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Dietary patterns and the risk of oral, pharyngeal and laryngeal cancer in Syria: a case control study

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Abstract

Background: No study has investigated the relationship between dietary patterns and the risk of oral, pharyngeal and laryngeal cancer in the Middle East and North Africa region. Thus, the present study aimed to investigate the association between dietary patterns and the risk of oral, pharyngeal and laryngeal cancer in Syria.

Methods: A hospital-based unmatched case–control study was conducted on 108 cases with histologically confirmed oral, pharyngeal or laryngeal squamous cell carcinoma and 105 healthy controls, who did not suffer from any diet-related diseases. Dietary intake data were collected by a face-to-face interview, using a food frequency questionnaire. Socio-demographic and health risk behavioural information was collected using a self-completed questionnaire. Factor analysis and logistic and linear regression analyses were performed. The level of significance was set at 5 %.

Results: The factor analysis revealed three dietary patterns labeled "Western", "Traditional Syrian" and "High Protein". The results of logistic regression analyses showed that consumption of Western food in the middle and high tertiles posed a significant increased oral, pharyngeal and laryngeal cancer risk of four and three-fold, respectively (adjusted OR = 4.05, 2.80; 95 % CI = 1.57–10.44, 1.05–7.51; $P = 0.004$, 0.041; respectively). In contrast, consumption of Traditional Syrian in the high tertile and High Protein in the middle and high tertiles displayed significant protective effects in relation to oral, pharyngeal and laryngeal cancer risk (adjusted OR = 0.28, 0.24, 0.10; 95 % CI = 0.10–0.80, 0.10–0.62, 0.03–0.25; $P = 0.018$, 0.003, <0.001; respectively). Compared to males, females were more likely to adhere to the High Protein dietary pattern. Traditional Syrian pattern's scores decreased with increasing level of education and smoking. High Protein pattern's scores decreased with age and smoking and increased with working status.

Conclusions: Traditional Syrian and High Protein dietary patterns were associated with a decreased oral, pharyngeal and laryngeal cancer risk, whereas Western pattern was associated with an increased oral, pharyngeal and laryngeal cancer risk.

Keywords: Dietary patterns, Oral cancer, Pharynx cancer, Larynx cancer, Risk, Case–control study, Factor analysis, Syria

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Background

Oral, pharyngeal and laryngeal cancer (OPLC) ranks 5th most prevalent cancer worldwide, accounting for over two-thirds of a million cancer incidences and around 375,000 cancer deaths annually. Over two-thirds of OPLC incidence and nearly 80 % of OPLC mortality occurs in developing countries [1]. OPLC incidence in developing countries, however, shows a large geographic variation, with such differences reaching up to 20 fold across different countries [2]. Underlying factors explaining these geographical variations are ethnic and racial differences which are postulated to play an important role in the etiology of OPLC [3]. In addition, these variations in incidence rates of the cancer have been attributed mainly to environmental factors [4] including tobacco use, alcohol consumption, and dietary intakes [5, 6]. While alcohol and tobacco have been extensively researched in association with OPLC risk [5–7], dietary factors remain to be fully explored [7].

It is postulated that diet has the potential to prevent up to half of OPLC incidences, based on estimates by the World Cancer Research Fund and American Institute for Cancer Research (WCRF/AICR) [8]. Risk reduction has been most significantly observed for increased consumption of fruits, non-starchy vegetables, and foods containing carotenoids, all of which showed a dose–response relationship [8, 9]. In addition, micronutrients such as β-carotene, vitamin C, and selected flavonoids have been associated with reduced OPLC risk, but their individual contributions have been difficult to separate from the effect of fruits and vegetables [10, 11]. Whole grains, as opposed to refined grains, have been related to a reduced OPLC risk [11, 12]. Other food groups had less consistent results and could be weakly associated with OPLC risk [11, 13]. Among these food groups are meat and meat products as well as fish [11, 13].

While studies focusing on individual nutrients or food groups have revealed many aspects of the association between diet and OPLC, this approach has limitations on both the conceptual and methodological levels. In the real world, foods are consumed in various characteristic combinations that deliver a variety of nutrients, which can have either synergistic or interactive metabolic actions. For this reason, it is often difficult to separate out the specific effects of nutrients or foods. Even when using methods that account for the interaction and synergistic effects of nutrients and foods, such as multiple linear and logistic regression models, the large number of correlated exogenous variables can make these models unstable and can miss significant associations while returning false associations as significant. Furthermore, aspects such as dietary diversity, which have been shown to reduce OPLC risk [14], is not accounted for in the single food or nutrient approach. Recently, nutrition epidemiologists have proposed studying dietary patterns as an alternative approach to evaluate diet-disease associations [15–17]. This alternate approach looks beyond the single nutrient or food and attempts to capture the broader picture of diet that is hypothesised to discriminate between health and disease [18]. Not only does this approach account for the collinearity or intercorrelations between nutrients or foods, it is also more culturally sensitive and can be more easily interpreted or translated into dietary recommendations for the public.

Several studies investigated the relationship between dietary patterns and OPLC risk [2, 7, 19–28] and offered valuable insight into how characteristic combinations of foods modulate OPLC risk. Overall, these studies showed a reduced OPLC risk for diets high in vegetables, fruits, and other fiber-rich foods as well as fish [29], characteristic of the ‘Prudent’ dietary pattern [2, 7, 25, 26] and Mediterranean diets [19–21, 27]. On the other hand, increased risk was observed in diets high in saturated fat, refined and processed foods, as well as fast foods [29], characteristic of a ‘Western’ dietary pattern [25, 26].

The Middle East and North Africa (MENA) region has been undergoing a fast rate of development and modernisation with concurrent shifts in food consumption and dietary patterns from a traditional towards a more ‘Western’ dietary pattern [30]. This shift is accompanied by an increase in cancer incidence, predicted to rise by 100 to 180 % over the next 15 years [31], with an estimated 40 % of cancer incidences preventable through modifiable factors as diet [32]. Despite the importance of dietary patterns in modulating the risk of cancer, few studies in the region have investigated this association [33, 34] and none have studied this relationship for OPLC. The main objective of this study is to investigate the association between dietary patterns and the risk of OPLC in Syria.

Methods

Study design

The current study adopted a hospital-based unmatched case–control design. The sample was obtained from all Damascus public hospitals where patients with head and neck carcinomas are referred to receive treatment. These hospitals are: Al-Bayrouny Hospital, Al-Mojtahed Hospital and Damascus University Dental Hospital. A minimum sample size of 210 subjects was proposed to demonstrate a 2.5-fold or greater odds ratio in explanatory variables between case and control groups. The calculation assumed 30 % frequency of exposure in controls. This calculation allowed for a power of the test at 80 % and the level of significance at 5 %. To account for any exclusion due to incomplete data, a total of 216 subjects were approached.

Ethics, consent and permissions

Ethical approval for the study protocol was obtained from Damascus University Faculty of Dentistry Research Ethics Committee (no. 2344/2011). Written informed consent was obtained from all participants and confidentiality was assured.

Study participants

The current study included only Syrian citizens, aged 40 years and above, dwelling in Damascus or sub-urban Damascus areas, with 20 or more teeth. A total of 108 new (incident) cases (with histologically confirmed oral, pharyngeal or laryngeal squamous cell carcinoma, in their 1st visit to start receiving treatment) and 108 healthy controls (attending the hospital as the cases' companions [family members/friends living in the same community] and did not suffer from any diet-related diseases such as diabetes or cardiovascular diseases) were recruited in this study. Pregnant women or subjects with syndromes were excluded.

The definition of included cancers was based on the International Classification of Diseases for Oncology [35]. Oral cancer was defined as the cancer of the lip, tongue, salivary glands and other sites in the mouth. Pharyngeal cancer included cancers of the nasopharynx, oropharynx and hypopharynx. Cancer of the larynx included cancers of the glottis, supraglottis, subglottis and laryngeal cartilage.

Participants were blind to the current study's specific scope to minimise the possibility of recall bias.

Data collection

The data collection was conducted at the hospitals' premises and included socio-demographic and health risk behavioural data. Socio-demographic data included age, gender, level of education and working status. Health risk behavioural data included tobacco smoking, alcohol drinking and dietary intake. All information was obtained by a self-completed questionnaire except the dietary intake information that was collected by a structured face-to-face interview and was carried out by a trained and calibrated researcher (AN). The training and calibration exercise took place in the American University of Beirut, Lebanon, by a nutrition expert (FN). The study protocol was piloted and data collection took place between October 2011 and April 2012.

Dietary intake assessment

A structured, semi quantitative food frequency questionnaire (FFQ) [36] was used to collect data on dietary intake. This FFQ was designed by a panel of nutritionists and included culture specific dishes and recipes. It was tested on a convenient sample ($n = 8$) to check for clarity and cultural sensitivity. The results of this pilot testing of the FFQ were used to modify and adapt the questionnaire to the dialect used by the study population and were not used in the data analysis of this study. The FFQ consisted of 128 foods and 11 beverages. For each food item, a standard portion size was indicated and five frequency choices were given: per day, per week, per month, per year or never. This partly-open-ended approach for recording frequency of consumption allows more flexibility as compared to the multiple choice frequency approach, and contributes to the reduction of misclassification errors [37]. Participants had the choice to report their intake either in terms of reference portion size or in grams. A reference portion, representing one standard serving expressed in household measures, was defined for each food item. Common household measures used were measuring cups, spoons, in addition to real portion size photos. The reported frequency of each food item and beverage was then converted to a daily portion intake. Daily gram intakes of food items, energy and macronutrients intake of participants were computed using the food composition database of the Nutritionist IV software [38]. The FFQ referred to food intake during the previous 12 months.

Derivation of the dietary patterns

For the purpose of the determination of dietary patterns, food items were grouped into 22 main food groups based on similarities in ingredients, nutrient profile and/or culinary usage (Additional file 1). Food items having a unique composition (eggs, burghul (parboiled wheat), tahini –sesame paste-) were classified individually (Additional file 1). The total consumption for each group was determined by summing up the daily portion intake of each item in this group. The derivation of dietary patterns in this study was conducted by factor analysis (FA). Prior to performing the latter, the suitability of the data for FA was assessed. Inspection of the correlation matrix should reveal the presence of many coefficients of 0.3 and above. The Kaiser-Meyer-Oklin value must be equal or above the recommended value of 0.5 [39]. Bartlett's Test of Sphericity [40] should reach statistical significance, supporting the factorability of the correlation matrix. Next, an exploratory FA was carried out on the 22 food groups to extract principal factors that account for most of the variability in the pattern of correlations amongst food groups. Factors were retained using two techniques: Kaiser's criterion (retaining factors with an eigenvalue of 1.0 or more) and Scree test (retaining factors above the elbow, or break in the plot). Thereafter, factor rotation and interpretation was carried out based on the orthogonal approach. When a food group loaded on more than one factor, the factor with the highest loading was considered for factor labeling.

Statistical analysis

Frequencies were used to describe various socio-demographic and behavioural characteristics of cases and controls. Pearson's correlation coefficients were used to examine the association between the derived dietary patterns energy, and energy adjusted nutrient intakes. Energy adjustment was carried out using the regression residual method [41]. The association between dietary patterns scores and odds of the cancer was assessed using simple and multivariable logistic regression models where each dietary pattern score was entered simultaneously as an independent variable. The scores of each pattern were categorised into tertiles corresponding to high, moderate and low levels of adherence to this pattern. Category boundaries were (-4.39335, -0.2503057), (-0.2503058, 0.4759720) and (0.4759721, 2.78291) for low, moderate and high levels of adherence to Western dietary pattern, respectively; (-.14897, -0.4175896), (-0.4175897, 0.4045281) and (0.4045282, 3.44407) for low, moderate and high levels of adherence to Traditional Syrian dietary pattern, respectively; and (-2.49921, -0.4724679), (-0.4724680, 0.5279658) and (0.5279659, 2.50196) for low, moderate and high levels of adherence to High Protein dietary pattern, respectively. Covariates considered in the multivariable models included age, gender, education level, tobacco smoking and total energy intake. Multiple linear regression analysis was performed to test the association between the socio-demographic and behavioural characteristics and dietary patterns. All analyses were two tailed and a *P*-value <0.05 was considered statistically significant. The Statistical Package for the Social Sciences (SPSS, IBM Corp., Released 2013, IBM SPSS Statistics for Windows, Version 20, Armonk, NY: IBM Corp) was used for all computations.

Results

A response rate of 100 % was obtained. Three controls were excluded due to incomplete data, resulting in a total number of 213 subjects (cases = 108, controls = 105). Cases group included 17 (15.7 %) oral, 20 (18.5 %) pharyngeal and 71 (65.7 %) laryngeal cancers. The socio-demographic and behavioural characteristics of the study sample are summarised in Table 1. Only one subject in the cases group reported alcohol consumption.

The suitability of the 22 food groups for factor analysis was assessed. Inspection of the correlation matrix revealed the presence of many coefficients of 0.3 and above. The Kaiser-Meyer-Oklin value was 0.521, which is above the recommended value of 0.5. Bartlett's Test of Sphericity reached statistical significance, supporting the factorability of the correlation matrix. The principal component analysis revealed the presence of three components with eigenvalues exceeding 1; explaining 9.94, 8.53 and 6.67 % of the variance; respectively (Fig. 1; Table 2). The three components accounted together for 25.13 % of the total variability within the sample (Table 2). An inspection of the screeplot revealed a clear break after the third component (Fig. 1). Eight food groups (green beverages, milk and dairy, potato, bread and pastas, soda, egg, sugar and desserts, and fast food) loaded highly on component one. Seven food groups (Syrian mixed dishes, fresh vegetables, olive and olive oil, fruits, traditional desserts, white rice, and burghul) loaded highly on component two. Seven food groups (caffeinated beverages, meat, poultry, fish, nuts and seeds, tahini, and legumes) loaded highly on component three. The first, second and third components were labeled "Western", "Traditional Syrian" and "High Protein", respectively.

Pearson's correlation coefficients describing the association among the identified patterns with energy and energy adjusted nutrients are presented in Table 3. Compared to other patterns, the scores of the Western pattern exhibited the highest correlations with intakes of saturated fatty acids ($r = 0.143$), cholesterol ($r = 0.287$), sodium ($r = 0.169$) and calcium ($r = 0.330$). A high negative association was noted between the scores of the Western pattern and fiber intake ($r = -0.430$). On the other hand, the scores of the Traditional Syrian" pattern were highly correlated with energy ($r = 0.596$),

Table 1 Frequency of socio-demographic and behavioural characteristics of the study sample ($n = 213$)

Variable	Total $N = 213$ (%)	Cases $N = 108$ (%)	Controls $N = 105$ (%)	*P* values (Chi-square)
Age groups (in years)				
40–49	104 (48.8)	36 (33.3)	68 (64.8)	
50–59	64 (30)	36 (33.3)	28 (26.7)	
60 and above	45 (21.1)	36 (33.3)	9 (8.6)	<0.001
Gender				
Male	122 (57.3)	83 (76.9)	39 (37.1)	
Female	91 (42.7)	25 (23.1)	66 (62.9)	<0.001
Education[a]				
High level	102 (47.9)	44 (40.7)	67 (63.8)	
Low level	111 (52.1)	64 (59.3)	38 (36.2)	0.001
Working status				
Working	134 (62.9)	79 (73.1)	55 (52.4)	
Not working	79 (37.1)	29 (26.9)	50 (47.6)	0.001
Tobacco smoking				
Not smoking	121 (56.8)	33 (30.6)	88 (83.8)	
Smoking[b]	92 (43.2)	75 (69.4)	17 (16.2)	<0.001

[a]High level included post-secondary school education (college, university and postgraduate studies) and low level included secondary school education and below
[b]Current or past smoker (within the last 10 years)

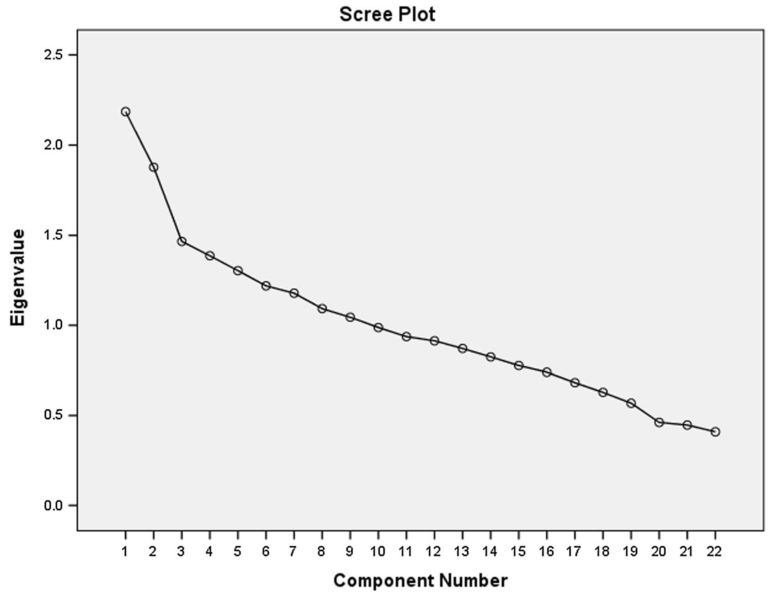

Fig. 1 Scree plot showing eigenvalues for 22 components, extracted in factor analysis of dietary data ($n = 213$)

carbohydrates ($r = 0.243$), monounsaturated fatty acids ($r = 0.146$) and dietary fibers ($r = 0.399$). The High Protein pattern, as its name depicts, was associated with a higher intake of proteins ($r = 0.399$). This pattern was also positively associated with cholesterol ($r = 0.192$) and fiber ($r = 0.155$) intakes and negatively associated with total fat ($r = -0.283$) and saturated fatty acids ($r = -0.136$).

The results of logistic regression analysis are summarised in Table 4. Consumption of Western food in the middle and high tertiles posed a significant increased OPLC risk of four and three-fold, respectively (OR = 4.05, 2.80; 95 % CI = 1.57–10.44, 1.05–7.51; $P = 0.004$, 0.041; respectively) (Table 4). In contrast, consumption of Traditional Syrian in the high tertile and High Protein in the middle and high tertiles displayed significant protective effects in relation to OPLC risk (adjusted OR = 0.28, 0.24, 0.10; 95 % CI = 0.10–0.80, 0.10–0.62, 0.03–0.25; $P = 0.018$, 0.003, <0.001; respectively) (Table 4).

The association between the identified patterns and the socio-demographic and behavioural characteristics are presented in Table 5. Compared to males, females were more likely to adhere to the High Protein dietary pattern (β = 0.48, 95 % CI: 0.04, 0.93). As for the Traditional Syrian pattern, its scores decreased with increasing level of education and with smoking (β = -0.40, 95 % CI: -0.69, -0.12 and β = -0.51, 95 % CI: -0.84, -0.18, respectively). Similarly, the scores of the High Protein pattern decreased with age and smoking and increased with working status (β = -0.09, 95 % CI: -0.18, 0; β = -0.51, 95 % CI: -0.83, -0.19 and β = 0.61, 95 % CI: 0.19, 1.03) (Table 5).

Discussion

This is the first study to report on the association between dietary patterns and OPLC risk in the Middle East and North Africa Region. The present study was conducted in Damascus, Syria, using a case–control design with 108 OPLC cases and 105 controls. Recently, there has been a growing appreciation that the overall dietary pattern, rather than any single nutrient, should be considered in relation to studying the association between diet and disease. Cancer, in particular, has complex etiology and it is unlikely that its development will be mediated by a single nutrient or food [42]. So conceptually the evaluation of the overall dietary patterns appears closer to real world as people “do not eat nutrients they eat food” [42]. In this study, using factor analysis, three dietary patterns were identified, 1) Western and 2) Traditional Syrian and 3) High Protein. Among these patterns, the Western was found to be positively associated with the odds of the OPLC. On the other hand, the Traditional Syrian and the High Protein patterns were both associated with lower odds of the cancer.

In the literature, most of the studies depicted two main patterns: A “Western” which, similar to the Western dietary pattern identified in this study, is energy dense and rich in refined grains, French fries, and sweets/desserts [42]. Another pattern also commonly reported in the literature is the “Prudent”/healthy pattern, which is generally characterised by vegetables, fruit, legumes, fish, and whole grains. In this study, instead of the commonly observed Prudent pattern, the Traditional Syrian and High Protein patterns were found. However,

Table 2 Food loadings for the three dietary patterns identified in the study population (*n* = 213)

Food group	Dietary patterns			Communality
	Western	Traditional Syrian	High Protein	
Green beverages	**−0.608**	0.331	0.189	0.514
Milk and dairy	**0.569**	0.237		0.383
Potato	**0.435**	0.171	−0.302	0.309
Bread and pasta	**0.379**		0.206	0.188
Carbonated beverages	**0.372**			0.144
Egg	**0.369**	0.321	0.237	0.295
Sugars and desserts	**0.191**	0.139	0.166	0.084
Fast food	**0.177**			0.031
Syrian Mixed dishes	0.306	**0.631**	0.118	0.505
Fresh vegetables	−0.239	**0.571**	0.254	0.448
Olives and olive oil	0.180	**0.537**	−0.122	0.336
Fruits	−0.169	**0.461**		0.243
Traditional desserts		**0.437**	−0.260	0.261
White rice		**0.335**	0.278	0.190
Burghol	0.133	**0.176**	0.148	0.070
Caffeinated beverages	0.477		**0.504**	0.486
Meat	0.128		**0.448**	0.217
Fish	−0.122		**0.440**	0.215
Poultry	0.380		**−0.410**	0.313
Nuts and seeds	0.104		**−0.387**	0.161
Tahini		0.213	**−0.216**	0.095
Legumes			**0.199**	0.041
Eigenvalues	2.186	1.877	1.466	
% explained variance	9.940	8.530	6.670	
% cumulative variance	9.940	18.470	25.130	

Bold indicates the highest loading of food groups for each dietary pattern

these patterns share significant similarities with the Prudent/healthy patterns as they consist of fruits and vegetables, fish and legumes. With the use of dietary pattern analysis becoming more widespread, traditional patterns have been identified for the ethnic or country specific diets, such as the "bean pattern" among women of Chinese or Japanese ancestry [43], the traditional Korean pattern [44], and the traditional Iranian pattern [45] and the traditional Lebanese pattern [46].

In this study, the positive association between the Western pattern and OPLC conforms to the results of similar studies. In fact, a recent study in Uruguay showed a 72 % increase in the odds of the upper aerodigestive tract cancers among subjects adhering to the Western dietary pattern. This increase was observed for oral/pharynx and larynx cancers [25]. Other studies have also shown an increase in oral cancer risk with patterns that, though had different nomenclatures, displayed many traits of the Western diet. For instance, in a case–control study in Jakarta, Indonesia, the 'Preferred' pattern which was associated with an almost two fold increase in the risk of oral cancer consisted of fast foods, fermented foods (including dairy), and desserts high in fat and sugar [23]. Similarly, another case–control study in Malaysia showed higher odds of oral cancer with the consumption of the 'Combination' pattern which consisted of dairy and meat as well as with the 'Traditional' pattern which included beverages and starches [7]. Many of the foods/food groups that constituted the aforementioned 'Preferred', 'Combination' and the 'Traditional' patterns were also shared by the Western pattern identified in our study, more specifically dairy products, starches (listed as potato, breads and pasta in our study), carbonated beverages and sugars and desserts. This observed increased in the risk of oral cancer associated with greater adherence to a Western or western-like patterns could be mediated by inflammation, the latter being a process central to most degenerative diseases including cancer. In their systematic review of the influence of dietary patterns on biomarkers of low-grade

Table 3 Pearson's correlation coefficients between pattern scores and energy and energy adjusted nutrient intakes[a]

	Western	Traditional Syrian	High Protein
Energy[b] (Kcal)	0.506**	0.596**	0.138*
Protein (g)	−0.430**	0.155*	0.399**
Carbohydrates (g)	−0.093	0.243**	0.105
Fat (g)	−0.067	−0.006	−0.283**
Saturated fatty acids (g)	0.143*	−0.131	−0.136*
Mono unsaturated fatty acids (g)	−0.085	0.146*	−0.130
Polyunsaturated fatty acids (g)	−0.151*	−0.169*	−0.296
Cholesterol (mg)	0.287**	0.101	0.192**
Dietary fibers (g)	−0.430**	0.399**	0.155*
Sodium (mg)	0.169*	−0.032	0.080
Calcium (mg)	0.330**	0.006	0.006

[a]Adjustment for energy was done by residual method described by Willett et al. [39]
[b]Absolute values are indicated for the correlation of dietary pattern scores with total energy intake
*Correlation is significant at $p < 0.05$
**Correlation is significant at $p < 0.01$

inflammation, Barbaresko et al. found that a Western pattern was positively correlated with higher concentration of C reactive proteins (CRP), a main biomarker of inflammation [47]. Furthermore, it is postulated that diets rich in high glycemic foods and protein-dense foods such as dairy products may lead to the increased formation of advanced glycated end (AGEs) products, which in turn lead to cellular damage at many levels. For instance, AGEs may cause alterations in the protein structure and function, aberrant cell signaling and dysfunction of extra cellular matrices. These damages to the normal cell functions are implicated in the etiology of most cancers including OPLC [48].

In this study, both the Traditional Syrian and the High Protein patterns were associated with significant reductions in the odds of OPLC. These findings are in line with a plethora of studies showing cancer risk reduction with a higher intake of Prudent/healthy diet, with which these patterns share many characteristics. According to the latest report by WCRF/AICR 2007 regarding the association between dietary patterns and cancer risk, recent meta-analyses (after 2007), have consistently conferred a protective effect of the prudent/healthy diet for most cancer sites, including OPLC [8]. In the Malaysian case–control study of dietary patterns and oral cancer, the 'Prudent' dietary pattern was associated with 47 % lower odds of the disease [7]. More recently, in Uruguay, adherence to the Prudent diet was associated with lower odds of cancers of the upper aerodigestive tract (OR = 0.52, 95 % CI = 0.34–0.76) [25]. The 'Combination' pattern described in the Jakarta case–control study had elements of both the Traditional Syrian and the High Protein patterns found in this study as it included red meat, fruits and poultry. Similar to our findings, adherence to this 'Combination' pattern was associated with 50 % decrease odds of oral cancer [23]. A closer examination of the Traditional Syrian and the High Protein patterns reveals many traits in common between these patterns with the Mediterranean diet. Syria is a country located along the side of the East Mediterranean basin and it is not surprising for its traditional dietary to have considerable similarities with the general definition of the Mediterranean diet. In fact, fruits, vegetables, olive oil, fish and legumes listed under the Traditional and

Table 4 Simple and multivariable logistic regression to predict odds of oral, pharyngeal and laryngeal cancer ($n = 213$)

Dietary pattern[a]	Base	Frequency of cases (%)	Unadjusted OR (95 % CI)	Adjusted OR (95 % CI)[b]
Western				
Low[1]	71.0	24.0 (33.8)	1	1
Moderate[2]	71.0	45.0 (63.4)	**3.39 (1.70–6.75)**	**4.05 (1.57–10.44)**
High[3]	71.0	39.0 (54.9)	**2.39 (1.21–4.70)**	**2.80 (1.05–7.51)**
Traditional Syrian				
Low[4]	71.0	44.0 (62)	1	1
Moderate[5]	71.0	40.0 (56.3)	0.79 (0.41–1.55)	0.59 (0.23–1.49)
High[6]	71.0	24.0 (33.8)	**0.31 (0.16–0.62)**	**0.28 (0.10–0.80)**
High Protein				
Low[7]	71.0	59.0 (83.1)	1	1
Moderate[8]	71.0	33.0 (46.5)	**0.18 (0.08–0.38)**	**0.24 (0.10–0.62)**
High[9]	71.0	16.0 (22.5)	**0.10 (0.03–0.14)**	**0.10 (0.03–0.25)**

[a]The scores of each pattern were categorized into tertiles corresponding to high, moderate and low levels of adherence to this pattern
[b]Adjusted for age, gender, education level, working status, tobacco smoking and total energy intake
Category boundaries: [1](−4.39335, −0.2503057); [2](−0.2503058, 0.4759720); [3](0.4759721, 2.78291); [4](−.14897, −0.4175896), [5](−0.4175897, 0.4045281); [6](0.4045282, 3.44407); [7](−2.49921, −0.4724679); [8](−0.4724680, 0.5279658); [9](0.5279659, 2.50196)
Bold indicates significance at $p < 0.05$

Table 5 Multivariable linear regression analysis of the association between dietary patterns and socio-demographic and behavioural characteristics ($n = 213$)

	Western		Traditional Syrian		High Protein	
Sociodemographic & behavioural characteristics	β	95 % CI	β	95 % CI	β	95 % CI
Age	−0.02	−0.12, 0.08	0	−0.10, 0.10	**−0.09**	**−0.18, 0**
Females vs males	−0.30	−0.76, 0.16	0.10	−0.36, 0.57	**0.48**	**0.04, 0.93**
Education	−0.21	−0.49, 0.07	**−0.40**	**−0.69, −0.12**	0.05	−0.22, 0.32
Working status	0.25	−0.18, 0.68	0.23	−0.21, 0.66	**0.61**	**0.19, 1.03**
Smoking	0.12	−0.21, 0.45	**−0.51**	**−0.84, −0.18**	**−0.51**	**−0.83, −0.19**

Bold indicates significance at $p < 0.05$

High Protein dietary patterns in this study are also common denominators to most of the definitions of the Mediterranean diets [49]. The protective effects of these patterns found in this study echo the accumulating evidence pointing to a lower risk of OPLC with higher adherence to the Mediterranean diet [20, 21]. Recently, using various different indices to assess the association of OPLC with adherence to the Mediterranean diet, Filomeno et al. and Li et al. found strong evidence for a beneficial role of this diet on OPLC risk [19, 27]. A recent review by Grosso et al. discussed many plausible biological mechanisms that explain the protective role patterns such as the Prudent/healthy and the Mediterranean have on the risk of cancer [50]. Fruits and vegetables are rich in antioxidants such as carotenoids, vitamin C, vitamin E, selenium, dietary fiber (and its components), dithiolthiones, glucosinolates (isothiocyanates and indoles), polyphenols, protease inhibitors, allium compounds, plant sterols, and limonene [51]. These compounds have been shown to decrease the risk of cancer possibly through attenuation of the effects of polycyclic aromatic hydrocarbons (PAHs) and nitrosamines, preventing the progression of different cancers, inhibition of multiple cancer-related biological pathways, such as carcinogen bio-activation, cell-signaling, cell cycle regulation, angiogenesis and inflammation [52]. Tyrosol and hydroxytyrosol, two main phenolic antioxidants found in olive oil, have been linked to decrease glutathione (GSH), the activation of the transcription factor Nuclear Factor-KB and cell death which may be implicated in the carcinogenetic processes [53]. In this study, green teas and herbal infusions were also part of the Traditional Syrian dietary patterns. These hot drinks are rich sources of polyphenols, especially epigallocatechin gallate (EGCG), gallocatechin (EGC), (−)-epicatechin gallae (ECG), (−)-catechin gallate (CG), (−)-epicatechin (EC), and (+)-catechin (C) [54]. These polyphenols seem to play an important role in the reduction of cell growth, induction of apoptosis, and inhibition of angiogenesis in oral cancer cell lines [55, 56].

A main difference between the Prudent/healthy, the Mediterranean diet and the High Protein dietary pattern in this study is the fact that the latter included red meat. The association between red meat and OPLC is still controversial. A meta-analysis of observational studies investigating this association showed that while the high consumption of processed meat was significantly associated with an increased risk of oral and pharyngeal cancer, there was no significant association between total red meat and white meat intake with the risk of cancer [57]. In Syria, meat is seldom consumed as processed or canned. Smoking, curing, salting or the addition of chemical preservatives to the meat is not common practices in the country and red meat is mostly consumed as fresh cuts simmered or, less frequently, barbecued.

The current study reported a high impact of different dietary patterns on OPLC risk. This could be explained based on the present study's population and food items. For example, in Hajizadeh et al. matched case–control study [34], conducted on an Iranian population regarding the risk of oesophageal cancer, the authors reported odds ratios of 10.3 for Western pattern and 0.17 for healthy pattern, which are both close to the current study's reported odds ratios of Western and Traditional Syrian/High Protein dietary patterns; respectively. Both Iranian and Syrian populations are similar racially and have similar food items. Thus, these large odds ratios observed in these populations might be linked to their racial and food items characteristics.

In addition to their association with cancer, the patterns identified in this study were also investigated in association with a few socio-demographic and behavioural characteristics.

Interestingly, the results of the present study highlight gender differentials in adherence to the High Protein dietary pattern, with females being significantly more likely to adhere to this pattern compared to males. This corroborates the findings of previous studies reporting females as being more health-conscious and followers of dietary recommendations than males [46, 49, 58, 59]. In a study investigating dietary patterns among a national sample of Lebanese adults, females adhered more to the prudent pattern while males were found to mainly follow the western pattern [46]. Also, in the present study, individuals from low socioeconomic position (having low education level or not working status) were significantly less likely to adhere to healthy dietary patterns compared to individuals from high socioeconomic position. This is in line with the findings of previous studies that reported individuals from high socioeconomic position as being more followers of healthy dietary recommendations than their counterparts from low socioeconomic position [60]. Furthermore, both the Traditional Syrian and the High Protein in this study were negatively associated with smoking. This finding supports the theory that food choices are part of a larger pattern of health-related characteristics and behaviour including not smoking. In fact, previous studies have also shown that Prudent and prudent-like patterns are associated with healthy behaviour, such as, no smoking, a higher level of physical activity, breakfast consumption and regular meals pattern [61–63]. The current study's population had a very low alcohol intake (only one subject in the cases group reported alcohol consumption). This could be explained based on the fact that the majority of Syrian population does not consume alcohol due to religious reasons.

One of the main strengths of the current study is the selection of newly diagnosed (incident) cases and population-based controls (cases' companions [mainly family members]), which both minimised the potential selection bias inherited with prevalent cases or hospital-based controls selection [64]. Selecting hospital-based controls, from those suffering from minor ailments, not related to diet, would have had posed a serious selection bias in the current study. Such hospital-based controls might not be from the same population that generated the cases. This is due to differences in the referral patterns for different diseases in the Syrian Health Care System. The current study's settings are the only public hospitals that provide cancer care in the southern region of Syria; whereas many other public hospitals provide care for other types of diseases and conditions. Another strength of the present study is the high participation level, both for cases and controls. The present study used a modern alternate approach to study the association between diet and OPLC in an understudied population such as in Syria. The dietary data reported and analysed were measured and collected by a trained researcher and were not self-reported, resulting in consistent interpretations and higher response and completion rates.

Despite the abovementioned strengths, the present study, like other hospital-based case–control studies, is not without limitations. Despite efforts to minimise the possibility of recall bias by blinding the participants to the current study's specific scope, this possibility could not be completely ruled out. The present study's effort to minimise selection bias, by recruiting population-based controls, might have had run the risk of overmatching and, hence, finding no significant differences between cases and controls. Yet, the large and significant differences, found in dietary patterns between cases and controls in the current study, suggest in the light of this possible overmatching, a rather stronger impact of identified dietary patterns on OPLC. Observer bias cannot be ruled out in the current study. The interviewer was not blinded to the present study hypothesis. Nevertheless, the appropriate training and calibration that the interviewer had received in collecting dietary data using FFQ by a strict structured interview protocol might have minimised considerably this potential bias. The reverse causality interpretation is one of the potential limitations of retrospective case–control studies. To minimise this, the current study selected new (incident) cases, where the time between the diagnosis and the referral to receive the treatment was on average less than 2 weeks. Dietary data were collected over the period of the last 12 months, therefore, the reverse causality (i.e. the presence of OPLC might have had changed the dietary patterns) is very unlikely. In contrast to matched case–control studies, the current unmatched study did not eliminate the potential confounding effect of age and gender in the design. This is because the present study targeted an understudied population, where unmatched design allowed for the exploration of the significance and impact of these socio-demographic factors, before adjusting statistically for their effect. Finally, it remains important to note that, although the FFQ used in the present study was not validated in our study population, it was previously used for the assessment of dietary patterns and their relationship with obesity and the metabolic syndrome and has yielded plausible findings among similar Arabic speaking subjects [46, 62]. In addition, the FFQ, used in the present study, was administered by a trained interviewer rather than being self-administered. This approach provides several advantages since self-administration of the FFQ requires a literate population, and may result in inconsistent interpretations of the food list and lower response and completion rates, each of which may jeopardise the validity of the data [65].

The current study's findings can be generalised to the current study's Syrian population. The current settings are the only public-settings that provide cancer care in the southern part of Syria.

The public health implications of the current study, both at the policy and population-based intervention levels, should be seen within a common risk factor approach perspective. The identified dietary patterns are a common determinant across a wide spectrum of cancers and other diet-related diseases. Therefore, the present study findings establish evidence to inform national health promoting policies and population-based programs in Syria.

In terms of clinical implications, the current findings imply the importance of incorporating dietary patterns assessment and advice within the general and dental practitioners' cancer preventive care package.

Conclusions

Traditional Syrian and High Protein dietary patterns were associated with a decreased OPLC risk, whereas Western pattern was associated with an increased OPLC risk. Compared to males, females were more likely to adhere to the High Protein dietary pattern. Traditional Syrian pattern's scores decreased with increasing level of education and smoking. High Protein pattern's scores decreased with age and smoking and increased with working status.

Additional file

Additional file 1: Table S1. Classification of food item. (PDF 47 kb)

Abbreviations

AGEs: Advanced glycated end; C: Catechin; CG: Catechin gallate; CRP: C reactive proteins; EC: Epicatechin; ECG: Epicatechin gallae; EGC: Gallocatechin; EGCG: Epigallocatechin gallate; FA: Factor analysis; OPLC: Oral, pharyngeal and laryngeal cancer; FFQ: Food frequency questionnaire; GSH: Glutathione; MENA: The Middle East and North Africa; PAHs: Polycyclic aromatic hydrocarbons; SPSS: Statistical Package for Social Science; WCRF/AICR: World Cancer Research Fund and American Institute for Cancer Research.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

EJ conceived the idea and designed the study; FN and AN contributed to the design of the study, EJ and FN analysed the data and wrote the manuscript; AN collected the data; LI and KN contributed to the data analyses; BR contributed to the writing of the introduction, AM contributed to the study conduct. All authors read and approved the final manuscript and critically reviewed the manuscript.

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