HHS Public Access
Author manuscript
Am J Gastroenterol. Author manuscript; available in PMC 2022 August 01.

Published in final edited form as:
Am J Gastroenterol. 2021 August 01; 116(8): 1667–1675. doi:10.14309/ajg.0000000000001229.

Red meat consumption and risk of Nonalcoholic Fatty Liver Disease in a population with low meat consumption: the Golestan Cohort Study

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SM, HP, FK, PB, SMD, CCA, AE and RM designed and implemented the study. HP, EJ, ARR, and AE contributed substantially to data collection and the follow-up process. MH, AE, NF, and CCA planned and conducted data analysis. MH and AE drafted the manuscript with important contributions from NF, AH, MSH, RS, SMD, CCA, and RM. All authors contributed to the interpretation of the study results and critical revision of the manuscript. All authors reviewed the manuscript and approved the final version for submission.

Conflict of interest: None declared

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Abstract

Introduction: Non-alcoholic fatty liver disease (NAFLD), as the most common liver disease in the world, can range from simple steatosis to steatohepatitis. We evaluated the association between meat consumption and risk of NAFLD in the Golestan Cohort Study (GCS).

Methods: The GCS enrolled 50,045 participants, aged 40 to 75 years in Iran. Dietary information was collected using a 116-item semi-quantitative FFQ at baseline (2004–2008). A random sample of 1612 cohort members participated in a liver focused study in 2011. NAFLD was ascertained via ultrasound. Total red meat and total white meat consumption were categorized into quartiles based on the GCS population, with the first quartile as the referent group. Multivariable logistic regression models were used to estimate odds ratios (OR) and 95% confidence intervals (CI).

Results: The median intake of total red meat was 17 and total white meat was 53 grams/day. During follow-up, 505 individuals (37.7%) were diagnosed with NAFLD, and 124 of them (9.2%) had elevated ALT. High total red meat consumption ($OR_{Q4\ vs\ Q1}$ =1.59, 95% CI=1.06 to 2.38, p trend=0.03) and organ meat consumption ($OR_{Q4\ vs\ Q1}$ =1.70, 95% CI=1.19 to 2.44, p trend=0.003) were associated with NAFLD. Total white meat, chicken or fish consumption did not show significant associations with NAFLD.

Conclusions: In this population with low consumption of red meat, individuals in the highest group of red meat intake were at increased odds of NAFLD. Furthermore, this is the first study to show an association between organ meat consumption and NAFLD.

Keywords

Non-alcoholic fatty liver disease; Non-alcoholic steatohepatitis; red meat; fish; diet

Introduction

Non-alcoholic fatty liver disease (NAFLD) occurs when fat is deposited in more than 5% of hepatocytes [1]. NAFLD is the most common liver disease in the world [2], affecting up to 17–46% of people in different countries [3]. The spectrum of abnormalities in NAFLD can range from simple steatosis called non-alcoholic fatty liver (NAFL), to hepatocellular inflammation and fibrosis called non-alcoholic steatohepatitis (NASH), which may progress to cirrhosis and hepatocellular carcinoma [1]. Cirrhosis caused by NASH is the second most common indication for liver transplantation in the United States [4], and between 1990 and 2017, the prevalence of cirrhosis due to NASH increased more than any other cause of cirrhosis [5]. This high prevalence of NAFLD and its severe consequences underline the importance of identifying its risk factors and advocating appropriate preventive strategies.

As obesity and metabolic syndrome are closely linked to NAFLD, weight loss remains the key component in the prevention and management of this disease [6]. Previous studies concluded that in addition to weight loss, the composition of the diet is important in managing NAFLD [7–9]. High fructose, carbohydrate, and red meat intake and low consumption of fish has been associated with high risk of NAFLD [10]. Consumption of total meat more than 1.1 portions per day and red meat and/or processed meat more than 0.33 portions per day has been associated with higher risk of NAFLD [11]. In a recent study, consumption of red meat more than 34 grams/day and processed meat more than 10 grams/day has been associated with NAFLD [12], although there have been relatively few studies.

While alcohol-related liver disease is not a major cause of liver failure in the Middle East and North Africa (due to low alcohol consumption in many countries), NAFLD is an important cause of liver damage in this region [5]. During the follow-up of the Golestan Cohort Study (GCS), one of the largest cohort studies in the Middle East, a random sample of participants underwent ultrasonographic assessment of NAFLD and liver function tests [13]. The availability of these data, along with extensive dietary information (including questions about consumption of organ meat) and anthropometric measurements at baseline provided the opportunity to investigate the association between meat intake and NAFLD (with or without abnormal liver function tests) in a population with low intake of red meat.

Materials and Methods

Study design and Participants

The GCS was launched in 2004 and enrolled 50,045 participants, aged 40 to 75 years, in Golestan Province, Northeastern Iran, to study major chronic disease and cause-specific mortality [14, 15]. At baseline, each participant completed a general questionnaire inquiring demographic and major risk factors of chronic disease and a food frequency questionnaire (FFQ). The design of the GCS has been described elsewhere [14].

A random sample of 1862 participant from Gonbad city were enrolled in a pragmatic trial for liver disease in 2011 [13]. The aim of the trial was to evaluate the effects of a combination pill (PolyPill) on cardiovascular diseases and liver-related outcomes [16], but we used baseline trial assessments before the intervention started. After excluding participants with viral or autoimmune hepatitis, hepatitis caused by drugs, iron overload or alpha_1_antitrypsin deficiency, a total of 1612 participants consented and underwent ultrasonographic assessment of NAFLD in addition to liver function tests [13].

The GCS was approved by the ethical review board of the Digestive Disease Research Institute, the Institutional Review Boards of the U.S. National Cancer Institute (NCI), the International Agency for Research on Cancer (IARC). All participants provided a written informed consent at baseline and for the liver study.

Regular alcohol use is not common in this population, but we still excluded participants with significant alcohol drinking at baseline, more than 30 g/day for men and 20 g/day for women (n=10) [1]. We also excluded participants who left more than 30 food items (26% of the total) blank in the FFQ or had an energy intake that was more than two interquartile ranges either above the 75th percentile (3690 kcal/day for women and 4145 kcal/day for men) or below the 25th percentile of energy intake (300 kcal/day for women and 525 kcal/day for men) (n=27) [17], and participants with a self-reported history of conditions that may have caused them to change their diets, such as cancer (other than non-melanoma skin cancer), diabetes, heart disease, or stroke (n=235). As a result, the analytic set for the present study included 1340 participants.

Exposure Assessment

Dietary information was collected using a 116-item semi-quantitative FFQ, validated against 24-hour dietary recall at baseline [18]. Participants were asked about their frequency of consumption of a given serving size of each food item daily, weekly, or monthly during the year leading up to their recruitment (Supplemental Table 1). Daily intake of each food item was calculated by multiplying the frequency of consumption by the typical portion size and the number of servings per day. Then daily intake of food items was converted to grams [19]. We created total red meat intake including unprocessed meat (lamb, beef, and hamburger), organ meat (liver, kidney, gizzard, and heart), and processed meat (sausage and deli meat). Total white meat intake included chicken and fish (Supplemental Table 2)

Anthropometrics were measured in the upright position with light clothes and without shoes by trained nutritionists at baseline. Waist circumferences were measured at the umbilical level. Body mass index was calculated as weight (kg) divided by height (m) squared. Physical activity was determined using a baseline questionnaire. All physical activities including physical activity at work and at leisure time were calculated to create metabolic equivalent of task (MET) and then categorized to tertiles. Ever users of tobacco or opium were defined as those who had used opium or tobacco at least once a week for more than six months. Smoking status was categorized to never tobacco users, former cigarette users, and current cigarette users. Opium status and alcohol consumption were categorized to ever and never users. The former cigarette users were defined as users who quit more than one year before enrollment [20, 21]. Wealth scores were calculated based on ownership of household appliances, vehicles, and other variables associated with wealth, using multiples correspondence analyses [22]. The tertiles of this composite score were used to create low, medium, and high wealth status.

Outcome Ascertainment

We used the ultrasonographic assessment conducted in 2011 (a median of 6 years after baseline) to ascertain NAFLD. Ultrasonography was performed using an Accuvix XQ ultrasound unit (Medison, Seoul, Korea), with high sensitivity (91.7%) and specificity (100%) for the histological diagnosis [23]. Hepatorenal echo contrast and/or liver brightness (0 to 3), deep attenuation (0 to 2), and vascular blurring (0 to 1) were used for scoring. A total score of at least 2, which includes the hepatorenal echo contrast and/or bright liver score of at least 1 was defined as NAFLD [13]. Since serum alanine transaminase (ALT) is often used in the clinic as a marker of liver injury, [24] we defined another outcome as NAFLD plus elevated ALT (levels above 45 and 30 IU/L for men and women, respectively). We also conducted a sensitivity analysis using ALT cutoffs of 30 IU/L for men and 20 IU/L for women.

Statistical Analysis

Descriptive values of variables were expressed as means ± standard deviations or percentages. Multivariable logistic regression models were used to estimate odds ratios (OR) and 95% confidence intervals (CI). Meat consumption variables were categorized into quartiles based on the whole Golestan Cohort Study population and the first quartiles were used as the referent group.

In multivariable models, we adjusted for age (years), sex (male, female), waist circumference (<88, ≥88 cm for females and <102, ≥102 cm for males), formal education (yes, no), smoking status (never, former, current), opium use (never, ever), physical activity (MET tertiles), ethnicity (Turkman, non-Turkman), wealth score (tertiles), alcohol drinking (ever, never), and total energy intake (quintile, kcal/d). In red meat models we also adjusted for white meat consumption (and vice versa), and in each meat subtype model (e.g. organ meat), we adjusted for other subtypes (e.g. processed and unprocessed meat). Since the correlation between BMI and waist circumferences was 85%, we only adjusted for waist circumference. Adding other obesity-associated conditions such as hypertriglyceridemia had little (<10%) impact on the estimates, so they were not included in the final models. Linear trends were evaluated using the median intake of each category.

We stratified the participants by potential effect modifiers including smoking status, opiate use, waist circumferences, and BMI then tested the interaction between these variables and meat consumption.

The levels of significance are indicated by P values. An alpha level of less than 0.05 was considered to indicate statistical significance. All statistical analyses were performed with SAS software, version 9.4 (SAS Institute, Inc., Cary, NC).

Results

In our study sample 51.6 % were men, with a mean age of 52.5±6.6 years and a mean BMI of 28.3±3 kg/m^2. The median intake was 17 grams/day for total red meat and 53 grams/day for total white meat. About 45% of the population reported no consumption of processed meat. The characteristics of participants by quartiles of total red meat consumption are summarized in Table 1. The first quartile includes two participants that their total red meat consumption was zero grams/day. The participants with higher red meat consumption had larger waist circumferences and higher energy intake. They were more likely to be men, Turkmen, current smokers, ever alcohol drinkers, and have a high wealth score.

The prevalence of NAFLD was 37.7% (n=505), and 9.2% (124) of the participants had elevated ALT in addition to NAFLD. The characteristic of participants with NAFLD (with and without elevated ALT) were compared with individuals without fatty liver changes in Table 2. The participants with NAFLD were younger and had higher BMIs and waist circumferences. They were also more likely to be women, and not to smoke or use opium.

The two highest categories of total red meat consumption were significantly associated with NAFLD in multivariable adjusted models ($OR_{Q3\ vs\ Q1}$=1.70 (95%CI: 1.15–2.53) and $OR_{Q4\ vs\ Q1}$=1.59 (95% CI: 1.06–2.38) with a significant trend across the categories (Table 3). Among different types of red meat, consumption of unprocessed red meat was significantly associated with NAFLD ($OR_{Q4\ vs\ Q1}$=1.73, 95% CI: 1.13–2.66). All three quartiles of unprocessed red meat consumption showed some degree of association compared with the reference (lowest) category, albeit the trend in ORs was not statistically significant. The highest category of organ meat consumption (>3.6 g/day) was significantly associated with NAFLD, and there was a significant trend across quartiles ($OR_{Q4\ vs\ Q1}$=1.70, 95% CI: 1.19–2.44, p trend=0.0025). Consumption of processed meat, total white meat, chicken or fish were not significantly associated with NAFLD (Table 3).

Although none of the quartiles of total red meat consumption showed a significant association with elevated ALT in the presence of NAFLD (Table 4), a trend in increasing odds of this outcome was suggested with higher consumption of total red meat ($OR_{Q4\ vs\ Q1}$=1.64, 95% CI=0.86–3.12, p trend=0.055). The highest category of unprocessed red meat consumption was significantly associated with the OR for elevated ALT in the presence of NAFLD ($OR_{Q4\ vs\ Q1}$=2.29; 95% CI=1.09–2.66). None of the other associations between meat intake and elevated ALT reached statistical significance, except for an inverse association with the third quartile of fish intake (Table 4). Using cut-off values of 20 and 30 IU/L for elevated ALT in women and men, respectively, led to small changes in the strengths of the observed associations and the NAFLD associations with the highest categories of total red meat ($OR_{Q4\ vs\ Q1}$=1.93; 95% CI=1.17–3.17), and organ meat consumption ($OR_{Q4\ vs\ Q1}$=1.73; 95% CI=1.11–2.71) became statistically significant (Supplemental Table 3).

We found no evidence that the associations between meat intake and NAFLD varied by smoking status (P for heterogeneity=0.94), opium status (P for heterogeneity=0.55), waist circumferences (P for heterogeneity=0.55), or BMI (P for interaction=0.98). Supplemental Table 4 shows the consumption of potential protective food groups in quartiles of total red meat intake. The table shows that the participants who consumed more red meat, also ate more fruits, vegetables, and less refine grains.

Discussion

We observed a high prevalence (37.7%) of fatty liver disease, with or without impaired ALT test in this population. Only 25% of these patients had elevated ALT, which is similar to previous reports showing that 75% of NAFLD patients have normal-range ALT [24]. Such high prevalence of fatty liver disease occurred in a background of obesity and high waist circumference. Although the intake of red and processed meat in this population was low, there was still a significant association between red meat intake and NAFLD. The median consumption of total red meat in our study was 17 grams/day. In the US, the mean consumption of red meat is 86 grams/day, and in Europe, it is 35 grams/day, ranging between 10 grams/day in Sweden and 110 grams/day in Austria [25]. Even in the Middle East and North Africa, mean red meat intake ranges between 29 grams/day in Afghanistan and 100 grams/day in United Arab Emirates [25]. Since many of the study participants used organ meat (liver, gizzard, and heart) regularly, we were also able to show an association between high intake of this kind of meat and NAFLD.

Our study is one of the large studies of meat intake and NAFLD using a FFQ collected in the context of a prospective cohort study before the disease diagnosis. Previously, the results of the Rotterdam cohort showed an association between high animal protein intake and NAFLD in an overweight, predominantly elderly European population [26]. The results of the Multiethnic study showed, consumption of red meat and processed meat were associated with NAFLD [12]. Two cross-sectional studies have also shown associations between red or processed meat and NAFLD [11, 27]. In the NIH-AARP cohort study, which followed about half a million people for over a median of 15 years, among different causes of death, the risk of death due to chronic liver disease had the strongest association with red meat consumption, and this association was present for both unprocessed and processed red meat [28]. We also observed associations between meat consumption and NAFLD plus elevated ALT, but some of these associations were not statistically significant due to the relatively small number of cases. A recent meta-analysis showed a significant association between “western” diet (i.e. heavily loaded with processed foods, red meat, refined grains, and high-fat dairy) and NAFLD [29]. The authors reported some degree of heterogeneity and publication bias, but the number of studies was too small to allow further exploration of the potential contributing factors such as ethnicity. These findings underscore the need for more studies of diet and NAFLD in populations with dietary and ethnic diversity.

Red meat consumption has been associated with insulin resistance [11] and the incidence of metabolic syndrome [30], and many researchers consider NAFLD is a characteristic of metabolic syndrome in the liver [31]. In addition to saturated fat and cholesterol, red meat contains L- carnitine, which is metabolized by gut microbiota to produce Trimethylamine (TMA) [32]. High TMA has been shown to be associated with NAFLD in insulin-resistant mice [33]. Trimethylamine-N-oxide (TMAO), derived from TMA in the liver, promotes atherosclerosis and is found in lower quantities in vegan and vegetarian people than in omnivores with the same intake of L-carnitine [32]. Red meat consumption may modify microbiota [34, 35] and the role of the microbiome and prebiotics in NAFLD and NASH has been shown in previous studies [36, 37]. The gut microbiota can affect hepatic carbohydrate and lipid metabolism and affect pro-inflammatory and anti-inflammatory balance in the

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liver, and consequently affect the progression of NAFLD to NASH [36]. In our study, although the participants who consumed more red meat, ate more fruits, vegetables, and less refine grains, these did not seem to nullify the observed association between red meat intake and NAFLD.

Besides total red meat, the intake of organ meat was associated with NAFLD in our study. Because the consumption of organ meat is not common in all populations, there is only one previous study exploring its association with NAFLD. Shi *et al.* showed that subjects with NAFLD consume more offal than subjects without NAFLD (9.7 vs. 3.4g/day, $P<0.05$) [27], which is consistent with our results. Organ meat is high in N-glycolylneuraminic acid, a chemical that may increase the risk of inflammation [38]. We did not observe any associations between processed meat and NAFLD, but it is important to note that using processed meat was not common in our study and the intake difference between the highest and lowest quartiles was very small.

Unlike red meat, white meat intake was not associated with the risk of NAFLD in our study, and there was even some evidence for a reduced risk of NAFLD plus elevated ALT associated with fish intake. Only one previous study has reported on the association between fish intake and NAFLD; this population-based cross-sectional study showed lower intake of fish rich in omega-3 among NAFLD patients, although this difference did not reach statistical significance [39]. Argo *et al.* showed that omega-3 fatty acid as much as 3000 mg/day for one year reduced liver fat measured by MRI, although it did not improve the histopathology or markers of hepatocyte injury in NASH patients [40]. Previous studies have shown that the Mediterranean diet, which includes abundant fish intake, moderate consumption of poultry and low consumption of red meat among others [19], is associated with decreased risk of NAFLD [41]. Our results are different from those of the Multiethnic Cohort study which showed that the consumption of poultry was positively associated with NAFLD [12]. On the other hand, white meat intake has been associated with lower risk of mortality due to liver disease [28]. These findings may reflect the lower level of components which contribute to insulin resistance and oxidative stress [42], such as saturated fat and heme iron, in white meat compared to red meat [43]. Further studies in other populations are needed to clarify the effect of poultry intake on the liver.

This study conducted in the context of a population-based cohort study after FFQ data were collected at baseline. This approach precludes concerns over recall bias as patients were not diagnosed with fatty liver when the nutritional data were collected. The GCS provided us extensive information on other risk factors of NAFLD. We successfully used ultrasound for a relatively large group. Although ultrasound has limited accuracy in the diagnosis of NAFLD, conducting liver biopsy in the general population is not feasible, so we could not determine the level of liver injury. We did report our findings in a group of NAFLD patients with abnormal ALT since it is commonly used in clinical practice, but abnormal ALT has not been shown to correlate with the clinical or histologic spectrum of NAFLD [44]. The ultrasound assessments were done 6 years after the dietary data collection, and the participants may have changed their diet during this period. Such changes could have potentially led to non-differential misclassification and bias towards null, meaning that the actual associations may be stronger than those observed in the study.

In conclusion, we found that even low consumption of red meat and organ meat, but not white meat, is associated with increase odds of NAFLD. This underlines the importance of dietary composition, in addition to calorie restriction and weight loss, in preventing fatty liver disease. We think that the results of our study can inform different dietary recommendations, such as American Dietary Guidelines, since in the absence of data on less studied conditions such as NAFLD, most of these recommendations are based on more extensively studied diet-related chronic diseases including cardiovascular disease and diabetes. We also believe that due to the high and increasing prevalence of NAFLD across the globe, more research on the role of diet on NAFLD prevention is needed in other ethnically diverse populations with different dietary patterns.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Financial support:

Tehran University of Medical Sciences, The Intramural Program of the US National Cancer Institute (NIH), and Cancer Research UK

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WHAT IS KNOWN

- Obesity and metabolic syndrome are closely linked to NAFLD.
- Weight loss remains the key component in the prevention and management of this disease.
- In addition to weight loss, the composition of the diet is important in managing NAFLD.
- High fructose, carbohydrate, and red meat intake and low consumption of fish has been associated with high risk of NAFLD in cross-sectional studies.

WHAT IS NEW HERE

- Even low consumption of red meat is associated with increased risk of NAFLD.
- Organ meat consumption is associated with increased risk of NAFLD.
- Total white meat, chicken or fish consumption did not show significant associations with NAFLD.

TRANSLATIONAL IMPACT.

- This study underlines the importance of dietary composition, in addition to calorie restriction and weight loss, in preventing fatty liver disease.
- Limiting red meat and organ meat consumption may prevent and manage NAFLD.

TABLE 1.

Baseline characteristics of subjects by quartiles of total red meat consumption in the Golestan Cohort Study

	Quartiles of total red meat consumption[1]				P value[2]
	Q1	**Q2**	**Q3**	**Q4**	
Median intake (IQR), grams/day	4 (3–6)	10 (8–12)	18 (15–21)	34 (28–44)	
Participants, n	206	296	393	445	
NAFLD[3], n (%)	65 (31.5)	102 (34.4)	159 (40.1)	179 (40.2)	0.07
NAFLD plus elevated ALT[3], n (%)	19 (9.2)	25 (8.4)	33 (8.3)	47 (10.6)	0.59
Age, years[4]	52.6±6.6	53.4±6.9	52.2±6.6	52.0±6.2	0.06
Sex, male (%)	89 (43.2)	127 (42.9)	192 (48.9)	283 (63.6)	**<0.0001**
Body Mass Index (kg/m^2)[4]	27.9±4.8	28.2±5.2	28.2±5.2	28.7±5.0	0.32
Waist circumference (cm)[4]	97.6±11.6	98.5±12.4	98.8±12.3	101.1±11.3	**0.0013**
Turkmen ethnicity (%)	92 (44.7)	162 (54.7)	244 (62.1)	237 (53.3)	**0.0006**
No formal education (%)	107 (15.4)	142 (48.0)	146 (37.2)	114 (25.6)	**<0.0001**
Physical Activity, highest tertile (%)	50 (24.9)	68 (23.3)	90 (23.7)	105 (23.9)	0.56
Wealth score, highest tertile (%)	112 (54.4)	189 (63.9)	275 (70.0)	341 (76.6)	**<0.0001**
Current smoker (%)	15 (7.3)	29 (9.8)	46 (11.7)	72 (16.2)	**0.0002**
Current Opium user (%)	17 (8.3)	17 (5.7)	29 (7.4)	31 (7.0)	0.73
Ever alcohol drinker (%)	6 (2.9)	23 (7.8)	38 (9.7)	69 (15.5)	**<0.0001**
Calorie intake[4]	1987±519	2146±486	2260±496	2507±559	**<0.0001**
Hypertriglyceridemia (%)	74 (35.9)	105 (35.5)	120 (30.5)	178 (40.0)	**0.04**

[1] Quartiles are based on the Golestan Cohort Study population

[2] Kruskal-Wallis Test or Chi square test

[3] NAFLD: non-alcoholic fatty liver disease; ALT: alanine transaminase

[4] Mean±SD

TABLE 2.

Baseline characteristics of subjects by Non Alcoholic Fatty Liver Diease (NAFLD) in the Golestan Cohort Study

	Normal ultrasonography (n=835)(reference)	NAFLD (n=505)	NAFLD plus elevated ALT (n=124)
Age[1]	52.9±6.8	51.8±6.1 **	50.7±5.6 **
Body Mass Index (kg/m^2)[1]	26.9±4.8	30.6±4.7 **	30.6±5.0 **
Waist circumference (cm)[1]	95.9±11.5	105.0±10.4 **	104.4±10.8 **
Calorie intake[1]	2274±551	2276±550	2259±534
Sex, male (%)	461 (55.2)	230(45.5) **	43 (34.7) **
Turkmen ethnicity (%)	482 (57.7)	253 (50.0) *	63 (50.8)
No formal education (%)	307(36.7)	202 (39.9)	58 (46.8) *
Physical Activity, highest tertile (%)	188 (22.9)	125 (25.4)	30 (24.4)
Wealth score, highest tertile (%)	562 (67.3)	355 (70.3)	88 (71)
Smoking status			
Current cigarette smoker (%)	130 (15.6)	32 (6.3) **	5 (4.0) **
Former cigarette smoker (%)	69 (8.3)	34 (6.7)	6 (4.8)
Never smoker (%)	636 (76.2)	439 (86.9)	113 (91.1)
Current Opium user (%)	76 (9.1)	18 (3.6) **[3]	3 (2.4) **[3]
Ever alcohol drinker (%)	48 (9.5)	88 (10.5)[3]	5 (4.0) *[3]
Hypertriglyceridemia (%)	230 (27.5)	247 (48.9) **	57 (46.0) **
Total Red meat, grams/day[2]	16.5 (8.9–27.4)	18.7 (10.5–29.5) *[4]	20.2 (9.95–30.5)[4]
Total white meat, grams/day[2]	51.8 (28.1–85.2)	54.9 (32.6–91.3)[4]	58.3 (35.9–91.9)[4]

[1] Mean±SD

[2] Median (IQR)

[3] Fisher's exact test

[4] Kruskal-Wallis Test

* <0.05

** <0.005

NAFLD: non-alcoholic fatty liver disease; ALT: alanine transaminase

TABLE 3.

Odds ratios (95% CIs) for Non Alcoholic Fatty Liver Disease (NAFLD) by quartiles of meat consumption in the Golestan Cohort Study

	Quartiles of meat consumption				
	Q1	**Q2**	**Q3**	**Q4**	***P* trend**
Total Red meat					
Case/participant, n	65/206	102/296	159/393	179/445	
Median intake (grams/day)	4	10	18	34	
Age and sex adjusted OR (95%CI)	1	1.18 (0.80–1.73)	**1.53 (1.07–2.19)**	**1.60 (1.12–2.29)**	**0.0075**
Fully adjusted OR (95%CI)[1]	1	1.17 (0.78–1.77)	**1.70 (1.15–2.53)**	**1.59 (1.06–2.38)**	**0.029**
Unprocessed red meat					
Median intake (grams/day)	2	6	12	25	
Age and sex adjusted OR (95%CI)	1	**1.64 (1.09–2.48)**	**1.63 (1.10–2.42)**	**1.63 (1.11–2.39)**	0.15
Fully adjusted OR (95%CI)[1]	1	**1.66 (1.07–2.59)**	**1.81 (1.17–2.79)**	**1.73 (1.13–2.66)**	0.16
Processed meat					
Median intake (grams/day)	0	0	1	5	
Age and sex adjusted OR (95%CI)	1	1	0.97 (0.74–1.27)	1.23 (0.94–1.61)	0.096
Fully adjusted OR (95%CI)[1]	1	1	1.03 (0.77–1.38)	1.08 (0.81–1.46)	0.60
Organ meat					
Median intake (grams/day)	0.05	0.4	2	7	
Age and sex adjusted OR (95%CI)	1	1.04 (0.77–1.40)	0.95 (0.69–1.31)	**1.68 (1.22–2.33)**	**0.0007**
Fully adjusted OR (95%CI)[1]	1	1.07 (0.78–1.47)	0.96 (0.68–1.34)	**1.70 (1.19–2.44)**	**0.0025**
Total white meat					
Case/participant, n	112/327	127/342	125/318	141/353	
Median intake (grams/day)	16	41	66	114	
Age and sex adjusted OR (95%CI)	1	1.14 (0.91–1.74)	1.26 (0.91–1.74)	1.27 (0.93–1.74)	0.14
Fully adjusted OR (95%CI)[1]	1	1.06 (0.75–1.50)	1.11 (0.76–1.58)	1.08 (0.76–1.55)	0.69
Chicken					
Median intake (grams/day)	10	34	57	103	
Age and sex adjusted OR (95%CI)	1	1.19 (0.89–1.61)	1.33 (0.96–1.83)	1.12 (0.81–1.54)	0.52

	Quartiles of meat consumption				
	Q1	Q2	Q3	Q4	*P* trend
Fully adjusted OR (95%CI) [1]	1	1.13 (0.82–1.56)	1.16 (0.82–1.66)	0.90 (0.63–1.28)	0.47
Fish					
Median intake (grams/day)	0	2	6	20	
Age and sex adjusted OR (95%CI)	1	0.83 (0.54–1.28)	0.71 (0.47–1.08)	0.89 (0.60–1.31)	0.59
Fully adjusted OR (95%CI) [1]	1	0.83 (0.52–1.32)	0.65 (0.41–1.03)	0.81 (0.52–1.27)	0.88

[1] Adjusted for age (years), sex (male, female), waist (<88, ≥88 for females and <102, ≥102 for males), formal education (yes, no), smoking status (never, former, current), opium use (never, ever), physical activity (tertile, MET), ethnicity (Turkman, non-Turkman), wealth score (tertile), alcohol drinker (ever, never), total energy intake (kcal/d); In red meat models we also adjusted for white meat consumption (and vice versa), and in each meat subtype model (e.g. organ meat) we adjusted for other subtypes (e.g. processed and unprocessed meat).

TABLE 4.

Odds ratios (95% CIs) for Non Alcoholic Fatty Liver Disease (NAFLD) plus elevated ALT* by quartiles of meat consumption in the Golestan Cohort Study

	Quartiles of meat consumption				
	Q1	**Q2**	**Q3**	**Q4**	***P* trend**
Total Red meat					
Case/participant, n	19/160	25/219	33/267	47/313	
Age and sex adjusted OR (95%CI)	1	1.03 (0.54–1.96)	1.13 (0.61–2.08)	1.61 (0.90–2.89)	**0.046**
Fully adjusted OR (95%CI)[1]	1	1.00 (0.51–1.97)	1.28 (0.67–2.48)	1.64 (0.86–3.12)	**0.055**
Unprocessed red meat					
Age and sex adjusted OR (95%CI)	1	**2.08 (1.03–4.23)**	1.24 (0.60–2.58)	1.93 (0.99–3.77)	0.22
Fully adjusted OR (95%CI)[1]	1	**2.39 (1.14–5.00)**	1.48 (0.68–3.21)	**2.29 (1.09–4.8)**	0.17
Processed meat					
Age and sex adjusted OR (95%CI)	1	1	0.75 (0.46–1.23)	1.12 (0.71–1.76)	0.41
Fully adjusted OR (95%CI)[1]	1	1	0.80 (0.49–1.33)	1.09 (0.67–1.76)	0.56
Organ meat					
Age and sex adjusted OR (95%CI)	1	1.21 (0.73–2.02)	1.13 (0.65–1.96)	1.61 (0.91–2.86)	0.13
Fully adjusted OR (95%CI)[1]	1	1.28 (0.75–2.17)	1.23 (0.69–2.17)	1.78 (0.97–3.29)	0.13
Total white meat					
Case/participant, n	112/327	127/342	125/318	141/353	
Age and sex adjusted OR (95%CI)	1	1.37 (0.77–2.44)	1.51 (0.84–2.70)	1.66 (0.95–2.89)	0.091
Fully adjusted OR (95%CI)[1]	1	1.27 (0.69–2.34)	1.43 (0.77–2.65)	1.54 (0.84–2.82)	0.22
Chicken					
Age and sex adjusted OR (95%CI)	1	1.25 (0.73–2.13)	1.67 (0.96–2.91)	1.33 (0.76–2.32)	0.29
Fully adjusted OR (95%CI) [1]	1	1.14 (0.65–2.00)	1.56 (0.87–2.82)	1.17 (0.64–2.13)	0.66
Fish					
Age and sex adjusted OR (95%CI)	1	0.69 (0.35–1.36)	**0.43 (0.22–0.86)**	0.76 (0.41–1.40)	0.56
Fully adjusted OR (95%CI) [1]	1	0.75 (0.37–1.54)	**0.42 (0.20–0.88)**	0.75 (0.37–1.51)	0.62

*defined as ALT>45 in men and ALT>30 in women

[1]Adjusted for age (years), sex (male, female), waist (<88, ≥88 for females and <102, ≥102 for males), formal education (yes, no), smoking status (never, former, current), opium use (never, ever), physical activity (tertile, MET), ethnicity (Turkman, non-Turkman), wealth score (tertile), alcohol drinker (ever, never), total energy intake (kcal/d); In red meat models we also adjusted for white meat consumption (and vice versa), and in each meat subtype model (e.g. organ meat) we adjusted for other subtypes (e.g. processed and unprocessed meat).