Review Article

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Malnutrition in Obesity: Is It Possible?

Milena Kobylińska Katarzyna Antosik Agnieszka Decyk Katarzyna Kurowska

Faculty of Medical and Health Sciences, Siedlce University of Natural Sciences and Humanities, Siedlce, Poland

Keywords

 $Obesity \cdot Malnutrition \cdot Microbiota \cdot Bariatric \ surgery \cdot Adults$

Abstract

Background: The World Health Organization (WHO) classifies malnutrition as the biggest threat to public health worldwide, and this condition is observed in 20-60% of hospitalized patients. Malnutrition is a state of the body in which due to insufficient supply or incorrect absorption of essential nutrients, the body composition changes and the body's functions are impaired. Malnutrition is associated not only with reduced body mass index but also with obesity. Summary: Obesity is defined as a paradoxical state of malnutrition, which despite excessive energy consumption is associated with a shortage of individual microelements. Deficiency or lack of homeostasis of essential micronutrients can significantly affect daily performance, intellectual and emotional state, but also the physical state of the body. Food deficiency can also contribute to further weight gain or the development of other metabolic diseases. Micronutrient deficiency may include not only incorrect dietary choices and insufficient access to nutrient-rich foods but also changes in the absorption, distribution or excretion of nutrients, and altered micronutrient metabolism resulting from systemic inflammation caused by obesity. An effective therapy method recommended for people with morbid obesity is bariatric surgery aimed at both weight loss and improving quality of

karger@karger.com www.karger.com/ofa

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Introduction

Malnutrition is a condition in which a deficiency of one or many nutrients has an adverse effect on cells, tissues, organs, and the body understood as a whole, which is manifested in the deterioration of its functioning and a negative change in the overall clinical picture [1]. The European Society for Clinical Nutrition and Metabolism (ESPEN) defines malnutrition as a state of the body in which due to insufficient supply or incorrect absorption

Correspondence to: Katarzyna Antosik, katarzyna.antosik@uph.edu.pl

of essential nutrients, body composition changes, physical and mental impairment of the body and adverse effects on the outcome of the underlying disease [2]. The World Health Organization (WHO) classifies malnutrition as the biggest threat to public health worldwide, and this condition is observed in 20-60% of hospitalized patients [3, 4]. Malnutrition is both medically and economically harmful. If detected early and treated appropriately, better clinical results and lower costs will be achieved. Malnutrition is an independent risk factor for patient morbidity and mortality and is associated with increased healthcare costs [1]. Malnutrition is associated not only with reduced body mass index, but also with obesity, in which adipose tissue is also a source of inflammatory cytokines [5]. Research suggests that the inflammatory process in the hypothalamus and mediators released at that time may also lead to a positive energy balance and, consequently, to the development of obesity. In experiments carried out on the animal model of obesity, a significant increase in inflammatory cytokine levels (tumor necrosis factor- α , interleukin-1 β , and interleukin-6) was observed both in adipose tissue and in the hypothalamus [6-8]. According to WHO, obesity is "pathological accumulation of body fat, exceeding its physiological needs and adaptability" [9]. Causes of obesity can result from various hormonal, genetic, and metabolic processes, but obesity is also a condition resulting from lifestyle factors, including excessive food consumption or insufficient physical activity [10]. Obesity increases the risk of other disease entities, referred to as concomitant diseases, which include, but are not limited to, diabetes, hypertension, tumors (in particular colorectal cancer), osteoarthritis, or lipid disorders [11, 12].

Data Sources and Searches

A literature search using PubMed and Google Scholar was performed using the following terms in various combinations: obesity, malnutrition, microbiota, bariatric, and adults. The search for literature was conducted in the period from November 30, 2020, to December 7, 2020, by all authors separately. Researchers used the same search words in both databases on different days to ensure that the search results were repeatable. All articles have been checked by title, abstract, and full text. Relevant articles have been reviewed and posted here. Language restrictions were not applied, but articles for which the full-text version could not be obtained were excluded.

Nutritional Deficiencies in the Diet and Serum Levels of Nutrients in Patients with Obesity

Diagnosing malnutrition in people with obesity is quite difficult. To determine the occurrence of malnutrition in a patient, an assessment of nutrition and nutritional status should be performed [13]. The most common methods of dietary assessment are 24/48-h dietary recall, ffq. Identification of malnutrition is also based on anthropometric measurements, blood biochemical tests, and physical parameters. An important element of assessing nutritional status and diet is dietary assessment consumed by people with obesity. This allows for early diagnosis and implementation of dietary treatment. Adequate supply of nutrients is particularly important when implementing a low-energy diet [13]. Studies by many authors [14-17] indicate that obesity is very often associated with the nutrition and qualitative malnutrition of the body. It is defined as a paradoxical state of malnutrition, which despite excessive energy consumption is associated with a shortage of individual microelements. Deficiency or lack of homeostasis of essential micronutrients can significantly affect daily performance, intellectual, and emotional state, but also the physical state of the body [18, 19]. Food deficiency can also contribute to further weight gain or the development of other metabolic diseases [20]. Nutrient deficiencies associated with obesity may be partly due to overconsumption of foods that are high in calories but have low-nutrient densities [21]. This phenomenon is most common in highly developed countries. For example, in children and adults living in the USA, about 27-30% of total daily calorie intake comes from low-nutrient foods, mainly from added sugars and desserts [22]. In turn, Astrup and Bügel [23] report that a diet in which >30% of energy demand is fat is characterized by a lower intake of vitamins A and C and folic acid. Micronutrient deficiency may include not only incorrect dietary choices, insufficient access to nutrientrich foods, but also changes in the absorption, distribution, or excretion of nutrients, and altered micronutrient metabolism resulting from systemic inflammation caused by obesity [15, 16, 24]. Studies by many authors indicate a higher incidence of food deficiency among people with excessive body weight, than in people with normal body weight of the same age and same sex [16, 25, 26]. Higher body weight resulting from increased body fat may result in lower serum vitamin D₃ levels. Vitamin D₃ deficiency in people with obesity may be associated with reduced physical activity, thus less exposure to the sun and increased storage of vitamin D₃ in adipose

tissue, where it is not available to regulate calcium metabolism [21, 27]. Deficiency of B vitamins is also observed in people with obesity [28]. Low levels of thiamine were found in 15-29% of people with obesity [29]. Higher body mass index is a significant clinical risk of thiamine deficiency. The explanatory mechanisms for the development of thiamine deficiency in people with obesity remain unclear. There are no data indicating that thiamine supplementation brings any clinical benefits in patients with excessive body weight [30]. While the mechanisms of thiamine deficiency in obese individuals remain unclear, there is some speculation that thiamine deficiency in obese individuals is caused by a diet high in simple sugars. These products are not only thiaminefree, but the metabolism of sugar-rich foods also requires relatively large amounts of thiamine, and therefore, consumption of these products may result in a deficiency of this vitamin [31]. In turn, abnormal levels of vitamin B_{12} were observed in 11% of people with morbid obesity [17, 32]. Vitamin B₁₂ supplementation has been shown to improve the deficiency rate to around 4%, but the use of multivitamins alone is usually not enough to prevent deficiency [21]. In turn, Vitolo et al. [33] showed an increased risk of insufficient folic acid intake in adolescents with a waist circumference above the 80th percentile. Studies in Brazil and Spain have shown a folic acid deficiency in 54.3% of adolescents and adults with obesity [32]. It has also been shown that almost 50% of people with obesity have insufficient levels of vitamin C (defined as serum vitamin C below the lower limit of the laboratory norm [<4.6 mg/L]) [34] and that a higher BMI is correlated with lower serum vitamin C levels [35]. Prospective studies demonstrating the clinical benefit of vitamin C supplementation in patients with obesity are therefore needed [23]. In addition, studies in people with obesity have shown that low magnesium levels are correlated with diseases associated with chronic inflammation [35, 36], while further analyses are needed to determine the relationship between magnesium content and obesity [37]. Research conducted in the USA among children with obesity and normal body weight showed that serum alpha-tocopherol levels were significantly lower in obese children than in children with normal body weight [38]. Another study found that men and women who were overweight and obese had lower serum levels of vitamin E than those of normal weight: this study showed a correlation between BMI and vitamin E levels - the higher the BMI value, the lower the serum vitamin E level [39]. The observed low vitamin E levels among people with overweight and obese may result from increased

systemic and adipose-specific oxidative stress for people with overweight, which may lead to increased oxidative catabolism of these fat-soluble nutrients [40, 41].

Astrup and Bügel [23] believe that along with recommendations for healthy eating and increased physical activity, supplementation with specific micronutrients or vitamins should be considered in people at highest risk or deficiencies. It should be noted that it is not recommended that increased intake of vitamins and minerals be based solely on food supplementation or fortification. Such strategies may discourage the use of healthy eating habits [42]. In addition, the bioavailability of nutrients in people with obesity is limited. Supplementation turns out not to be the best solution in the case of large nutritional deficiencies [19].

Microbiota Dysfunction in People with Obesity

Pilot studies conducted by Damms-Machado et al. [25] did not show an improvement in the levels of selected microelements after the introduction of a balanced low-calorie diet for people with obesity. The diet covered 100% of the demand for micronutrients in accordance with adult standards. The lack of a positive effect can be explained by the dysfunction of the intestinal microbiota in these people. Recently, it has been promoting the role of the intestinal microbiota in the pathogenesis of obesity. Gut bacteria are a source of lipopolysaccharide (LPS), which induces chronic inflammation. LPS is recognized by immunocytes through toll-like receptor 4, to which it binds with high affinity, thereby stimulating immune cells to produce pro-inflammatory cytokines that trigger inflammation [43]. Increased LPS levels in plasma and intestines are observed in people with obesity. Intestinal barrier disorders in people with obesity may result from long-term poor eating habits [44]. Another area of research concerns the metabolic role of intestinal microbes in energy production, storage, and expenditure related to obesity. The results of studies suggest that the composition of the intestinal microflora is different in lean people with obesity and animals [16]. Studies on germ-free mice that have been transplanted with the intestinal bacteria of obese mice and mice with normal body weight have demonstrated the relationship between intestinal microflora and obesity. Using the same diet in both groups, it was observed that germ-free mice transplanted with excess weight mice also became obese. In addition, obese mice showed a 50% decrease in the number of Bacteroides and a proportional increase in

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Firmicutes [45]. Composition, variety, and metabolic activity of gut microbiota (GM) are closely related to nutrient intake and dietary patterns. Specific dietary patterns and nutritional factors alter GM profiles that may regulate or influence the progression of obesity [46]. Many dietary patterns, such as the Western diet, vegan diet, vegetarian diet, gluten-free diet, and Mediterranean diet, have been shown to influence the marked diversity of the gut microflora that can affect the host metabolism [47]. However, more research is needed to understand the impact of dietary patterns on obesity-related GM changes [46]. Evidence linking gut bacteria to host metabolism could enable the development of new therapeutic strategies based on the modulation of the gut microflora to treat or prevent obesity [48]. In people with obesity, the ratio of Bacteroidetes to Firmicutes was also disturbed in favor of the latter. Weight reduction is associated with an increase in the number of Bacteroidetes bacteria proportional to the number of kilos lost [49]. It has been proven that a 20% increase in the number of Firmicutes and an analogous decrease in the number of Bacteroidetes are responsible for an increase by 150 kcal of energy intake from food [50]. What is more, as a result of bariatric surgery (Roux-en-Y gastric bypass [RYGB] - bypass gastrointestinal anastomosis with Roux-en-Y loop), leading to weight loss in people with obesity, researchers observed an increase in the number of Bacteroidetes in them [51]. A study of pregnant women who are overweight and pregnant women who have normal weight showed that the composition of the microflora is different, with a proportionally higher number of Bacteroidetes and Staphylococcus in women who are overweight during pregnancy [52]. In addition, intestinal dysbiosis can alter the production of gastrointestinal peptides associated with satiety, resulting in increased food intake [53]. At this point, however, it should be mentioned that not all studies confirm such a significant contribution of the intestinal microbiota in the pathogenesis of obesity. Ley et al. [54] found identical numbers of Bacteroidetes and Firmicutes in people with obesity who were fed a high-fat diet after changing to a low-calorie diet. There have also been studies suggesting no relationship between Bacteroidetes/Firmicutes and diet and body mass index [55]. This topic still requires a lot of research and analysis, taking into account all possible factors that affect the credibility of the results [56]. The heterogeneity of the methods used to quantify the level of the gut microflora does not allow a proper comparison of the results obtained from different studies, as each technique is burdened with issues of accuracy, sensitivity, or specificity. Therefore, there is a need to standardize the techniques used to detect and classify the composition of the intestinal microflora in obese people [57]. Gender, age, genotype, and environmental conditions also affect the composition of the intestinal microbiota outside of the diet. Intestinal microbiota changes with age, as shown by comparing the microbiota of children, adults, and the elderly [58, 59]. It is possible to directly modulate the intestinal microflora with probiotics, prebiotics, antibiotics, or other therapeutic interventions. While several randomized controlled trials have been conducted on probiotics in obesity, the results are not yet convincing. Therefore, there is a lack of more randomized, placebo-controlled in this regard [57].

Bariatric Obesity Treatment and Nutritional Deficiencies

An effective therapy method recommended for people with morbid obesity (BMI \ge 40) is surgical treatment of obesity, that is, bariatric surgery aimed at both weight loss and improving quality of life [60]. Unfortunately, the effects of these treatments are often medium- and longterm complications associated with micronutrient deficiency as a result of reduced consumption or absorption [21, 61]. Therefore, the use of bariatric surgery in patients with extreme obesity can affect the metabolism of microelements and increase the risk of nutritional deficiencies [62]. The type of bariatric surgery performed may also affect the occurrence of nutritional deficiencies, especially of some microelements and macroelements, depending on which part of the gastrointestinal tract is bypassed [23]. A study by Guan et al. [63] showed that nutritional deficiencies were common in patients undergoing RYGB and sleeve gastrectomy. Vitamin D deficiency was the most severe (78.8%), followed by vitamin B_1 (39.2%), vitamin B₆ (28.0%), folate (26.8%), vitamin C (18.0%), albumin (13.4%), transferrin (11.6%), phosphorus (11.5%), and vitamin B_{12} (3.3%). One year after surgery, folate deficiency was found in 4% of RYGB patients and 10.8% of sleeve gastrectomy patients. The authors noted that despite postoperative routine multivitamin supplementation, the incidence of vitamin B₁₂ deficiency increased significantly in the RYGB group (16%) 12 months after surgery. Additionally, preoperative vitamin B₁₂ levels were independently associated with postoperative decline, and preoperative vitamin B₆ deficiency was a predictor of deficiency 1 year after surgery [64]. Newer procedures such as one anastomosis gastric bypass and single

anastomosis duodenal ileostomy are likely to have better metabolic effects, but the risk of malnutrition and vitamin A deficiency is higher [65]. For example, iodine is absorbed in the stomach and small intestine [66]. Copper is absorbed in both the stomach and duodenum, while vitamin B₁₂ must bind to internal factors in the stomach before it is absorbed in the ileum. Other microelements, including iron, zinc, selenium, chromium, manganese, vitamins A, C, E, and K, thiamine, riboflavin, folic acid, niacin, biotin, pyridoxine, pantothenate, and calcium, are absorbed in the duodenum or jejunum [62]. According to Correia-Horvath et al. [67], food consumption before bariatric surgery in people with obesity is a factor that requires more careful examination, as it can help regain and maintain proper nutritional status in the postoperative period. Calorie intake in people with obesity is usually excessive, but there may be insufficient amounts of essential nutrients, leading to undiagnosed deficiencies. Studies indicate that nutritional deficiencies are observed in patients qualified for surgery before surgery (so-called preoperative deficiencies), which particularly affect iron, calcium, folic acid, vitamin D, and vitamin B₁₂ [68]. Iron deficiency may occur in patients with obesity before surgery due to constant inflammation. One of the basic mechanisms may be the production of hepcidin, which reduces serum iron levels. Bariatric operations may exacerbate this [69]. In addition to the above-mentioned components, deficiencies of vitamin A, copper, zinc, and selenium are also observed [23, 70, 71]. Thiamine deficiency in the range of 16–47% among patients with obesity undergoing bariatric surgery has also been demonstrated [72]. Observation and taking action to compensate for preoperative deficits is an important element in avoiding more serious complications after bariatric procedures [73].

Summary

Conducting research on the role of malnutrition and micronutrient deficiencies is important not only in the context of obesity, but also in the pathophysiology of comorbidities [17]. Actions aimed at reducing body weight should be undertaken with the greatest possible care, as they may be associated with a reduced intake of nutrients [19]. Monitoring the concentration of minerals and vitamins in blood serum is a good practice in the treatment of obesity. The proper nutritional status of the body affects not only the state of health, but also the effectiveness of therapy [13].

Conclusion

- 1. Before and during the implementation of diet therapy in patients with obesity, a comprehensive assessment of nutritional status should be performed. This examination should be performed by a specialist using subjective and objective parameters such as nutritional interview, clinical history, anthropometric measurements, physical parameters, and laboratory results. Systematic screening for nutritional risk and standardized nutritional management of people with obesity can also help reduce healthcare costs.
- 2. The obesity medical care plan should include a lifestyle change, choosing healthy, high-nutrient foods to prevent malnutrition. Fortified foods should also be included to prevent shortages. The use of specific vitamin supplements can be incorporated into this practice. The current recommended nutrition standards are standard, but it seems necessary to develop specific standards for people with obesity. There is a need to conduct further research explaining the factors shaping nutritional deficiencies in people who are overweight or obese, as well as appropriate treatment strategies to prevent them.
- 3. Physicians, dietetics, and nutritionists should be aware of potentially preexisting nutritional deficiencies in overweight or patients with obesity, as well as nutritional deficiencies following bariatric procedures. Observation and taking action to compensate for preoperative deficiencies is an important element in avoiding complications after bariatric surgeries.
- 4. The complex interaction of gut bacteria with the host should be elucidated, as well as the possible influence of variables such as diet, gender, age, and exercise. Future evidence may help by using the modulation of these variables to transform the gut microflora into a healthier profile.
- 5. Modifying the composition of the GM with a mixture of probiotic strains may be a promising strategy for treating obesity. However, further research is needed.
- 6. Further research should be carried out using standardized next-generation sequencing technologies on the actual association of gut microflora composition with specific obesity-related phenotypes.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

All authors provided substantial contribution to the design and implementation of this study and to the generation of the manuscript. The contributions of each author are as follows: M. Kobylińska and K. Antosik conceived the design and purpose of the work. M. Kobylińska, K. Antosik, A. Decyk, and K. Kurowska analyzed the data and interpreted the results based on the available literature. M. Kobylińska, K. Antosik, and A. Decyk drafted the manuscript. A. Decyk, K. Antosik, K. Kurowska, and M. Kobylińska provided critical revisions and final approval of the version submitted.

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