ARTICLE

Nutrition in acute and chronic diseases

The association between dairy products and the risk of COVID-19

Mina Darand [1], Shirin Hassanizadeh[1], Ameneh Marzban[2], Masoud Mirzaei[3] and Mahdieh Hosseinzadeh [4,5 ✉]

BACKGROUND: The fast spread of the coronavirus disease 2019 (COVID-19) epidemic and its high mortality were quickly noticed by the health community. Dairy products have been recognized as part of a healthy diet that helps strengthen body immunity and prevent infections. The present study can provide a comprehensive picture of the associations between dairy products consumption and COVID-19 incidence.
METHODS: This study was undertaken on 8801 adults participants of Yazd Health Study (YaHS) and Taghzieh Mardom-e-Yazd (TAMIZ) study aged 20 to 70 years. Data on dietary intakes were obtained using a validated food frequency questionnaire (FFQ). Multivariable logistic regression analysis was used to assess the association between dairy consumption and COVID-19.
RESULT: Our finding indicated that moderate intake of total dairy (OR: 0.63, 95% CI 0.46–0.87, P-trend = 0.97) could reduce the odds of COVID-19 and higher intake of low-fat dairy products (OR: 0.51 CI: 0.37–0.69, p-trend < 0.001) and low-fat milk (OR: 0.47 CI: 0.35–0.64, p-trend < 0.001) had a protective effect on COVID-19 after adjusting for confounders. However, higher intake of high-fat-dairy-product (OR: 1.40 CI: 1.09–1.92, p-trend = 0.03), high-fat milk (OR: 1.54 CI: 1.20–1.97, p-trend < 0.001), total yogurt (OR: 1.40 CI: 1.04–1.89, p-trend = 0.01), cheese (OR: 1.80 CI: 1.27–2.56, p-trend = 0.001), and butter (OR: 1.80 CI: 1.04–3.11, p-trend = 0.02) were related to increase the odds of COVID-19.
CONCLUSIONS: Moderate intake of total dairy could reduce odds of COVID-19 by 37% and, a higher intake of low-fat dairy products had a protective role on COVID-19. Although our study has promising results, stronger clinical studies are needed.

European Journal of Clinical Nutrition; https://doi.org/10.1038/s41430-022-01149-8

INTRODUCTION

Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), named after the 2019 novel coronavirus (COVID-19), is a viral disease that first outbreak in late 2019 in Wuhan City Hubei Province of China, and it is spreading rapidly all over the world [1]. As of August 16, 2021, the incidence of coronavirus in the world is 207 million people and, the mortality rate is 4.36 million people. In Iran, 97,828 people have lost their lives due to coronavirus [https://g.co/kgs/yW8djw]. Currently, the uncontrollable prevalence of COVID-19 is the chief public health problem [2]. This disease imposes a heavy economic [3, 4] on world people and the health system and has drastically reduced the quality of life of people [5, 6]. Evidence shows that the severity of clinical manifestations and mortality rate of COVID-19 varies from person to person [7], and the immune system of individuals and factors affecting it play a critical role in COVID disease [8].

Nutrition and dietary components, as well food security as a modifiable factor, might contribute to these conditions by influencing immune system [9–11]. Dairy products have been recognized as part of a healthy diet [12] that help strengthen body

immunity and prevent infections, especially viral infections [13]. Milk have some high biologic proteins including caseins and whey proteins that reduce pro-inflammatory and oxidative stress factors [14]. In addition, CLA (Conjugated linoleic acid) in as one of the fatty acids of dairy products, could reduce inflammation markers [15]. Given the anti-inflammatory, antioxidant, and immune-boosting effects of dairy products, it is hypothesized that dairy consumption can reduce the risk of COVID-19 [14, 16]. Few studies have been conducted on the association between dairy consumption and the risk of COVID-19 [16, 17]. The findings of one study revealed that intake of dough and yogurt reduces the incidence of COVID-19 [17]. A narrative review of Gouda et al. showed that yogurt consumption due to its probiotics and bioactive peptides improved manifestations of COVID-19 [18]. In contrast, in another study, a higher milk consumption was associated with increase COVID-19 infection rate [10]. As dairy products are revealed to be diverse categories and their health effects are dependent on several complex specifications such as probiotics in yogurt, kashk, and dough, and also fermentation of cheese and others, this study can provide a comprehensive

---

[1]Department of Clinical Nutrition, School of Nutrition and Food Science, Food Security Research Center, Isfahan University of Medical Sciences, Isfahan, Iran. [2]Department of Health in Disasters and Emergencies, School of Health Management and Information Sciences, Iran University of Medical Sciences, Tehran, Iran. [3]Yazd Cardiovascular Research Centre, Shahid Sadoughi University of Medical Sciences, Yazd, Iran. [4]Nutrition and Food Security Research Center, Shahid Sadoughi University of Medical Sciences, Yazd, Iran. [5]Department of Nutrition, School of public health, Shahid Sadughi University of Medical Sciences, Yazd, Iran. ✉email: hoseinzade.mahdie@gmail.com

picture of the milk and, its derivatives include some traditional eastern products that can be efficiently applied in the community to reduce COVID-19. Therefore, the present study was conducted to investigate the association between dairy consumption and COVID-19 incidents.

MATERIALS AND METHODS
Study population
This study was conducted on the recruitment phase data of Yazd Health Study (YAHS) and Taghzieh Mardom-e-Yazd (TAMIZ) that were conducted in a large sample of Iranians (www.yahs-ziba.com). YaHS is a population-based prospective cohort study, designed to assess the changing incidence of variety of chronic diseases and their associated risk factors among Iranian adults (20–70 years) in Yazd, Iran. Our survey initially included 10208 adults, but 1407 were excluded due to unusual dietary intake and cancer, so we ended up with 8801 adults for final analysis. Please see the participants' selection algorithm (https://academic.oup.com/ije/article/47/3/697/4658812). The participants were selected during September 2014 to March 2016 based on the two-stage cluster sampling method according to the WHO STEP guidelines. Briefly, first, 200 clusters were randomly selected based on postal code of the city of residence. Second, the study was presented to them by interviewers and organize a meeting time at their domiciles. Finally, interviewers met 50 participants defined to each cluster (25 men and 25 women) to interview based on the study protocol. There are five persons in each 10-year classified age group (20–29, 30–39, 40–49, 50–59 and 60–69 years). On the other hand, due to the cohort nature of the YaHS study, the information is updated every 5 Years and, the incidence of various diseases is measured. According to the worldwide COVID-19 epidemic, the incidence of COVID-19 among participants was measured.

The ethics committee of Shahid Sadoughi University of Medical Sciences approved the study protocol (Ethical approval code: IR.SSU.SPH.REC.1400.201).

First, all participants signed informed written consent. Data on participants' general characteristics, history of chronic disease, physical activity, smoking history, anthropometric measurements, and dietary assessment were collected using validated questionnaires. In order to evaluate the validity and reliability of the questionnaires, a pilot study was conducted on 50 participants before the start of the main study and the results were reported and published by experts in each section. The reliability of the questionnaires was also confirmed by Cronbach's alpha 0.89. More details of YaHS have been published elsewhere [19]. In addition to the previous questionnaires, a specific COVID-19 questionnaire was completed over the phone for all participants who were diagnosed with COVID-19 during February 2020 to February 2021 according to Yazd Central Health database. In this questionnaire they were asked whether or not they had undergone a diagnostic test for COVID-19.

COVID-19 incidence measurement
We used polymerase chain reaction (PCR) test to diagnose cases of COVID-19 [20]. Also, serologic assays were used to estimate IgM and IgG antibodies in symptomatic or asymptomatic COVID subjects recovered from the disease. Serologic assays involving IgM and IgG antibodies to detect antibodies against SARS-CoV-2 were used as these antibodies can be detected from the second week of the start of COVID-19 symptoms where IgM can be detected after the fourth day of infection and IgG has been found after the eighth day of disease onset. Serologic assays provide quick diagnostic by avoiding PCR false positive/false negative results as well as these provide antibody patterns for estimation of strength and duration of humoral immunity [21].

Dietary assessment
Dietary intake was assessed in 2014–2016 using a 178-item semi-quantitative food frequency questionnaire (FFQ) consisting of 551 questions about dietary intake over the past year [22]. The FFQ used in YaHS was a modified version of a previously validated 168-item food frequency questionnaire applied for the Tehran Lipid and Glucose Study (TLGS) [22].10 items commonly consumed by Yazdi adults were added to the original 168- item FFQ, resulting in a 178-item FFQ. Further, the 168-item FFQ used in TLGS was designed to be open-ended in its original form; however, we changed the questionnaire to a multiple-choice one in YaHS. Also in order to accurate estimates, we rendered the portion size of food as

a unit using a photo book for all participants. Two types of questions were asked from the participants about each food item: (1) the frequency of food consumption (number of times per month, week, or day the food was consumed) in the previous year, and (2) the amount of the food that was usually consumed every time (portion size based on the standard serving sizes commonly consumed by Iranians). All reported intakes were converted to g/day by using household measures of consumed foods. Then we used Nutritionist IV software to calculate nutrients intakes [23]. Given that eating habits usually take longer than 4 years to change, each person's eating habits may not change over many years [24–27] unless a specific disease incident changes his/her eating pattern (of course we excluded them or adjusted the effect of the disease). So the diet has been almost constant during this follow-up period. In addition, we recently looked at relative food intakes and compared those in the highest dairy group to the lowest, and if the change is due to socio-economic changes, it will affect the whole population, so it would not have a significant effect on the odds in our study. Also, reconsidering the cohort nature of YaHS's study and the effect of dietary patterns on the immune system over time [28], the association is justifiable because the immune system has a direct effect on the incidence of the disease. Moreover, dairy intake data from all sources were classified into total dairy, high-fat and low-fat dairy. In this study, six dairy products, including milk, yogurt, cheese, kashk, butter, and yogurt drink were examined. Dairy products (milk and yogurt) are classified into two categories based on fat amount. Dairy products that have more and less than 3% fat are in the high-fat and low-fat categories, respectively. Cheese, butter, Kashk, and Yogurt drink were also considered high-fat dairy products. The questionnaire was designed by a trained reviewer.

Anthropometric measurements
Participants' weight was measured using a portable digital scale and the body analyzer (Omron Inc. Osaka, Japan), with the accuracy of 0.1 kg, with a minimum of clothing and without shoes.

Height was measured in a standing position without shoes and their heads placed in the Frankfurt position, shoulder blades, and heels touching the straight wall to which the tape was fixed. Body mass index (BMI) (kg/m^2) was calculated by dividing weight (kg) by height squared (m^2).

Physical activity assessment
The level of daily PA was assessed using the short form of the International Physical Activity Questionnaire (IPAQ). PA classified as low, medium, and high according to guidelines of IPAQ short form [29]. Persian translation validation of IPAQ has previously been confirmed by Moghaddam et al. [30].

Statistical analysis
Study participants were categorized into tertiles base on their dairy food intake levels in 3 models. Frequency and percentage were used to describe the qualitative variables. Multivariable Logistic regression analysis was performed in different models to find the association between dairy products and COVID-19. In model 1, we adjusted only age and total energy intake. In model 2, smoking status, physical activity, marital status, educational levels, chronic disease, gender, physical activity, job status, house status (home-owner or tenant), family size (less than 4, more than five), ethnicity (from Yazd or not from Yazd) were additionally adjusted. Final adjustments were performed for BMI. Logistic regression results were reported as the odds ratio (OR) and 95% confidence interval (95% CI). All analyses were performed using the SPSS software (version22; SPSS Inc, Chicago IL, USA). P values <0.05 were considered statistically significant.

RESULTS
Characteristics of participants
A summary of the general characteristics of the study population is shown in Table 1. Four hundred seventy-four out of 8801 participants were infected with Coronavirus (5.4%). Participants were mostly under 50 years old, while 40% were over 50. Furthermore, 84.9% of participants were married, 15.4% graduated from university, 86.7% had never smoked, and 64.5% were obese or overweight.

Furthermore, dairy intake did not differ significantly between the underweight, normal, overweight, and obese participants (P > 0.05) Supplementary Table 1. However, there is a significant difference

Table 1. Distribution of Yazd Health Study (YaHS) participants according to general characteristics.

Variables	Total (n = 8801) N (%)
Sex	
Male	4305 (50.3%)
Female	4252 (49.7%)
Age groups (years)	
20–29	1683 (19.7%)
30–39	1715 (20.1%)
40–49	1783 (20.9%)
50–59	1697 (19.9%)
60–69	1664 (19.4%)
Education level	
Some primary/high school, diploma and graduate diploma	7195 (84.6%)
Bachelors	1086 (12.8%)
Masters and PhD	223 (2.6%)
Smoking	
Never smoker	7231 (86.7%)
Current smoker	933 (11.3%)
Ex –smoker	168 (2%)
Marital status	
Married	7259 (84.9%)
Single	904 (10.6%)
Widowed or divorced	383 (4.5%)
BMI	
Low weight (< 18.5)	330 (3.9%)
Normal (18.5–24.9)	2681 (31.6%)
Overweight (25.0–29.9)	3219 (37.9%)
Obesity (≥ 30.0)	2262 (26.6%)
COVID-19 status	
Yes	474 (5.4%)
No	8327 (94.6%)

BMI body mass index (calculated as weight in kilograms divided by height in meters squared).

between dairy intake based on tertiles of consumption ($P < 0.05$) Supplementary Table 2.

Dairy intake and coronavirus in the whole population

Table 2 presents the multivariable-adjusted odds ratios and 95% confidence intervals for COVID-19 based on the tertiles of dairy intake. Higher intake of low-fat dairy products (OR: 0. 51 CI: 0.37–0.69, p-trend < 0.001) and low-fat milk (OR: 0.47 CI: 0.35–0.64, p-trend < 0.001) had a protective role on COVID-19 after adjusting for age, energy intake, smoking status, physical activity, marital status, educational levels, chronic disease, gender, job status, house status, family size, ethnicity, and BMI.

Higher intake of total milk was associated with lower odds of COVID-19 after adjusting for age and energy intake (OR: 0.72 CI: 0.55–0.94 p-trend = 0.01). Moderate intake of total dairy (OR: 0.63, 95% CI 0.46–0.87, P-trend = 0.97) could reduce odds of COVID-19 after full adjustments for confounders. However, higher intake of high-fat-dairy-product (OR:1.40 CI:1.09–1.92, p-trend = 0.03), high-fat milk (OR: 1.54 CI: 1.20–1.97, p-trend < 0.001), total yogurt (OR: 1.40 CI: 1.04–1.89, p-trend = 0.01), cheese (OR: 1.80 CI: 1.27–2.56, p-trend 0.001), and butter (OR: 1.80 CI: 1.04–3.11, p-trend = 0.02)

were related to increase the odds of COVID-19. On the basis of model 2, yogurt drink consumption was associated with an increase in COVID-19 (OR: 1.41 CI:1.01–1.96, p-trend = 0.09). This significant relationship disappeared after further adjustment for BMI (OR:1.37, CI: 0.98–1.91, p-trend = 0.12). Our findings indicated no significant relationship between low-fat yogurt (OR: 1. 12, CI: 0.82–1.52, p-trend = 0.31), high-fat yogurt (OR: 1. 21, CI: 0.93–1.59, p-trend = 0.27), and Kashk consumption (OR: 1. 06 CI: 0.79–1.44, p-trend 0.65) and COVID-19.

Subgroup analysis based on sex

Stratified analysis based on gender indicated that women in the highest tertile of low-fat dairy products (OR: 0.53, CI: 0.34–0.81, p-trend = 003) and low-fat milk (OR: 0.50, CI: 0.30–0.76, p-trend < 0.001) had lower odds of COVID-19 after full adjustments for confounders. The results were similar for men as well (OR low fat dairy products: 0.50, CI: 0.32– 0.78, p- trend =0.001), (OR low fat milk: 0.45, CI: 0.29–0.70, p- trend < 0.001).

High consumption of cheese (OR: 2.13, CI: 1.26– 3.59, p-trend = 0.006) could significantly increase the odds of COVID-19 in women after controlling for confounders, but men's results were marginally significant (OR 1.59, 95% CI 0.98–2.58, P-trend = 0.06).

In addition, consumption of high-fat milk (OR: 1.68, CI: 1.18–2.37, p-trend = 0.003) could increase the odds of COVID-19 in men after controlling for confounders. In women, high-fat milk consumption was marginally associated with COVID-19 (OR: 1.42, 95% CI 0.99–2.03, P-trend =0.03).

The main difference between men and women was in butter consumption and the odds of COVID-19. Women who consumed high butter had an increased odds of COVID-19 after full adjustments for confounders (OR: 3.16, CI: 1.23–8.08, p-trend = 0.003), whereas the association between butter intake and COVID-19 was not significant among men (Table 3).

DISCUSSION

In this study, the associations between milk and its products' intake and COVID-19 incidence in a large sample of the adult population were explored using a comprehensive multivariable analysis. In the best of my knowledge, the present study is the first investigated the association between dairy and its product consumption and COVID-19. Our finding indicated that moderate intake of total dairy could reduce odds of COVID-19 and, a higher intake of low-fat dairy products had a protective role on COVID-19. However, higher intake of high-fat-dairy-product, high-fat milk, total yogurt, cheese, and butter were related to increasing the odds of COVID-19. Our findings indicated no significant relationship between other dairy products intake and COVID-19. Stratified analysis based on gender indicated that women who consumed higher amount of butter had an increased odds of COVID-19 compared with men.

So far, few studies have been conducted on the association between dairy and the risk of COVID-19 [10, 16, 17]. Cobre et al. that evaluated the influence of foods and nutrients on COVID-19 recovery, reported that animal protein including milk had a protective effect on recovery from COVID-19 [16]. Inconsistently, in a study by Abdulah et al. examining the association between dietary factors and the rate of infection and mortality from COVID-19 among 158 countries, the countries with higher infection rates between 1500 and above had a higher total milk consumption [10]. We examined more extensively the association between various types of dairy products (both high and low fat) and COVID-19 incidences. Overall, a moderate intake of total dairy could reduce the odds of COVID-19. Higher consumption of low-fat dairy and milk had a protective effect against COVID-19. As well, higher consumption of high-fat and low-fat dairy products had a significant effect on increasing and decreasing the incidence of COVID-19 respectively, while yogurt consumption increased the

Table 2. Multivariable-adjusted odds ratios and 95% CI for COVID-19 across tertiles of dairy intake.

Variables	Tertile1	Tertile2	Tertile3	P-trend
Low-fat dairy product				
Model 1	1	0.62 (0.48–0.79)	0.48 (0.37–0.63)	<0.001[a]
Model 2	1	0.63 (0.47–0.84)	0.52 (0.38–0.71)	<0.001[a]
Model 3	1	0.63 (0.47–0.84)	0.51 (0.37–0.69)	<0.001[a]
High-fat-dairy-product				
Model 1	1	1.04 (0.79–1.36)	1.49 (1.13–1.95)	<0.001[a]
Model 2	1	0.93 (0.68–1.28)	1.37 (1.00–1.88)	0.05
Model 3	1	0.94 (0.68–1.29)	1.40 (1.09–1.92)	0.03a
Total dairy				
Model 1	1	0.63 (0.48–0.83)	0.99 (0.76–1.28)	0.81
Model 2	1	0.63 (0.45–0.86)	1.02 (0.75–1.38)	0.82
Model 3	1	0.63 (0.46–0.87)	1.03 (0.76–1.39)	0.97
Low-fat milk				
Model 1	1	0.54 (0.38–0.75)	0.45 (0.35–0.59)	<0.001[a]
Model 2	1	0.49 (0.32–0.73)	0.50 (0.37–0.67)	<0.001[a]
Model 3	1	0.49 (0.33–0.73)	0.47 (0.35–0.64)	<0.001[a]
High-fat milk				
Model 1	1	1.18 (0.28–4.95)	1.45 (1.17–1.79)	<0.001[a]
Model 2	1	1.56 (0.36–6.66)	1.56 (1.22–1.99)	<0.001[a]
Model 3	1	1.58 (0.37–6.73)	1.54 (1.20–1.97)	<0.001[a]
Total milk				
Model 1	1	0.90 (0.70–1.17)	0.72 (0.55–0.94)	0.01[a]
Model 2	1	0.97 (0.72–1.30)	0.75 (0.55–1.02)	0.06
Model 3	1	0.97 (0.72–1.30)	0.74 (0.54–1.01)	0.06
Low-fat yogurt				
Model 1	1	1.08 (0.83–1.41)	1.13 (0.87–1.46)	0.36
Model 2	1	1.15 (0.85–1.57)	1.10 (0.81–1.50)	0.30
Model 3	1	1.16 (0.85–1.58)	1.12 (0.82–1.52)	0.31
High-fat yogurt				
Model 1	1	0.74 (0.53–1.02)	1.21 (0.96–1.52)	0.15
Model 2	1	0.75 (0.51–1.10)	1.20 (0.92–1.56)	0.31
Model 3	1	0.69 (0.47–1.03)	1.21 (0.93–1.59)	0.27
Total yogurt				
Model 1	1	1.03 (0.78–1.34)	1.25 (0.97–1.61)	0.07
Model 2	1	1.14 (0.83–1.55)	1.36 (1.01–1.84)	0.01[a]
Model 3	1	1.15 (0.84–1.58)	1.40 (1.04–1.89)	0.01[a]
Cheese				
Model 1	1	1.84 (1.40–2.41)	1.77 (1.32–2.38)	<0.001[a]
Model 2	1	2.02 (1.46–2.78)	1.80 (1.27–2.55)	0.001[a]
Model 3		2.01 (1.45–2.78)	1.80 (1.27–2.56)	0.001[a]
Yogurt drink				
Model 1	1	1.01 (0.76–1.34)	1.19 (0.91–1.55)	0.18
Model 2	1	1.42 (1.01–1.99)	1.41 (1.01–1.96)	0.09
Model 3	1	1.37 (0.98–1.92)	1.37 (0.98–1.91)	0.12
Kashk[b]				
Model 1	1	0.90 (0.69–1.18)	0.91 (0.71–1.18)	0.51
Model 2	1	1.16 (0.85–1.60)	1.09 (0.81–1.48)	0.56
Model 3	1	1.12 (0.81–1.54)	1.06 (0.79–1.44)	0.65
Butter				
Model 1	1	0.97 (0.65–1.46)	1.30 (0.86–1.97)	0.02[a]
Model 2	1	1.45 (0.85–2.46)	1.83 (1.06–3.16)	0.01[a]
Model 3	1	1.4 4 (0.85–2.46)	1.80 (1.04–3.11)	0.02[a]

Values are reported as odds ratio and 95% confidence interval.
Model 1: Adjusted for age and energy intake.
Model 2: model 1+ further adjustment for smoking status, physical activity, marital status, educational levels, chronic disease, gender, job status, house status (home-owner or tenant), family size (less than 4, more than five), ethnicity (from Yazd or not from Yazd).
Model 3: model 2+ further adjustment for BMI.
[a]Significant association.
[b]Kashk is made from drained yogurt or Yogurt drink by shaping it and letting it dry.

Table 3. Multivariable-adjusted odds ratios and 95% CI for COVID-19 based on dairy intake tertile stratifying by sex.

Variables	Tertile1	Tertile2	Tertile3	P-trend
Low-fat dairy product				
Men	1	0.73 (0.49–1.09)	0.50 (0.32–0.78)	0.001*
Women	1	0.55 (0.35–0.86)	0.53 (0.34–0.81)	0.003*
High-fat-dairy-product				
Men	1	0.94 (0.60–1.48)	1.38 (0.88–2.17)	0.18
Women	1	0.92 (0.58–1.45)	1.41 (0.90–2.38)	0.11
Total dairy				
Men	1	0.52 (0.33–0.82)	0.89 (0.58–1.37)	0.49
Women	1	0.73 (0.46–1.17)	1.19 (0.77–1.85)	0.53
Low-fat milk				
Men	1	0.62 (0.37–1.02)	0.45 (0.29–0.70)	<0.001*
Women	1	0.39 (0.20–0.74)	0.50 (0.30–0.76)	<0.001*
High-fat milk				
Men	1	1.58 (1.08–2.59)	1.68 (1.18–2.37)	0.003*
Women	1	2.60 (0.57–11.83)	1.42 (0.99–2.03)	0.03*
Total milk				
Men	1	0.80 (0.52–1.22)	0.74(0.48–1.13)	0.14
Women	1	1.22 (0.81–1.86)	0.74(0.46–1.17)	0.23
Low-fat yogurt				
Men	1	1.10 (0.71–1.68)	0.99 (0.64–1.53)	0.93
Women	1	1.20 (0.76–1.89)	1.27 (0.81–1.98)	0.18
High-fat yogurt				
Men	1	0.76 (0.43–1.34)	1.38 (0.95–2.01)	0.12
Women	1	0.65 (0.36–1.16)	1.07 (0.72–1.58)	0.93
Total yogurt				
Men	1	1.11 (0.71–1.73)	1.32 (0.87–2.02)	0.22
Women	1	1.17 (0.74–1.86)	1.49 (0.96–2.29)	0.03*
Cheese				
Men	1	1.82 (1.17–2.83)	1.59 (0.98–2.58)	0.06
Women	1	2.25 (1.38–3.65)	2.13 (1.26–3.59)	0.006*
Yogurt drink				
Men	1	1.52 (0.95–2.44)	1.29 (0.80–2.06)	0.41
Women	1	1.26 (0.76–2.08)	1.47 (0.91–2.38)	0.15
Kashk				
Men	1	1.08 (0.69–1.69)	1.00 (0.65–1.52)	0.97
Women	1	1.20 (0.76–1.90)	1.10 (0.71–1.71)	0.66
Butter				
Men	1	1.11 (0.57–2.13)	1.14 (0.57–2.28)	0.76
Women	1	2.10 (0.83–5.31)	3.16 (1.23–8.08)	0.003*

Values are reported as odds ratio and 95% confidence interval.
All models are adjusted for age, energy intake, smoking status, physical activity, marital status, educational levels, chronic disease, job status, house status (home-owner or tenant), family size (less than 4, more than five), ethnicity (from Yazd or not from Yazd), and BMI.
*Denotes statistically significant.

risk of COVID-19. In contrast, in another study conducted in Iran, consumption of yogurt and doogh (yogurt drink) significantly reduced the occurrence of COVID-19, and type of dairy (low-fat, medium-fat, high-fat dairy) did not affect the incidence of COVID-19. Although, in this study, the beneficial effect of yogurt has been mainly attributed to its probiotics [17]. In addition, our findings contradict a narrative review article that [18] theoretically addresses the benefits of yogurt-derived probiotics and peptides in patients with COVID-19. Although the causes of these discrepancies cannot be explained definitely, the logical causes include differences in the prevalence and severity of COVID-19

symptoms in different parts of the world, differences in the type of dairy products studied (milk, yogurt, or low-fat versus high-fat) and differences in the amount of dairy consumption. Moreover, the difference in the adjusted confounders factors between previous studies and our study is another reason for this discrepancy. Stratified analysis based on gender indicated that the main difference between men and women was in butter consumption and the odds of COVID-19. Women who consumed high butter had an increased odds of COVID-19 compared to men. The cause is unclear, but differences in the amount of butter consumed, study duration, and physiological differences between

men and women, including differences in the immune systems [31] and gut microbiota [32], can be potential causes. Factors affecting sex differences in the gut microbiota include sex hormones [33], diet [34], drugs [35], BMI [36], and colonic transit time [37].

There are some hypotheses about the etiology of relation between dairy consumption and COVID-19. Milk and dairy products are rich in protein, zinc, selenium, vitamin A, vitamin D [38] as well as vitamin B12 [39]. Dietary selenium makes up the antioxidant enzymes glutathione peroxidase and thyroxine reductase, which are expressed highly in immune cells like T lymphocytes and macrophages. The beneficial effects of selenium have been reported almost solely for RNA virus infections [40]. Zinc is needed as a critical cofactor for the function of many enzymes and the development of immune cells [41]. Sufficient zinc intake from food sources helps maintain immune cell health and reduces susceptibility to various infections, including pneumonia [42, 43]. Vitamins A is important regulators of the differentiation and function of immune cells such as monocytes and T cells [44]. Vitamin D affects the host's immune pathway [45]. Evidence offer that vitamin D3 supplementation may reduce susceptibility to respiratory infection [46] or improve recovery from COVID-19 [47], influenza, recurrent pneumonia, and tuberculosis [48]. In addition, proteins in dairy and peptides derived from them including, casein and whey protein, have antioxidant anti-viral, anti-inflammatory properties in lung cells and regulate immune responses [13]. Also, some fatty acids in milk, including conjugated linoleic acid, have been proposed to have gut anti-inflammatory properties, which may, in turn, improve immune activity [49]. On the other hand, many Iranians use traditional yogurt, which is high in fat and rich in saturated fatty acids. High-fat dairy products increase the population of harmful bacteria in the gut and the production of highly inflammatory endotoxin molecules [50]. Therefore, although in the present study, consuming more low-dairy products had a protective effect in preventing COVID-19, it is recommended that each person normally consume 2–3 servings of low-fat dairy products per day.

Our research has several strengths. First, we control many potentials confounders that might influence the association. Second, the large sample size with a wide age span increases the study power. Third, we examined the association between dairy consumption and its products such as milk, yogurt, cheese, and yogurt drink both low and high-fat products and COVID-19 individually. In addition, the questionnaire was designed by a trained reviewer.

The present study also has limitations that need to be considered. Although we have identified several potential confounders, the effect of residual confounders cannot be controlled. Measurement bias is a feature existed in any dietary assessment.

CONCLUSION
In conclusion, the present study illustrated higher intake of low fat dairy products, and low-fat milk) had a protective role on COVID-19. However, higher intake of high-fat-dairy-product, high-fat milk, total yogurt, cheese, and butter were related to increase the odds of COVID-19. Although our study has promising results, up to now, the number of researches in this field is not enough to provide reliable nutritional recommendations, and stronger clinical studies are needed to prove these hypotheses.

DATA AVAILABILITY

REFERENCES
1. Olwenyi OA, Dyavar SR, Acharya A, Podany AT, Fletcher CV, Ng CL. et al.Immuno epidemiologyand pathophysiology of coronavirus disease 2019 (COVID-19). Journal of Molecular Medicine. 2020;98:1369–83.
2. McArthur L, Sakthivel D, Ataide R, Chan F, Richards JS, Narh CA. Review of burden, clinical definitions, and management of COVID-19 cases. Am J tropical Med Hyg. 2020;103:625–38.
3. Jin H, Wang H, Li X, Zheng W, Ye S, Zhang S, et al. Economic burden of COVID-19, China, January–March, 2020: a cost-of-illness study. Bull World Health Organ. 2021;99:112.
4. Burhamah W, AlKhayyat A, Oroszlányová M, AlKenane A, Almansouri A, Behbehani M, et al. The psychological burden of the COVID-19 pandemic and associated lockdown measures: experience from 4000 participants. J Affect Disord. 2020;277:977–85.
5. Ferreira LN, Pereira LN, da Fé Brás M, Ilchuk K. Quality of life under the COVID-19 quarantine. Qual Life Res. 2021;30:1389–405.
6. Izzo L, Santonastaso A, Cotticelli G, Federico A, Pacifico S, Castaldo L, et al. An Italian survey on dietary habits and changes during the COVID-19 lockdown. Nutrients. 2021;13:1197.
7. Baj J, Karakula-Juchnowicz H, Teresinski G, Buszewicz G, Ciesielka M, Sitarz E. et al. COVID-19: specific and non-specific clinical manifestations and symptoms: the current state of knowledge. J Clin Med. 2020;9:1753.
8. Paces J, Strizova Z, Daniel SM, Cerny J. COVID-19 and the immune system. Physiological research. 2020;69:379
9. Perez-Araluce R, Martinez-Gonzalez MA, Fernández-Lázaro CI, Bes-Rastrollo M, Gea A, Carlos S. Mediterranean diet and the risk of COVID-19 in the 'Seguimiento Universidad de Navarra'cohort. Clinical Nutrition. 2021 Apr 15.
10. Abdulah DM, Hassan AB. Relation of dietary factors with infection and mortality rates of COVID-19 across the world. The journal of nutrition, health & aging. 2020;24:1011–8.
11. Mirzadehahari Z, Mohammadi-Nasrabadi F, Eini-Zinab H, Khosravi M, Mousavi N, Agasi M. Survey of association between major depression disorder in women and household food insecurity. Iran J Nutr Sci Food Technol. 2015;10:9–20.
12. Mahdavifar B, Hosseinzadeh M, Salehi-Abargouei A, Mirzaei M, Vafa M. The association between dairy products and psychological disorders in a large sample of Iranian adults. Nutritional Neuroscience. 2021;10:1.
13. Batiha GE-S, Awad DA, Algammal AM, Nyamota R, Wahed MI, Shah MA, et al. Dairy-derived and egg white proteins in enhancing immune system against COVID-19. Front Nutr. 2021;8:394.
14. Young D, Mine Y. Anti-inflammatory/oxidative stress proteins and peptides. Bioactive proteins and peptides as functional foods and nutraceuticals. 2010;30:13–27.
15. Reynolds C, Roche H. Conjugated linoleic acid and inflammatory cell signalling. Prostaglandins Leukot Essent Fat Acids. 2010;82:199–204.
16. Cobre AF, Surek M, Vilhena RO, Böger B, Fachi MM, Momade DR, et al. Influence of foods and nutrients on COVID-19 recovery: a multivariate analysis of data from 170 countries using a generalized linear model. Clin Nutr. 2021.
17. Mohseni H, Amini S, Abiri B, Kalantar M, Kaydani M, Barati B, et al. Are history of dietary intake and food habits of patients with clinical symptoms of COVID 19 different from healthy controls? A case–control study. Clin Nutr Espen. 2021;42:280–5.
18. Gouda AS, Adbelruhman FG, Alenezi HS, M,garbane B. Theoretical benefits of yogurt-derived bioactive peptides and probiotics in COVID-19 patients-A narrative review and hypotheses. Saudi Journal of Biological Sciences. 2021;28:5897–905.
19. Mirzaei M, Salehi-Abargouei A, Mirzaei M, Mohsenpour MA. Cohort profile: the Yazd Health Study (YaHS): a population-based study of adults aged 20–70 years (study design and baseline population data). Int J Epidemiol. 2018;47:697–8h.
20. Tahamtan A, Ardebili A. Real-time RT-PCR in COVID-19 detection: issues affecting the results. Expert Rev Mol Diagn. 2020;20:453–4.
21. Nakano Y, Kurano M, Morita Y, Shimura T, Yokoyama R, Qian C, et al. Time course of the sensitivity and specificity of anti-SARS-CoV-2 IgM and IgG antibodies for symptomatic COVID-19 in Japan. Sci Rep. 2021;11:1–10.
22. Esfahani FH, Asghari G, Mirmiran P, Azizi F. Reproducibility and relative validity of food group intake in a food frequency questionnaire developed for the Tehran Lipid and Glucose Study. J Epidemiol. 2010;20:150–8.
23. Bodner-Montville J, Ahuja JK, Ingwersen LA, Haggerty ES, Enns CW, Perloff BP. USDA food and nutrient database for dietary studies: released on the web. J Food Composition Anal. 2006;19:S100–S7.
24. Weismayer C, Anderson JG, Wolk A. Changes in the stability of dietary patterns in a study of middle-aged Swedish women. J Nutr. 2006;136:1582–7.
25. Batis C, Sotres-Alvarez D, Gordon-Larsen P, Mendez MA, Adair L, Popkin B. Longitudinal analysis of dietary patterns in Chinese adults from 1991 to 2009. Br J Nutr. 2014;111:1441–51.
26. Lim H, Kim SY, Wang Y, Lee SJ, Oh K, Sohn CY, et al. Preservation of a traditional Korean dietary pattern and emergence of a fruit and dairy dietary pattern among

adults in South Korea: secular transitions in dietary patterns of a prospective study from 1998 to 2010. Nutr Res. 2014;34:760–70.

27. Forman M. Nutritional epidemiology: Willett, W, editor. 1998, 514 pages. New York: Oxford University Press; 1999.

28. Aljadani H. Impact of different dietary patterns and micronutrients on the immune system and COVID-19 infection. Curr Res Nutr Food Sci. 2021;9:127.

29. Committee IR. Guidelines for data processing and analysis of the International Physical Activity Questionnaire (IPAQ)-short and long forms. 2005. http://www.ipaqkise/scoring.pdf.

30. Moghaddam MB, Aghdam FB, Jafarabadi MA, Allahverdipour H, Nikookheslat SD, Safarpour S. The Iranian Version of International Physical Activity Questionnaire (IPAQ) in Iran: content and construct validity, factor structure, internal consistency and stability. World Appl Sci J. 2012;18:1073–80.

31. Takahashi T, Ellingson MK, Wong P, Israelow B, Lucas C, Klein J, et al. Sex differences in immune responses that underlie COVID-19 disease outcomes. Nature. 2020;588:315–20.

32. Kim YS, Unno T, Kim B-Y, Park M-S. Sex differences in gut microbiota. World J Men's Health. 2020;38:48–60.

33. Markle JG, Frank DN, Mortin-Toth S, Robertson CE, Feazel LM, Rolle-Kampczyk U, et al. Sex differences in the gut microbiome drive hormone-dependent regulation of autoimmunity. Science. 2013;339:1084–8.

34. Bolnick DI, Snowberg LK, Hirsch PE, Lauber CL, Org E, Parks B, et al. Individual diet has sex-dependent effects on vertebrate gut microbiota. Nat Commun. 2014;5:1–13.

35. Maier L, Pruteanu M, Kuhn M, Zeller G, Telzerow A, Anderson EE, et al. Extensive impact of non-antibiotic drugs on human gut bacteria. Nature. 2018;555:623–8.

36. Ley RE, Bäckhed F, Turnbaugh P, Lozupone CA, Knight RD, Gordon JI. Obesity alters gut microbial ecology. Proc Natl Acad Sci USA . 2005;102:11070–5.

37. Tottey W, Feria-Gervasio D, Gaci N, Laillet B, Pujos E, Martin J-F, et al. Colonic transit time is a driven force of the gut microbiota composition and metabolism: in vitro evidence. J Neurogastroenterol Motil. 2017;23:124.

38. Vissers PA, Streppel MT, Feskens EJ, de Groot LC. The contribution of dairy products to micronutrient intake in the Netherlands. J Am Coll Nutr. 2011;30:415S–421SS.

39. Khosravi M, Sotoudeh G, Amini M, Raisi F, Mansoori A, Hosseinzadeh M. The relationship between dietary patterns and depression mediated by serum levels of Folate and vitamin B12. BMC Psychiatry. 2020;20:1–8.

40. Steinbrenner H, Al-Quraishy S, Dkhil MA, Wunderlich F, Sies H. Dietary selenium in adjuvant therapy of viral and bacterial infections. Adv Nutr. 2015;6:73–82.

41. Prasad AS. Zinc in human health: effect of zinc on immune cells. Mol Med. 2008;14:353–7.

42. Walker CF, Black RE. Zinc and the risk for infectious disease. Annu Rev Nutr. 2004;24:255–75.

43. Hess SY, Lönnerdal B, Hotz C, Rivera JA, Brown KH. Recent advances in knowledge of zinc nutrition and human health. Food Nutr Bull. 2009;30:S5–S11.

44. Huang Z, Liu Y, Qi G, Brand D, Zheng SG. Role of vitamin A in the immune system. J Clin Med. 2018;7:258.

45. Bikle DD. Vitamin D and immune function: understanding common pathways. Curr Osteoporos Rep. 2009;7:58–63.

46. Rhodes JM, Subramanian S, Laird E, Kenny RA. low population mortality from COVID-19 in countries south of latitude 35 degrees North supports vitamin D as a factor determining severity. Alimentary Pharmacol Ther. 2020;51:1434.

47. Bleizgys A. Vitamin D and COVID-19: It is time to act. Int J Clin Pract. 2021;75: e13748.

48. Martineau AR, Jolliffe DA, Hooper RL, Greenberg L, Aloia JF, Bergman P. et al. Vitamin D supplementation to prevent acute respiratory tract infections: systematic review and meta-analysis of individual participant data. BMJ. 2017;356: i6583.

49. Bassaganya-Riera J, Hontecillas R. Dietary CLA and n-3 PUFA in inflammatory bowel disease. Curr Opin Clin Nutr Metab Care. 2010;13:569.

50. Onishi J, Häggblom M, Shapses S. Can dietary fatty acids affect the COVID-19 infection outcome in vulnerable populations? Mbio. 2020;11:e01723–20.

AUTHOR CONTRIBUTIONS
MH: supervision, study concept and design analysis of data, review and editing; MD: drafting the manuscript; SH: analysis of data, statistical analysis; AM: data collection; MM: revising the manuscript.

COMPETING INTERESTS
The authors declare no competing interests.

ADDITIONAL INFORMATION
Supplementary information The online version contains supplementary material available at https://doi.org/10.1038/s41430-022-01149-8.

Correspondence and requests for materials should be addressed to Mahdieh Hosseinzadeh.

Reprints and permission information is available at http://www.nature.com/reprints

Publisher's note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.