this study, VAS is filled one time by subject’s parent/caregiver expressing current time child’s appetite.

Covid-19 pandemics has altered many aspect of the society including the eating habits that has impacts on children’ nutritional status. In long term, this will lead to altered zinc status and it’s function. The aim of this study is to determine the correlation between zinc intake with hair zinc level and appetite in children aged 2-3 years in Jakarta.

Methods

This cross-sectional study design was carried out during the Covid-19 pandemic, from September to October 2020 in Kampung Melayu Sub-district, East Jakarta. Location of the study was chosen because it was the only limited resources that provided permission to do data collection due to Covid-19 pandemic.

Subjects

The subjects of this study were apparently healthy children aged 2-3 years old, with permission to participate in the study from their parents. Subject selection was carried out by total population sampling. The subject’s parents or guardians were explained about the purpose, benefits and examinations that would be taken. Parents who agreed to take part in this study signed the consent form. Children with acute and chronic infection, severe malnutrition, liver disorders, malabsorption syndrome, congenital diseases, and hair length didn’t sufficient for sampling were excluded from

the study. Total 70 samples were met the criteria for this study and furthered analyzed.

Characteristic Data

Data on subjects' characteristics include: age, gender, maternal education, family income, income during pandemic, and the impact of the pandemic on children's food were collected from interviews. Maternal education was categorized into high (high school education and above) and low (below high school education). Family income was categorized based on minimum wage (UMP) DKI Jakarta 2020 (Rp. 4.276.350) to be more or equal to the UMP and less than the UMP.

Zinc intake, anthropometric measurement, and appetite assessment

Assessment of food intake was taken using a semi quantitative questionnaire (SQ-FFQ) to determine the subjects' zinc intake. Interviews were conducted using a food photo book. Anthropometric measurement taken were body weight and height. Subjects' body weight was measured using SECA digital scale, with accuracy 0,1 kg. Subject's height was measured using a SECA stadiometer with accuracy 0,1 cm. Each measurement was taken twice and the average value was calculated. Nutritional status was determined based on the WHO growth chart Z-score weight/height. Appetite was assessed by using Visual Analog Scale (VAS) which have 3 questions with extreme value in each side of the 100 mm line. The questions were asked to the parents or guardian of the subjects.

Laboratory examination

Hair samples were collected to check the level of hair zinc. The hair zinc test was conducted in collaboration with Prodia Laboratory. Hair sample was taken in the Kampung Melayu Sub-district office by laboratory staff. The number of hair 10-15 strands and taken at 5 different places, was cut as close as possible to the hair roots, taken 2.5 cm from the closest to the base of the hair and the rest discarded. Then the hair samples were taken to Prodia laboratory for analysis. Examination of hair zinc levels using the Atomic Absorption Spectrophotometry (AAS) method using Agilent Inductively Coupled Plasma-Mass Spectrometry (ICP-MS) 7700 series.

Data analysis

Data were analyzed using SPSS version 20.0. Normality of the data distribution was determined by Kolmogorov Smirnof test. Data distribution was considered normal when p value ≥ 0,05. Data are presented in the form of mean ± standard deviation (SD) if normally distributed ($p \geq 0.05$), and in the form of median (minimum-maximum) if not normally distributed ($p < 0.05$). Categorical data were presented in the form of frequency distribution (n,%). Continuous data were presented in the form of median (minimum-maximum). The correlation between two variables was analyzed using the Pearson correlation test if the data distribution was normal, or the Spearman Rank correlation test if the data distribution was not normal. The possible range of values for the correlation coefficient (r) is -1 to 1. A correlation of -1 indicates a perfect negative correlation, and a correlation of 1 indicates a perfect positive correlation. Value 0,8 to 1 indicate very strong correlation, 0,6 to 0,8 indicate strong correlation, 0,4 to 0,6 indicate moderate correlation, 0,2 to 0,4 indicate weak correlation, and < 0,2 indicate very weak correlation. If the correlation coefficient is greater than zero, it is a positive relationship. Conversely, if the value is less than zero, it is a negative relationship. The correlations were considered significant if the p value < 0,05. Nutrisurvey 2007 was used to perform analysis of zinc intake.

Results

From 70 subjects, the median age was 30 (24-36) months. The majority of subjects had normal nutritional status and family income below UMP DKI Jakarta. Data on subjects' characteristics can be seen in **Table 1.**

Table 1. Subjects' characteristics

Characteristics	Mean/Median Value	Results (n=70)
Age (months)	30 (24-36)*	
Gender, n (%)		
Male		30 (42.9)
Female		40 (57.1)
Nutritional status, n (%)		
Severely wasted		-
Wasted		5 (7,1)
Normal		63 (90)
Overweight		1 (1,4)
Obese		1 (1,4)
Mother' education, n (%)		
Low		27 (38.6)
High		43 (61.4)
Family income, n (%)		
< UMP		50 (71,4)
⩾ UMP		20 (28,6)
In this		
Zinc intake, n (%)	6 (1,2-22,5)*	
Insufficient		14 (20)
Sufficient		56 (80)
VAS appetite score	54.8 ± 20.5**	
Income during pandemic, n (%)		
Decreased		53 (75,7)
Same as before		15 (21,4)
Impact of the pandemic on children's food, n (%)		
Changed		23 (32,9)
Same as before		45 (64,3)
Number of children in the family, n (%)		
One		16 (22.9)
Two		30 (42.9)
Three or more		24 (34.3)
Hair zinc level, n (%)	132 (30-451)*	
Insufficient		12 (17,1)
Sufficient		58 (82,9)

* Median (min-max)
** Mean ±SD

Table 2. Correlation of zinc intake and VAS appetite score with hair zinc level

Correlation test	Hair zinc level µg/g	
	r	p
Zinc intake	-0.077	0.528
VAS appetite	0,247	0,039*

* statistically significant

In this study, the median value of zinc intake was 6 (1,2-22,5) mg/day. Compared to Indonesia RDA 2019 adequacy, it was found that 20% of the subjects had insufficient zinc intake. The results can be seen in **Table 1**. The median (minimum-maximum) hair zinc value was 132 (30-451) µg/g. Compared to the cut off value of normal hair zinc level (≥ 80 µg/g), there were 17,1% subjects with insufficient hair zinc value. The adequacy of hair zinc can be seen in Table 1. The mean ± SD for VAS appetite assessment by the parents was 54.8 ± 20.5 mm.

The correlation between zinc intake and VAS appetite with hair zinc levels can be seen in **Table 2**. There was not significant very weak negative correlation between zinc intake and hair zinc levels (r = -0.077, p = 0.528). There was a weak positive correlation between VAS appetite and hair zinc levels (r = 0,247, p = 0,039).

Discussion

In this study, majority of subjects had adequate zinc intake, 20% of subjects had insufficient zinc intake. The median intake of zinc was 6 (1.2-22.5) mg, this result was not much different from the study on children under five in Semarang who got an average zinc intake of 5.2 ± 2.5 mg with 29.5% insufficient intake.[12] Although intake of zinc was adequate, children are still considered as an age group at high risk for zinc deficiency, because the important role of zinc in cell division and protein synthesis is very much needed during the growth period. Indonesia RDA 2019 stated that 3 mg/day is sufficient for children aged 1-3 years with notes that it comes from sources with high and moderate bioavailability.[6] Zinc with high bioavailability is found in "expensive foods" such as fish and meat. The RDA of zinc for Southeast Asia should be considered regarding bioavailability of the diet compared to the western diet, Asians generally tend to consume less animal products and more plant products that are rich in phytate.[13] Approximately 17.3% of the world's population is at risk of zinc deficiency which can be absorbed, with the highest risk in countries in Southeast and South Asia.[14] It was found that 82.9% had adequate hair zinc levels and median hair zinc value was 132 (30-451) µg/g. The median is similar to the mean hair zinc value in the Brazilian study by Beinner et al.[15] Beinner got an average hair zinc level 134.3 ± 110.3 µg/g.

This study showed there was not significant very weak negative correlation between zinc intake and hair zinc levels (r = -0.077, p = 0.528). This result is similar to the study of Beinner et al.[15] which found that there was no correlation between zinc intake and hair zinc level in Brazilian children. This result is different from the results of the study by Siahaan which obtained a strong and significant correlation with (r = 0.707, p = 0.000), but the study was conducted on a population of children with autism.[16] Another study in children in Brazil concluded that the physiological signs of zinc depletion are described with diverse biochemical functions rather than with specific functions, which makes it difficult to recognize zinc biomarkers. Prolonged and severe decrease in zinc intake can significantly reduce zinc stores in the body.[17,18] Chronic zinc deficiency can be best assessed by examining hair zinc levels.[15] It was also found in this study that adequate zinc intake had higher mean of hair zinc levels (169.93±112.009) compared to the group with inadequate zinc intake (137.07±79.11), but this increase was not significant **(Table 3).** This result is also similar with Beinner's study where in the increased zinc consumption group, the average hair zinc level also increased, but this increase was also not significant. There was a weak positive correlation between VAS appetite and hair zinc levels (r = 0,247, p = 0,039). This indicates with adequate zinc status, children appetite tend to be good, and the otherwise. This is similar to the study of Daniels et al.[19] which obtain that increased food fussiness score or lack of appetite may result in decrease zinc concentration, or increase in zinc

Table 3. Average hair zinc levels based on categorized variable

Variable	n=70	Hair zinc level µg/g (mean ±SD)	p
Zinc intake			
Insufficient	14	137,07 ± 79,11	0,45 [mw]
Sufficient	56	169,93 ± 112,009	
VAS appetite			
Poor (<40)	11	124.36 ± 66.22	
Acceptable (40-70)	39	147.38 ± 101.025	0,049 [kw]
Good (> 70)	20	215.95 ± 119.167	

mw= Mann Whitney, kw=Kruskal

concentration could result in a lower food fussiness score or bigger appetite.

Zinc is required for the metabolic activity of 300 enzymes of the body, and is essential for cell division and the synthesis of DNA and proteins. This enzyme is involved with the metabolism of proteins, carbohydrates, and fats. Zinc is also important for wound healing, taste acuity, tissue growth and maintenance, immune system function, prostaglandin production, bone mineralization, thyroid function, blood clotting, cognitive function.[7] Hence when zinc needs are not met, it will affect optimal child growth and development. Therefore, this study took subjects aged 2 to 3 years old because this period is an important transition period from children eating complimentary food to family food, and optimal time to catch up growth after the golden period, where if there is insufficient nutrients such as zinc, it can be quickly resolved. Based on Indonesian RDA, the recommendation of zinc consumption in children aged 2-3 years is 3 mg/day.[6] Hopefully zinc needs can be fulfilled from variety of foods that are rich in zinc. Food rich in zinc include seafood, meat, whole grains, nuts, and dairy products. Most developing countries had children lack the intake of foods rich in easily absorbed zinc, such as liver, red meat, poultry, and seafood. The difference between zinc intake and absorption must be considered, because even if zinc intake is adequate, levels of inhibitors (fiber and phytate) in the diet can prevent zinc from being absorbed adequately. Traditional staple foods, such as cereals, and legumes contain zinc, but the presence of phytates, fiber, and lignin reduces their bioavailability. These substances form insoluble complexes with zinc and prevent its absorption.[7] Although the median of zinc intake of subjects in this study (6 mg/day) was higher than the recommendation in Indonesian RDA, however 20% of the subjects did not have sufficient zinc intake. Continuous lack of zinc intake will cause decrease in the body's zinc reserves. A study by Jackson et al.[20] on experimental animals, found zinc loss was not similar in all tissues. Hair, skin, heart and muscle zinc levels remained constant, while plasma, liver, bone zinc levels fell significantly. It is interesting that hair zinc concentrations did not change in this experimental animal study. Hair zinc levels are expected to change with marginal intake over the long term but not with severe depletion as studied in these experimental animals.[20]

Questionnaire of VAS was filled in by the subject's parents by marking with a vertical sign on a 100 mm horizontal line based on how they currently feel about the child's appetite with consideration that the extreme labels at both ends were the least hungry and the most hungry the child had experienced so far. In this study, mean of VAS score was 54,5 mm. When compared to the cut off from El Sayed Ahmad et al.[21] study in pediatric patients of tonsillotomy which categorized between 40 and 70 mm as "acceptable appetite", the mean

VAS score of this study can be said to be "acceptable appetite". The plausible mechanism for correlation between appetite score and hair zinc status as showed in Daniels et al.[19] study if toddler is lack of appetite or food fussy, then they may eat fewer foods that are high in zinc, and zinc status could decreased. However, there is also evidence for the opposite pathway from low zinc status to decrease appetite. Lower zinc status can result in impaired taste acuity in children[22,23,24], which may result in lower appetite.[25]

Zinc plays a role in activating areas of the brain that receive and process information from taste and smell sensors. So that zinc levels affect taste, taste preferences and increase taste sharpness.[26] Research shows that zinc can increase appetite, energy intake and increase fat-free mass.[27] Zinc can increase calorie intake because it can increase children's appetite.[28] Research conducted animal studies have shown that oral zinc administration rapidly stimulates food intake during early-stage zinc deficiency without decreasing plasma and tissue zinc concentrations. Zinc supplementation increases appetite and weight in children with poor appetite and growth failure due to unspecified causes. In a study of zinc supplementation in malnourished children conducted in Taiwan, it was found that the effect of increasing appetite was significantly better in children whose initial zinc level was low.[3] Other studies have shown that zinc supplementation can increase appetite and caloric intake in children aged 2-6 years.[28] Zinc also stimulates the growth and function of taste buds on the tongue, thereby affecting appetite.[29,30] Zinc is a component of gustin, an important protein involved in sharpness of taste.[8]

There were some limitation of this study. It was carried out during the Covid-19 pandemic, thus limited available resources in the data collecting. The parents of prospective subject were also hesitate to participate because concerning of pandemic situation. There are also possibility of memory bias during assessment zinc intake of children with SQ-FFQ.

Conclusion

From this study it can be concluded that zinc intake had no significant correlation with hair zinc level. Another finding in this study, appetite had a positive correlation with hair zinc level. Among subjects there are 20% that had zinc intake below the daily requirement. Zinc is needed in the development and growth of children, thus it is important to pay attention the adequacy of zinc intake. Health service centers can provide counseling to parents during visits regarding the importance of zinc sources for children's health and growth, instructions for the amount of zinc sources, especially from animal sources that are affordable for the community. Information needs to be carried out either directly or through social media, for example through infographics, regarding the importance of adequate intake of nutrients to meet the needs of zinc which can support children's growth and health. Further research is needed on zinc intake and status by considering albumin status, and grouping zinc sources from high and low bioavailability.

Conflict of Interest

Authors declared no conflict of interest regarding this article.

Acknowledgment

We would like to convey our gratitude to all those who helped in this study, including but not limited to, the study subjects, *Puskesmas* Kampung Melayu and its sub-district office. The authors would like to thank Universitas Indonesia for funding this research though PUTI Grant with contract number NKB-4707/UN2.RST/HKP.05.00/2020

References

1. Nasar SS, Pulungan BA. Masalah makan pada anak. Makalah lengkap konggres nutririon growth-development, continuing professional development IDAI, Jakarta; 2006, hal. 53-68
2. Dewi A. Gambaran asupan zat gizi mikro pada balita di Kota Semarang. *Journal of Nutrition and Health*. 2015; 3(2)
3. Chao HC, Chang YJ, Huang WL. Cut-off Serum Zinc Concentration Affecting the Appetite, Growth, and Nutrition Status of Undernourished Children Supplemented With Zinc. Nutrition in Clinical Practice published, American Society for Parenteral and Enteral Nutrition. Wiley Periodicals Inc. 2018;33(5):701-9
4. Caulfield LE, Black RE. Zinc deficiency. Diakses tanggal 6 Maret 2020 :www.who.int/publications/cra/chapters/volume1/0257-0280pdf.
5. Gibson RS. Principle of Nutritional Assessment.Second edition.Oxford University Press. 2005: p.380.
6. Kemenkes. Peraturan Menteri Kesehatan Republik Indonesia nomor 28 tahun 2019 tentang angka kecukupan gizi yang dianjurkan untuk masyarakat Indonesia, 2019.
7. Deshpande JD, Joshi MM, Giri PA. Zinc: The Trace Element Of Major Importance In Human Nutrition And Health. *International Journal of Medical Science and Public Health*. Vol 2 Issue 1. 2013;1-4.
8. Stubbs RJ, Hughes DA, A, Johnstone M, Rowley E, Reid C, Elia M, Stratton R, Delargy H, King N, Blundell JE. The use of visual analogue scales to assess motivation to eat in human subjects: a review of their reliability and validity with an evaluation of new hand-held computerized systems for temporal tracking of appetite ratings. *British Journal of Nutrition*. 2000, 84, p405
9. Allison DB, Baskin ML. Handbook of assessment methods for eating behaviours and weight-related problems. Second edition. SAGE publication. 2009, p454-6, 296-9
10. Alarcon PA, Lin LH, Noche M, Hernandez VC, Cimafranca L, Lam W, Comer GM. Effect of oral supplemental on catch-up growth in picky eaters. Clin Pediatr 2003;42:209–17.
11. Huynh DT, Estorninos E, Capeding RZ, Oliver JS, Low YL, Rosales FJ. Longitudinal growth and health outcomes in nutritionally at-risk children who received long-term nutritional intervention. J Hum Nutr Diet 2015;28:623–35.
12. Sundari E, Nuryanto. Hubungan Asupan Protein, Seng, Zat Besi, dan Riwayat Penyakit Infeksi dengan Z-Score TB/U pada Balita, Journal of Nutrition College Volume 5, Nomor 4, 2016 : 520-529
13. Tee ES, Florentino R. Recommended Dietary Allowances (RDA) Harmonization in Southeast Asia. Monograph Series. Singapore: International Life Sciences Institute, Southeast Asia Region, 2005
14. Galetti V. Zinc Deficiency and Stunting. Pada: Preedy V., Patel V. (eds) Handbook of Famine, Starvation, and Nutrient Deprivation. Springer, Cham. 2018. https://doi.org/10.1007/978-3-319-40007-5_93-1
15. Beinner MA, Menezes MADBC, da Silva JBB, de Amorim FR, Jansen AK, Lamounier JA. Plasma Zinc and Hair Zinc Levels, Anthropometric Status and Food Intake of Children in a Rural Area of Brazil, Revista de Nutricao, 2010
16. Siahaan DK. Hubungan Asupan Seng (Zn) dan Protein terhadap Kadar Seng (Zn) Rambut pada Anak Autis di Kota Medan, 2019. http://repo.poltekkes-medan.ac.id/xmlui/handle/123456789/1045
17. Cousins RJ. Systemic transport of zinc. In: Mills CF, editor. Zinc in human biology. New York: Springer-Verlag; 1989. pp. 79–93. [Google Scholar] [Ref list]
18. Han TH, Lee J, Kim YJ. Hair Zinc Level Analysis and Correlative Micronutrients in Children Presenting with Malnutrition and Poor Growth. Pediatr Gastroenterol Hepatol Nutr. 2016;19(4):259-268. doi:10.5223/pghn.2016.19.4.259
19. Daniels L, Williams SM, Gibson RS, Taylor RW, Samman S, Heath AM. Modifiable "Predictors" of Zinc Status in Toddlers. Nutrients. 2018 Mar 5;10(3):306. doi: 10.3390/nu10030306. PMID: 29510562; PMCID: PMC5872724.
20. Jackson, M. J., Jones, D. A. Edwards, R.H.T. Tissue zinc levels as an index of body zinc status. Clin. Physiol.1982, 2:333–343.
21. El Sayed Ahmad Y, Nehme J, Moukarzel N. Comparison of Postoperative Pain and Appetite in Pediatric Patients Undergoing Monopolar Tonsillotomy and Cold Steel Tonsillectomy. Int J Otolaryngol. 2020;2020:8060971. Published 2020 May 18. doi:10.1155/2020/8060971
22. Cavan, K.R.; Gibson, R.S.; Grazioso, C.F.; Isalgue, A.M.; Ruz, M.; Solomons, N.W. Growth and Body Composition of Periurban Guatemalan Children in Relation to Zinc Status—A Cross-Sectional Study. Am. J.Clin. Nutr. 1993, 57, 334–343.
23. Buzina, R.; Jusi´c, M.; Sapunar, J.; Milanovi´c, N. Zinc nutrition and taste acuity in school children with impaired growth. Am. J. Clin. Nutr. 1980, 33, 2262–2267.
24. Gibson, R.S.; Vanderkooy, P.; MacDonald, A.C.; Goldman, A.; Ryan, B.A.; Berry, M. A Growth-Limiting, Mild Zinc-Deficiency Syndrome in Some Southern Ontario Boys with Low Height Percentiles. Am. J. Clin. Nutr.1989, 49, 1266–1273.
25. Hambidge, K.M.; Hambidge, C.; Jacobs, M.; Baum, J.D. Low-Levels of Zinc in Hair, Anorexia, Poor Growth, and Hypogeusia in Children. Pediatr. Res. 1972, 6, 868–874.

26. Kusumastuti AC, Ardiaria M, Hendrianingtyas M, Effect of Zinc and Iron Supplementation on Appetite, Nutritional Status and Intelligence Quotient in Young Children, The Indonesian Biomedical Journal, Vol.10, No.2, August 2018, p.133-9
27. Arsenault JE, Romaña DL, Penny ME, Loan MDV, Brown KH. Additional zinc delivered in a liquid supplement, but not in a fortified porridge, increased fat-free mass accrual among young peruvian children with mild-to-moderate stunting. J Nutr. 2008; 138: 108-14
28. Khademian M, Farhangpajouh N, Shahsanaee A, Bahreynian M, Mirshamsi M Kelishadi R. Effects of zinc supplementation on subscales of anorexia in children: A randomized controlled trial. Pak J Med Sci. 2014; 30: 1213-7.
29. Suzuki H, Asakawa A, Li JB, Tsai M, Amitani H, Ohinata K, et al. Zinc as an appetite stimulator - the possible role of zinc in the progression of diseases such as cachexia and sarcopenia. *Recent Patents on Food, Nutrition & Agriculture* (2011) 3: 226-31. Bentham Science Publisher
30. Yagi T, Asakawa A, Ueda H, Ikeda S, Inui SMA. The role of zinc in the treatment of taste disorders. *Recent Pat Food Nutr Agric*. 2013; 5: 44-51.

World Nutrition Journal |eISSN 2580-7013

LITERATURE REVIEW

Nutritional management in children with disease-related malnutrition : what's the guideline?

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Received 21 October 2021
Accepted 21 February 2022
Published: 28 February 2022

Link to DOI:
10.25220/WNJ.V05.i2.0006

Citation: Sidiartha IGL. Nutritional management in children with disease-related malnutrition: what's the guideline?. World Nutrition Journal.2022 Feb 28, 5(2):32-41.

Website :
http://www.worldnutrijournal.org/

Abstract

Background: Disease-related malnutrition (DRM) is one of the most common problems in pediatric patients. Both cancer and congenital heart diseases (CHD) are commonly associated with DRM. Altered nutrition utilization, reduced intake, malabsorption, and hypermetabolism are the main pathophysiology in DRM.

Method: A systematic literature searching was performed through Pubmed and Google Scholar websites. Thirty-six articles were included into the study.

Results: Malnutrition screening should be performed as soon as possible since early feeding can benefit the patients. One of the most commonly used tools is Screening Tool for Risk on Nutritional Status and Growth ($STRONG_{kids}$), which was proven to be valid, reproducible, and applicable in pediatric patients with malnutrition. Following screening and assessment, nutrition support can ensue, preferably in the form of enteral nutrition, unless contraindicated. Nutrient-dense formula, also known as protein and energy-enriched formula, aims to aid infants to reach nutrition target rapidly and stimulate anabolism. This formula has been studied in various population, mostly infants with CHD and studies showed favorable outcomes with its administration, namely faster improvement, reduced diuretics use and oxygen supplementation, decreased length of hospital stay, and less antibiotic use. Nutrient-dense formula is also safe and well-tolerated.

Conclusion: Proper screening and management should be performed with multidisciplinary approach to achieve the best outcome in children with DRM.

Keywords: nutritional management, disease-related malnutrition. cancer, congenital heart disease, nutrient-dense formula

Introduction

Malnutrition, one of the most common problems encountered in pediatric patients, is defined as a condition of excess or lack of protein, energy, or other nutrients which affects the function and structure of the body.[1] Hence, malnutrition implies obesity and undernutrition. Double burden malnutrition (DBM) is a concerning problem worldwide where obesity and undernutrition occur together.[2] Approximately 165 million children experience undernutrition worldwide with 90% of the cases are from Asia and Africa.[3] Indonesia, a middle-income country, is affected by this DBM as well. About 37% of the children aged under 5 years old in Indonesia experience stunting and 12% of the same population experience wasting.[2] On the other hand, approximately 11,5% of children aged 6-12 years old in Indonesia experience obesity.[4]

Based on the chronicity, malnutrition is classified into acute malnutrition for duration less than 3 months and chronic malnutrition for duration of 3

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months or longer. Acute malnutrition is often associated with burns, infectious diseases, and trauma as chronic malnutrition is associated with chronic diseases, such as chronic pulmonary disorders, malignancies, and cystic fibrosis. As for etiologic classification, malnutrition is classified into disease-related malnutrition (DRM) and not DRM, which relates to environmental, behavioral, and socioeconomical factors.[5]

Disease-related malnutrition is identified in 6-51% of hospitalized pediatric patients. However, this is often underdiagnosed.[5] DRM is mostly associated with infectious disease, gastrointestinal disorders, endocrine disorders, metabolic disorders, as well as neuropsychiatric disorders. This condition might predispose the pediatric patients to poor outcomes, such as disrupted wound healing process, higher infection rates, longer length of stay (LOS), poor quality of life, and higher risk of surgical and medical complications. As for the stakeholders, this can lead to increased costs which affects the country's economic status.[6]

As this DRM can increase the pediatric patients' morbidity and mortality rates, a proper screening and management algorithm is necessary. Multidisciplinary approach should be implemented to achieve an optimal outcome.[7] Therefore, this review aims to discuss the guidelines for nutritional management in children with DRM.

Methods

Search of literatures were performed through Pubmed and Google Scholar websites using keywords "Disease-related Malnutrition", "Children", "Congenital Heart Disease", "Cancer", and "Nutrient-dense formula". A total of 530 articles were found. After screening, 35 articles were included. Most articles were review articles and four articles were randomized controlled trials. The articles were published between 2010 and 2021. Article selection process is shown in **Figure 1**.

Result

Disease-related malnutrition in children with congenital heart diseases

The prevalence of congenital heart disease (CHD) is approximately 4-10 cases per 1000 newborns. Pediatric patients with CHD are known to be prone to growth retardation and failure to thrive. Acute malnutrition can be identified in 33-51% of pediatric patients with CHD while chronic malnutrition can be identified in 40-64% of pediatric patients with CHD.[8] Hassan et al.[9] reported higher prevalence of malnutrition in Egypt which was 84% with 71.4% of the children experienced severe malnutrition.

The main mechanism of malnutrition in CHD is increased energy expenditure due to cardiac changes which leads to inadequate nutrients. In addition, the hemodynamic status is unstable which affects the children's growth. As the child grows, the cardiovascular system works harder, the basal temperature increases corresponding to increase metabolic rate, and the sympathetic nervous system is activated. Alterations in cardiovascular function manifest as hypoxia and edema which induces malabsorption. Also, the children will suffer from early satiety and anorexia which will reduce dietary intakes. The predictors for malnutrition in CHD include older age at presentation, anemia, pulmonary hypertension, heart failure, decreased oxygen saturation, high metabolic rate, energy disequilibrium, feeding difficulties, and born with high APGAR score.[9-11]

As the CHD causes weight loss, the respiratory and heart muscles are affected as well which further compromises the respiratory and myocardial functions, immunologic responses, and healing capacity.[10] These children will have longer LOS, repeated hospitalizations, increased diuretic needs, and more likely to be transferred to intensive care unit (ICU). Therefore, malnutrition will significantly increase mortality and morbidity of pediatric patients with CHD.[12]

Disease related malnutrition in children with cancers

One of the most common conditions associated with malnutrition in pediatric patients is cancer. Fifty percent of pediatric patients with neuroblastoma suffers from malnutrition while only 0-10% of pediatric patients with leukemia suffers from

malnutrition. Pediatric patients with medulloblastoma and solid tumors often experience weight loss although criteria for nutritional status do not include weight loss. Furthermore, pediatric patients with solid tumors and leukemia suffers from fat free mass (FFM) loss which can predispose them to infections, frailty, and decreased quality of life.[13]

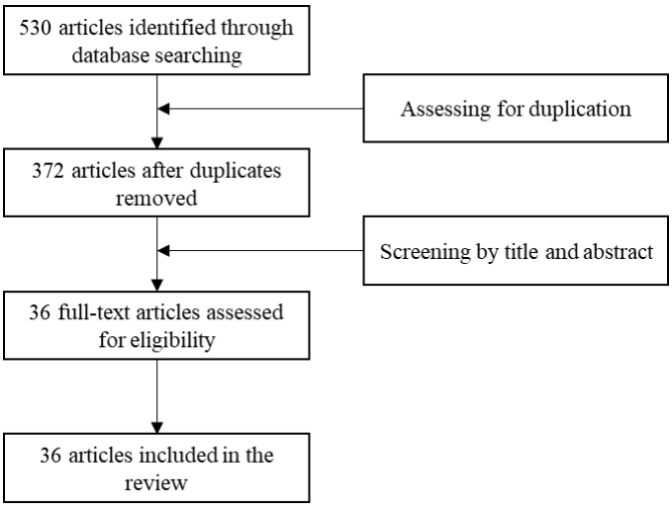

Figure 1. Article selection process

The possible mechanisms of DRM in pediatric patients are less physical activity or altered nutrition utilization, reduced intake, increased metabolic rate or hypermetabolism, as well as loss from vomiting, diarrhea, and malabsorption. In addition, patients who receive corticosteroids might undergo increased catabolism of muscle protein, which leads to reduced FFM.[13] Zimmermann et al.[1] found that patients diagnosed at age over 10 years old, having body mass index standard deviation score (BMI SDS) ≤1.0 when diagnosed, and diagnosed with medulloblastoma had strong association with malnutrition during treatment. Several parameters used for defining malnutrition in pediatric patients are body weight, body height, mid upper arm circumference, and skin folds. These parameters are incorporated to determine the Z-scores and then plotted into the reference charts, which are Multicenter Growth Reference Study (MGRS) by World Health Organization (WHO) for children aged 0-2 years old and reference chart by Center for Disease Control and Prevention (CDC) for children aged over 2 years old.[5]

Pediatric patients with cancer have lower survival rates when they suffer from DRM. Rapid weight loss will increase their risk of febrile neutropenia with bacteremia.[14] In addition, their quality of life is significantly impaired. While pediatric patients with undernutrition have poor social participation and activities, those with obesity also have psychosocial and cognitive problems.[15] Difference between disease-related malnutrition in children with congenital heart disease and cancers is shown in **Table 1.**

Screening for children with disease-related malnutrition

In order to prevent morbidity and mortality caused by DRM in hospitalized pediatric patients, proper and aggressive treatment should be implemented immediately.[12] Screening tools for malnutrition should be practical, cost-effective, applicable, and have high reproducibility so it can be performed by physicians, nurses, or dieticians.[18] To date, there has been no guidelines for screening disease-related malnutrition in pediatric patients. A systematic review by Klanjsek et al.[19] identified 3 assessment tools and 14 screening tools for malnutrition. The study included 8 screening tools, comprising nutritional risk screening tool in cystic fibrosis (CF), nutritional risk screening tool for pediatric patients with CF, Neonatal Nutrition Screening Tool (NNST), Paediatric Nutrition Screening Tool (PNST), Pediatric Yorkhill Malnutrition Score (PYMS), Nutrition Screening Tool for Childhood Cancer (SCAN), Screening Tool for the Assessment of Malnutrition in Paediatrics; (STAMP), and Screening Tool for Risk on Nutritional Status and Growth ($STRONG_{kids}$). Other screening tools which did not have validation study consisted of Nutrition Risk Score (NRS), Pediatric Digital Scaled MAlnutrition Risk Screening Tool (PeDiSMART), St Andrew's Nutrition Screening Instrument (SANSI), Simple Pediatric Nutrition Risk Score (SPNRS), a malnutrition screening tool for children under 2 years old in Zambia, and a screening tool for infants and young children with special health care

Table 1. Difference between disease-related malnutrition in children with congenital heart disease and cancers[13,16,17]

Congenital heart disease-related malnutrition	Cancer related malnutrition
Mostly born with normal weight	Involuntary skeletal muscle and adipose tissue loss
Pathogenesis □ Decreased nutrition intake (+++) □ Malabsorption or loss of nutrients (++) □ Increased nutrition requirement (+) □ Impaired utilization (+/-)	Pathogenesis □ Increased nutrition requirement (+++) □ Decreased nutrition intake (++) □ Malabsorption or loss of nutrients (+) □ Impaired utilization (+/-)
Cyanotic children are more common to suffer from failure to thrive compared to non-cyanotic children	Cause prolonged hospital stay and expenses
Feeding intolerance indicated by □ Abdominal pain □ Abdominal distention □ Vomiting □ Reduced or diminished bowel sound □ Addition of residual gastric volume	Feeding intolerance indicated by Anorexia Nausea and vomiting
Complication □ Fluid overload □ Deteriorating of catabolic response induced by stress □ Impaired wound healing □ Disruption of myocardial and muscle work □ Increased incidence of postoperative complications □ Long-term impaired cognitive function	Complication □ Impaired functional progressively □ Complications due to treatment □ Impaired quality of life
Poor prognosis	Poor prognosis Conservative nutritional management might partially revert the condition
Nutritional management □ Tube feeding is preferred due to inadequate intake □ High-energy density formula is preferred due to fluid restriction and increased demand □ Semi- or elemental formula is preferrable for cyanotic children	Nutritional management □ Enteral supplementation and tube feeding can be administered if necessary □ High-energy density formula is preferred due to increased demand □ Standard formula is preferrable although semi- or elemental formula might be necessary in some cases

needs. Three assessment tools include Clinical Assessment of Nutritional Status (CANS), Subjective Global Assessment (SGA), and Subjective Global Nutritional Assessment (SGNA).[19]

While Klansjek et al.[19] recommended PYMS along with full nutritional assessment for malnutrition screening in hospitalized pediatric patients, SCAN was developed to screen malnutrition in pediatric patients with cancer. This screening tool includes 5 questions with 1 to 2-point score. Pediatric patients with cancer who get 3 or more points will be referred to get a full nutritional assessment from a dietician. This tool is proven to be highly sensitive (100%) with 39% specificity, 56% positive predictive value and 100% negative predictive value which is ideal for a screening tool. As it is easy to use and valid, SCAN can help to identify malnutrition in pediatric patients early in order to prevent bad outcomes.[20]

Aside from screening tool, there are several key points which indicate high risk for malnutrition should be noted in pediatric patients with cancer. These points consist of age under 2 months old, low socioeconomic status, presence of malnutrition or wasting at diagnosis, history of relapse, getting stem

cell transplant, receiving emetogenic medications, receiving radiation to gastrointestinal (GI) tract, getting regimens with potential GI complications, getting chemotherapy with GI adverse effects or affecting appetite, and experiencing surgical complications related to GI tract. These patients should be monitored for their body mass index (BMI) and laboratory abnormalities. Measurements for body weight, height, and arm circumference are necessary to estimate BMI, adipose density, and lean body mass. For laboratory examination, prealbumin level can indicate acute malnutrition.[21] In addition, ratio of C-reactive protein (CRP) level to albumin level can predict acute malnutrition risk. Higher ratio infers to high risk of acute malnutrition.[22] Other necessary examinations include glucose panel, lipid panel, liver function test, and renal function test to evaluate dietary impact on the patients' body. If the patients are deemed to have a high risk for malnutrition, experiencing weight loss for 5% or more since the diagnosis, having low BMI for age or arm circumference, being obese or overweight, having difficulty receiving oral nutrient (less than 80%), feeding with nasogastric tube, and advised to receive total parenteral nutrition, the patients should be referred immediately to a dietician.[21]

Similarly, there has been no guideline for nutritional screening for pediatric patients with CHD. Traditionally, body weight, height, and arm circumference are used to determine the nutritional status. However, the BMI should be interpreted cautiously in this population because body fat can be overestimated if the patients suffer from edema or have more lean body mass. Pediatric patients with CHD often experience edema due to increase fluid from the cardiac problems; hence, it will mask the wasting or fat loss. Radman et al.[23] suggested the measurement of triceps skin fold to measure the fat mass more appropriately in pediatric patients with CHD. Another study by Gu et al.[24] used $STRONG_{kids}$ scoring for infants with CHD. This screening tool was proven to have high accuracy (81.9%) on predicting malnutrition in infant with CHD. Another screening tool was developed by St. Pierre et al.[25] This checklist comprised 24 items concerning cardiac diagnosis, chromosomal abnormalities, brain injury, vocal cord paresis, weight, diet, use of feeding tube, GI tolerance, physiological status, vocal cord status, and feeding problems. Although this screening tool is deemed valid and reliable for malnutrition screening in pediatric patients with CHD, there have been no other studies evaluating its use.

$STRONG_{kids}$ was published in 2010. It was originally tested on children aged 1 month old to 18 years old at 44 hospitals in the Netherlands. The tool screened for subjective findings of fat and muscle loss, reduced nutrient intake, existing high-risk disorders or major surgical plan, loss of body weight or insufficient weight improvement, as well as GI symptoms (nausea, vomiting, diarrhea, and pain). Final score was subtracted and 0 defined as low risk, 1-3 defined as moderate risk, and 4-5 defined as high risk. This screening tool has been proven to be valid, has good reproducibility, and very applicable for screening malnutrition in pediatric patients.[18]

Nutritional management for infants with disease-related malnutrition

For pediatric patients with CHD, enteral nutrition is advisable because it exerts less complication than parenteral nutrition and better effect on intestines. As it is cheaper than parenteral nutrition, its availability and accessibility are better in developing countries. If the pediatric patients do not experience gastroesophageal reflux or poor tolerance, intragastric feeding is preferrable. Neonates and infants should be instructed to get breast milk as it is free, good for immune system, aids trace elements' absorption, and associated with low risk of necrotizing enterocolitis. Patients with fluid restriction should increase the feeding's energy density about 1 kcal/ml although osmotic diarrhea can occur.[26] High-calorie feeding to as high as 125% of standard feeding are recommended for optimal growth. Another alternative is continuous feeding can be considered if the patients do not respond to high-calorie feeding.[27] For patients with gastroesophageal reflux, severe weight faltering, or aspiration, gastrostomy or jejunostomy can be an alternative. If the patients were undergone surgery, enteral nutrition should be administered as soon as possible. Use of parenteral nutrition within a week

after surgery is associated with unfavorable outcomes.[26] Monitoring of the laboratory markers which represent the patient's nutritional status should be performed. These include CRP, albumin, prealbumin, creatinine, urea, 3-methylhistidine, insulin-like growth factor I, retinol-binding protein, transferrin, and transerythrin.[8,27]

Similarly in pediatric patients with cancer with DRM, enteral nutrition is preferred than parenteral nutrition. Enteral nutrition is associated with good tolerability, improvement of quality of live, better survival rates, and prevent worsening of nutrition status.[28] Use of enteral tube feeding (ETF) help increasing body weight, relatively easy and safe. In this population, oral supplementation alone can not meet the nutrition requirement. ETF should be used for only 4-6 weeks. If the enteral feeding is necessary for more than 6 weeks, an ostomy will be needed.[29] Enteral nutrition can be given in bolus, intermittent drip, or continuous administration. Intermittent drip and bolus method is preferred for feeding with gastrostomy because this can simulate normal feeding cycle. On the other hand, continuous feeding is preferred in case of small bowel problems or patients who cannot tolerate other methods.[28]

Formulation for enteral feeding can be classified into standard formula (polymeric), specialized formula, and elemental formula. Standard formula is indicated for patients with intact GI tract.[28] Nutrient-dense formula can also be a choice for enteral feeding.[29] This formula is indicated for patients who cannot tolerate high volume diet. Elemental formula is indicated for patients with pancreatic disorders and malabsorption. Specialized formula is specially prepared for certain diseases, such as diabetes mellitus, renal disorders, pulmonary disorders, and liver diseases.[28]

Parenteral nutrition is not preferrable because it increases risks of cholestasis, hyperglycemia, hypertriglyceridemia, and infections. It is indicated if the patients cannot tolerate the enteral nutrition or have difficulty absorbing enteral nutrition.[29] Several contraindications for parenteral nutrition include difficult intravenous access, well-functioned GI tract, and duration of therapy less than 5 days.[28] Limitations of this parenteral nutrition are high cost and needs of trained professionals. Administration of parenteral nutrition with peripheral access should not be longer than 2 weeks while central access can allow longer duration.[29] Parenteral nutrition should be started slowly at 15-20 calories/kg body weight/day and limit of 1000 calories per day. The calories should be reduced slowly and parenteral nutrition should be stopped if the patients have achieved more than 60% of protein and energy needs.[28] Monitoring of complications should be performed regularly and nutrition status should be re-assessed every two weeks.[29]

One thing should be taken into account when treating children with malnutrition is refeeding syndrome.[28] This syndrome happened when patients with malnutrition getting aggressive nutrition therapy. Refeeding syndrome occurs due to shifting from catabolism to anabolism, leading to increased insulin secretion and resistance. Hyperinsulinemia and hyperglycemia co-occur along with hypokalemia, hypophosphatemia, hypomagnesemia, and increased fluid volume. Almost all organ systems are affected, such as respiratory, cardiovascular, GI, neurological, musculoskeletal, and hematological systems. This refeeding syndrome can be catastrophic and leads to organ failure, ultimately death.[30] Patients with DRM for more than two weeks is highly possible to suffer from refeeding syndrome. In order to prevent this, metabolic disorders should be manage properly before initiating parenteral nutrition.[28] The author develop an algorithm for disease-related malnutrition management in pediatric patient with congenital heart disease and cancers based on several literatures which is shown in **Figure 2.**[26-30]

Role of nutrient-dense formula for infants with disease-related malnutrition

Nutrient-dense formula, also known as protein and energy-enriched formula, is a high protein and energy formula formulated for infants to reach the nutrition targets faster and stimulate anabolism.[31,32] Prior to the development of this formula, clinicians tried to add triglycerides or glucose to the formula or breastmilk or concentrate the formula in order to increase the energy density. However, there were limitations to these methods. First, the infants need

all nutrients, not only glucose and triglycerides, also the protein-derived energy decreased. Second, this concentrated formula could be too complex for the parents and increased possibility of microorganism contamination. Nutrient-dense formula came as a more cost-effective, highly accessible, and ready to-use alternative.[33]

This formula might help infants with DRM because they are prone to fast reduction of nutrition and have very little or no reserve. Nutrient-dense formula are preferrable in pediatric patients with CHD, especially who have fluid restriction, since they have more energy per milk volume. It can decrease 33% volume intake while providing similar energy intake as standard formula.[32] Various studies have been conducted to assess the use of nutrient-dense formula in critically-ill pediatric patients. This formula is proven to be associated with good outcomes and well-tolerated in pediatric patients with congenital heart disease following surgery, viral bronchiolitis, and pediatric patients on mechanical ventilator.[34]

Cui et al.[32] reported that use of nutrient-dense formula in infants with CHD showed good results. The infants tolerated the formula well and they reach the target faster than infants who received standard formula. The intervention group also showed faster anabolism process, proven by positive nitrogen balance and presence of essential amino acids. This positive nitrogen balance points toward anabolism while negative balance points toward catabolism. When an infant undergoes cardiac operation, the inadequate metabolic reserve induces low amino

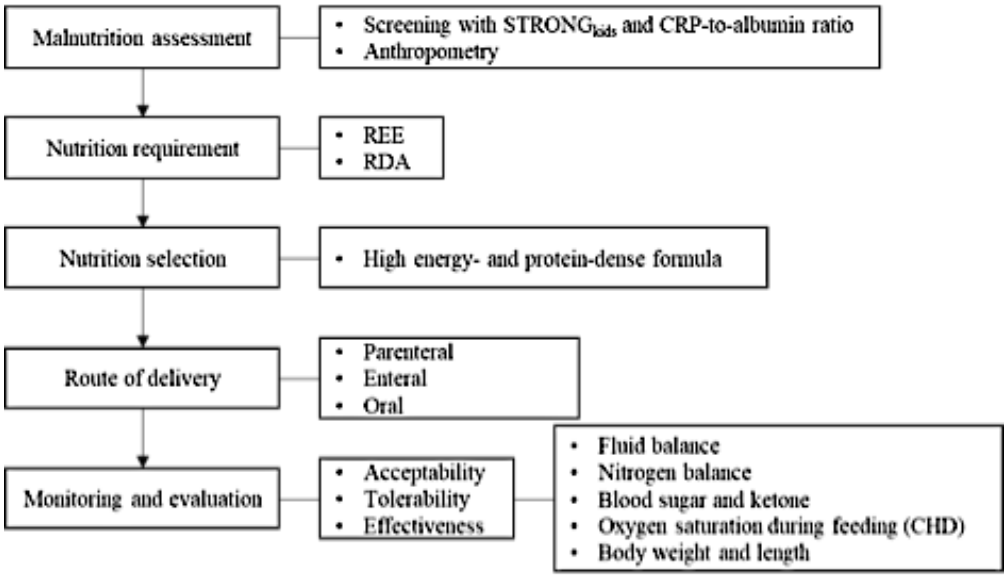

Figure 2. Algorithm for disease-related malnutrition management in pediatric patient with congenital heart disease and cancers[26-30]
CHD: congenital heart disease; CRP: C-reactive protein; RDA: recommended dietary allowance; REE: resting energy expenditure; $STRONG_{kids}$: screening tool for risk on nutritional status and growth

Table 2. Benefits of using nutrient-dense formula for infants with disease-related malnutrition[31-36]

Benefits of using nutrient-dense formula for infants with disease-related malnutrition
Decrease 33% volume intake while providing similar energy intake as standard formula
Reach the nutrition target faster
Prevent weight loss
Faster anabolism process, positive nitrogen balance and presence of essential amino acid
Prevent proteolysis
Increase protein synthesis
Improve protein breakdown
Improve hepatocytes restoration
Improve insulin resistance
Increase albumin level
Reduce feeding intolerance
Decrease length of stay
Decrease postoperative infection and use of antibiotics
Mild adverse events
Good tolerability
Cost-effective

acid levels and substantial proteolysis. Adequate protein and energy intake will prevent this proteolysis which is proven by the administration of nutrient-dense formula in this population. As for the essential amino acids acquired from the formula, they will help increasing protein synthesis as well as improving protein breakdown, hepatocytes restoration, and insulin resistance which leads to improvement of infants' survival and quality of life.[32]

Similarly, Zhang et al.[31] reported that infants with CHD received more energy and gained weight better with nutrition-dense formula. Also, the patients had increased serum albumin levels which indicated improvement of nutrition status.[31] Another study by Scheefer et al.[35] linked the use of nutrient-dense formula with decreased LOS and use of antibiotics during 30 days after CHD surgery. Favorable effects were also shown by reduced use of diuretics and oxygen supplementation.[35] Favorable outcomes were also reported by Eveleens et al.[34], who found that critically-ill infants experience weight-for-age (WFA) Z-score following administration of nutrient-dense food. These patients achieved the energy target which was determined to be two-fold of the resting energy expenditure.[34] Benefits of using nutrient-dense formula for infants with disease-related malnutrition are shown in Table 2.

Despite no significant different of adverse events in intervention and control group, vomit, diarrhea, and gastric retention were reported in infants getting nutrient-dense formula.[32] Nutrient-dense formula

exerts more osmotic pressure, leading to increase risk of GI symptoms, such as gastric retention, diarrhea, nausea, and vomiting. However, these symptoms can be easily managed by medication. The GI system might probably tolerate the formula if given with increasing density.[31]

Conclusion

To conclude, DRM in pediatric patients with CHD and cancer needs to be identified as soon as possible. Proper screening and management should be performed with multidisciplinary approach to achieve the best outcome. The guidelines for DRM management include assessment of malnutrition, nutrition requirement, nutrition selection, route of delivery, as well as monitoring and evaluation.

Conflict of Interest

Authors declared no conflict of interest regarding this article.

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References

1. Zimmermann K, Ammann RA, Kuehni CE, De Geest S, Cignacco E. Malnutrition in pediatric patients with cancer at diagnosis and throughout therapy: A multicenter cohort study. Pediatr Blood Cancer. 2013;60:642-9.
2. Maehara M, Rah JH, Roshita A, Suryantan J, Rachmadewi A, Izwardy D. Patterns and risk factors of double burden of malnutrition among adolescent girls and boys in Indonesia. PLoS One. 2019;14:e0221273.
3. De Silva I, Sumarto S. Child Malnutrition in Indonesia: Can Education, Sanitation and Healthcare Augment the Role of Income? Journal of International Development. 2018;30:837-64.
4. Rachmi CN, Li M, Alison Baur L. Overweight and obesity in Indonesia: prevalence and risk factors-a literature review. Public Health. 2017;147:20-9.
5. Mehta NM, Corkins MR, Lyman B, Malone A, Goday PS, Carney LN, et al. Defining pediatric malnutrition: a paradigm shift toward etiology-related definitions. JPEN J Parenter Enteral Nutr. 2013;37:460-81.
6. Freijer K, van Puffelen E, Joosten KF, Hulst JM, Koopmanschap MA. The costs of disease related malnutrition in hospitalized children. Clin Nutr ESPEN. 2018;23:228-33.
7. Guenter P, Jensen G, Patel V, Miller S, Mogensen KM, Malone A, et al. Addressing Disease-Related Malnutrition in Hospitalized Patients: A Call for a National Goal. The Joint Commission Journal on Quality and Patient Safety. 2015;41:469-73.
8. Toole BJ, Toole LE, Kyle UG, Cabrera AG, Orellana RA, Coss-Bu JA. Perioperative nutritional support and malnutrition in infants and children with congenital heart disease. Congenit Heart Dis. 2014;9:15-25.
9. Hassan BA, Albanna EA, Morsy SM, Siam AG, Al Shafie MM, Elsaadany HF, et al. Nutritional Status in Children with Un-Operated Congenital Heart Disease: An Egyptian Center Experience. Front Pediatr. 2015;3:53.
10. Monteiro FPM, Araujo TLd, Lopes MVdO, Chaves DBR, Beltrão BA, Costa AGdS. Nutritional status of children with congenital heart disease. Rev Latino-Am Enfermagem. 2012;20:1024-32.
11. Arodiwe I, Chinawa J, Ujunwa F, Adiele D, Ukoha M, Obidike E. Nutritional status of congenital heart disease (CHD) patients: Burden and determinant of malnutrition at university of Nigeria teaching hospital Ituku - Ozalla, Enugu. Pak J Med Sci. 2015;31:1140-5.
12. Hubschman LE. Malnutrition in Congenital Heart Disease. ICAN: Infant, Child, & Adolescent Nutrition. 2013;5:170-6.
13. Brinksma A, Huizinga G, Sulkers E, Kamps W, Roodbol P, Tissing W. Malnutrition in childhood cancer patients: a review on its prevalence and possible causes. Crit Rev Oncol Hematol. 2012;83:249-75.
14. Loeffen EA, Brinksma A, Miedema KG, de Bock GH, Tissing WJ. Clinical implications of malnutrition in childhood cancer patients--infections and mortality. Support Care Cancer. 2015;23:143-50.
15. Brinksma A, Sanderman R, Roodbol PF, Sulkers E, Burgerhof JG, de Bont ES, et al. Malnutrition is associated with worse health-related quality of life in children with cancer. Support Care Cancer. 2015;23:3043-52.
16. Schiessel DL, Baracos VE. Barriers to cancer nutrition therapy: excess catabolism of muscle and adipose tissues induced by tumour products and chemotherapy. Proceedings of the Nutrition Society. 2018;77:394-402.
17. Martini S, Beghetti I, Annunziata M, Aceti A, Galletti S, Ragni L, et al. Enteral Nutrition in Term Infants with Congenital Heart Disease: Knowledge Gaps and Future

Directions to Improve Clinical Practice. Nutrients. 2021;13.
18. Dos Santos CA, Ribeiro AQ, Rosa COB, de Araujo VE, Franceschini S. Nutritional risk in pediatrics by StrongKids: a systematic review. Eur J Clin Nutr. 2019;73:1441-9.
19. Klanjsek P, Pajnkihar M, Marcun Varda N, Povalej Brzan P. Screening and assessment tools for early detection of malnutrition in hospitalised children: a systematic review of validation studies. BMJ Open. 2019;9:e025444.
20. Murphy AJ, White M, Viani K, Mosby TT. Evaluation of the nutrition screening tool for childhood cancer (SCAN). Clin Nutr. 2016;35:219-24.
21. Joffe L, Ladas EJ. Nutrition during childhood cancer treatment: current understanding and a path for future research. The Lancet Child & Adolescent Health. 2020;4:465-75.
22. Sidiartha IGL, Wati DK, Subanada IB, Suwarba IGNM. High C-reactive protein/albumin ratio increased risk of acute malnutrition during hospitalization in pediatric patients. International journal of health sciences. 2020;4:32-8.
23. Radman M, Mack R, Barnoya J, Castaneda A, Rosales M, Azakie A, et al. The effect of preoperative nutritional status on postoperative outcomes in children undergoing surgery for congenital heart defects in San Francisco (UCSF) and Guatemala City (UNICAR). J Thorac Cardiovasc Surg. 2014;147:442-50.
24. Gu Y, Hu Y, Zhang H, Fu W, Yang Y, Latour JM. Implementation of an Evidence-Based Guideline of Enteral Nutrition for Infants With Congenital Heart Disease: A Controlled Before-and-After Study. Pediatr Crit Care Med. 2020;21:e369-e77.
25. St Pierre A, Khattra P, Johnson M, Cender L, Manzano S, Holsti L. Content validation of the infant malnutrition and feeding checklist for congenital heart disease: a tool to identify risk of malnutrition and feeding difficulties in infants with congenital heart disease. J Pediatr Nurs. 2010;25:367-74.
26. Argent AC, Balachandran R, Vaidyanathan B, Khan A, Kumar RK. Management of undernutrition and failure to thrive in children with congenital heart disease in low- and middle-income countries. Cardiol Young. 2017;27:S22-S30.
27. Wong JJ, Cheifetz IM, Ong C, Nakao M, Lee JH. Nutrition Support for Children Undergoing Congenital Heart Surgeries: A Narrative Review. World J Pediatr Congenit Heart Surg. 2015;6:443-54.
28. Ackerman D, Laszlo M, Provisor A, Yu A. Nutrition Management for the Head and Neck Cancer Patient. Cancer Treat Res. 2018;174:187-208.
29. Viani K. Parenteral and enteral nutrition for pediatric oncology in low- and middle-income countries. Indian J Cancer. 2015;52:182-4.
30. Obeid OA, Hachem DH, Ayoub JJ. Refeeding and metabolic syndromes: two sides of the same coin. Nutr Diabetes. 2014;4:e120.
31. Zhang H, Gu Y, Mi Y, Jin Y, Fu W, Latour JM. High-energy nutrition in paediatric cardiac critical care patients: a randomized controlled trial. Nurs Crit Care. 2019;24:97-102.
32. Cui Y, Li L, Hu C, Shi H, Li J, Gupta RK, et al. Effects and Tolerance of Protein and Energy-Enriched Formula in Infants Following Congenital Heart Surgery: A Randomized Controlled Trial. JPEN J Parenter Enteral Nutr. 2018;42:196-204.
33. Clarke SE, Evans S, Macdonald A, Davies P, Booth IW. Randomized comparison of a nutrient-dense formula with an energy-supplemented formula for infants with faltering growth. J Hum Nutr Diet. 2007;20:329-39.
34. Eveleens RD, Dungen DK, Verbruggen S, Hulst JM, Joosten KFM. Weight improvement with the use of protein and energy enriched nutritional formula in infants with a prolonged PICU stay. J Hum Nutr Diet. 2019;32:3-10.
35. Scheeffer VA, Ricachinevsky CP, Freitas AT, Salamon F, Rodrigues FFN, Brondani TG, et al. Tolerability and Effects of the Use of Energy-Enriched Infant Formula After Congenital Heart Surgery: A Randomized Controlled Trial. JPEN J Parenter Enteral Nutr. 2020;44:348-54.
36. Marino LV, Meyer R, Cooke ML. Cost comparison between powdered versus energy dense infant formula for undernourished children in a hospital setting. e-SPEN Journal. 2013;8:e145-e9.

World Nutrition Journal |eISSN 2580-7013

LITERATURE REVIEW

Disease-related malnutrition in children with cancer: what's the risk and impact on patient outcome

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Received 27 October 2021
Accepted 26 February 2022
Published: 28 February 2022

Link to DOI:
10.25220/WNJ.V05.i2.0007

Citation: Sudarmanto B, Primavita C. Disease-related malnutrition in children with cancer: what's the risk and impact in patient outcome. World Nutrition Journal.2022 Feb 28, 5(2): 42-51.

Website :
http://www.worldnutrijournal.org/

Abstract

Background: Malnutrition in children with cancer is a common problem, particularly in low-income countries. Risk factors, effects on outcome, and feasible interventions are important to comprehend in managing patients.

Objectives: To identify the risk and impact of malnutrition in children with cancer.

Method: The authors searched for articles through PubMed and Google Scholar, using a combination of the following keywords: "Impact and Risk", "Effects of Malnutrition", and "Children with Cancer". Article searches were performed in July to September 2021**.** The articles reviewed in this manuscript are English language articles, with full text available. A total of 31 articles were used in this review.

Discussion: Children with cancer are at risk of suffering from malnutrition. Malnutrition occurs due to energy imbalance and results from multifactorial interactions, including type of tumors and therapy. Malnutrition can contribute to poor clinical outcome and decreased quality of life. Management of malnutrition in pediatric patients with cancer include screening and nutritional interventions with suitable route of administration based on patient condition.

Conclusion: Pediatric cancer patients are at increased risk of malnutrition, with a disproportionate burden between low- and middle-income versus high-income countries. Malnutrition is a threat to pediatric cancer patients because it can interfere with the course of chemotherapy treatment, although chemotherapy is considered to have a role in triggering malnutrition itself. Malnutrition has a short-term and long-term impact on children with cancer such as delays in treatment, impaired growth and development, to the emergence of other medical problems that lead to a worsening quality of life. Malnutrition is considered to cause high rates of morbidity and mortality in pediatric cancer patients. Malnutrition should be carefully screened and assessed early as it affects patient outcome.

Keywords: malnutrition, cancer, risk, outcome

Introduction

Children with cancer are at increased risk of severe mortality and morbidity. An important challenge is the inequality of survival rates between children in high-income and low-income countries. According to the World Health Organization, in high-income countries, where comprehensive services are generally accessible, more than 80% of children with cancer are cured while in low- and middle-income countries (LMICs), less than 30% are cured. Some contributing factors of this inequality include diagnostic delay, advanced disease, lack of diagnostic accuracy, lack of accessible therapy, treatment abandonment, death due to toxicity as

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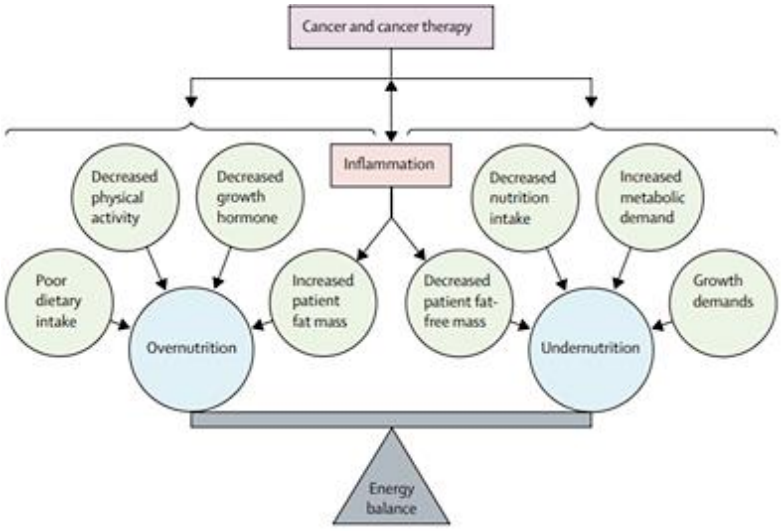

Figure 1. Energy balance in pediatric cancer[3]

treatment side effects, and avoidable relapse. Due to its magnitude, WHO considers childhood cancer a public health issue and therefore developed the Global Initiative for Childhood Cancer. The Global Initiative aims to "at least achieve 60% survival and to reduce suffering for all children with cancer by 2030, by increasing capacity of countries to provide quality services for children with cancer as well as increasing prioritization of childhood cancer at the global, regional, and national levels". The Global Initiative targeted that those efforts will be implemented across 6-10 countries by 2019-2020 and 18-25 countries by 2021-2023.[1]

Managing childhood cancer as well as its comorbidities is an important goal of the WHO, Malnutrition is one of well-known comorbidities of childhood cancer patients. Successful childhood cancer management is in line with the second Sustainable Development Goals (SDG)[2], which is "end hunger", as the Global Initiative stated that "Reducing cancer and malnutrition improves childhood cancer outcome".

It is well known that significant association exists between childhood cancer and malnutrition. The main problem that arises from the aforementioned association is the likely impact on patient outcome, i.e. the effect of malnutrition in childhood cancer and its influence on variables such such as mortality, treatment outcomes, and other clinical conditions. This review will describe disease-related malnutrition in children with cancer, as well as its risk and impact on patient outcome.

Methods

The authors searched for articles through PubMed sources and Google Scholar, using a combination of keywords including "Impact and Risk", "Effects of Malnutrition", and "Children with Cancer". Article searches were performed in July to September 2021**.** The articles reviewed in this manuscript are English articles, with full text is available. After screening through the titles and abstracts of the articles found for relevancy to the topic, 31 articles were used in this review.

Risk factors of malnutrition in children with cancer

Children with cancer are at increased risk of malnutrition. Malnutrition can manifest as undernutrition or overnutrition, as pediatric cancer interferes with energy balance. The interference of cancer with energy balance occurs through the process of inflammation for both overnutrition and undernutrition. For overnutrition, contributing factors include poor dietary intake, decreased physical activity, decreased growth hormones, decreased nutrition intake; whereas for undernutrition, contributing factors include

decreased nutrition intake, increased metabolic demand, and growth demands **(Figure 1)**.[3]

Several risk factors for malnutrition can be categorized into three factors such as the characteristics of tumor itself, factors related to treatment, factors related to symptoms, demographics, anthropometry, and dietary intake. Characteristics of tumor itself include solid tumors in advanced stages (such as neuroblastoma, Wilms tumor, rhabdomyosarcoma, Ewing sarcoma), central nervous system tumors (craniopharyngioma, medulloblastoma, astrocytoma, ependymoma), high-risk acute lymphoblastic leukemia, lymphoma, nasopharyngeal carcinoma, as well as multiple relapsed and high-risk leukemias.[4] More specifically, tumor characteristics can be further divided into high risk factor for undernourishment, moderate risk factor for undernourishment, and high risk factor for fat accumulation **(Table 1).**[5]

The second contributing factors (factors related to treatment) include gastrointestinal tract irradiation, high-dose cranial/craniospinal radiotherapy, prolonged corticosteroid therapy with large doses, major abdominal surgery, undergoing haematopoietic stem cell transplantation (HSCT) or presenting graft vs host disease. Symptoms that are considered contributing factors to malnutrition include nausea, vomiting, diarrhea, and severe mucositis. Compared to other demographical groups, infants have higher risk of malnutrition. Anthropometry risk factors include weight-for-high (W/H) or body mass index (BMI) for age (A) BMI/A Z-score of less than −2 or more than +2, mid-upper arm circumference (MUAC) of less than percentile 10 or more than percentile 90, and weight loss or poor weight gain during the last few weeks. Factors related to dietary intake include unmet energy and protein needs for the last few days.[4] More practically, patients with childhood cancer have taste and smell dysfunction, altered appetite regulation (varibility in ghrelin and leptin levels), and disturbed eating habits (such as lack of exposure to a variety of nutritious foods during treatment).[6] Specifically, taste dysfunction seemed to be more prominent than smell.

A study by Lemos et al.[7] in Brazil showed that the prevalence of malnutrition in children and adolescents with cancer, both solid and hematological, were higher compared to those without cancer. This study, performed in a total of

Table 1. Tumor types associated with malnutrition for pediatric oncology patients. Adapted from Bauer et al.[5]

High risk factor for undernourishment	Moderate risk factor for undernourishment	High risk factor for fat accumulation
Solid tumor with advanced stages	Nonmetastatic solid tumors	Acute lymphoblastic leukemia receiving cranial irradiation
Wilms tumor	Uncomplicated acute lymphoblastic leukemia	Craniopharyngioma
Neuroblastoma stage III and IV	Advanced diseases in remission during maintenance treatment	Malignancies with large and prolong doses of corticosteroid therapy or other drugs increasing body fat stores
Rhabdomyosarcoma Ewing sarcoma Medulloblastoma Multiple relapsed leukemia and lymphoma Head and neck tumors Post stem cell transplantation (graft vs host disease) Diencephalic tumors		Total body or abdominal or cranial irradiation

1154 patients, showed that at the diagnosis of disease, the BMI of 12.2% of children in the solid tumor group and 9.52% of children in the hematologic group were below the adequate threshold, therefore classified as undernourished. Interestingly, this study found that malnutrition could be masked in some types of tumors, especially when the evaluation of malnutrition was performed by using only BMI. Therefore, multiple anthropometrical measurements other than BMI such as weight, height, triceps skinfold thickness (TSFT), mid-upper arm circumference (MUAC), arm muscle circumference (AMC), and percentage weight loss should be used as evaluation tools.

In malnourished children diagnosed with cancer, the problems became more complex. The side effects of a worsening nutritional status are mainly found during treatment, such as a decrease in the child's tolerance for chemotherapy, changes in drug metabolism due to inadequate absorption and digestion, decreased immunity due to malnutrition, increased risk of infection and decreased quality of life of children. This impact varies greatly from child to child. Malnutrition in children with cancer is dynamic and its development tend to become more visible during subsequent treatment. [13]

A clinical study reported that about 28% pediatric cancer patients have a high risk of experiencing severe malnutrition. This is further exacerbated by the increased risk of mortality and infection which are significantly increased by malnutrition and rapid weight loss in the initial phase of treatment (3-6 months after diagnosis).[24] Chemotherapy is a common treatment for cancer patients. Although needed, it also plays an active role in triggering nutritional problems in children. Chemotherapy agents affect and damage other normal cells in the body, such as cells of the digestive tract, mouth, hair follicles, and bone marrow. Depending on the type and dose of the drug given and the length of treatment, side effects of chemotherapy include canker sores (mucositis), stomatitis, dysphagia, changes in taste and smell, anemia, depression, anorexia, anxiety, nausea, vomiting and diarrhea may lead to malnutrition. Almost about 84% of children (boys and girls) with cancer have below normal Body Mass Index. On the other hand, chemotherapy is very necessary for treatment, but poor nutritional status will disrupt the course of treatment.[25]

The incidence of malnutrition in children with cancer not only affects the frequency and continuity of chemotherapy, but also gives birth to other clinical problems, such developmental and growth disorders. Malnutrition among pediatric oncology patients has been recognized as a negative prognostic factor associated with increased morbidity or decreased survival. Moreover, these children are at greater risk of experiencing nutritional deficiencies due to their faster metabolic rate and greater caloric requirements for growth and development.[26] This increases the likelihood of malnutrition, leading to children with cancer experiencing growth delays such as stunting, especially in children with cancer at an early age. Poor nutritional intake and inadequate treatment have the potential to disrupt cognitive brain development. This demonstrated that untreated malnutrition worsens the children's quality of life.[27] Considering the burden severity of malnutrition in children in cancer, malnutrition in children with cancer should be well screened. Before using any specific screening tools, history taking is critical as an initial step. Important aspects to ask during history taking include current patient clinical state (subjective symptoms, treatment given, treatment effect nutrient intake, absorption and retention), patient history (dietary pattern before cancer diagnosis, previous data on growth, previous antitumor therapy and its effect on nutritional status), developmental status (feeding skill milestone and swallowing function), food allergies and intolerance, medications with special attentions to gastrointestinal side effects), family history, and social history.[8]

Nutrition screening tool for childhood cancer (SCAN) is a screening tool specifically developed to diagnose malnutrition in childhood cancer, with a score of three or more indicating at risk of malnutrition **(Table 2).** In an explanation of this questionnaire by Murphy et al.[9] type of cancer that is considered high risk depends on hospitals criteria and include patients on high risk treatment protocols, infants, and the presence of

comorbidities. In addition, treatment that are considered high intensity are chemotherapy, radiotherapy, and HSCT. Signs of undernutrition include visible muscle wasting, edema (including bilateral pedal), skin manifestations (dry, thin, shiny or wrinkled), hair manifestations (thin, sparse and easily pulled out), or evidence of micronutrient deficiencies.

Table 2. Nutrition screening tool for childhood cancer. Adapted from Murphy et al (2016)

Item	
Does the patient have a high risk cancer?	1
Is the patient currently undergoing intensive treatment?	1
Does the patient have any symptoms relating to the GI tract?	2
Has the patient had poor intake over the past week?	2
Has the patient had any weight loss over the past month?	2
Does the patient show signs of under nutrition?	2
Total	
Score indication ≥3 At risk of malnutrition – Refer to dietitian for further assessment	

The impact of disease-related malnutrition in patient outcome

The burden of malnutrition in childhood cancer is unequally distributed between low-and-middle income countries and high-income countries. More than 80% of children and adolescents with cancer are found in low-and-middle income countries. At the same time, low-and-middle income countries also face undernutrition as another entity, making the burden even greater.[10]

Malnutrition in pediatric cancer patients poses several consequences that influence outcome. The consequences can be generally categorized into short-term and long-term. Short-term consequences include wasting of muscle and fat mass, decreased tolerance of chemotherapy, unfavorable response to chemotherapy, treatment delays, fatigue, biochemical disturbances (anemia and hypoalbuminemia), delayed recovery of normal marrow function, changes in body composition, drug dose alteration, decreased quality and productivity of life, greater levels of psychological distress, and higher susceptibility of infections. On the other hand, long-term consequences include growth impairment, reduced final height, decreased long-term survival (in several tumor types), impairment of several functions (motor, cognitive, and neurodevelopment), increased risk for several medical conditions (metabolic syndrome, secondary cancers, aging) increased mortality rate, retardation of skeletal maturation, abnormal bone mineral density, and decreased quality of life.[5] The overall long-term impact is the accumulated result of the previous short-term impacts. Poor nutritional status affects the patient's survival ability and is closely related with an increase in patient treatment failure. The incidence of under-nutrition and malnutrition has been investigated as risk factors for the patient's worsening condition, posing critical risks for the child's growth and development. Limited nutritional reserves despite large nutritional requirements rendered the patients more vulnerable to high morbidity and mortality rates.[30] Magri Teles et al.[31]'s study on 155 pediatric cancer patients reported 18.1% patients had a Z-score of <-2 for BMI, and had to be treated with intubation/mechanical ventilation.

Besides those short-term and long-term consequences, clinical consequences of malnutrition in patients with cancer include increased infection risk, poor wound healing, poor quality of life, and

possible increased referral to tertiary care centers. Specifically, related to the cancer itself, malnutrition results in a reduced response to cancer treatment, increased side effects, and a possibility of reduced survival.[11] In addition, pediatric cancer patients with malnutrition have worse quality of life. Brinksma et al.[12] studied quality of life of 104 children aged 2–18 years diagnosed with hematological, solid, or brain malignancies. They found that undernutrition and weight loss were associated with worse physical and social functioning domains of health-related quality of life, whereas overnutrition and weight gain affected the emotional and social domains.

A review by Barr and Mosby[10] reported that malnutrition in pediatric patients results in altered tolerance of chemotherapy, comorbidities, abandonment of treatment, relapse of disease, and death. Regarding altered tolerance of chemotherapy, the specifics are perturbations of drug metabolism, with resulting delays in chemotherapy, increased toxicity, and compromised survival. In addition, this review also stated that underweight or overweight/obese patients, using acute myelogenous leukemia (AML) patients as an example, had lower survival chance. Malnutrition at the time of diagnosis of malignancy is also a risk factor of unfavorable outcome.[13] Overweight/obese pediatric acute lymphoblastic leukemia (ALL) patients who already presented with overnutrition at the time of diagnosis also had poorer outcome such as higher rates of minimal residual disease at the end of induction therapy as well as poorer event-free survival, regardless of their minimal residual disease status.[10]

A study by Pribnow et al.[14] in Nicaragua showed that that the proportion of pediatric cancer patients with adequate nutritional status was 59.1%, higher compared to a proportion of 52.9% of event-free survival in moderately and severely malnourished patients. The study classified adequate nutrition, moderate malnutrition, and severe malnutrition as shown in **Table 3** (moderate and severe malnutrition are grouped together as inadequate nutrition). [14] Types of cancer included in this study were ALL, AML, Hodgkin lymphoma, Burkitt lymphoma, and Wilms tumor. Among the aforementioned types, Wilms tumor (85.7%), followed by Burkitt lymphoma (75%), and AML (74.%) had the highest percentage of inadequate nutrition among each group.

Table 3. Classification of malnutrition. Adapted from Pribnow et al.[14]

Classification	Item
Adequate nutrition	triceps skinfold thickness (TSFT) > 10th percentile AND
	Mid-upper arm circumference (MUAC) > 10th percentile AND
	Body mass index (BMI) > 5th percentile AND
	Serum albumin > 3.5 g/dL (when available)
Moderate malnutrition	TSFT 5-10th percentile OR
	MUAC 5-10th percentile OR
	BMI 3-5th percentile OR
	Serum albumin 3.2-3.5 g/dL (when available)
Severe malnutrition	TSFT <5th percentile OR
	MUAC <5th percentile OR
	BMI <3rd percentile OR
	Serum albumin <3.2 g/dL (when available)

Malnutrition also increased the risk of febrile neutropenia in childhood cancer. A study by Agnes et al.[15] in Indonesia showed a significant correlation between malnutrition and febrile neutropenia in patients with ALL. In addition, a recent study in

India found that malnutrition, in this case severe underweight, together with profound neutropenia and non-remission status of bone marrow served as predisposing factors of recurrent fever in patients with ALL.[16]

A study by Sakthikumar on 306 children with cancer showed that 37% had poor nutritional status at the time of diagnosis. (9.52%). This risk factor for the impact of malnutrition can lead to poor treatment outcomes that lead to recurrence, severity and even death.[28] Significantly, the type of tumor greatly affects the child's survival and severe impact. Low BMI values are significantly associated with poor histologic response in patients with tumor necrosis (90%) and worsening of the condition in children with Ewing sarcoma.[29]

A systematic review of 46 studies reviewing the prevalence of malnutrition in pediatric cancer patients as well as the effects of pediatric cancer and its treatment on nutritional status showed that the prevalence range of undernutrition and overnutrition in pediatric cancer patient is 0% to 65% and 8% to 78%, respectively.[17] In particular, a study by Mejia-Arangure assessed in this systematic review that is considered strong in quality, showed that in patients with ALL, undernutrition is associated with higher risk of mortality.[18]

What's the goal/target of cancer management? Discussion

The goal of cancer management can first be classified into therapeutic and palliative goals. Therapeutically, cancer management aims to improve function and outcome by preventing and treating undernutrition, enhance antitumor treatment effects, reduce adverse effects of antitumor therapies, and improve quality of life. Regarding the first goal (preventing and treating undernutrition), in curative oncology treatment, nutritional intervention aims to "reduce the number of complications and to shorten hospitalization"; whereas in palliative oncology treatment, the aim of nutritional intervention is to "sustain or enhance recovery of patient performance in everyday life, their well-being and their quality of life.[19]

In general, to achieve the nutritional goals for pediatric cancer patients, several steps can be taken. First, nutritional status should be assessed. After nutritional status is assessed, the requirement is calculated and gastrointestinal function is evaluated. Then, route of food administration is determined and food regimen is decided. Route of food administration varies, depending on patient indications **(see Table 4).** Finally, evaluation of result is performed. The process should be patient-centered with team-based collaboration.[5]

Specifically, the goal of nutrition management in cancer patients can be broken down to be specific points. First, to reduce stress, as some patients has a desire to eat, but unable to do so due to their cancer conditions. Second, to ensure food safety, as cancer patients has specific dietary requirements to prevent further infection and complications, by having neutropenic diet, low bacteria diet, and sterile food. Third, to stimulate the gut, as the gut muscle needs to be stimulated or it will atrophy. Fourth, to meet caloric requirements, as calorie requirement during treatment are usually higher, and protein requirement are also higher. Fifth, to meet micronutrients and macronutrients requirements, by a balanced combinations of carbohydrate, lipids, protein, mineral, vitamin, and fiber.[5]

When is the critical time to optimize the management of cancer by stage?

Regarding the time of optimization, nutritional assessment of pediatric cancer should be frequently performed. In addition, nutrition intervention should be initiated early when deficit are detected. In general, nutrition therapy should be started if undernutrition already exist or if it is anticipated that the patient will be unable to eat at 7 days. During chemoradiation, intensive dietary advice and oral nutrition supplement is advised to increase dietary intake to prevent therapy association with weight loss and interrupted radiation therapy. During chemotherapy, routine enteral nutrition during chemotherapy has no effect of tumor response to chemotherapy or on chemotherapy associated unwanted effect.[8]

Table 4. Nutritional strategies for children with cancer. Adapted from Bauer et al.[5]

Nutritional strategies	Indications
Enteral route	In all patients with functional gastrointestinal tract Meeting > 95–100% of estimated energy needs
Tube feeding (nasogastric)	Inability to ingest full energy requirements (.90%) through oral diet for 3–5 d Severe mucositis <3 d
PEG jejunostomy	Inability to meet full energy needs through tube diet for 3–5 d Severe vomiting for 3–5 d Weight loss despite tube feeding
Parenteral nutrition	Altered gastrointestinal absorption for 3–5 d Severe vomiting and diarrhea Severe pancreatitis Intestinal manifestation of graft vs. host disease Paralytic ileus

Benefit of improving disease-related malnutrition in patient with cancer during cancer treatment?

Evidence showed that improving disease-related malnutrition in pediatric cancer patient will lead to more favorable outcomes. A review by Barr and Mosby suggested that restoration of lean body mass, mainly skeletal muscle, is an important aim of nutritional intervention. The review also discussed the impact of nutritional interventions in pediatric patients with leukemia in low- and middle-income countries. It was shown that in particular, fortified snack was shown to be beneficial in improving nutritional status and tolerance of chemotherapy.[10] A study in Malawi explored a peanut-butter based ready-to-use-therapeutic food (RUTF) called 'chiponde'. This study showed that the preoperative nutritional status of children with Wilms' tumor during neo-adjuvant chemotherapy was improved using the aforementioned food as an intervention. In addition, it also improve tumor response significantly.[20] A study in Guatemala by Antillon et al.[21] showed that an RUTF based on a mixture of maize and soy flours called 'incaparina' is beneficial for improving the prognosis of ALL patients who were malnourished at the time of diagnosis. Energy-enriched formula given through nasogastric tube also showed beneficial effect in improving nutritional status of pediatric cancer patients. A trial conducted by Broeder et al.[22] showed that energy-enriched formula was more effective in improving the nutritional status of children with cancer. In that study, the authors compared two equal volumes of tube feeding, standard (1 kcal/mL) versus a high energy density (1.5 kcal/mL) on 27 children with solid tumor undergoing intensive phase treatment with weekly assessments of nutritional status. The same author also conducted a study showing that aggressive nasogastric tube feeding protocol has a positive impact to improve nutritional status of newly diagnosed pediatric cancer patients,[23] as well as to decrease the occurrence of infection in pediatric cancer patients with solid tumor.[24] A more recent evidence from a study by Sacks et al.[32] also supported the aforementioned results, showed that proactive enteral tube feeding is feasible and beneficial for children with cancer.

Conclusion

In conclusion, pediatric cancer patients are at increased risk of malnutrition, with a disproportionate burden between low- and middle-income versus high-income countries. Malnutrition is a threat to pediatric cancer patients because it can interfere with the course of chemotherapy treatment, although chemotherapy is considered to have a role in triggering malnutrition itself. Malnutrition has a short-term and long-term impact on children with cancer such as delays in treatment, impaired growth and development, to the emergence of other medical problems that lead to a worsening quality of life.

Malnutrition is considered to cause high rates of morbidity and mortality in pediatric cancer patients, and should be carefully screened and assessed early as it affects patient outcome. Management of malnutrition should be in line with the therapeutic or palliative goals of cancer treatment. Correcting disease-related malnutrition in pediatric cancer patients, including using an energy-fortified formula administered via a nasogastric tube, has shown beneficial effects.

Conflict of Interest

Authors declared no conflict of interest regarding this article.

Acknowledgment

The authors would like to thank DANONE SN Indonesia for funding the publication of this article.

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References

1. World Health Organization. Childhood cancer. (2021). Available from: https://www.who.int/news-room/fact-sheets/detail/cancer-in-children.
2. United Nations. Sustainable development goals (2021). Available from: https://sdgs.un.org/goals.
3. Joffe L, Ladas EJ. Nutrition during childhood cancer treatment: current understanding and a path for future research. Lancet Child Adolesc Health. 2020 Jun;4(6):465-75.
4. Viani K, Trehan A, Manzoli B, Schoeman J. Assessment of nutritional status in children with cancer: A narrative review. Pediatr Blood Cancer. 2020 Jun;67 Suppl 3:e28211.
5. Bauer J, Jurgens H, Fruhwald MC. Important aspects of nutrition in children with cancer. Adv Nutr. 2011 Mar;2(2):67-77.
6. Cohen J, Collins L, Gregerson L, Chandra J, Cohn RJ. Nutritional concerns of survivors of childhood cancer: A "First World" perspective. Pediatr Blood Cancer. 2020 Jun;67 Suppl 3:e28193.
7. Lemos Pdos S, de Oliveira FL, Caran EM. Nutritional status of children and adolescents at diagnosis of hematological and solid malignancies. Rev Bras Hematol Hemoter. 2014 Nov-Dec;36(6):420-3.
8. Viani K, Trehan A, Manzoli B, Schoeman J. Assessment of nutritional status in children with cancer: A narrative review. Pediatr Blood Cancer.2020;67(Suppl.3):e28211.
9. Murphy AJ, White M, Viani K, Mosby TT. Evaluation of the nutrition screening tool for childhood cancer (SCAN). Clin Nutr. 2016 Feb;35(1):219-24.
10. Barr RD, Mosby TT. Nutritional status in children and adolescents with leukemia: An emphasis on clinical outcomes in low and middle income countries. Hematology. 2016 May;21(4):199-205.
11. Srivastava R, Pushpam D, Dhawan D, Bakhshi S. Indicators of malnutrition in children with cancer: A study of 690 patients from a tertiary care cancer center. Indian J Cancer. 2015 Apr-Jun;52(2):199-201.
12. Brinksma A, Sanderman R, Roodbol PF, Sulkers E, Burgerhof JG, de Bont ES, et al. Malnutrition is associated with worse health-related quality of life in children with cancer. Support Care Cancer. 2015 Oct;23(10):3043-52.
13. Diakatou V, Vassilakou T. Nutritional Status of Pediatric Cancer Patients at Diagnosis and Correlations with Treatment, Clinical Outcome and the Long-Term Growth and Health of Survivors. Children (Basel). 2020 Nov 7;7(11).
14. Pribnow AK, Ortiz R, Baez LF, Mendieta L, Luna-Fineman S. Effects of malnutrition on treatment-related morbidity and survival of children with cancer in Nicaragua. Pediatr Blood Cancer. 2017 Nov;64(11).
15. Agnes M, Widjajanto PH, W D. Impact of malnutrition on febrile neutropenia in children with acute lymphoblastic leukemia during induction phase chemotherapy Paediatr Indones,. 2018;58:298-304
16. Ramamoorthy JG, Radhakrishnan V, Ganesan P, Dhanushkodi M, Ganesan TS, TD S. Malnutrition is a predisposing factor for developing recurrent fever following febrile neutropenia in children with acute lymphoblastic leukemia. Pediatric Hematology Oncology Journal. 2020;5:75-9.
17. Iniesta RR, Paciarotti I, Brougham MF, McKenzie JM, Wilson DC. Effects of pediatric cancer and its treatment on nutritional status: a systematic review. Nutr Rev. 2015 May;73(5):276-95.
18. Mejia-Arangure JM, Fajardo-Gutierrez A, Reyes-Ruiz NI, Bernaldez-Rios R, Mejia-Dominguez AM, Navarrete-Navarro S, et al. Malnutrition in childhood lymphoblastic leukemia: a predictor of early mortality during the induction-to-remission phase of the treatment. Arch Med Res. 1999 Mar-Apr;30(2):150-3.

19. Akbulut G. New perspective for nutritional support of cancer patients: Enteral/parenteral nutrition. Exp Ther Med. 2011 Jul;2(4):675-84.
20. Israels T, Borgstein E, Jamali M, de Kraker J, Caron HN, Molyneux EM. Acute malnutrition is common in Malawian patients with a Wilms tumour: A role for peanut butter. Pediatr Blood Cancer. 2009 Dec 15;53(7):1221-6.
21. Antillon F, Rossi E, Molina AL, Sala A, Pencharz P, Valsecchi MG, et al. Nutritional status of children during treatment for acute lymphoblastic leukemia in Guatemala. Pediatr Blood Cancer. 2013 Jun;60(6):911-5.
22. den Broeder E, Lippens RJ, van 't Hof MA, Tolboom JJ, Sengers RC, van den Berg AM, et al. Nasogastric tube feeding in children with cancer: the effect of two different formulas on weight, body composition, and serum protein concentrations. JPEN J Parenter Enteral Nutr. 2000 Nov-Dec;24(6):351-60.
23. den Broeder E, Lippens RJ, van't Hof MA, Tolboom JJ, van Staveren WA, Hofman Z, et al. Effects of naso-gastric tube feeding on the nutritional status of children with cancer. Eur J Clin Nutr. 1998 Jul;52(7):494-500.
24. Triarico, R., et al. Impact of malnutrition on survival and infections among pediatric patients with cancer: A retrospective study. European Review for Medical and Pharmacological Sciences. 2019;23(3):1165-1175.
25. Sudersanadas K, Alsharidah AS, Al Harthy N, Philip W, Qureshi S. Effect of Chemotherapy on Nutritional Status of Pediatric Subjects with Hematological Malignancies - A Retrospective Longitudinal Study. Journal of Medical Science and Clinical Research. 2017;05(05):21201-21215.
26. Sakthikumar, Lakshmanan, Latha M. Sneha, Shobana Chandran, and Et Al, 'Clinical Implications of Undernutrition in Childhood Cancer: A Single Centre Experience from a Developing Country', *International Journal of Nutrition, Pharmacology, Neurological Diseases* |, 11.2 (2021) https://doi.org/10.4103/ijnpnd.ijnpnd_112_20
27. Galler, Janina R., Maria L. Bringas-Vega, Qin Tang, Arielle G. Rabinowitz, Kamarul Imran Musa, Wen Jia Chai, and others, 'Neurodevelopmental Effects of Childhood Malnutrition: A Neuroimaging Perspective', *NeuroImage*, 231.October 2020 (2021), 117828 <https://doi.org/10.1016/j.neuroimage.2021.117828>
28. Yazbeck N, Samia L, Saab R, Abboud MR, Solh H, Muwakkit S. Effect of malnutrition at diagnosis on clinical outcomes of children with acute lymphoblastic leukemia. J Pediatr Hematol Oncol 2016;38:107-10.
29. Goldstein G, Shemesh E, Frenkel T, Jacobson JM, Toren A. Abnormal body mass index at diagnois in patients with Ewing Sarcoma is associated with inferior tumor necrosis. Pediatr Blood Cancer 2015;62:1982-6.
30. Han WM, Koo JY, Lim YY*, et al* Implementation of a nutrition screening tool to improve nutritional status of children with cancer in Singapore's largest paediatric hospital *BMJ Open Quality* 2021;10**:**e000944. doi: 10.1136/bmjoq-2020-000944
31. Magri Teles ND, Silva DCBD, Araujo OR, Maia Lemos PDS, Oliveira FLC. Undernutrition as an Aggravating Risk for Hospital Death in Critically Ill Children with Cancer. *Nutr Cancer*. 2021;73(11-12):2627-2632. doi: 10.1080/01635581.2020.1844244. Epub 2020 Nov 5. PMID: 33153333.
32. Sacks N, Hwang WT, Lange BJ, Tan KS, Sandler ES, Rogers PC, et al. Proactive enteral tube feeding in pediatric patients undergoing chemotherapy. Pediatr Blood Cancer. 2014 Feb;61(2):281-5.