ISSN 1948-5182 (online)

World Journal of *Hepatology*

World J Hepatol 2022 August 27; 14(8): 1530-1693

Published by Baishideng Publishing Group Inc

World Journal of Hepatology

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INDEXING/ABSTRACTING

The *WJH* is now abstracted and indexed in PubMed, PubMed Central, Emerging Sources Citation Index (Web of Science), Scopus, Reference Citation Analysis, China National Knowledge Infrastructure, China Science and Technology Journal Database, and Superstar Journals Database. The 2022 edition of Journal Citation Reports® cites the 2021 Journal Citation Indicator (JCI) for *WJH* as 0.52. The *WJH*'s CiteScore for 2021 is 3.6 and Scopus CiteScore rank 2021: Hepatology is 42/70.

RESPONSIBLE EDITORS FOR THIS ISSUE

Production Editor: *Yi-Xuan Cai*; **Production Department Director:** *Xiang Li*; **Editorial Office Director:** *Xiang Li*.

NAME OF JOURNAL
World Journal of Hepatology

ISSN
ISSN 1948-5182 (online)

LAUNCH DATE
October 31, 2009

FREQUENCY
Monthly

EDITORS-IN-CHIEF
Nikolaos Pyrsopoulos, Ke-Qin Hu, Koo Jeong Kang

EDITORIAL BOARD MEMBERS
https://www.wjgnet.com/1948-5182/editorialboard.htm

PUBLICATION DATE
August 27, 2022

INSTRUCTIONS TO AUTHORS
https://www.wjgnet.com/bpg/gerinfo/204

GUIDELINES FOR ETHICS DOCUMENTS
https://www.wjgnet.com/bpg/GerInfo/287

GUIDELINES FOR NON-NATIVE SPEAKERS OF ENGLISH
https://www.wjgnet.com/bpg/gerinfo/240

PUBLICATION ETHICS
https://www.wjgnet.com/bpg/GerInfo/288

PUBLICATION MISCONDUCT
https://www.wjgnet.com/bpg/gerinfo/208

ARTICLE PROCESSING CHARGE
https://www.wjgnet.com/bpg/gerinfo/242

STEPS FOR SUBMITTING MANUSCRIPTS
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World Journal of Hepatology

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World J Hepatol 2022 August 27; 14(8): 1643-1651

DOI: 10.4254/wjh.v14.i8.1643

ISSN 1948-5182 (online)

ORIGINAL ARTICLE

Observational Study

Prevalence of sarcopenia using different methods in patients with non-alcoholic fatty liver disease

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Specialty type: Nutrition and dietetics

Provenance and peer review: Invited article; Externally peer reviewed.

Peer-review model: Single blind

Peer-review report's scientific quality classification

Grade A (Excellent): 0
Grade B (Very good): B, B
Grade C (Good): 0
Grade D (Fair): D
Grade E (Poor): 0

P-Reviewer: Ghoneim S, United States; Pham TTT, Vietnam

Received: March 17, 2022
Peer-review started: March 17, 2022
First decision: April 28, 2022
Revised: May 11, 2022
Accepted: July 26, 2022
Article in press: July 26, 2022
Published online: August 27, 2022

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Abstract

BACKGROUND

Sarcopenia is a clinical condition associated with several liver diseases and it includes non-alcoholic fatty liver disease (NAFLD) in its broad spectrum as steatosis, steatohepatitis and fibrosis. However, the criteria to define sarcopenia are diverse, and even those established in consensus have been discussed regarding their performance in making an accurate diagnosis.

AIM

To evaluate the prevalence of sarcopenia, using different methods, in patients with NAFLD, and its association with clinical-anthropometric parameters.

METHODS

This was an observational study of outpatients with NAFLD. Sarcopenia was defined by the European Working Group Consensus on Sarcopenia in Older People of 2010 (EWGSOP1) and 2018 (EWGSOP2). The skeletal muscle index was used to estimate muscle mass, handgrip strength was assessed using the dynamometer and physical performance by walking a distance of four meters at usual walking speed. The non-invasive fibrosis scores, fibrosis-4 (FIB-4) index and Aspartate aminotransferase to platelet ratio index (APRI), were used to assess the absence and presence of fibrosis.

RESULTS

Fifty-seven individuals with NAFLD were evaluated, the mean age (SD) was 52.7 (11.3) years and 75.4% were female. Fibrosis assessed by FIB-4 and APRI was observed in 3.7% and 16.6% of patients with NAFLD, respectively. The diagnosis of sarcopenia was identified only by EWGSOP1 in 3.5% of NAFLD patients, and the prevalence of probable/pre-sarcopenia was higher using the EWGSOP2 consensus at 26.3%, when compared to 1.8% with EWGSOP1. Sarcopenia defined by EWGSOP1, was associated with grade I steatosis, but without overweight ($P < 0.05$). An association between sarcopenia and fibrosis was not observed ($P > 0.05$). EWGSOP2 showed a greater number of patients with probable sarcopenia, and who were overweight (12 (80.0%)), with a higher degree of steatosis [11 (73.3%) and presence of fibrosis (1 (6.7%), FIB-4 and 3 (20.0%), APRI] compared to EWGSOP1 [1 (100%), 0 (0.0%), 0 (0.0%), FIB-4 and 0 (0.0%), APRI, respectively].

CONCLUSION

The present study showed that sarcopenia in NAFLD was not predominant in patients without fibrosis, by both diagnostic methods. In addition, the prevalence of probable sarcopenia also depends on the method applied.

Key Words: Non-alcoholic fatty liver disease; Sarcopenia; Muscle strength; Physical performance; Liver fibrosis

Core Tip: In Non-Alcoholic Fatty Liver Disease (NAFLD), sarcopenia has been associated with the presence and severity of the disease. However, the diagnostic criteria for sarcopenia are still under evaluation and undergoing constant changes. In patients with NAFLD, sarcopenia was not common, but a higher prevalence of probable sarcopenia was observed by the most current European Working Group Consensus on Sarcopenia in Older People, 2018. This increased sensitivity to the possible early stage of sarcopenia may be an opportunity for accurate and early interventions in this population, preventing the development of sarcopenia and the worse evolution of NAFLD.

Citation: Almeida NS, Rocha R, de Souza CA, da Cruz ACS, Ribeiro BDR, Vieira LV, Daltro C, Silva R, Sarno M, Cotrim HP. Prevalence of sarcopenia using different methods in patients with non-alcoholic fatty liver disease. *World J Hepatol* 2022; 14(8): 1643-1651
URL: https://www.wjgnet.com/1948-5182/full/v14/i8/1643.htm
DOI: https://dx.doi.org/10.4254/wjh.v14.i8.1643

INTRODUCTION

Non-alcoholic fatty liver disease (NAFLD) is considered the most prevalent liver disease and affects approximately 25% to 30% of the world population[1]. Among obese and/or diabetic individuals, the prevalence is even higher, reaching around 75%-90% in these populations[2]. The increased prevalence in these groups may be justified by the association of NAFLD with several metabolic disorders, including insulin resistance, inflammation and altered lipid metabolism[3].

Sarcopenia, defined as the progressive loss of muscle mass, strength and muscle function, shares some pathophysiological mechanisms with NAFLD such as insulin resistance, which is the main link between these two diseases[3-6].

Skeletal muscle is an active endocrine organ responsible for insulin-mediated glucose elimination. Thus, muscle depletion can lead to a reduction in the primary target tissue of insulin action with consequent resistance to it[7,8].

Sarcopenia was considered a diagnostic code muscle disease, in which low muscle strength is the main determinant for triggering diagnostic investigation, surpassing low muscle mass, prioritized by the first publication of the European Working Group on Sarcopenia in Older Persons (EWGSOP)[9,10]. The primary difference between the two consensuses (EWGSOP1 2010 and EWGSOP2 2018) is in the triggering criteria for diagnostic investigation, defined as "pre-sarcopenia".

Although experts in the field accept the use of EWGSOP2, the effect on the identification of sarcopenia has raised concern. To date, all consensuses have agreed on two crucial components in defining sarcopenia, the involvement of both structural damage (low muscle mass) and impaired function (low muscle strength). However, the cut point reductions suggested in EWGSOP2 seem to have lower sensitivity[11,12].

The present study aimed to evaluate the prevalence of sarcopenia using different diagnostic methods in patients with NAFLD, and its association with the severity of this disease.

MATERIALS AND METHODS

Study design and population

A cross-sectional study was conducted at the Nonalcoholic Steatohepatitis Outpatient Clinic (NASH) - Federal University of Bahia, Brazil.

A consecutive and voluntary sample of patients including both sexes aged over 18 years with NAFLD was selected from January 2019 to December 2021. The criteria for NAFLD included the presence of hepatic steatosis on abdominal ultrasound; negative history of ethanol intake (< 140 g of ethanol per week); exclusion of other liver diseases such as hepatitis B and C virus infection; hemochromatosis, and autoimmune hepatitis. Patients with hypothyroidism, pregnant and lactating women, those with hepatomegaly or splenomegaly, ascites, abdominal tumors and recent abdominal surgeries, or any physical limitation that compromised the anthropometric assessment were excluded.

Abdominal ultrasound

All patients underwent ultrasound of the upper abdomen by a single evaluator to measure intrahepatic fat, in a specialized clinic, using the Xario 100 Canon Medical Systems device®.

Non-invasive fibrosis scores

Non-invasive fibrosis scores were used to assess the absence and presence of fibrosis. The fibrosis-4 index (FIB-4), considered the absence of fibrosis to be FIB-4 < 1.30, indeterminate FIB-4 1.30–2.67 and fibrosis FIB-4 > 2.67[13,14]. For the Aspartate aminotransferase to platelet ratio index (APRI), absence of fibrosis was APRI ≤ 0.50, indeterminate APRI > 0.5 - < 1.49 and fibrosis APRI > 1.50[15].

Anthropometric assessment

Anthropometric measurements were performed in duplicate by a trained and standardized team. Body weight (kg) and height (cm) were measured with light clothes and without shoes, using a digital scale with a resolution of 100 g and a stadiometer with 0.5 cm[16]. The body mass index (BMI) was obtained using the formula weight (kg)/height^2 (m^2)[17] and for better interpretation of the data, overweight and non-overweight categorizations were used. To this end, adult individuals were considered overweight when the BMI ≥ 25 kg/m^2 and in the elderly, when BMI ≥ 28 kg/m^2[17,18].

Sarcopenia assessment

As diagnostic criteria, the 2010 European Consensus was used (EWGSOP1)[9], which recommends muscle mass, muscle strength and physical performance for the diagnosis, and the 2018 European Consensus (EWGSOP2)[10] that uses muscle strength and muscle quantity/quality, in that order, maintaining physical performance only as a way of categorizing the severity of the disease (Table 1).

Muscle mass

Muscle mass was evaluated by calculating skeletal muscle mass (SMM), using the prediction equation proposed by Janssen *et al*[19], where height is measured in cm, resistance in ohms, male = 1, female = 0, and age is measured in years.

The resistance value was obtained through bioelectrical impedance, using the tetrapolar Biodynamics®, model 450. The technique and previous procedures were performed according to Kyle *et al*[20]. From the SMM, the equation skeletal muscle index (SMI) calculated the SMI = MM/height^2[19].

Low muscle mass was defined according to the cutoff points predicted by the EWGSOP1[9] (women < 6.42 kg/m^2, men < 8.87 kg/m^2) and EWGSOP2[10] (women < 5.5 kg/m^2, men < 7 kg/m^2).

Muscle strength

Muscle strength was assessed by the maximal handgrip strength test, with a portable handheld dynamometer SAEHAN Spring Hand Dynamometer (Smedley-Type SH5002), and a 0-100 kg/force grading scale (kg/f).

Two measurements were taken on each hand, alternately, with 1 min of rest between them. The average between each pair of measurements was obtained and the highest average obtained was considered for analysis. For EWGSOP1, low muscle strength is defined as < 30 kgf for men and < 20 kgf for women[9] and for EWGSOP2, < 27 kgf for men and < 16 kgf for women[10].

Physical performance

Usual gait speed was measured in meters per second (m/s). The patient walked four meters in a straight and flat environment, at their usual walking speed. The test was repeated twice, and the shortest time spent was used for analysis. Individuals with gait speed < 0.8 m/s were evaluated with reduced gait

Table 1 Classification of the diagnosis of sarcopenia according to the European Working Group on Sarcopenia in Older People, 2010 and 2018

Diagnosis	EWGSOP1	EWGSOP2
No sarcopenia	MM + MS + PP adequate	MQ + MS + P adequate
Pre-sarcopenia/Probablesarcopenia	MM insufficient	MS insufficient
Sarcopenia	MM + (MS or PP)insufficient	MS + MQ insufficient
Severe sarcopenia	MM + MS + PP insufficient	MS + MQ + P insufficient

EWGSOP1: European Working Group of Sarcopenia in Older People, 2010; EWGSOP2: European Working Group of Sarcopenia in Older People, 2018. MM: Muscle mass; MS: Muscle strength; PP: Physical performance; MQ: Muscle quantity; P: Performance.

speed or poor physical performance[9,10].

Statistical analysis

For tabulation and analysis of the data, the statistical program Statistical Package for the Social Sciences® (SPSS) version 20.0 was used. The results of categorical variables were expressed as absolute and relative frequency and continuous variables were expressed as mean and standard deviation. Pearson's chi-square test was used to compare qualitative variables. Values of $P < 0.05$ were considered statistically significant.

RESULTS

Characteristics of the population studied

The study included fifty-seven patients with NAFLD. A total of 75.4% were female, and the ages ranged between 26 and 73 years, mean (SD) of 52.7 (11.3) years. 84.2% of patients were overweight, 63.1% had grade II and III steatosis. Hepatic fibrosis by FIB-4 was observed in 3.7% of the NAFLD patients and in 16.6% by APRI.

Prevalence of EWGSOP1 vs EWGSOP2 Sarcopenia

The diagnosis of sarcopenia in these NAFLD patients was identified only by EWGSOP1, in 3.5% patients. The prevalence of probable/pre-sarcopenia was higher when using the EWGSOP2 consensus when compared to EWGSOP1, 26.3% *vs* 1.8% of patients with NAFLD.

When evaluated separately by the items that define sarcopenia, most patients had preserved muscle mass and physical performance, both by EWGSOP1 and EWGSOP2. However, it is observed that the number of people with preserved muscle strength was higher by the EWGSOP2 (71.9%), when compared to those evaluated by the EWGSOP1 (47.4%) (Table 2).

Prevalence of sarcopenia according to BMI, degrees of steatosis and fibrosis

Patients with NAFLD diagnosed with sarcopenia by EWGSOP1 presented grade I steatosis and were not overweight ($P = 0.027$ and $P = 0.003$, respectively). However, no association was observed between sarcopenia and fibrosis, either by FIB-4 or APRI ($P > 0.05$) (Table 3).

By EWGSOP2, no association was observed between probable-sarcopenia and degree of steatosis or probable-sarcopenia and excess weight ($P > 0.05$). However, using this method, a greater number of patients with probable sarcopenia and who were overweight, with a higher degree of steatosis and presence of fibrosis were observed (Table 3).

DISCUSSION

This sample of NAFLD patients was composed mostly of overweight adult women, who had the highest degrees of hepatic steatosis, but without fibrosis. The diagnosis of sarcopenia was identified by EWGSOP1 criteria, and the EWGSOP2 algorithm identified probable sarcopenia or pre-sarcopenia major. According to the EWGSOP2, we observed more cases of NAFLD with probable sarcopenia, who were overweight, had a higher degree of steatosis and the presence of fibrosis.

Due to the wide variety of methods available, the identification of sarcopenia varies, and consequently discrepancies are observed between the prevalence of sarcopenia when applying the EWGSOP1 and EWGSOP2 criteria[21]. A systematic review, which compared the prevalence of sarcopenia in the geriatric population based on these two consensuses found 6.2% to 35.3% had sarcopenia by EWGSOP1

Table 2 Variables for the definition of sarcopenia by the European Working Group of Sarcopenia in Older People, 2010 and 2018

Variable	EWGSOP1	EWGSOP2
Muscle mass, *n* (%)		
Adequate	54 (94.7)	57 (100)
Low	3 (5.3)	0 (0.0)
Muscle strength, *n* (%)		
Adequate	27 (47.4)	41 (71.9)
Low	30 (52.6)	16 (28.1)
Physical performance, *n* (%)		
Adequate	48 (84.2)	41 (71.9)
Low	9 (15.8)	16 (28.1)

EWGSOP1: European Working Group of Sarcopenia in Older People, 2010; EWGSOP2: European Working Group of Sarcopenia in Older People, 2018.

Table 3 Association of sarcopenia with the classification of body mass index, degrees of steatosis and presence of fibrosis (Pearson's chi-square test)

Variable	EWGSOP1				EWGSOP2		
	No Sarcopenia, *n* = 54	Pre-sarcopenia, *n* = 1	Sarcopenia, *n* = 2	*P* value	No sarcopenia, *n* = 42	Probable sarcopenia, *n* = 15	*P* value
BMI, *n* (%)							
No excess weight	7 (13.0)	0 (0.0)	2 (100.0)	0.003	6 (14.3)	3 (20.0)	0.685
Overweight	47 (87.0)	1 (100.0)	0 (0.0)		36 (85.7)	12 (80.0)	
Degree of steatosis, *n* (%)							
Grade I	18 (33.3)	1 (100.0)	2 (100.0)	0.027	17 (40.5)	4 (26.7)	0.534
Grade II-III	36 (66.7)	0 (0.0)	0 (0.0)		25 (59.5)	11 (73.3)	
FIB-4[1]							
No fibrosis	49 (96.1)	1 (100.0)	2 (100.0)	0.740	38 (97.4)	14 (93.3)	0.484
Fibrosis	2 (3.9)	0 (0.0)	0 (0.0)		1 (2.6)	1 (6.7)	
APRI[1]							
No fibrosis	42 (82.4)	1 (100.0)	2 (100.0)	0.448	33 (84.6)	12 (80.0)	0.688
Fibrosis	9 (17.6)	0 (0.0)	0 (0.0)		6 (15.4)	3 (20.0)	

[1]*n* = 54, considering three patients who did not have biochemical tests.

EWGSOP1: European Working Group of Sarcopenia in Older People, 2010; EWGSOP2: European Working Group of Sarcopenia in Older People, 2018; BMI: Body mass index; FIB-4: Fibrosis-4 index; APRI: Aspartate aminotransferase to platelet ratio index.

and 3.2% to 26.3% by EWGSOP2[22]. Some studies have shown that EWGSOP1 seems to have great sensitivity in identifying individuals at higher risk for health outcomes[12,21,23]. However, the sensitivity assessment of both methods has been, in its entirety, applied in geriatric populations associated with other diseases.

Sarcopenia has been associated with an increased incidence and risk of NAFLD[24,25]. Despite the divergence of methods used to identify sarcopenia in several studies, and considering the specific characteristics of each population, the literature shows a positive association between sarcopenia and NAFLD, with a significant prevalence in this population[24,26,27].

The association of steatosis with fibrosis in patients with sarcopenia was evaluated by scores FIB-4 and APRI[26-28]. The currently available scores, including FIB-4 and APRI, have some limitations in the diagnosis of fibrosis. There is also difficulty in defining a cutoff point capable of differentiating between the absence of fibrosis or the presence of advanced fibrosis in NAFLD. In general, predictive fibrosis scores have a good Negative Predictive Value to exclude advanced fibrosis with low Positive Predictive

Value. Therefore, these scores can be safely used for basal risk stratification to exclude advanced and nonexistent fibrosis. There is an interval considered undetermined or gray area. In these cases, other methods such as liver biopsy may be necessary for the diagnosis of fibrosis[14,29].

Different methods have been used for the diagnosis of sarcopenia in these studies, among them, the ratio between appendicular skeletal muscle mass and BMI with different cutoff points, and fibrosis identified through liver biopsy and/or non-invasive markers.

The association between sarcopenia and NAFLD still requires further evaluation, considering the standardization and identification of the best diagnostic method for both sarcopenia and hepatic fibrosis.

Considering that sarcopenia is often not noticeable in the preliminary stages, detecting probable sarcopenia is important so that appropriate intervention can be established early[30,31]. In our population, EWGSOP2 better identified cases of probable sarcopenia when compared to EWGSOP1. In addition to the difference in cutoff points, the criteria used in the initial screening are different between the consensuses (muscle mass *vs* muscle strength). In a longitudinal analysis performed in the geriatric population, a higher prevalence of low muscle strength was observed[32].

The cohort study by Xia *et al*[33] found that hand pressure strength is inversely associated with the incidence of NAFLD. This finding had been demonstrated in other studies, which also pointed to a probable relationship between NAFLD and muscle strength[34,35]. Patients with NAFLD seem to be more likely to have low muscle strength when compared to controls, and a higher prevalence of NAFLD was identified in those with low muscle strength. Thus, the evaluation of muscle strength, prioritized by the EWGSOP2, in patients with NAFLD may be a more valuable parameter to identify the early stages of sarcopenia when compared to the analysis of muscle mass[33].

These study results suggest that prioritization of muscle strength by EWGSOP2 may allow greater identification of early cases of sarcopenia in individuals with NAFLD. The measurement of muscle strength is easy to perform and of low cost, which is a positive factor for clinical applicability when compared with the measurement of muscle mass. From a clinical viewpoint, early detection of cases is essential, considering that it is better to prevent skeletal muscle depletion than to try to restore it once it has progressed[36,37].

This seems to be one the first studies to investigate the impact of using the two most frequently used consensuses for the detection of sarcopenia in patients with NAFLD. Although the cross-sectional design limits the possibility of inferring causality, and the small sample size restricts the extrapolation of results to the entire NAFLD population, our results suggest a new clinical approach to sarcopenia in patients with NAFLD.

CONCLUSION

In conclusion, the prevalence of sarcopenia varies depending on the sensitivity of the method applied. In addition, due to the pathophysiological association of sarcopenia with NAFLD, it is important to identify the best method for early detection of loss of muscle function in this population.

It is also possible to identify viable strategies to screen for sarcopenia in clinical practice, using muscle strength as a primary diagnostic indicator, as determined by the EWGSOP2. Thus, this method makes it easier to identify probable sarcopenia in the initial screening at an outpatient level, and consequently the early detection of cases of sarcopenia in this population.

ARTICLE HIGHLIGHTS

Research background

Sarcopenia is a clinical condition possibly associated with Non-Alcoholic Fatty Liver Disease (NAFLD) as they share common pathophysiological mechanisms, such as insulin resistance. The diagnostic criteria available in the literature to define sarcopenia are diverse, and even those established in consensus have been questioned in relation to their diagnostic accuracy.

Research motivation

Previous studies demonstrated an association between sarcopenia and NAFLD. However, the assessment of sarcopenia is performed by various diagnostic methods, which implies discrepant prevalence. The search for the best method led to the two most used consensuses in the scientific community for the diagnosis of sarcopenia in the population and that were not previously investigated in patients with NAFLD.

Research objectives

To evaluate the prevalence of sarcopenia, using different methods, in patients with NAFLD, and its association with the severity of this disease.

Research methods

Sarcopenia was defined by the European Working Group Consensus on Sarcopenia in Older People of 2010 (EWGSOP1) and 2018 (EWGSOP2). Abdominal ultrasound was used to diagnose hepatic steatosis. The non-invasive fibrosis scores, FIB-4 and APRI, were used to assess the absence and presence of fibrosis.

Research results

The diagnosis of sarcopenia was identified only by EWGSOP1, and the EWGSOP2 algorithm identified probable sarcopenia or pre-sarcopenia. Sarcopenia, defined by EWGSOP1, was associated with grade I steatosis, but without excess weight ($P < 0.05$). EWGSOP2 showed a greater number of patients with probable sarcopenia, overweight, with a greater degree of steatosis and presence of fibrosis compared to EWGSOP1.

Research conclusions

Sarcopenia in NAFLD was not predominant in patients without fibrosis, by both consensuses. In addition, the prevalence of probable sarcopenia, a promising early indicator of sarcopenia, was higher by the EWGSOP2 method.

Research perspectives

Validation of muscle strength measurement in the early identification of sarcopenia is essential in NAFLD patients.

ACKNOWLEDGEMENTS

Fundação de Amparo à Pesquisa do Estado da Bahia (FAPESB), Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES), Programa Institucional de Bolsas de Iniciação Científica (PIBIC), Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CNPq) and Programa Permanecer.

FOOTNOTES

Author contributions: Almeida NS, da Cruz ACS, de Souza CA, Rocha R, Ribeiro BR participation in the literature review, analysis and interpretation of data, and final writing of the manuscript; Daltro C, Cotrim HP, data analysis and interpretation, literature review and analysis, and final writing of the manuscript; Vieira LV, Silva R, Sarno M data collection; all authors provided critical contributions and approved the manuscript.

Institutional review board statement: This study was reviewed and approved by the Research Ethics Committee of the School of Nutrition of the Federal University of Bahia (Approval No. 2.443.762).

Informed consent statement: All study participants, or their legal guardian, provided informed written consent prior to study enrollment.

Conflict-of-interest statement: All the authors have no conflicts of interest to declare.

Data sharing statement: Technical appendix, statistical code, and dataset available from the corresponding author at email address raquelrocha2@yahoo.com.br. Participants gave informed consent for data sharing. No additional data are available.

Country/Territory of origin: Brazil

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S-Editor: Liu JH
L-Editor: Webster JR
P-Editor: Liu JH

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