

NAZARBAYEV UNIVERSITY
SCHOOL OF MEDICINE

**NUTRITIONAL AND BEHAVIORAL RISK FACTORS FOR GASTRITIS IN
KAZAKHSTANI POPULATION: PRELIMINARY RESULTS.**

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Table of Contents

Abstract.....	2
Introduction.	3
General Information.....	3
Aims and objectives.....	4
Methods and Materials.	5
Study population.....	5
Data analysis.....	6
Results.	7
Discussion.....	11
Limitations.....	16
References.	17
List of appropriate journals, where this study might be published.....	22

Abstract.

Gastritis is characterized as inflammation in stomach, and it can be acute and chronic. Acute gastritis can go away in several days, while chronic gastritis can persist for years. The latter is implicated with increased risk for gastric cancer. Risk factors for gastritis include *H.pylori* infection, family history, psychological stress, use of drugs, and lifestyle habits. Since Kazakhstan holds the fifth place among the highest stomach cancer mortality rates worldwide, epidemiology of risk factors for gastric cancer and its potential precursors are needed to study. To address this issue, lifestyle habits and family history were studied for association with chronic non-atrophic gastritis. The survey on nutrition and behavioral habits was given to patients, who underwent gastroendoscopy in two hospitals of Astana, and then further analyzed with bivariate non-parametric and bivariate logistic regression tests. Data from total of 19 gastritis patients and 14 non-gastritis patients were obtained. Though no statistical significance was found during analysis, higher frequency of alcohol drinking, kazy/shuzhyk eating, drinking piped water, having family history of cancer, and hypertension were detected in gastritis patients comparing with controls. Kumys/shubat drinking, eating fresh fruits, and overweight and obesity was less present in gastritis group than in controls. These findings supported existing knowledge on risk factors for gastritis and gave more specific evidence for chronic non-atrophic gastritis. Moreover, more research is needed on larger sample size to elucidate role of food in risk of developing chronic gastritis in people living in Kazakhstan.

Introduction.

Background Information.

Gastritis is defined as inflammation of gastric mucosa, which is protective lining of the stomach (Papavassiliou et al, 2008). Based on the level of inflammation, gastritis is divided into two types, acute and chronic. The former type involves noticeable symptoms such as problems in stomach and bowel, which can be self-limiting. Meanwhile, the latter type can occur unnoticed with irregular complaints in the stomach, last for years, and have a high risk of proceeding to precancerous lesions (atrophic gastritis, intestinal metaplasia, dysplasia) or even gastric cancer proposed as Correa pathway (Correa, 1988). Chronic gastritis itself has two types: non-atrophic (NAG) and atrophic (AG), (Dixon et al, 1996). If non-atrophic gastritis is defined as chronic inflammation of the stomach, then atrophic gastritis is also accompanied with loss of secretory glands, which are responsible for production of essential digestive substances. Atrophic gastritis has been numerously reported with increased risk of gastric cancer development, while role of chronic non-atrophic gastritis in susceptibility for gastric cancer is often underrated, though it is one of the predecessors of atrophic gastritis (Correa, 1992; Sipponen et al, 1987; Jewell, 1992). Indeed, various risk factors for atrophic gastritis have been studied widely including infection with *H.pylori*, genetics, autoimmune diseases, and diet (Freedman et al, 2010; Kamangar et al, 2011; Karimi et al, 2014; Uemura et al, 2001; Leung, Sung, 2002). On the other hand, chronic gastritis is also associated with these factors in along with chemicals (non-steroid anti-inflammatory drugs, bile acid reflux) and stress though role of diet remains controversial (Hawkey, Langman, 2003; Levenstein et al, 2015).

Numerous studies on diet and risk of atrophic gastritis were carried out in the East Asian region, where gastric cancer rates are the highest in the world. For example, eating salty food, which is especially widespread in Japan, has been reported to increase risk of developing atrophic gastritis and metaplasia but few studies did it on non-atrophic type (Song et al, 2017; Ddine et al, 2012; Chen et al, 1990; Shibata et al, 2002). Meanwhile, eating spicy food,

processed meat, canned food, and smoked food also were found to increase risk for atrophic gastritis (Kang et al, 2012; Kim et al, 2008; Joo et al, 2013). Furthermore, other habits were regarded as risky ones such as drinking alcohol and smoking (Stermer, 2002; Namiot et al, 2007). In contrast, consumption of fresh vegetables was found to improve gastric mucosa of Chinese patients that is useful during gastritis (Chooi et al, 2012). However, even in wide range of studies on these factors, their role in developing particularly in non-atrophic gastritis remains elusive.

However, most of the studies focus on East Asian countries, while the Central Asia region with second highest occurrence of gastric cancer remains underreported. Kazakhstan holds the fifth place in mortality rates, and 7th highest incidence rate of 21.6 per 100,000 in 2012 (Rafiei et al, 2016; Moore, 2013). It is also unclear whether local traditional food and drinks, namely kazy/shuzhyk (homemade horse meat sausages) and kumys/shubat (fermented milk of mare and camel respectively), have an effect on risk of chronic non-atrophic gastritis. Therefore, the role of dietary factors (salty food, canned food, smoked food, fresh vegetables) and Kazakh traditional food and drinks (kazy, shuzhyk, kumys, shubat) in development of chronic non-atrophic gastritis, would be addressed in the group of Kazakhstani patients.

Aims and objectives.

1. Find out the effect of nutritional aspects of Kazakhstani diet including traditional food, kazy/shuzhyk and kumys/shubat on risk of gastritis.
2. Study an association between behavioral habits, namely alcohol drinking, smoking, engaging into sports, and gastritis.
3. Look at influence of sociodemographic characteristics and comorbidities (hypertension, overweight/obesity) on gastritis development.

Methods and Materials.

Study population.

This study was approved by the Nazarbayev University School of Medicine Ethics Committee. Patients were recruited by trained interviewers from two Astana hospitals: Republican Diagnostic Center (University Medical Center) and Oncology Center in Astana city, Kazakhstan. The Oncology center has capacity of 380 visits per shift, while the Republican Diagnostic Center can provide services to 500 patients per day (Onko-Astana, 2017; UMC, 2018). Endoscopy departments were chosen in both Centers for data collection because their primary focus was endoscopy diagnostics of stomach, which was crucial for this study. The former Center is more specialized on patients with high probability of having gastric cancer and those after gastric surgery. In the Oncology Center, around 40-45 endoscopic patients are examined per week, and among of them about 3-5 cases of gastritis occur. Meanwhile, in the latter Center most of the patients come with gastric issues other than gastric cancer and routine health check-up. The approximate number of endoscopy patients can be 50-60 people weekly, and with gastritis there can be around 5-7.

The case-control study was conducted via convenient nonrandom sampling method in the hospital settings from February 2018 till March 2018. Potential participants were approached before or after endoscopy examination to ask about taking part in the research. They were considered for study if they came for primary check-up. Participants were also eligible if they were 18 years and older, did not have mental illnesses, any type of cancer, and if they were not critically ill. The diagnosis was identified by physician from endoscopy examination. Once participants filled the survey, their diagnosis was transferred from medical records to the questionnaire.

Participants were provided with a prior verbal explanation about the research and given consent form to sign. Participants were administered a 10-15-minute questionnaire, which was

adapted from the National Institute of Health Diet History Questionnaire II (NIH, n.d). Patients diagnosed with chronic non-atrophic gastritis (superficial gastritis, erosive gastritis, diffuse antral gastritis, chronic active gastritis, and non-ulcer pangastritis) were defined as cases, while patients with other gastric illnesses or healthy state were categorized as controls except those with any type of cancer.

In the survey, the following data was collected, and further used as variables in the analysis: sociodemographic characteristics (age, sex, ethnicity, occupation, residence), comorbidities (hypertension, weight, height), dietary intake characteristics (kumys/shubat, kazy/shuzhyk, salted, processed, pickled, canned, smoked, fresh food, water type), behavioral habits (smoking, drinking alcohol, doing sports) as well as family history of cancer diseases and cooking source. Moreover, survey consisted of questions regarding frequency and size of each food/drink, which were further categorized during the analysis. The diagnosis of chronic non-atrophic gastritis was an outcome variable.

BMI was calculated based on weight and height data. Subsequently, BMI values were categorized as overweight/obese and non-overweight/obese according to the World Health Organization classification (WHO, 2017).

Data analysis.

The collected data were analyzed using STATA version 12.0 software (StataCorp LP, TX, USA). Particularly, it included univariate, bivariate non-parametric and bivariate logistic analyses with gastritis as the outcome. The univariate and bivariate tests (non-parametric Mann-Whitney U and Fisher's exact test) were performed for primary evaluation of the collected data, and to identify statistically significant differences between cases and controls. Non-parametric tests (Mann-Whitney U, Fisher's exact test) were chosen due to small sample size. Due to the same reason, simple logistic regression with stratification (according to median age=58) was

chosen instead of multivariate alternative, and thus ensuring adjustment for the most common confounder, namely age. Statistical significance was defined at $\alpha=0.05$ level.

Results.

Sociodemographic characteristics were shown in Table 1 including mean age and BMI as well as sex, BMI categories, ethnicity, hypertension status, residence distributions. Total of 40 participants were recruited, however, after removing samples according to exclusion criteria, the final number was 33 with n=19 of gastritis patients and n=14 of controls. Though bivariate analysis did not show statistical significance, following trends can be suggested. Namely, cases had higher percentage distribution of females, namely 73.7% in cases and 42.9% in controls. Next, percentage of hypertensive individuals with gastritis was almost two-fold larger than in controls, 26.3% versus 14.3% accordingly. Furthermore, controls tended to be more overweight and obese than normal and overweight in comparison with gastritis patients, whose distribution of BMI ≤ 25 and BMI > 25 was close to each other. Additionally, mean BMI in cases was notably smaller than in controls.

Table 1. Sociodemographic characteristics.

Variable	Type	Total	Cases, n=19	Controls, n=14	p-value
Mean Age, years \pm S.D. ¹		53.87 \pm 17.37	49.62 \pm 4.51	50.73 \pm 4.93	0.794 ²
Sex, n (%)	Female	25 (62.50%)	14 (73.68%)	6 (42.86%)	0.148 ³
	Male	15 (37.50%)	5 (26.32%)	8 (57.14%)	
BMI, kg/m ² \pm S.D. ¹		27.17 \pm 5.79	25.93 \pm 4.67	29.09 \pm 6.05	0.188 ²
BMI category, n (%)	<25	11 (33.3%)	8 (42.1%)	3 (21.5%)	0.278 ³
	≥ 25	22 (67.7%)	11 (57.9%)	11 (78.6%)	
Ethnicity, n (%)	Kazakh	32 (82.05%)	16 (88.89%)	11 (78.57%)	0.631 ³
	Other	7 (17.95%)	2 (11.11%)	3 (21.43%)	
Hypertension, n (%)	No	32 (80%)	14 (73.68%)	12 (85.71%)	0.670 ³
	Yes	8 (20%)	5 (26.32%)	2 (14.29%)	
Residence, n (%)	Urban	32 (80%)	17 (89.5%)	9 (69.2%)	0.194 ³
	Rural	8 (20%)	2 (10.5%)	4 (30.8%)	

¹ Standard deviation. ² p-value obtained from Mann-Whitney U test. ³ p-value obtained from

Fisher's exact test.

Nutritional and behavioral habits of participants were outlined in Table 2. Bivariate analysis also revealed distribution trends but did not provide p-values below significance level. In terms of smoking in the past, larger proportion of gastritis patients (42.9%) had this habit than controls (22.2%). Cases also tended to in smaller amounts, 78.9% drank less than 1 standard unit of alcohol (beer bottle or can, a glass of wine, shot of vodka/cognac/whiskey) than controls (64.3%), though their frequency of alcohol consumption was almost the same. Furthermore, drinking kumys/shubat also appeared to be less frequent (84.2%) in gastritis patients than in control group (71.4%). In contrast, engaging in sports activities was more popular in cases (78.9%) comparing with controls (50%). Though consuming processed food was twice smaller in cases, eating traditional sausage, namely kazy/shuzhyk, was considerably more often in former ones (57.9%) than in controls (35.7%). Moreover, higher percentage of gastritis patients tended to eat more than 100 grams of kazy/shuzhyk than non-gastritis participants. Canned food was consumed more frequently by controls than cases. Though larger proportion of gastritis patients ate fresh vegetables than controls, 68.4% and 35.7% accordingly, fresh fruits were eaten more often by the latter ones (57.1%) than former patients (47.4%). Presence of family members with history of cancer was in higher extent in cases than in controls by almost 30%. Finally, majority of cases (89.5%) were from urban area, comparing with controls, whose 69.2% of participants came from cities.

Table 2. Summary of behavioral and eating habits.

Variable	Status	Total, n (%)	Cases, n (%)	Controls, n (%)	p-value ¹
Current smoking status	No	32 (86.49%)	17 (89.47)	12 (85.71%)	1.000
	Yes	5 (13.51%)	2 (10.53%)	2 (14.29%)	
Past smoking status	No	21 (72.41%)	8 (57.14%)	7 (77.78%)	0.429
	Yes	8 (27.59%)	6 (42.86%)	2 (22.22%)	
Smoking shisha	No	32 (91.43%)	15 (88.23%)	10 (90.91%)	1.000
	Yes	3 (8.57%)	2 (11.77%)	1 (9.09%)	
Kumys/Shubat	No	27(71.05%)	16 (84.21%)	10 (71.43%)	

frequency	≥ 2 times/month	11 (28.95%)	3 (15.79%)	4 (28.57%)	0.422
Kumys/Shubat size	< 1 regular size tea cup ≥ 1 regular size tea cup	12 (50%) 12 (50.0%)	6 (31.58%) 13 (68.42%)	5 (35.71%) 9 (64.29%)	1.000
Alcohol frequency	No ≥ 1 time/ month	20 (54.05%) 17 (45.95%)	11 (57.89%) 8 (42.11%)	7 (50%) 7 (50%)	0.733
Alcohol size, 1 regular size (beer bottle/ can, glass of wine, shot of vodka/cognac/ whisky)	< 1 regular size 1 to 3 regular size	5 (33.33%) 10 (66.67%)	15 (78.95%) 4 (21.05%)	9 (64.29%) 5 (35.71%)	0.422
Sports time	No ≥ 15 min	26 (68.42%) 12 (31.58%)	4 (21.05%) 15 (78.95%)	7 (50%) 7 (50%)	0.136
Processed meat frequency	No ≥ 2 times/month	16 (42.11%) 22 (57.89%)	10 (52.63%) 9 (47.37%)	8 (57.14%) 6 (42.86%)	1.000
Processed meat size	<100 gr ≥ 100	12 (36.36%) 21 (63.63%)	11 (57.9%) 8 (42.1%)	4 (28.57%) 10 (71.43%)	0.158
Kazy/shuzhyk frequency	No ≥ 2 times/month	17 (44.73%) 20 (55.27%)	8 (42.1%) 11 (57.9%)	9 (64.3%) 5 (35.7%)	0.296
Kazy/shuzhyk size	< 100 gr ≥ 100 gr	22 (64.71%) 12 (35.29%)	13 (68.4%) 6 (35.7%)	11 (78.6%) 3 (21.4%)	0.698
Pickled vegetables frequency	No ≥ 2 times/month	17 (45.94%) 20 (54.06%)	14 (73.7%) 5 (26.3%)	9 (64.3%) 5 (35.7%)	0.707
Pickled vegetables size	< 1 regular-size pickled vegetable ≥ 1 regular-size pickled vegetable	13 (37.14%) 22 (62.86%)	8 (42.1%) 11 (57.9%)	5 (35.7%) 9 (64.3%)	1.000
Salted snack frequency	No ≥ 2 times/month	26 (70.27%) 11 (29.73%)	13 (68.4%) 6 (31.6%)	9 (64.3%) 5 (35.7%)	1.000
Salted snack size	< 1 regular package ≥ 1 regular package	14 (77.78%) 4 (22.3%)	7 (70%) 3 (30%)	6 (85.7%) 1 (14.3%)	0.603
Smoked food frequency	No ≥ 2 times/month	27 (72.97%) 1 (27.03%)	15 (78.9%) 4 (21.1%)	11 (78.6%) 3 (21.4%)	1.000
Smoked food size	< 100 gr 100 to 300 gr	15 (62.5%) 9 (37.5%)	15 (78.9%) 4 (21.1%)	11 (78.6%) 3 (21.4%)	1.000
Canned food frequency	No ≥ 2 time/month	15 (41.67%) 21 (58.33%)	10 (52.6%) 9 (47.4%)	5 (35.7%) 9 (64.3%)	0.482
Fresh vegetables frequency	≤ 2 times/week > 3 times/week	16 (44.45%) 20 (55.55%)	6 (31.6%) 13 (68.4%)	9 (64.3%) 5 (35.7%)	0.085

Fresh vegetable size	< 1 plate 1 to 3 plates	28 (80.0%) 7 (20.0%)	14 (73.7%) 5 (26.3%)	12 (85.7%) 2 (14.3%)	0.670
Fresh fruit frequency	≤ 2 times/week > 3 times/week	16 (44.45%) 20 (55.55%)	10 (52.6%) 9 (47.4%)	6 (42.9%) 8 (57.1%)	0.728
Fresh fruit size	< 1 regular sized fruit ≥ 1 regular sized fruit	9 (25.0%) 27 (75%)	4 (21.1%) 15 (78.9%)	4 (28.6%) 10 (71.4%)	0.695
Water type	Bottled water Piped water	21 (58.33%) 15 (41.67%)	7 (36.8%) 12 (63.2%)	7 (50%) 7 (50%)	0.497
Cooking source	Electric stove Gas stove	15 (71.43%) 6 (28.57%)	9 (75%) 3 (25%)	4 (57.1%) 3 (42.9%)	0.617
Family Cancer	No Yes	21 (60.0%) 14 (40.0%)	11 (57.9%) 8 (42.1%)	12 (85.7%) 2 (14.3%)	0.131

¹ p-values obtained from Fisher's Exact Test.

Selected logistic regression results were presented in Table 3. None of the models reached significance level. First, BMI \geq 25 occurred to be have odds less than 1 (OR, 0.38; 95% CI, 0.08-1.80) comparing to those with BMI<25. Next, having hypertension appeared to increase odds of getting gastritis (OR, 2.14; 95% CI, 0.35-13.12) as well as history of family cancer (OR, 3.6; 95% CI, 0.76-25.1). Next, eating fresh fruits tended to decrease odds ratio of getting gastritis (OR, 0.68; 95% CI, 0.17-2.71). Eating processed meat increased odds of having gastritis by 1.2 times (95% CI, 0.29-4.82). For those eating kazy/shuzhyk odds of having gastritis were equal to 2.48 (95% CI, 0.59-10.27). Next, drinking alcohol appeared to decreased odds for gastritis (OR, 0.73; 95% CI, 0.18-2.92). Drinking kumys/shubat had higher odds than those that did not drink these beverages (OR, 0.47; 95% CI, 0.09-2.55). Finally, drinking piped water combined increased odds of having gastritis by 1.71 times (95% CI, 0.42-6.97). Stratification for age groups (Age \leq 58 and Age>58) revealed that odds ratio for having gastritis tended to increase in elder group comparing with younger one in alcohol drinking, kazy/shuzhyk eating, family history of cancer, fresh vegetables, processed meat eating. P-values for having family of cancer, eating fresh vegetables, and eating kazy/shuzhyk approached significance level, and they were around 0.06. Meanwhile, odds for gastritis dropped in elder age group for those with BMI>25.

Table 3. Bivariate logistic regression with gastritis as outcome.

Variable	Status	Total		Age≤58		Age>58	
		OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value
BMI	<25	1		1		1	0.217
	≥25	0.38 (0.08-1.80)	0.220	0.63 (0.07-5.35)	0.668	0.21 (0.02-2.48)	
Hypertension	No	1				1	
	Yes	2.14 (0.35-13.12)	0.410	Cannot be determined		1.28 (0.16-10.45)	0.814
Kumys/Shubat frequency	< 1 regular size tea cup	1				1	
	≥ 1 regular size tea cup	0.47 (0.09-2.55)	0.380	Cannot be determined		1.29 (0.16-10.45)	0.814
Alcohol frequency	No	1		1		1	
	≥ 1 time/month	0.73 (0.18-2.92)	0.653	0.4 (0.05-3.42)	0.403	1.11 (0.16-7.51)	0.914
Alcohol size	< 1 regular size	1		1		1	
	1 to 3 regular size	0.48 (0.10-2.27)	0.354	0.13 (0.01-1.72)	0.120	1.29 (0.16-10.45)	0.814
Processed meat frequency	No	1		1		1	
	≥ 2 time/month	1.2 (0.29-4.82)	0.797	0.625 (0.07-5.35)	0.668	2 (0.26-15.38)	0.505
Kazy/shuzhyk frequency	No	1		1		1	
	≥2 times/month	2.48 (0.59-10.27)	0.212	0.625 (0.07-5.35)	0.668	10.5 (0.91-121.39)	0.06
Fresh vegetable frequency	≤2 times/week	1		1		1	
	≥ 3 times/week	3.9 (0.91-16.79)	0.068	2 (0.24-16.61)	0.521	7 (0.86-56.89)	0.069
Fresh fruit frequency	≤ 2 times/week	1		1		1	
	≥ 3 times/week	0.68 (0.17-2.71)	0.579	0.4 (0.05-3.42)	0.403	1 (0.16-6.42)	1.000
Family cancer	No	1		1		1	
	Yes	36 (0.76-25.1)	0.099	1.43 (0.09-20.4)	0.793	10.5 (0.91-121.4)	0.06
Water Type	Bottled	1		1		1	
	Piped	1.71 (0.42-6.97)	0.451	1.25 (0.16-9.92)	0.833	2.33 (0.34-16.18)	0.391

Discussion.

In summary, this thesis studied nutritional and behavioral habits, which can serve as possible risk factors for gastritis. Though none of the results showed statistical significance, several speculations and recommendations can be made for further studies. First, analysis of sociodemographic analysis showed that gastritis patients were more likely female and having

hypertension than controls. However, cases had lower mean BMI than controls. Further analysis of answers on questions about diet and alcohol/tobacco consumption revealed that gastritis patients tended to eat kazy, fresh vegetables and smoke in the past more often than control group. However, drinking alcohol and kumys/shubat, eating fresh fruits were less frequent habits in the cases comparing with non-gastritis patients. Furthermore, larger proportion of participants with gastritis drank piped water and had family history of cancer. Finally, logistic regression suggested that several habits can be either risk or protective factors for gastritis. Kumys/shubat, fresh fruits, BMI, and alcohol decreased odds for having gastritis, while hypertension, processed meat, kazy/shuzhyk, family cancer, and piped water increased risk of being diagnosed with gastric inflammation. Finally, stratification for age groups revealed that variable acquired stronger protective/risk feature comparing with the younger group, and thus suggesting that age can be a potential confounder for having gastritis due to thinning stomach lining as people get older (Kekki et al, 1990).

Gastritis is considered as one of the common side-effects of taking non-steroidal anti-inflammatory drugs (NSAIDs) during hypertension treatment (Assaad et al, 2016; Lanas et al, 2013; Chaterjee, 2015). Remarkably, in this study, both frequency and logistic analysis also revealed trend towards larger proportion hypertensive patients in gastritis group and increased odds for having gastritis. Therefore, NSAIDs intake can be a major contributor for gastritis development in hypertensive individuals.

Obesity and overweight had been widely reported for their association with gastritis development (Yamamoto, 2012; Kim, 2007; Yamamoto et al, 2011). Inflammatory cytokines released from adipocytes are believed to be linked with increased inflammation in stomach. For example, BMI was significantly higher in Japanese and Korean patients with erosive gastritis (Kim, 2007; Yamamoto et al, 2011). However, our study revealed that people with BMI higher than 25 kg/m^2 had decreased odds of being diagnosed with gastritis. Similarly, studies on

relationship between atrophic gastritis and BMI also found that patients with atrophic gastritis had significantly lower BMI values than non-atrophic gastritis group in Japanese patients (Watabe et al, 2009; Suto et al, 2010). Therefore, this finding also should be considered for future studies to monitor relationship of BMI and different types of gastritis for more conclusive results.

Kazy/shuzhyk consumption was high in cases than in controls, and logistic regression analysis results also suggested it to be a risk factor for gastritis. Though there are very few studies on this type of food, several reports imply that high concentration of salt in kazy/shuzhyk and carcinogenic compounds in shuzhyk, namely nitrosamines, can play role in gastric and esophageal cancer development. Particularly, several Soviet-time studies reported that average proportion of salt to meat is 3 g to 100 g and 4 g to 100 g in kazy and shuzhyk respectively (Barmintsev, 1980; Tuleulov, 1986). Since in this study majority of gastritis patients eat kazy/shuzhyk in range of 100 g to 300 g, then their salt consumption would exceed the recommendations by WHO. Next, other Soviet-period researchers found out that shuzhyk concentration of carcinogenic compounds, nitrosamines, exceed healthy range, which were 7 $\mu\text{g}/\text{kg}$ and 5 $\mu\text{g}/\text{kg}$ accordingly (Stermermann, 1981; Aidjanov, 1982). Meanwhile, in homemade kazy this characteristic was lower than 0.9 $\mu\text{g}/\text{kg}$, which was regarded as safe dose of nitrosamines. Importantly, nitrosamines can cause inflammation in stomach, while continuous exposure was associated with development of atrophic gastritis, intestinal metaplasia, and eventually gastric cancer (Pourfarzi et al, 2009; Haenszel et al, 1972; Schlag et al, 1980). Therefore, at least these two aspects, salt and nitrosamines, should be considered in contributing of kazy/shuzhyk to increase odds for gastritis.

Having kumys/shubat in diet revealed to be less frequent in cases in our research, it also decreased odds against gastritis, and thus suggesting protective feature of kumys/shubat drinking. These characteristics of kumys/shubat can be attributed due to immunomodulating and

antimicrobial properties. First, shubat was found to contain peptidoglycan recognition protein, lactoferrin, lactoperoxidase and other proteins, which stimulate host immunity and possess antimicrobial activity against *E.coli*, *Salmonella* and *Pseudomonas* species, rotavirus, *L. monocytogenes* (Gul et al, 2015; Hosam et al, 2013; Abbas et al, 2013; Benkerroum et al, 2004; Al-Majali et al, 2007). Meanwhile, kumys contains lactoferrin, lysozyme that exert antibacterial effect inhibiting growth of *S.typhimurium*, *L.monocytogenes* and *C.botulinum* (Guri et al, 2015; Wulijideligen et al, 2015). Furthermore, probiotic bacteria strain found in kumys, namely *L.helveticus* NS8, was shown to exhibit anti-inflammatory activities through activation of IL-10 interleukin production in mouse macrophage cell line (Rong et al, 2015). Next, a study on Mongolian patients with gastric cancer found out that drinking kumys decreased risk of getting gastric cancer, thus suggesting that protective mechanisms of kumys/shubat might also work on gastritis as well (Tsegmed et al, 2012). Finally, kumys and shubat therapy was found to be successful in treating peptic ulcer patients by healing wounds in 93% and 90% of patients treated by kumys and shubat respectively (Sharmanov et al, 1981).

In terms of alcohol drinking, our study revealed that though alcohol consumption does not differ notably between case and control groups, it can also have protective features against gastritis. Alcohol consumption has been implicated in many gastrointestinal complications in a dose-dependent manner. Studies report that heavy alcohol consumption induces acute inflammation in the stomach, and thus can play role in development of chronic gastritis (Gao et al, 2009; Dixon et al, 1994; Anderson et al, 1973). However, it also found that alcoholic beverages with less than 5% of ethanol concentration can trigger acid production inside the stomach, while those with higher ethanol percentage did not have such effect (Mincis et al, 1995). Furthermore, red wine has been linked with anti-bacterial effect in the stomach including *H.pylori*, *E.coli*, *Shigella* and *Salmonella* species (Blaser, 2006; Brenner et al, 2001). Additionally, other studies emphasized role of moderate consumption, which can be beneficial

for people in contrast with heavy drinking episodes (Weisse et al, 2015; Taylor et al, 2005). In comparison, most of the participants of our study drank up to three regular drinks, which is a recommended dosage for both women and men (CDC, 2013). Therefore, protective features of alcohol found in this study could be because of moderate consumption pattern.

Fresh fruits and vegetables were not found to have significantly associated with gastritis, though fresh fruits are suggested to have protective features in logistic regression analysis. Numerous studies found fresh vegetables and fruits to decrease risk of gastric cancer (Kato et al, 1990; Inoue et al, 1995; Mirvish, 1983; Kato et al, 1995). They contain plenty of micronutrients such as Vitamin C that can protect from cancer development. Regarding gastritis there are controversial reports with some arguing for beneficial features, while others obtaining no statistically significant results (Chooi et al, 2012; Shibata et al, 2002; Tsugane et al, 1993; Kato et al, 1992). Japanese researchers suggest that fruits and vegetables can have advantageous effect against stomach cancer but may lack such features for atrophic gastritis (Ozasa et al, 1999). However, this statement is yet arguable because atrophic gastritis is frequently linked with risk of gastric cancer itself, and therefore more studies should be performed in area of fresh fruits/vegetables and gastritis.

Our analysis whether water source had associations with gastritis showed that larger proportion of cases used piped water, and increased risk of having the disease. Water sources have been linked with gastrointestinal diseases mostly due to inadequate sanitation, and subsequent infection with bacterial or parasitic pathogens (Eichelberger et al, 2015; Carballo et al, 1997; Klein et al, 1991). Recent study showed that in Kazakhstan has access to sanitized water in 84% of urban area and only in 10% of rural area (GWP, 2009). Since majority of participants and cases were from urban area, this might imply that cities can have issues with proper chlorination of water. Moreover, *H.Pylori* infection and quality of water were either

poorly studied or not examined at all, future studies can address these areas to better understand impact of water quality on health of Kazakhstani citizens.

Family history of cancer, especially gastric cancer, has been found to be a risk factor mostly for atrophic gastritis across studies (Gao et al, 1997; Sepulveda et al, 2002; Nishizawa et al, 2017). We also found positive but insignificant trend for gastritis in patients with familial history of cancer, suggesting its role in development of gastritis as well. The studies suggest that familial history increases susceptibility and response to major risk factor such as *H.pylori*, and possibly lifestyle habits.

Limitations.

One of the major limitations was the small sample size, which did not allow to reach statistically significant results, and could also lead to spurious results. The study was performed during one-and-a-half-month period in two hospitals, and thus longer time is needed for future studies. Next, most of the patients were not tested for *H.pylori* infection, which is one of the major risk factors. Furthermore, other possible risk factors (psychological well-being, water quality, carbonated drinks, fast food) were omitted, thus it can undermine statistical analysis, and draw inconclusive results.

In conclusion, various lifestyle habits were studied for association with risk of developing gastritis. Alcohol, smoking, kazy/shuzhyk, history of family cancer, piped water type, overweight and obesity, and hypertension were found among potential risk factors. Meanwhile, consumption of fresh fruits and drinking kumys/shubat were suggested as protective factors. This study expanded knowledge in terms of effect of nutrition and behavior on risk of having chronic non-atrophic gastritis, while the previous researches were mostly done on atrophic type. Moreover, novel discovery of kazy/shuzhyk as a risk factor for having chronic gastritis is suggested for further studies and recommendations on diet. Finally, more research is needed for more evidence for the proposed risk and protective factors.

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List of appropriate journals, where this study might be published.

1. Journal of Gastrointestinal and Digestive System
2. Gastric Disorders and Therapy | Open Access Journals
3. Digestive diseases - Gastric, bowel and liver diseases : Free medical journal
4. Stomach Disorders
5. Global Journal of Digestive Diseases