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Original article

Nutrition

A clinical retrospective study — the investigation of folic acid concentration in caucasian cancer patients

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Introduction. Folates are one of the essential coenzymes for the proper synthesis, stability, and repair of DNA, playing a crucial role in renewing the population of rapidly dividing cells. Folates may act as a "double-edged sword". Folate in the diet may reduce the risk of cancer. However, folates may contribute to the progression of precancerous conditions or cancer. The study's primary objective was to evaluate the frequency of folic acid deficiency (FAD) in cancer patients and determine clinical factors associated with FAD.

Material and methods. Retrospective data were analyzed from 150 consecutive Caucasian cancer patients admitted to a major oncology hospital for cancer treatment. Folic acid (FA) plasma concentration, cancer and treatment type, histology, staging, comorbidities, nutritional status, body composition, and medical history of ailments were recorded.

Results. FAD was diagnosed in 18% of cancer patients. FAD was significantly more frequent in women than in men (81.5 *vs.* 18.5%; $p = 0.028$), in squamous cell carcinoma $p < 0.001$, in patients undergoing radiotherapy $p < 0.001$ and in dysphagic patients $p = 0.011$. The anthropometric and biochemical data analysis had no significant relationship with the occurrence of FAD.

Conclusions. FAD is more common in women with cancer than in men, regardless of the nutritional status determined by anthropometric or biochemical methods. Gender may play a role when assessing micronutrient status. Nutritional guidelines for cancer patients should include screening for micronutrient deficiencies. Further studies are needed to determine the role, dosage, and duration of FA supplementation recommended for specific cancer diagnoses and gender.

Keywords: cancer, folate, folic acid, folic acid deficiency, vitamins

Introduction

Folates in the general population

Folic acid (FA) and its derivatives belong to the group of folates, and differ in the degree of oxidation of the pyridine ring and the number of glutamic acid residues [1]. Folate is a naturally occurring form of vitamin B9 in food, while FA is a synthetic compound manifesting as a food additive or dietary supplement. Food folates have lower bioavailability than synthetic FA, 50% and 85%, respectively. Due to differences in the bioavailability of folates from food, their total amount is defined as the Dietary Folate Equivalent (DFE), where 1 µg of DFE is 1 µg of dietary folate, which in turn is equal to 0.6 µg of FA from fortified foods and dietary supplements or 0.5 µg of FA from a dietary supplement taken on an empty stomach [2].

The primary sources of folate are green vegetables such as spinach, parsley, asparagus, brussels sprouts, and broccoli. Legume seeds contain significant folates — edamame, beans, peas, and broad beans. Animal products are also sources

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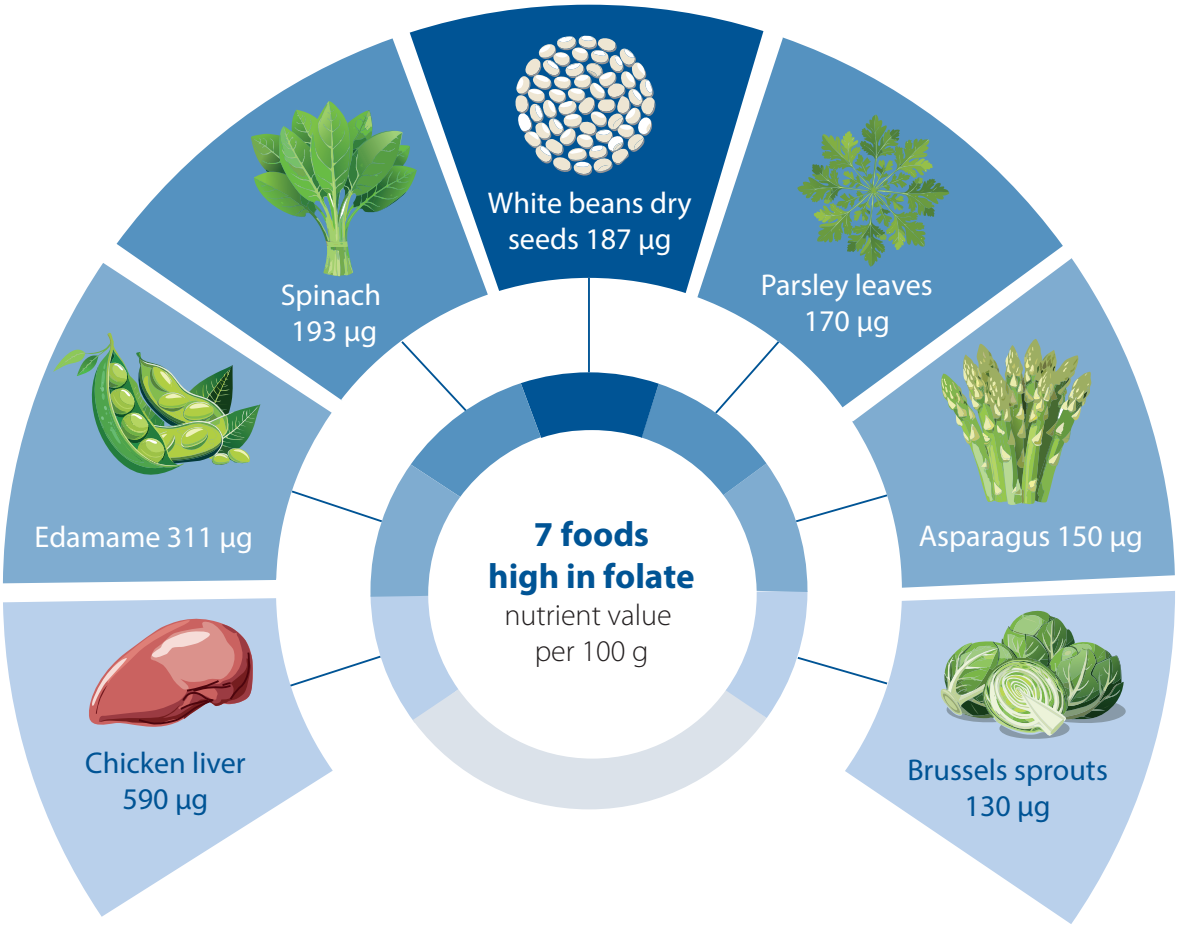

Figure 1. Folate content in food

of folates – mainly liver and egg yolks [3]. The richest sources of folate are shown in Figure 1.

Folates found in food products are unstable and sensitive to high temperatures, sunlight, oxygen, copper and iron ions, and the acidic pH of the environment. Significant folate losses occur during thermal processing — up to 30% during bread baking and up to 80% during cooking. The presence of ascorbic acid in food products has significantly reduced folates loss [4, 5].

There can be many causes of folate deficiency, including insufficient supply from the diet, alcohol consumption, malabsorption syndrome (inflammatory bowel disease, celiac disease, chronic intestinal failure), increased demand (pregnancy and lactation, inflammatory and cancer diseases, dialysis, dermatological diseases), taking certain medications (sulfasalazine, methotrexate, anticonvulsants, metformin) [6]. The National Institutes of Health (NIH) recommends 400 µg DFE for the American population for both women and men. Pregnant and breastfeeding women require 600 and 500 µg of DFE daily [1]. The guidelines of the European Food Safety Authority (EFSA) suggest a supply of 330 µg for the general population and a double dose for pregnant and breastfeeding women [7]. The European Society of Clinical Nutrition and Metabolism recommends a daily supply of 400–600 µg of FA. The upper level (UL) for adults for FA from fortified food or supplements (not including folate from food) is set at 1,000 µg a day. The harmful effects of FA overdosing have not been described [8].

Data from the 2013–2014 National Health and Nutrition Examination Survey (NHANES) show that most people in the United States consume adequate amounts of folates. The average daily intake of folate from food among adults is 602 µg DFE for men and 455 µg DFE for women. Still, certain groups, including women of childbearing age and African American women, are at risk of inadequate folate intake. In order to prevent complications resulting from folate deficiency, the US Food and Drug Administration (FDA) in January 1998 introduced the obligation to fortify certain food products with FA [9, 10]. The analysis of studies on folate intake in the Polish population in 2000–2010 showed that the average folate intake among adults ranged from 110 to 352 µg/person/ /day, depending on the subpopulation studied. In Poland, like in many European countries, there is no obligation to enrich

food products with FA, but there is still a growing range of fortified products, mainly breakfast cereals, juices, drinks, sweets, flour, cocoa, and margarine [11].

Folates and its derivatives are transformed in the human body into the biologically active form of tetrahydrofolate. It functions as a coenzyme in transferring one-carbon formalyl and hydroxymethyl groups and synthesizing purine and pyrimidine bases — the fundamental components of nucleic acids. Therefore, folates are necessary for all body cells to survive and proliferate, especially those that divide frequently (blood cells, epithelia). Folates also plays a significant role in the metabolism of amino acids, thanks to which it is possible to remethylate homocysteine to methionine, which is necessary for methylation reactions.

Folate deficiency leads to impaired cell division and methylation reactions necessary to regulate gene expression, as well as to the accumulation of toxic metabolites. Folic acid supplementation may reduce the risk of death from cardiovascular disease, which may be attributable to a reduction in serum homocysteine concentrations [12]. Due to improving nitric oxide bioavailability, folates can prevent and reverse endothelial dysfunction, a significant risk factor for cardiovascular disease [13]. Folic acid supplementation was associated with a lower risk of certain pregnancy complications — neural tube defect, megaloblastic anemia, low fetal weight, cleft lip and palate, preeclampsia, and congenital heart defects [14, 15].

Folates in the cancer patient population

Epidemiologic studies have suggested the protective role of folates on the risk of cancer of the colon, lungs, pancreas, esophagus, stomach, cervix, ovary, and breast [16]. Perinatal supplementation of FA reduces the incidence of neuroblastoma among children aged ≤ 17 years [17, 18]. Beneficial observations from epidemiological studies and the undeniable value of FA supplementation in reducing the risk of severe congenital neural tube defects and cardiovascular disease contributed to the introduction of mandatory food fortification with FA in North America, South Africa, Canada, and Australia in 1998. However, in subsequent years, studies have suggested the negative impact on transforming precancerous colorectal adenomas into malignant tumors [19–21]. The Aspirin and Folic Acid Polyp Prevention Study [19] reported in 2007 an unexpected increase in the incidence of advanced colorectal adenomas and prostate cancer during seven years of treatment with FA. Aspirin (300 mg/day) but not folate (0.5 mg/day) use was found to reduce the risk of colorectal adenoma recurrence in 945 patients in a double-blind, randomized trial by Logan and colleagues [20].

Moreover, the hypothesis that a temporal association exists between FA fortification and an increase in colorectal cancer raised more doubts about the safety of FA supplementation [22]. Based on animal studies, it has been observed that FA can act as a double-edged sword. On the one hand, its supplementation reduces the risk of cancer in healthy tissues. However, in the case of precancerous or already malignant lesions, it may be the cause of their accelerated progression [23]. In neoplastic cells, where DNA replication and cell division occur at an accelerated rate, interruption of folate metabolism causes ineffective DNA synthesis, inhibiting tumor growth. The first valuable lesson was learned in 1940 when Sidney Faber tried to use FA conjugates as a treatment in oncology. In a group of children with leukemia, the disease progressed rapidly after using FA [24]. This observation became the starting point for work on drugs from the antimetabolites group that block the action of folates, DNA replication, and restoration of the cancer cell population. Indeed, this has been the basis for cancer chemotherapy with several antifolate agents like methotrexate and 5-fluorouracil. All these contradictory and unclear reports on the role of folates and FA in carcinogenesis led to a meta-analysis involving 13 randomized trials and 50,000 individuals by Vollset E.S. and colleagues in 2013 [25]. During a weighted average scheduled treatment duration of 5 years, allocation to FA quadrupled plasma concentrations of FA (57,3 nmol/L for the FA groups *vs.* 13,5 nmol/L for the placebo groups) but had no significant effect on overall cancer incidence (1904 cancers in the FA groups *vs.* 1809 cancers in the placebo groups [risk ratio (RR) = 1.06; 95% confidence interval (CI) 0.99–1.13; p = 0, 10]. Supplemented dosage of FA was 0,5-5mg daily; only in one study was the dosage 40 mg daily.

Moreover, there was no significant effect of FA supplementation on the incidence of cancer of the large intestine, prostate, lung, breast, or any other specific site. Folic acid supplementation does not substantially increase or decrease cancer incidence during the first five years of treatment. Food fortification with FA is safe, and the amount of FA delivered with fortified food is definitely below the doses used in clinical trials.

Material and methods

The study population comprised 150 consecutive outpatients of the Maria Skłodowska-Curie National Research Institute of Oncology in Warsaw, recruited for the study between June 2022 and June 2023. The study received the positive opinion of Bioethics Committee (KB-078-10/24). The study population were divided into six cancer groups: head and neck, upper gastrointestinal tract, pancreas, colon, breast, and gynecological. The groups were equal in size, 25 patients each.

The primary goal of the analysis was the prevalence of FA deficiency in cancer patients. Then, we tried to find clinical factors associated with FA deficiency (FAD). The concentration of FA was determined during the patient's first visit to the Institute's nutritional outpatient clinic.

Data about the type and stage of cancer, histopathological diagnosis, treatment type, nutritional status, and ailments were collected. Nutritional status was determined based on anthropometric analysis [body weight, body mass index (BMI), weight loss over the last six months], body composition [lean body

mass and adipose tissue from bioelectrical impedance testing (BIA), Body Composition Analyzer MC-780MA] and laboratory parameters (albumin, blood cells count). The local laboratory has established a folate concentration in blood samples with a cut-off value of 4.80 to 37.30 ng/mL. Folic acid deficiency was defined as < 4.80 ng/mL. Folic acid concentration was determined in serum using the electrochemiluminescence method Elecsys® Folate III on a Roche Cobas analyzer. Measuring range is 0.6–20.0 ng/mL or 1.36–45.4 nmol/L, with limit of detection = 1.2 ng/mL (2.72 nmol/L). Blood for testing was collected on an empty stomach.

Statistical analysis was performed using IBM SPSS Statistics v. 29.0. To determine the relationship between qualitative variables, Fisher's exact test was performed. The phi coefficient for 2×2 tables or the Cramers'V coefficient for larger tables were used as the effect size. To compare the two groups in terms of quantitative variables, an analysis was performed using the Mann-Whitney U test. The significance level was taken as $\alpha \leq 0.05$.

Results

The general group characteristic n = 150, divided into six equal groups according to a cancer diagnosis is presented in Table I. The investigated group was assessed using clinical variables like sex, age, cancer type, histopathology, ailments, BMI, BIA, albumin concentration, and blood count.

Folic acid deficiency and gender

Folic acid deficiency was recognized in 18% of patients in the study group (Tab. II) and statistically more often in women than in men (81,5 *vs.* 18,5% p = 0,028) (Tab. III).

Folic acid deficiency and cancer type

Folic acid deficiency was more common with head and neck cancer than pancreas (32% *vs.* 4%; p = 0.023; φ = 0.36), with gynecological cancer more common than colorectal (40% *vs.* 8%; p = 0.018; φ = 0.38), pancreas (40% *vs.* 4%; p = 0.005; φ = 0.44). No differences were noted between the other types (p > 0.05). Data presented in Table IV.

Folic acid deficiency and histopathology

The squamous cell carcinoma group had a higher incidence of FAD than the adenocarcinoma group (40% *vs.* 10.5%; p < 0.001; φ = 0.33). No differences were noted between the other groups (p > 0.05). Data presented in Table V.

Folic acid deficiency and oncological treatment

It was shown that among patients undergoing radiotherapy, the percentage of FAD was significantly more frequent than among patients undergoing chemotherapy (64.3% *vs.* 6.1%; p < 0.001, φ = 0.62), hormonotherapy (64.3% *vs.* 16.7%; p = 0.010; φ = 0.49) and cancer survivors (64.3% *vs.* 16.1%; p < 0.001; φ = 0.44). Folic acid deficiency was more common among patients undergoing surgery than chemotherapy (37.5% *vs.* 6.1%; p = 0.031; φ = 0.36). Data presented in Table VI.

Folic acid deficiency and ailments

During oncological treatment, various symptoms were recorded: nausea and vomiting, diarrhea, constipation, dysphagia, pain, smell and taste disturbances, anorexia, and dry mouth. Other symptoms reported by patients were tiredness and flatulence.

Among patients experiencing dysphagia, FAD was significantly more frequently than when experiencing pain (40% *vs.* 0%; p = 0.005; φ = 0.48) and in the group with no ailments (40% *vs.* 14.8%; p = 0.028; φ = 0.27; Tab. VII).

The analysis did not show a significant relationship between the concentration of FA and age or nutritional status — body mass index, lean and fat body mass, albumin concentration or blood count.

No significant association was found between disease advancement (local *vs.* metastatic) and FAD.

Discussion

A deficiency of vitamins and trace elements in oncological patients is common. Recommendations regarding micronutrient supplementation are dedicated to the general population, not cancer patients. The current ESPEN recommendation on the use of micronutrient supplementation does not recommend exceeding the recommended dietary allowance (RDA), adequate intake (AI) in the group of cancer patients [5]. Nevertheless, it is known that the demand for micronutrients in oncological patients may be significantly increased in various clinical situations and concerns primarily water-soluble vitamins and zinc [26, 27].

Vitamin D deficiency in cancer patients examined in the same oncology center reached 66.8% [28], and zinc deficiency 68% [29]. Deficiencies of micronutrients such as vitamin D, zinc or folate have been considered an important factor in increasing cancer risk [30, 31].

There is little data in the literature on the prevalence of FAD in the general population, in older adults it is 12.6–16.4% [32]. However, there is no data on the frequency of FAD in oncological patients. Therefore, FAD found in our study, reaching 18%, can be defined as a significant clinical problem.

Scarce data are available for FAD in cancer patients in association with gender. In the Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial (PLCO), dietary folate intake was investigated, and the risk of pancreatic cancer among women with the highest folate intake significantly decreased [hazard ratio (HR) = 0.47; 95% CI: 0.23–0.94; p for trend = 0.09)] but not among men [33]. In a study based on a self-administered dietary questionnaire analysis filled out by 56,837 women enrolled in the Canadian National Breast Screening Study, folate intake was inversely associated with colorectal cancer risk in women [incidence rate ratio (IRR) = 0.6;

Table I. General group characteristics

Variable	Statistics
Sex, n (%)	
Women	93 (62.0%)
Men	57 (38.0%)
Age, mean (SD)	62.67 (11.13)
Cancer type, n (%)	
Head and neck	25 (16.7%)
Esophagus and stomach	25 (16.7%)
Colorectal	25 (16.7%)
Breast	25 (16.7%)
Pancreas	25 (16.7%)
Gynecological	25 (16.7%)
Histopathology, n (%)	
Squamous cell carcinoma	35 (23.3%)
Adenocarcinoma	105 (70.0%)
Low-differentiated or undifferentiated cancer	8 (5.3%)
Sarcoma	2 (1.3%)
Ailments, n (%)	
Smell or taste disorders	8 (5.3%)
Nausea and vomiting	5 (3.3%)
Lack of appetite	49 (32.7%)
Early satiety	54 (36.0%)
Dysphagia	20 (13.3%)
Dry mouth	7 (4.7%)
Diarrhea	19 (12.7%)
Constipation	25 (16.7%)
Pain	16 (10.7%)
Aphthae	1 (0.7%)
Other	9 (6.0%)
No ailments	21 (14.0%)
BMI [kg/m^2], n (%)	
< 18.9	21 (14.0%)
19–24.9	68 (45.3%)
25–29.9	44 (29.3%)
30–34.9	12 (8.0%)
> 35	5 (3.3%)
BIA — lean body mass — FFM, n (%)	
Deficiency	8
Standard	54
Excess	29
BIA — adipose tissue, n (%)	
Deficiency	23
Standard	46
Excess	22
Treatment, n (%)	
Chemotherapy	48 (32.0%)
Radiotherapy	14 (9.3%)
Chemoradiotherapy	3 (2.0%)
Immunotherapy	1 (0.7%)
Surgery	10 (6.7%)
Hormone therapy	18 (12.0%)
Cancer survivors	56 (37.3%)
Albumin concentration, [g/L] M (SD)	39.21 (3.15)
WBC [g/L], M (SD)	6.91 (5.12)
Hbg [g/dL], M(SD)	12.22 (1.60)
MCV [fl], M (SD)	90.10 (8.16)
Neutrocytes [g/L], M (SD)	4.51 (4.55)
Lymphocytes [g/L], M (SD)	1.57 (0.75)

BIA study norms:
Body fat women: deficiency < 24%, standard ≥ 24%, < 36%, excess ≥ 36%
Body fat men: deficiency < 12%, standard ≥ 12%, < 25%, excess ≥ 25%
Lean body mass women: deficiency: < 50%, standard ≥ 50%
Lean body mass men: deficiency: < 53%, standard ≥ 53%
BIA — bioelectrical impedance analysis; BMI — body mass index; FFM — fat-free mass; SD — standard deviation

95% CI: 0.4–1.1; p for trend = 0.25] [34]. Dietary folate intake, especially in case of alcohol consumption > 4 g/daily, was associated with a 25% decrease in the risk of ovarian cancer for the highest *versus* the lowest quartile level of intake [35]. Female gender and high folate intake probably play a role in the risk of developing some types of cancer. In our study, the reproductive organ patient group has a significantly higher incidence of FAD. However, how to treat the deficiency of FA in this group of patients needs to be investigated. Folates are crucial for the DNA metabolism of any cell, including cancer cells. Folate receptor alpha (FRα) is a folate-binding protein overexpressed on ovarian cancer cells (72% of primary and 82% of recurrent ovarian cancers) [36]. Folate receptor alpha, encoded by the FOLR1 gene, responsible for adequate neural and cardiovascular system development, has attracted considerable interest due to its high expression

Table II. Analysis of the prevalence of folic acid deficiency in the study sample

Concentration	Folic acid	
	n	[%]
Deficiency	27	18.0
Norm	123	82.0

in several lung, renal, and breast cancer types. Despite their anti-tumor effects in preclinical models, folate-cytotoxic drug conjugates and no conjugated humanized antibody have yet to demonstrate clinical efficacies [37]. Phase III trials with farletuzumab (anti-FRα antibody) showed a favorable toxicity profile but controversial antitumor activity [38]. Therefore,

Table III. Fisher's exact test for the prevalence of folic acid deficiency depending on gender

Gender	Folic acid concentration					
	Deficiency		Norm			
	n	[%]	n	[%]	p	φ
Women	22	81.5	71	57.7	**0.028**	0.19
Men	5	18.5	52	42.3		

Table IV. The prevalence of folic acid deficiency depending on cancer type

Cancer type	Folic acid concentration (deficiency)	
	n	[%]
Head and neck	8	32.0
Esophagus and stomach	3	12.0
Colorectal	2	8.0
Pancreas	1	4.0
Breast	4	16.0
Gynecological	10	40.0

Table V. The prevalence of folic acid deficiency depending on histopathology

Histopathology	Deficiency	
	n	%
Squamous cell carcinoma	14	40.0
Adenocarcinoma	11	10.5
Low-differentiated or undifferentiated cancer	2	25.0
Sarcoma	0	0.0

Table VI. The prevalence of folic acid deficiency depending on the oncological treatment type

Oncological treatment type	Deficiency	
	n	[%]
Chemotherapy	3	6.1
Radiotherapy	9	64.3
Surgery	3	37.5
Hormonotherapy	3	16.7
Cancer survivors	9	16.1

Table VII. The prevalence of folic acid deficiency depending on ailments

Ailments	Deficiency	
	n	[%]
Smell or taste disturbances	1	12.5
Nausea and vomiting	0	0.0
Lack of appetite	9	18.4
Dysphagia	8	40.0
Dry mouth	0	0.0
Diarrhea	2	10.5
Constipation	8	32.0
Pain	0	0.0
Aphthae	0	0.0
Other (tiredness)	4	19.0
No ailments	8	14.8

the results of our study, where FAD is significantly more common in women, prompt us not only to look for FAD but also to interpret the results in the context of gender. The finding may be significant for women of reproductive age who plan to have children after cancer therapy. Based on previous literature data, no relationship has ever been found between high, natural dietary folate intake and the risk of cancer progression. When comparing the highest to lowest intake of folate, higher intake was associated with a nearly 50% decreased risk for squamous cell carcinoma of the head and neck, analyses have shown that every 100 mcg/day increase in folate intake was associated with a 4.3% decrease in risk of head and neck cancer [39]. Another study found a 35% reduced risk for oral cavity and pharyngeal, 41% reduced risk of esophageal, 34% reduction in pancreatic, and 16% reduction in bladder cancers [40]. Furthermore, FA daily intake up to 5 mg does not appear to influence the risk of cancer progression [12]. Therefore, perhaps adopting a strategy of offering a folate-rich diet and moderate oral FA supplementation is a safe strategy for cancer patients with FAD. On the other hand, other factors may influence folate metabolism. One of them is gene polymorphism; the other is ethnicity [41]. Gene encoding methylenetetrahydrofolate reductase (MTHFR) directly affects DNA synthesis and methylation due to affecting nutrient bioavailability, and has been associated with an increased risk of certain cancers. A different mutation in the MTHFR genes has been associated with increased risk of lung, hepatocellular, breast, brain, and ovarian cancer in Asian populations and breast cancer in Turkish population [28].

Finally, our study draws attention to a dangerous triangle of variables with significantly frequent co-occurrence, namely squamous cell carcinoma — radiotherapy — dysphagia and micronutrient deficiency. We described similar observations among patients of our center when examining vitamin D and zinc deficiency [16, 17]. Squamous cell carcinomas are the dominant histopathological type among head and neck cancers. One of the primary methods of treating this group of cancers, apart from surgery, is chemoradiotherapy. Chemoradiation is an aggressive treatment method associated with numerous side effects, primarily post-radiation mucositis, which is stage III in 60% of patients [42]. Severe radiation exposure leads to dysphagia, weight loss, and the development of deficiencies in numerous micronutrients, including FAD. Various supportive treatment strategies were undertaken, including supplementation of micronutrients such as glutamine, arginine, omega-3 fatty acids, zinc and FA to reduce the severity of mucositis [43]. The more significant the FAD, the greater the risk of occurrence and severity of radiation-mucositis, especially in head and neck cancer patients [44]. In a preclinical study, FAD led to the misincorporation of uracyl into DNA, non-effective DNA repair, and chromosome breakage. This same ability has ionising radiation responsible for DNA and chromosome damage. Antioxidants during radiotherapy diminish free radicals' activity, managing inflammatory responses, and attenuating apoptosis signaling pathways in radiosensitive organs. Folic acid deficiency and radiotherapy work synergistically. Aneuploidy of chromosome 21, apoptosis, and necrosis were increased by FAD [45]. In a randomized trial, 540 patients diagnosed with head and neck cancer undergoing radiotherapy were enrolled in the study investigating the influence of antioxidants on adverse events like mucositis and QoL. The reduction of adverse events was statistically significant in antioxidants group (OR = 0.38; 95% CI: 0.21–0.71). However, the rate of local recurrence of the head and neck tumor tended to be higher in the supplement arm of the trial (HR = 1.37; 95% CI: 0.93 to 2.02) [46]. Several studies have shown that antioxidants can effectively reduce the toxicity of radiotherapy, but unfortunately, they also reduce the therapeutic effect of this treatment method [47, 48]. However, whether antioxidants alter antitumor effects during radiotherapy remains unclear. The systematic review with 49 RCTs concludes that the harm caused by antioxidant supplementation remains unclear for cancer therapy patients except for smokers undergoing radiotherapy, where it is significantly harmful [49].

Study limitations

The heterogeneity of the study group and, consequently, different methods of oncological treatment may have different effects on FA resources in the body. In addition, variables related to lifestyle (addictions, physical activity, diet), the presence of other chronic diseases, and medications used may also affect the obtained results.

Conclusions

Folic acid deficiency in cancer patients is common, especially in women, regardless of nutritional status measured by anthropometric or biochemical tools. Although folates may be involved in many ways in cancer proliferation, it seems to be underestimated. The question of how to treat FAD during active oncological treatment, especially radiotherapy, seems particularly interesting. In light of the results of our study, patients with reproductive organ cancer should be particularly screened for FAD. Nutrition guidelines for cancer patients should include screening for micronutrient deficiencies. Further studies are needed to determine the role, dosage, duration, and form of the supplementation recommended for specific cancer diagnoses and gender.

Article information and declarations

Data availability statement

Data are not available.

Ethics statement

The study received a positive opinion of Bioethics Committee (KB-078-10/24).

Authors contributions

Aleksandra Kapała — conceptualization, formal analysis, methodology, supervision, validation, writing — original draft preparation, writing — review & editing.
Katarzyna Różycka — data curation, investigation, visualization, writing — original draft preparation.
Marta Dąbrowska-Bender — data curation, investigation.

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Conflict of interest

The authors declare no conflict of interest.

Supplementary material

None.

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