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MATERNAL NUTRITION FACTORS AND SOCIO-ECONOMIC STATUS IN CHILDHOOD CANCER

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Abstract – *Objective:* *Cancer is described as a condition in which cells divide without control. Dietary pattern plays an important role in some cancer incidence. The aim of this study was to determine nutritional risk factors and socio-economic status (SES) in childhood cancer.*

Materials and Methods: *This cross-sectional study was conducted on 71 cancerous children for 2 years. Their mothers were asked about nutritional habits' information during pregnancy as well as SES. In addition, data of the breast-feeding of these children was assessed. Data were collected through a face-to-face interview with mothers. Data were analysed by descriptive analysis and chi-square test with SPSS (Statistical Package for Social Sciences, version 16) software.*

Results: *Mean age of these children was 0-16 years old, and 54.9% of them were girls. 81.2% of them were from urban areas and 18.3% were from rural areas. Among of these children, 41.4% suffered from Acute Lymphoblastic Leukemia (ALL). About 83.1% of their mothers consumed routine supplements (iron, foliate and multivitamin) during pregnancy. 75% of these children consumed nutritional supplements (vitamin A and D) in the first two years of life. 74.6% of their mothers drank tea daily. There was no significant difference between the children breastfeeding, complementary feeding information and the type of cancer.*

Conclusions: *Among all the considered factors, just in the case of tea consumption (as a known risk factor) we achieve a parallel result to our assumed hypothesis. Since diet is a modifiable factor, therefore, assessing the nutritional status of cancer patients is a good approach to understanding the risk factors for cancer.*

KEYWORDS: *Childhood cancer, Nutrition factors, SES.*

INTRODUCTION

Cancer consists of a diverse mix of diseases occurring in every part of the body and is one of the major public health problems. It has shifted from the third cause of mortality in 1990 to the second cause after cardiovascular diseases (CVDs). Incidence and type of the cancer in children is different from adults. The most common types of childhood cancers are leukemia, brain tumors, central nervous system (CNS) and lymphoma[1,2]. Childhood cancer incidence has shown an increase over time since the mid of the last century and its incidence range raised from 130 to 160 cases per million children[3]. Cancers are assumed to be a multifactorial disease that progress as a complex and chronic process[4,5]. The main reason of cancer is unknown; however, common well-known risk factors include genetic, environmental, and exogenous factors such as tobacco smoking, alcohol consumption, diet, overweight and obesity[6,7].

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Tobacco is one of the major risk factors for different malignancies like myeloid leukemia. Some studies have indicated that parental smoking is highly important for the manifestation of childhood leukemia[8,9]. Many epidemiological studies suggest that dietary pattern plays an important role in cancer incidence. The evidence indicates that 1/3 of cancers is associated with consumed foods, and nutrition plays a crucial role in decreasing the risk of some solid tumors in adults[10,11]. In the last years, maternal and child dietary pattern has received considerable attention to risk of Acute Lymphoblastic Leukemia (ALL) in children[12,13]. Intake of N-nitroso resources by mothers during pregnancy and children in the first years of life could result in carcinogenic formation and transference of these compounds to the brain tissue[14]. In some other studies, the association between other dietary compounds, including oranges/bananas and orange juice consumption by children or maternal coffee, vegetable and protein intake during pregnancy, and some kinds of childhood cancer (brain tumors, ALL, Acute Myeloid Leukemia (AML), etc.) has been considered[15,16].

Breast-feeding is another studied factor in relation to the childhood cancer. Mother milk has different protective, anti-infective and immune modulating properties that have been confirmed in some studies. The studies have also indicated that breastfeeding has a protective effect on ALL and AML[17-19]. Since there were limited studies in the field of the effects of maternal diet during pregnancy and child's diet on the risk of childhood cancers, we aimed to assess nutritional and environmental risk factors (parental age and smoking…) on the childhood cancer.

MATERIALS AND METHODS

Study design and population

This cross-sectional study was conducted on 71 cancerous children admitted to Mohammad Kermanshahi Hospital in Kermanshah Province (West of Iran). Sample size was calculated based on the total cancerous children with a 95% confidence interval and 90% study power. Patients were randomly selected using the convenience sampling method. We used a questionnaire to collect data about nutritional and some environmental risk factors (parental smoking, occupational status, etc.). The validity and reliability of the questionnaire were confirmed under supervision of several nutritionists and by conducting a pilot study (results are not shown).

Inclusion criteria were hospitalization in the Oncology Department of Mohammad Kermanshahi Hospital and the parental consent to participate in this study. Mothers who did not provide the complete information about their pregnancy condition were excluded from our study.

At the beginning of the study, demographic information and socio-economic status (SES) were entered into the first part of the questionnaire. This part contains some demographic information, including gender, age, habitat, parental educational level, and parental occupational status.

Part 2: To determine information about mother's confinement and maternal nutritional factors during pregnancy, we asked the mothers about childbirth type, their age in delivery time, number of delivery order, their pregnancy duration, nutritional risk factors (including consumption of fast food, fruits, vegetables, tea and coffee), height, and weight before pregnancy. According to height and weight before pregnancy, we calculated the body mass index (BMI) (kg/ m^2) by weight (kg) divided height square (m^2). Afterward, it was divided according to World Health Organization (WHO) criteria for the Asian population. Therefore, BMI< 18.5 kg/ m^2 was considered underweight; 18.5–24.9 kg/ m^2, normal weight; 25.0–29.9 kg/ m^2, overweight; and ≥ 30 kg/ m^2 was considered obesity[20].

The last part was related to children breastfeeding and complementary feeding information, including birth weight, breastfeeding duration, exclusive breastfeeding, artificial milk consumption and complementary feeding.

All data were collected through a face-to-face interview with mothers by trained experts within 2 years.

Statistical analysis

The data were analyzed by the SPSS (Statistical Package for Social Sciences, version 16, SPSS Inc., Chicago, IL, USA) software. Descriptive statistics were used to examine the data (frequency and percentage) that were reported in tables and graph. Chi-square was used to determine the difference between the qualitative variables (including age, children gender, SES, information about mother's confinement, maternal nutritional factors during pregnancy, children breastfeeding and complementary feeding information) and type of cancer. In all tests, *p*-value was considered lower than 0.05.

RESULTS

In the present study, the participants were aged 0-16 years old (39.4% ≤5 years) from Kermanshah and the surrounding provinces of Loristan (Ilam, Kurdistan). In this regard, 54.9% of the participants were female and 45.1% were male, and 81.2% of them

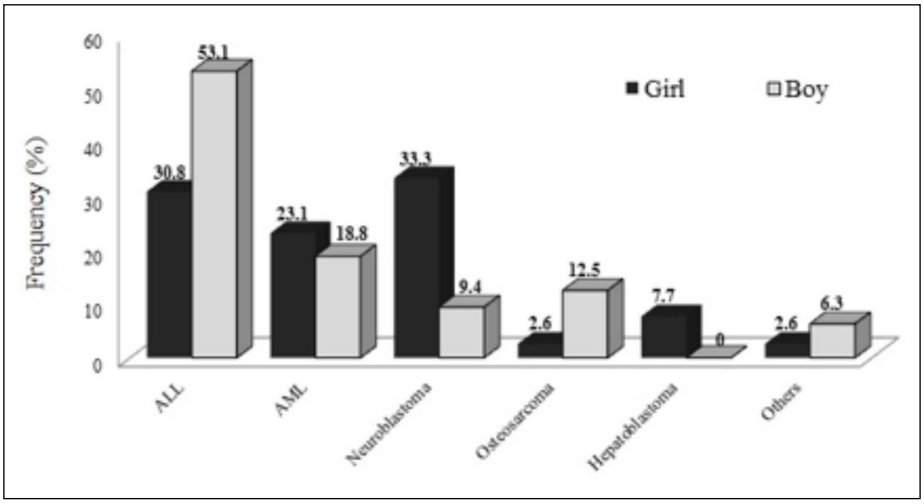

Fig. 1. The malignancies prevalence in studied subjects in both sexes.

were inhabited in urban areas and the rest of them lived in rural areas.

In this study, the prevalence of ALL was higher than that of another type of cancer in males (53.1%). Figure 1 presents the malignancies prevalence percentage in both sexes. According to the chi-square test, a significant difference was observed between gender and type of cancer (p= 0.015). There was no significant difference between data about SES and type of cancer (Table 1).

Our results also showed that only 20% of the participants had a family history of cancer. In the case of childbirth type, 57.1% of the participants were born from natural childbirth, and the rest (42.9%) were born with cesarean-section (C/S). Table 2 presents the information about childbirth type, number of delivery order, mother's age, and BMI before pregnancy based on the type of cancer. In this study, among information about mother's confinement, only pregnancy duration had a significant difference with type of cancer (p= 0.024).

Our findings have indicated that approximately 83.1% of mothers consumed routine supplements (iron, foliate and multivitamin) during pregnancy. Concerning parental smoking pattern, we found that 98.6% of the mothers did not smoke during pregnancy and after delivery. In addition, our results indicated that only 22.5% of their fathers were smokers, and there was no significant difference between parental smoking and type of cancer (p= 0.137). Findings related to the maternal dietary during pregnancy showed that frequency of tea consumption was higher than that of other nutritional factors (Table 3).

The results of this study indicated that approximately 75% of these children consumed supplements (iron, Vitamin A+D) in the first two years of life. Most studied children had normal weight at birth and were breastfed in the first two years of life. Table 4 shows no significant difference between children breastfeeding, complementary feeding information, and type of cancer.

DISCUSSION

Cancer is the most common cause of disease-related death in children and accounts for 94% of all deaths in children aged 0–14 years [3,20]. Different childhood cancer therapies, such as surgery, radiotherapy, and chemotherapy, have progressed considerably. Despite these advances, most children with cancer live in low- or middle-income countries, where new cancer therapies are not readily accessible; therefore, a focus on nutritional aspects could serve to raise the standard of care feasibly [21,22].

The primary focus of the current study was on describing nutritional and SES risk factors for childhood cancer among children under 16 years of age, mother dietary pattern during pregnancy, parental occupational class, other SES factors, children birth weight, exclusive breastfeeding, and complementary feeding before being sick. In previous studies, the relationship between some environmental, socioeconomical and nutritional factors such as parental smoking pattern, educational level, family history of cancer, breastfeeding, occupational status, and childhood cancer was considered [6,7]. A number of animal and human studies indicated that preconception maternal nutrition and specific dietary factors (folic acid supplementation and fruit and vegetables, risk related to cured meat consumption) were associated with risk of ALL in children and following generations [15, 23].

According to the results of our study, approximately 84% of mothers daily consume usual supplements (iron, folate, multivitamin etc.) during pregnancy and 50% and 30% daily consume fruits and vegetables sources, respectively (the most common source of folate and other vitamins).

TABLE 1. Difference between SES and type of cancer in studied subjects (n=71).

Variables	*Category*	*ALL**	*AML*	*Neuroblastoma*	*Osteosarcoma*	*Hepatoblastoma*	*Others*	*p***
Gender of children	Boy (n=32)	17 (53.1)	6 (18.8)	3 (9.4)	4 (12.5)	0 (0)	2 (6.2)	0.015
	Girl (n=39)	12 (31.6)	9(23.7)	13 (34.2)	1 (2.6)	3 (7.9)	0 (0)	
Habitat	Urban (n=58)	22 (40)	12 (21.8)	15 (27.3)	3 (5.5)	2 (3.6)	1 (1.8)	0.245
	Rural (n=13)	6 (46.2)	3 (23.1)	0 (0)	2 (15.4)	1 (7.7)	1 (7.7)	
Mothers' educational level	Illiterate (n=4)	1 (25)	0 (0)	1 (25)	1 (25)	0 (0)	1 (25)	0.632
	< Diploma (n=42)	16 (39)	12 (29.3)	7 (17.1)	3 (7.3)	3 (7.3)	0 (0)	
	Diploma (n=19)	10 (52.6)	1 (5.3)	7 (36.8)	0 (0)	0 (0)	1 (5.3)	
	Academic educational (n=6)	2 (33)	2 (33)	1 (16.7)	1 (16.7)	0 (0)	0 (0)	
Fathers' educational level	Illiterate (n=4)	2 (50)	0 (0)	1 (25)	1 (25)	0 (0)	0 (0)	0.349
	< Diploma (n=34)	14 (41.2)	9 (26.5)	4 (11.8)	3 (8.8)	3 (8.8)	1 (2.9)	
	Diploma (n=15)	7 (50)	3 (21.4)	4 (28.6)	0 (0)	0 (0)	0 (0)	
	Academic educational (n=18)	6 (35.3)	3 (17.6)	6 (35.3)	1 (5.9)	0 (0)	1 (5.9)	
Mothers' occupational status	Householder (n=68)	28 (42.4)	14 (21.2)	15 (22.7)	4 (6.1)	3 (4.5)	2 (3)	0.443
	Workingwoman (n=0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	
	self-employment (n=0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	
	Employee (n=3)	0 (0)	1 (33)	1 (33)	1 (33)	0 (0)	0 (0)	
	Dead (n=0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	
	Retired (n=0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	
Fathers' occupational status	Unemployed (n=4)	1 (25)	1 (25)	0 (0)	1 (25)	1 (25)	0 (0)	0.128
	Workingman (n=17)	11 (68.8)	1 (6.2)	2 (12.5)	1 (6.2)	0 (0)	1 (6.2)	
	self-employment (n=31)	12 (41.4)	10 (34.5)	4 (13.8)	1 (3.4)	2 (6.9)	0 (0)	
	Employee (n=17)	5 (29.4)	2 (11.8)	8 (47.1)	1 (5.9)	0 (0)	1 (5.9)	
	Dead (n=1)	0 (0)	0 (0)	1 (100)	0 (0)	0 (0)	0 (0)	
	Retired (n=1)	0 (0)	1 (100)	0 (0)	0 (0)	0 (0)	0 (0)	

*ALL: Acute Lymphoid Leukemia; AML: Acute Myeloid Leukemia.
** p was obtained by Chi- Square.

TABLE 2. Difference between information about mother's confinement and type of cancer in studied subjects (n=71).

Variables	*Category*	*ALL**	*AML*	*Neuroblastoma*	*Osteosarcoma*	*Hepatoblastoma*	*Others*	*p***
Childbirth type	Natural	12 (30.8)	9 (23.1)	9 (23.1)	4 (10.3)	3(7.7)	2 (5.1)	0.208
	Cesarean- Section (C/S)	16 (53.3)	6 (20)	7 (23.3)	1 (3.3)	0 (0)	0 (0)	
Mothers' age in delivery time	< 18 years	2 (28.6)	4 (57.1)	0 (0)	1 (14.3)	0 (0)	0 (0)	0.331
	18-35 years	24 (44.4)	9 (16.7)	12 (22.2)	4 (7.4)	3 (5.6)	2 (3.7)	
	> 35 years	3 (33.3)	2 (22.2)	4 (44.4)	0 (0)	0 (0)	0 (0)	
Number of delivery order	≤ 3	25 (42.5)	12 (20.3)	13 (22)	4 (6.8)	3 (5.1)	2 (3.4)	0.864
	> 3	3 (30)	3 (30)	3 (30)	1 (10)	0 (0)	0 (0)	
Pregnancy duration	≤ 8 month	5 (83.3)	0 (0)	0 (0)	1 (16.7)	0 (0)	0 (0)	0.024
	> 8 month	24 (37.5)	15 (23.4)	16 (25)	4 (6.2)	3 (4.7)	2 (3.1)	
Mothers' BMI before pregnancy	< 18.5	5 (71.4)	0 (0)	1 (14.3)	1 (14.3)	0 (0)	0 (0)	0.376
	18.5- 24.99	19 (50)	8 (21.1)	6 (15.8)	2 (5.3)	2 (5.3)	1 (2.6)	
	25- 29.99	4 (20)	5 (25)	8 (40)	2 (10)	1 (5)	0 (0)	
	≥ 30	0 (0)	2 (66.7)	1 (33.3)	0 (0)	0 (0)	0 (0)	

*ALL: Acute Lymphoid Leukemia; AML: Acute Myeloid Leukemia.
**p was obtained by Chi- Square.

TABLE 3. Maternal dietary intakes during pregnancy.

N (%)	Variable
Fast-food consumption	
Weekly	13 (18.4)
Monthly	7 (9.9)
Seldom	27 (38)
Never	24 (33.1)
Fruit consumption	
Daily	35 (49.3)
Weekly	26 (36.6)
Monthly	3 (4.2)
Seldom	7 (9.9)
Vegetable consumption	
Daily	20 (28.2)
Weekly	36 (50.7)
Monthly	13 (18.3)
Seldom	2 (2.8)
Tea consumption	
≥ 5 cup per day	53 (74.6)
5-7 cup weekly	7 (9.9)
Monthly	9 (12.6)
Never	2 (2.9)
Coffee consumption	
1-2 cup daily	1 (1.4)
3-4 cup weekly	1 (1.4)
Monthly	1 (1.4)
Never	68 (95.8)

Some specific nutrients, including folate and vitamin B12 (which are methyl group donors) can alter DNA methylation and subsequently cause alterations in epigenetic mechanisms, and deficiency of them can lead to creation of different phenotypes or diseases, including cancers in the following generations. Bailey et al[24] showed that higher levels of dietary folate and vitamin B12 of pregnant mothers appeared to be related to a reduced risk of ALL [24]. Metayer et al[25] indicated that maternal prenatal use of vitamins and folic acid reduced the risk of both ALL and AML.

Furthermore, fruits and vegetables are good sources of vitamin C, which is an antioxidant that can protect DNA from oxidative damages and prevent the production of carcinogenic agents, including N-nitroso compounds in the GI tract [26]. Bunin et al[27] investigated the effect of some supplements on medulloblastoma during pregnancy. They demonstrated the protective role of multivitamins, iron, and calcium in pregnancy and the preconception period. Tower et al[28] showed that the absence of the folate supplementation consumption by mothers was related to an increased risk of the childhood leukemia.

In the current study, we also assessed children's birth weight. The results indicated that 8.5% of children had birth weight lower than 2500 g (LBW), 4.2% had birth weight higher than 4000 g and the rest (87.3%) had normal birth weight (2500–4000 g). Young et al[26] investigated the protective relationship between high birth weight and childhood leukemia. Smulevich et al[29] also reported that LBW was significantly related to the leukemia risk. Three supposed mechanisms of the association between birth weight higher than 4000 g (HBW) and risk of malignancies in children are illustrated. The first one is mainly related to the Insulin-like growth factor 1 (IGF-1). It is assumed that children with higher birth weight have higher levels of IGF-1, and this factor has a stimulating effect on the proliferation of progenitor and pre-malignant cells. The second mechanism demonstrates that massive bone marrow subsequently in HBV children increases the existence chance of at-risk cells to being malignant and ultimately the third theory, which indicates IGF-1 secreted from pre-malignant cells that can increase birth weight [28].

Based on the reported results of our study, 98.6% of mothers did not smoke during pregnancy and after delivery, and only 22.5% of fathers were smokers. Several studies have addressed the relationship between parental smoking and childhood cancer. Some of them reported no significant association and a positive association between parental smoking and risk of malignancies, especially leukemia, in the next generation [23,30].

The previous studies demonstrated that the preconception or exposure to carcinogenic compounds through smoking during pregnancy can cause DNA damage. They may also have indirect effects through affecting metabolism, finally leading to develop some cancers such as leukemia, malignant CNS, and other tumors[15, 31].

In this study, almost 82% of mothers drank tea daily during pregnancy and only 1.4% drank coffee daily. The results of the meta-analysis conducted by Cheng et al[32] demonstrated that coffee consumption by mothers during pregnancy increased risk of the childhood ALL. Dietary DNA Topoisomerase II (DNAt2) inhibitor (coffee, tea etc.) intake by mothers during pregnancy is associated with childhood AML and CNS tumors. These compounds can cause chromosomal damage [15,33].

Breastfeeding is another important factor assumed to be associated with childhood cancers, especially ALL. In our study, 83% of the considered patients had exclusive breastfeeding and only lower than 5% of them consumed formula completely instead of the mothers' milk. Smulevich et al[29] confirmed that breastfeeding had a protective effect on almost all types of childhood cancers.

In the present study, almost 92% of the mothers and the fathers had a low education level. In this regard, 96% of the mothers were homemakers and 43.5% of the fathers were self-employed individuals. Individually, 24.6% were employees, and the rest were unemployed, retired or dead.

TABLE 4. Difference between children breastfeeding and complementary feeding information and type of cancer in studied subjects (n=71)

Variables	*Category*	*ALL**	*AML*	*Neuroblastoma*	*Osteosarcoma*	*Hepatoblastoma*	*Others*	*p***
Birth weight	< 2500 gr	2 (33.3)	1 (16.7)	1 (16.7)	2 (33.3)	0 (0)	0 (0)	0.549
	2500-4000 gr	25 (41)	13 (21.3)	15 (24.6)	3 (4.9)	3 (4.9)	2 (3.3)	
	> 4000 gr	2 (66.7)	1 (33.3)	0 (0)	0 (0)	0 (0)	0 (0)	
Breastfeeding duration	Less than one year	1 (25)	1 (25)	1 (25)	1 (25)	0 (0)	0 (0)	0.596
	The end of year 1	2 (22.2)	2 (22.2)	2 (22.2)	1 (11.1)	2 (22.2)	0 (0)	
	Less than two year	8 (57.1)	2 (14.3)	3 (21.4)	1 (7.1)	0 (0)	0 (0)	
	The end of year 2	18 (42.9)	10 (23.8)	10 (23.8)	2 (4.8)	1 (2.4)	1 (2.4)	
Exclusive breastfeeding	Yes	25 (43.9)	13 (22.8)	12 (21.1)	3 (5.3)	3 (5.3)	1 (1.8)	0.594
	No	4 (33.3)	2 (16.7)	4 (33.3)	2 (16.7)	0 (0)	0 (0)	
Artificial milk consumption	Supporting	0 (0)	1 (33.3)	1 (33.3)	1 (33.3)	0 (0)	0 (0)	0.790
	Completely	3 (42.9)	1 (14.3)	2 (28.6)	1 (14.3)	0 (0)	0 (0)	
	No	26 (44.1)	13 (22)	13 (22)	3 (5.1)	3 (5.1)	1 (1.7)	
Complementary feeding	Before 6 month	5 (45.5)	1 (9.1)	3 (27.3)	1 (9.1)	1 (9.1)	0 (0)	0.638
	The end of 6 month	19 (37.3)	13 (25.5)	12 (23.5)	4 (7.8)	2 (3.9)	1 (2)	
	After 7 month	4 (100)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	

*ALL: Acute Lymphoid Leukemia; AML: Acute Myeloid Leukemia.
** *p* was obtained by Chi- Square test.

According to these results, it could be concluded that most of the studied population were from lower SES levels. Factors related to SES and their relationship to the childhood cancers were studied frequently. The results are completely contradictory. Several studies indicated a positive association between high SES levels and the childhood leukemia. Although, a number of them concluded a different result, and others found no association [34-36]. Poole et al[34] indicated that low levels of some SES factors, including parental education level and higher occupational level, were related to higher rates of leukemia. Smith et al[35] and Njoku et al[36] found no association between SES and the childhood cancer.

The last related factor considered is parental age, which is likely a leading synergetic agent in epigenetic changes, especially in sperm cells; in this case, fathers' age is a determinant factor. It has been demonstrated that maternal age is also important in leukemia risk in the offspring[23]. Our study indicated that approximately 78% of mothers were young (18-37 years) in delivery time, and only 12% of them were under 18 years old or over 35 years old while confinement.

CONCLUSIONS

Indisputably, our study had some limitations. Unfortunately, we did not have access to a larger sample size. We could study 71 children for two years and owing to cultural reasons, we could not check some risk factors, including mothers' alcohol consumption during and after conception. In fact, it is extremely difficult to interview a mother who had a child with cancer. We presumably had misreporting by interviewees about their dietary pattern, breastfeeding, complementary feeding, smoking and so forth. These can be probable reasons confirming why our results are not parallel to some other studies. However, it should be noted that this is the first time that almost all known risk factors related to childhood cancer are considered altogether, and this study can be a base for future studies. Another limitation of this study is the recall bias of dietary intakes, which is an inherent characteristic of nutritional questionnaires. Although collecting dietary information of some samples was conducted more than 10 years earlier, it is important to note that people's diet is often difficult to change and is stable throughout their lives. Therefore, we recommend that investigators conduct more studies with a larger sample size.

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Conflict of Interest:

The Authors declare that they have no conflict of interests.

Ethical Committee:

The study was conducted according to the Institutional requirements and Helsinki Declaration.

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