Adherence to low-carbohydrate diet in relation to gastric cancer: findings from a case-contrl study in Iran

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FT and KZ designed the study, BS and MH supervised data collection and cleaning. FT analyzed the data and drafted the manuscript. MH helped in data analysis and manuscript drafting. AE contributed in study conception, data analysis and manuscript drafting. All authors reviewed and approved the final version of the manuscript.

ABSTRACT:

Background: No earlier study has examined the association between adherence to low carbohydrate diets (LCD) and odds of Gastric Cancer (GC).

Objective: This study examined the association between adherence to LCD and risk of GC.

Design: This hospital-based case-control study was conducted in Iran Cancer Institute, Tehran, Iran between 2010 and 2012. Totally, 178 patients with GC and 276 apparently healthy controls participated in this study. Cases were histo-pathologically confirmed gastric cancer patients aged ≥40 years that diagnosed with gastric cancer in the last year, elapsing no more than 1 year of the diagnosis. Dietary intakes were assessed using a validated 146-item Diet History Questionnaire. Participants were classified into deciles based on their percentage of energy intake from fats, proteins and carbohydrates. Participants with the highest intake of fats and proteins received 10 points and those in the lowest deciles of these macronutrients were given the score of 1. For dietary carbohydrate intake, we did vice versa. Then, the scores of these three macronutrients were summed up to obtain the total LCD score. The same method was applied to compute animal and vegetable LCD score, in which we used percent of energy from carbohydrates, animal- or vegetable-fats and animal- or vegetable-proteins for scoring.

Results: Patients with GC were older (60.8 vs. 53.2 y, P<0.001) and more likely to be male (74.2 vs. 63.8%, P=0.02), married (97.8 vs. 86.6%, P<0.001) and illiterate (62.4% vs. 26.1%, P<0.001) than controls. Comparing across tertiles of LCD score, we found that those with the greatest adherence to LCD had a higher mean BMI than those in the second tertile (27.7 vs. 25.6 Kg/m^2, P<0.001). Before adjusting for covarients, adherence to LCD-diet was not associated with risk of GC (OR 1.31; 95% CI 0.82,2.09 for highest vs. lowest tertile; P_{trend}<0.26). Adjustments for several potential confounders including H-pylori infection did

not alter the association (OR 1.08; 95% CI 0.62,1.89 for highest vs. lowest tertile; P_{trend}<0.76). After additional controlling for BMI, paticipants in the highest tertile of LCD score were 7% more likely to have GC than those in the lowest tertile; however, this association was not statistically significant (OR 1.07; 95% CI 0.59,1.95 for highest vs. lowest tertile; P_{trend}<0.79). No significant association was also seen between adherence to animal- or veghetable-based LCD diet and risk of GC.

Conclusion: In conclusion, we failed to find any evidence on the association between consumption of low carbohydrate diet (LCD) and odds of gastric cancer. Further studies, in particular of prospective design, are required to confirm these findings.

INTRODUCTION:

Gastric cancer is one of the most common cancers worldwide. Its incidence has decreased dramatically in several countries; however, it is still a major public health problem, as the third cause of malignancy death, in the world (1-3). Despite improvements in sanitary conditions in Iran, the prevalence of gastric cancer is rising in Iran. The age-standardized incidence rate in Iran was 26.1 men and 11.1 in women in 100,000 (4). Moreover, gastric cancer becomes symptomatic just in advanced stages and its five-year survival rate is dramatically low (ranges from 10% to 30%) (1, 3, 5). Therefore, identification of contributing factor to gastric cancer in order to prevent its incidence is of high priority (5).

In addition to H-Pylori infection, tobacco smoking and drinking alcohol, several dietary factors including high sodium intake, consumption of salt-cured foods and red and processed meats have been reported as contributing factors to gastric cancer (1-3, 5). Despite for reducing trend in most parts of the world, gastric cancer is still highly prevalent in geographic areas where refined grains are staple foods. This is relevant for Iran, Japan and south Asian countries (?). In Iran, the traditional dietary pattern has been composed of large amounts of carbohydrates, in particular refined carbohydrates from white bread and rice (6). Carbohydrate intake has earlier been investigated in relation to several cancers, including breast, colon and gastric cancer (?). High carbohydrate diets especially those with a high glycemic index result in elevated blood glucose and finally insulin levels, through which they might influence the initiation of several cancer by activating the pathways of oxidative stress, inflammation and proliferation (2). Hyperinsulinemia increases Insulin-like Growth Factor-I (IGF-I), which can in turn raise cell proliferation and inhibit apoptosis (7, 8). On the other hand, Prospective studies have indicated that consumption of low GI diets have been associated with a reduced risk of GC (), while diets with greater dietary GI and GL were

positively associated with incident GC (). In addition to quality, the quantity of dietary carbohydrate intake was also linked with GC (). However, most of such investigations have considered carbohydrate intake alone and did not take into account the contribution of the other two macronutrients. Low Carbohydrate-Diet (LCD) score, developed by Halton et al (?), considers dietary intake of carbohydrates, fats and proteins together. Therefore, examining the association of LCD score with health outcomes seems more important than the relation of an individual macronutrient. Several studies have investigated the relation between LCD and different health outcomes including metabolic syndrome, obesity and cardiovascular diseases (?). Such association was also examined with some cancers including colorectal, lung, prostate and breast cancer. However, we are aware of no study linking LCD with risk of gastric cancer. Given the high intake of carbohydrates and fats in Middle Eastern countries on one hand and alarming prevalence of GC in these countries on the other hand, the present study was done to examine the association between adherence to Low-Carbohydrate Diet (overall, plant-based and animal-based) and risk of gastric cancer Iranian adults.

METHODS:

Study population: The present hospital-based case-control study was conducted between May 2010 and June 2012 in Cancer Institute of Iran, which is a referral hospital in Imam Khomeini complex in Tehran, capital city of Iran. In this study, cases were histo-pathologically confirmed gastric cancer patients who aged ≥40 years that diagnosed with gastric cancer in the last year, elapsing no more than 1 year of the diagnosis. Controls were healthy relatives of other patients hospitalized in other wards of the hospital. The response rate was 95% among cases and 70% among controls.

In the current analysis, we excluded individuals with implausible energy intakes (defined as less or more than 3 standard deviations from the mean energy intakes). This left 178 cases and 278 controls in the current study. Written inform consent was taken from all participants after face-to- face description of the study protocol. The participants were free to find more information on study protocol from main releasers trough phone call. This study was approved by Ethics Committee of Tehran University of Medical Sciences (no.17198).

Dietary assessment: Dietary intakes were assessed using a Diet History Questionnaire (DHQ) that was consisted of 146 questions about consumption of food items and mixed dishes during the preceding year. Detailed description and validity of the questionnaire has been reported previously (?). Patients with gastric cancer were requested to report their usual dietary intakes before the diagnosis of the cancer. Controls were asked to report their routine usual dietary intakes. All information about diet was collected through phone call by trained dietitians. Each question in the DHQ was consisted of two parts. The first part was about frequency of food and mixed dishes based on its consumption in a day, week or month. Participants were able to report their consumption frequency based on multiple-choice frequency response categories. The second part was about the quantity of foods consumed, which was designed based on standardized Iranian food portion sizes. Daily intake of each food item was calculated given the quantities of foods along with frequency response categories. Total energy and nutrient intakes were then computed using the translated version of McCance and Widdowson's Food composition table (10) and Iranian food composition table (11).

Validation study revealed acceptable correlation coefficients between energy and nutrients intakes assessed by DHQ and multiple 24-hour recalls. Deattenuated Spearman correlation coefficients between DHQ and 24-hour recall were 0.63 for carbohydrate, 0.59 for protein and 0.31 for fat.

Low Carbohydrate-Diet scoring: We computed the LCD score trough the protocol explained by Halton (12). Firstly, we divided participants into deciles in terms of their percentage of energy intake from fats, proteins and carbohydrates. Participants with the highest intake of fats and proteins received 10 points (the highest scores) and those in the lowest deciles of these macronutrients were given the score of 1. Other deciles received their corresponding scores. For dietary carbohydrate intake, we did vice versa, those with the highest intake received the lowest score (score 1) and individuals with the lowest intake received the highest score (10). Then, the scores of these three macronutrients were summed up to obtain the total LCD score, which ranged from 3 to 30. The same method was applied to compute animal and vegetable low-carbohydrate diet score, in which we used percent of energy from carbohydrates, animal- or vegetable-fats and animal- or vegetable-proteins for scoring.

Assessment of gastric cancer: Gastroscopic or surgical biopsy of patients was assessed by an experienced pathologist. Patients with histologically confirmed stomach cancer, as defined by second edition of the International Classification of Diseases for Oncology (ICDO-c16) (ref), were enrolled**.**

Assessment of covariates: A structured questionnaire was used through face to face interview to collect information on demographic variables and general characteristics. Data on usual weight and height were collected through self-reported method. As patients with gastric cancer might lose weight, we did not examine current weight. Body Mass Index (BMI) was calculated as usual weight in kilograms divided by height in meters squared. Smoking status was examined through asking participants about their usual behavior on smoking during the last year. They were classified as current smokers and non-smokers. To examine H. Pylori infection, 10 mL venous blood samples were collected. Serum samples were evaluated for IgG antibody using ELISA kits. Experienced technicians performed the

serologic assays, while they were not aware of the study design and case/control status of participants. The validity of this method was ascertained by repeating the H-pylori antibody test in a random selection of serums. The seropositivity was defined as the presence of antibody and seropositivity >0.87 was considered as positive .

Statistical analysis: To compare general characteristics between cases and controls, we applied Student's independent t test for continuous variables and chi-square test for categorical variables. Participants were classified into tertiles of LCD score and then comparison of general characteristics of study participants across tertiles of LCD score was done using chi-square test for categorical and one-way ANOVA for continuous variables. To determine the association of LCD score and gastric cancer, we applied unconditional logistic regression models, in which several potential confounding variables were taken into account. In the first model, we considered age (continuous), sex (male, female) and energy intake (continuous) as covariates. In the second model, we additionally adjusted for education (categorical), marital status (single, married) and residential place (Tehran, other cities), alcohol intake (g/day), smoking status (ever vs. never) and H-pylori infection (positive, negative). To determine if the associations are mediated through obesity, we controlled for BMI (continuous) in an additional model. In all analyses, we considered the first tertile as a reference category and odds ratios (ORs) and 95% CIs for gastric cancer were considered. The trend of odds ratios was examined by considering tertiles of LCD as continuous variable. All statistical analyses were carried out using STATA (STATA, version 14, State Corp., College station, TX).

RESULTS:

Study participants were 178 patients with gastric cancer and 276 healthy controls. General charactristics of participants are shown in **Table 1**. Patients with GC were older (60.8 vs.

53.2 y, P<0.001) and more likely to be male (74.2 vs. 63.8%, P=0.02), married (97.8 vs. 86.6%, P<0.001) and illiterate (62.4% vs. 26.1%, P<0.001) than controls. They were less affected with H-Pylori (38.2 vs. 56.2%, P<0.001) and were more likely to be current smokers (45.5 vs. 30.8, P<0.001) than controls. Comparing across tertiles of LCD score, we found that those with the greatest adherence to LCD had a higher mean BMI than those in the second tertile (27.7 vs. 25.6 Kg/m^2, P<0.001). In addition, those in the top tertile of LCD score were less likely to be reseidents of Tehran (39.9% vs. 60%, P=0.001) and dranke more alcohol (10.7 d vs. 0.8 g/d, P<0.001) than those in the lowest tertile. No other significant differences were seen in terms of other variables across tertiles of LCD score.

Dieary intakes of participants are provided in **Table 2**. Compared with conrlos, patients with gastric cancer had lower intakes of fruits (355 vs. 531 g/d, P<0.001) and vegetables (254 vs. 394 g/d, P<0.001). As expected, higher LCD score was associated with higher intake of fats, animal fat, vegetable fat, animal proteins, saturated fatty acids, mono-saturated fatyy acids and poly saturated fatty acids (P<0.001 for all). Participants with the greatest adherence to LCD diet, took greater percentage of their energy from fats and proteins and lower percent from carbohydrates (P<0.001 for all). Dietary intakes of energy, fiber and sugar were lower among participants with the highest LCD score than those with the lowest score (P<0.001 for all).

Multivariable-adjusted odds ratios and 95% CIs for GC across tertiles of LCD score are provided in **Table 3**. Before adjusting for covarients, adherence to LCD-diet was not associated with risk of GC (OR 1.31; 95% CI 0.82,2.09 for highest vs. lowest tertile; P_{trend}<0.26). Adjustments for several potential confounders including H-pylori infection did not alter the association (OR 1.08; 95% CI 0.62,1.89 for highest vs. lowest tertile; P_{trend}<0.76). After additional controlling for BMI, paticipants in the highest tertile of LCD score were 7% more likely to have GC than those in the lowest tertile; however, this

association was not statistically significant (OR 1.07; 95% CI 0.59,1.95 for highest vs. lowest tertile; P_{trend}<0.79).

When we computed LCD score based on animal or vegetable sources of macronutrients, again no significant association was seen between adherence to LCD diet and risk of GC.

DISCUSSION:

In this hospital-based case-control study, we found no significant association between adherence to LCD diet and odds of GC. To the best of our knowledge, this study is the first examining the association between adherence to LCD diet and GC.

Although the association of LCD diet with GC has not been assessed before, several studies have investigated the association of dietary glycemic index and glycemic load or dietary macronutrient intakes with GC. In a hospital-based case-control study in Italy, high dietary GI and GL was associated with a greater odds of GC (A). A swidish population-based cohort study failed to reach any significant association between dietary GL, GI or total carbohydrate intake and risk of GC (B). Some studies have investigated the association of macronutrients intake and risk of GC; however, they reached to controversial findings. A case-control study in Italy demonstrated no significant association between total protein,vegetable or animal protein intake as well as total fat, vegetable or animal fat and risk of GC (C). Findings from a a case-control study in Venezuela revealed a positive relationship between dietary protein and fat intake and risk of GC, while an inverse association between dietary carbohydrate intake and risk of GC (D). Similar findings were reported from China (E). In addition, the beneficial effect of low carbohydrate ketogenic diet on several cancers has also been shown (37)(38). Overall, it seems that the quantity of dietary carbohydrate intake alone cannot determine the risk of several cancers and all macronutriwents hshould be considered together to have a definite conclusion about their contribution to several cancers. The low-carbohydrate dietary pattern, we focused on here, is usually characterized by low intakes of carbohydrates and

high intakes of proteins and fats (36). This approach considers the whole macronutrients in the diet and it might provide better insight into the link between macronutrient intakes and risk of several cancers.

High carbohydrate intake is associated with elevated blood glucose and insulin levels. Insulin resistance might result in decreased levels of insulin-like growth factor (IGF) binding proteins 1 and 2, and therefore, the availability of IGF-I, which can in turn increase tumor cell proliferation, would increase (45, 46). Therefore, adherence to a diet with low quantity of carbohydrates might suppress tumor cell proliferation and regulate apoptosis via cell signaling pathways, the PI3K/Akt/Mtor and RAS/RAF/MEK/ERK sequences, which are insulin or IGF-I-dependent (7, 46, 49). In addition, Warburg et al expressed that cancer cells depend on glucose as a fuel (44).

Earlier studies on the association between dietary carbohydrate intake and several outcomes have mostly examined considering total carbohydrate intake alone or in the context of low-carbohydrate, high-protein (LCHP) or low-carbohydrate, high-fat diets (2, 17, 23, 33-35).

In spite of a strong association between *H pylori* infection and GC, prevalence of *H-Pylori* infection was lower in patients with gastric cancer than controls in this study. Such findings were previously reported in other case-control studies (43). This could be attributed to reverse causation in such study designs. We evaluated *H-Pylori* infection by assessing Ig G antibody, which might be eradicated during the gastric atrophy and development of gastric cancer (42). In addition, patients with gastric cancer might have received anti *H-pylori* treatments and their infection had eradicated before diagnosis of gastric cancer (43). It was shown that *H pylori* infection by CagA and VacA would provide stringer evidence on the association with Gastric Cancer (42). Measurement of

H pylori infection with CagA/VacA or conducting prospective study is needed in future studies further examine the role of this infection in gastric cancer.

High rates of participation, similar socioeconomic status of patients and controls, considering the seropositivity of H-Pylori as a risk factor for gastric cancer and the use of a validated FFQ for dietary assessment are among strengths of this study. However, several limitations should also be noted. As with all epidemiological studies applying FFQ, misclassification of study participants based on their dietary intakes is unavoidable [49]. Although we controlled for several confounders, the possibility of residual confounding cannot be excluded. A relatively small number of cases, which did not allow meaningful analysis by histological type or tumor site, is another concern. Given the case-control design of the study, the inherent limitations of recall and selection bias should also be considered [50].

In conclusion, we failed to find any evidence on the association between consumption of low carbohydrate diet (LCD) and odds of gastric cancer. Further studies, in particular of prospective design, are required to confirm these findings.

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Table1. General characteristic of participants across tertiles of LCD score[1]

Characteristics	Groups				Tertile of LCD score			
	Cases (n=178)	**Controls (n=276)**	**P[2]**		**Lowest**	**Middle**	**Highest**	**P[2]**
Age (years)	60.8±12.0	53.2±11.9	<0.001		55.4±12.7	56.2±12.2	57.3±12.5	0.88
Gender (Male, %)	132(74.2)	176(63.8)	0.02		114(69.1)	104(66.7)	90(67.7)	0.89
Marital status (Married, %)	174(97.8)	239(86.6)	<0.001		148(89.7)	141(90.4)	124(93.2)	0.54
Education (illiterate, %)	111(62.4)	72(26.1)	<0.001		62(37.6)	61(39.1)	60(45.1)	0.54
Residential (Tehran, %)	93(52.3)	140(50.8)	0.751		99(60.0)	81(51.9)	53(39.9)	0.001
Smoking (yes %)	81(45.51)	85(30.8)	0.001		68(41.2)	52(33.3)	46(34.6)	0.292
H-pylori (positive, %)	68(38.2)	155(56.2)	<0.001		81(49.1)	76(48.7)	66(49.6)	0.99
Alcohol intake (g/day)	6.8±86.4	1.7±11.7	0.3		0.8±8.11	1.6±10.4	10.7±104.73	<0.001
BMI (kg/m2)	27.8+16.4	26.0+8.2	0.12		27.0(9.6)	25.6(4.8)	27.7(18.9)	<0.001

[1] Reported figures are means±SDs unless indicated.

[2]Obtained from chi-square test for categorical variables and independent student's t-test for continuous variables.

[3] Obtained from chi-square test for categorical and one-way ANOVA for continuous variables.

[4]based on self-reported data.

Table2. Dietary intakes of participants across tertiles of LCD score								
Nutrient /food group	Groups				Tertiles of LCD score			
	Cases (n=178)	Controls (n=276)	P[1]		1	2	3	P[2]
Energy (Kcal/d)	2853±1241	2782±1252	0.55		2962.9±1374.6	2872.8±1117.7	2545.3±1188.4	0.012
Vegetables (g/d)	254.1±176.4	394.9±225.6	<0.001		351.8±230.6	334.8±222.1	330.7±199.4	0.67
Fruits (g/d)	355.0±270.2	531.0±373.8	<0.001		462.9±333.6	459.5±346.1	463.9±368.1	0.994
Red meats (g/d)	15.9±13.4	17.8±15.2	0.356		15.6±19.5	18.3±20.8	17.5±19.8	0.447
Processed meats (g/d)	5.7±14.8	9.1±20.7	0.056		4.6±11.9	10.9±23.2	8.1±18.9	0.010
Fats (g/d)	104.6±57.9	97.7±60.5	0.234		81.8±44.8	107.9±53.8	114.6±74.7	<0.001
Proteins (g/d)	126.2±47.2	122.9±50.8	0.497		120.9±52.6	126.7±45.3	125.3±47.2	0.545
Carbohydrates (g/d)	367.2±180.8	365.1±176.9	0.904		447.6±210.84	364.6±136.7	265.7±115.5	<0.001
Animal fat (g/d)	45.1±28.3	41.4±24.3	0.137		35.9±23.7	44.3±24.6	50.0±28.0	<0.001
Vegetable fat (g/d)	59.4±47.2	56.3±51.2	0.517		45.9±32.3	63.7±46.2	64.6±66.2	<0.001
Animal protein (g/d)	89.3±42.7	86.3±38.6	0.438		72.9±36.8	91.7±36.7	100.7±42.9	<0.001

Vegetable protein (g/d)	36.8±21.1	36.7±21.9	0.934		48.0±26.1	35.0±15.6	24.7±12.5	<0.001
Saturated fatty acids(g/d)	29.4±17.3	26.4±15.3	0.054		22.9±14.8	29.1±14.5	31.7±18.3	<0.001
Mono unsaturated fatty acids	35.7±29.1	33.9±31.3	0.526		21.4±11.2	27.9±13.4	30.1±17.5	<0.001
Poly unsaturated fatty acids	27.5±14.5	25.4±14.5	0.134		26.1±19.2	38.4±28.0	40.7±40.7	<0.001
Fiber (g/d)	19.9±10.7	18.9±9.16	0.364		22.2±10.8	19.6±9.1	15.4±7.8	<0.001
Sugar (g/d)	170.3±82.3	169.5±81.9	0.918		179.2±93.1	178.6±75.5	147.9±70.1	0.0012
Energy from fats (%)	32.5±8.9	30.9±8.2	0.051		24.5±5.3	32.8±6.2	38.7±7.3	<0.001
Energy from proteins (%)	18.4±4.9	18.7±4.7	0.633		16.82±3.4	18.4±4.7	20.9±5.4	<0.001
Energy from Carbohydrates (%)	51.3±8.7	52.6±8.7	0.125		60.7±5.4	51.1±2.9	42.5±4.9	<0.001
[1]using independent student T-test [2] using one-way ANOVA								

Table3. Odd Ratios (ORs) and 95% confidence Intervals (CIs) for gastric cancer across tertiles of LCD score[1]

	OR (95%CI)			P trend[1]
Total No. of cases/controls (178/276)	Tertile 1	Tertile 2	Tertile 3	
Crude	1.00	1.12(0.72-1.77)	1.31(0.82-2.09)	0.256
Model A[2]	1.00	1.11(0.69-1.79)	1.27(0.78-2.09)	0.341
Model B[3]	1.00	1.16 (0.69-1.97)	1.08 (0.62-1.89)	0.756
Model C[4]	1.00	1.27 (0.71-2.26)	1.07(0.59-1.95)	0.789

[1] Trend was analysed considering tertiles of LCD as continuous variable.

[2]Adjusted for age(continuous), sex(male/female) and energy intake(continuous)

[3]Further adjusted for education (illiterate/literate), marital status (married/single) and residential place (Tehran/others), alcohol intake(continuous), smoking status(smoker/nonsmoker) and H-pylori infection(positive/negative)

[4] Additionally controlled for BMI(continuous)

Table4. Odd Ratios (ORs) and 95% confidence Intervals (CIs) for gastric cancer across tertiles of animal LCD score[1]

	OR (95%CI)					
Total No. of cases/controls (178/276)	Tertile 1		Tertile 2		Tertile 3	P trend[1]
Crude	1.00		1.30(0.83-2.06)		1.11(0.69-1.77)	0.645
Model A[2]	1.00		1.31(0.81-2.12)		1.13(0.68-1.87)	0.610
Model B[3]	1.00		1.23(0.71-2.11)		0.95(0.53-1.69)	0.868
Model C[4]	1.00		1.12(0.62-2.01)		0.81(0.44-1.52)	0.531

[1] Trend was analysed considering tertiles of LCD as continuous variable.

[2]Adjusted for age(continuous), sex(male/female) and energy intake(continuous)

[3]Further adjusted for education (illiterate/literate), marital status (married/single) and residential place (Tehran/others), alcohol intake(continuous), smoking status(smoker/nonsmoker) and H-pylori infection(positive/negative)

[4] Additionally controlled for BMI(continuous)

Table4. Odd Ratios (ORs) and 95% confidence Intervals (CIs) for gastric cancer across tertiles of vegetable LCD score[1]

	OR (95%CI)					
Total No. of cases/controls (178/276)	Tertile 1		Tertile 2		Tertile 3	P trend[1]
Crude	1.00		0.97(0.62-1.52)		1.52(0.94-2.45)	0.103
Model A[2]	1.00		0.86(0.54-1.38)		1.33(0.80-2.21)	0.294
Model B[3]	1.00		0.75(0.49-1.28)		1.13(0.64-1.99)	0.699
Model C[4]	1.00		0.83(0.46-1.48)		1.25(0.67-2.31)	0.483

[1] Trend was analysed considering tertiles of LCD as continuous variable.

[2]Adjusted for age(continuous), sex(male/female) and energy intake(continuous)

[3]Further adjusted for education (illiterate/literate), marital status (married/single) and residential place (Tehran/others), alcohol intake(continuous), smoking status(smoker/nonsmoker) and H-pylori infection(positive/negative)

[4] Additionally controlled for BMI(continuous)