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Gender-specific associations between dietary inflammatory and antioxidant indices and gallstone risk and their mediating mechanisms: A cross-sectional analysis

Chang Chen[1,2], Yueyu Zhang[2], He Wang[2], Mengfei Cao[1,2], Zhui Ke[3]*, and Ming Jiang[1,2]*

[1]Department of General Surgery, Graduate School of Wan Nan Medical University, Wuhu, Anhui, China

[2]Department of General Surgery, The Hefei Second People's Hospital, Hefei, Anhui, China

[3]Department of Oncology, The Tenth People's Hospital, School of Medicine, Tongji University, Shanghai, China

***Corresponding authors:**
Ming Jiang
(jiangming8088@yeah.net)
Zhui Ke
(kezhui1314@163.com)

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Abstract

Gallstones are common, and dietary inflammatory and antioxidant characteristics may influence their development, but sex-specific associations remain unclear. We evaluated three dietary indices in relation to gallstone prevalence and explored potential obesity-related pathways. This cross-sectional analysis included 3,904 adults from the 2017–2018 National Health and Nutrition Examination Survey. The Healthy Eating Index-2015 (HEI-2015), Dietary Inflammatory Index (DII), and Comprehensive Dietary Antioxidant Index (CDAI) were derived from two 24-h dietary recalls. Survey-weighted sex-stratified logistic regression, curve fitting, threshold and subgroup analyses, and exploratory mediation analyses of body mass index (BMI) and body fat percentage (BFP) were performed. Overall, 426 participants (10.91%) reported gallstones. In females, compared with the lowest tertile, the highest DII tertile was associated with higher gallstone odds (odds ratio [OR] = 1.45, 95% confidence interval [CI] 1.04–2.01; $p = 0.0282$), whereas the highest CDAI tertile was associated with lower odds (OR = 0.68, 95% CI 0.49–0.95; $p = 0.0219$). HEI-2015 was not significantly associated with gallstones. No significant associations were observed in males. In females, BMI and BFP showed exploratory indirect effects in the DII and CDAI associations, with mediated proportions of 19.47% and 26.35% for DII and 10.91% and 15.84% for CDAI, respectively. Fully adjusted models yielded an area under the curve of approximately 0.71. Higher dietary inflammatory potential and lower dietary antioxidant capacity were associated with gallstones in females, but not males. Prospective studies are needed to confirm temporality and causality.

Keywords: Gallstones; Healthy Eating Index-2015 (HEI-2015); Dietary Inflammatory Index (DII); Comprehensive Dietary Antioxidant Index (CDAI); National Health and Nutrition Examination Survey (NHANES)

1. Introduction

Gallstones, as a globally prevalent digestive disease, have emerged as a major public health concern requiring urgent prevention and control. Approximately 6% of the global population is affected by gallstones, with higher incidence rates observed in South America, females, and developing countries adopting Western lifestyles.[1,2] Gallstones are also frequently associated with numerous severe complications, such as cholecystitis, common bile duct stones, and acute pancreatitis[3–6], imposing a heavy burden on public health systems.

Furthermore, gallstones are significantly associated with various physical conditions, including cardiovascular diseases, metabolic disorders, mental disorders, and sarcopenia.[7–9] Therefore, investigating the risk factors for gallstones and formulating effective prevention and control strategies are of paramount importance. As a key modifiable lifestyle factor, diet is closely linked to the development of gallstones. Compared to traditional single-nutrient indicators, comprehensive dietary indices can more systematically and comprehensively assess overall dietary quality or specific dietary characteristics. Existing studies have shown that comprehensive dietary indices (e.g., Dietary Approaches to Stop Hypertension diet, Mediterranean diet, and Dietary Inflammatory Index [DII]) may influence gallstone risk through multiple mechanisms, such as anti-inflammation, antioxidation, and regulation of lipid metabolism.[10–13]

This study focuses on the associations between three comprehensive dietary indices—Healthy Eating Index-2015 (HEI-2015), DII, and Comprehensive Dietary Antioxidant Index (CDAI)—and gallstone risk, offering distinct advantages over traditional single-nutrient analyses (e.g., fat or cholesterol) while comparing the performance of these three indices. HEI-2015 comprises 13 dietary components, comprehensively evaluating adherence to dietary guidelines and objectively reflecting overall dietary quality.[14] DII is calculated by weighting the effects of 27 nutrients on inflammatory markers, enabling precise quantification of the inflammatory potential of the diet.[15] These comprehensive indices can more systematically and comprehensively reveal the mechanisms underlying the diet-gallstone association, providing a more reliable analytical dimension for the study. Body mass index (BMI) and body fat percentage (BFP) are not only core mediating variables in the dietary-metabolic pathway but also recognized risk factors for gallstones. Obesity and insulin resistance can increase gallstone risk by altering cholesterol metabolism, bile acid homeostasis, and gallbladder motility[16], highlighting the need to consider the mediating role of BMI when investigating the diet-gallstone relationship. However, gallstone status was confirmed via self-report, and the three dietary indices were calculated based on two 24-h dietary recalls, which may be subject to recall bias. Additionally, two recalls may not fully represent long-term dietary habits.

Based on data from the National Health and Nutrition Examination Survey (NHANES), this study systematically evaluated the associations between three comprehensive dietary indices and gallstone risk, and further explored the potential mediating effects of BMI and BFP. Simultaneously, it investigated the association patterns between comprehensive dietary quality, dietary inflammatory properties, and gallstones, aiming to provide a more scientific and comprehensive basis for preventing gallstones through dietary intervention. In particular, it offers targeted guidance for dietary management and body fat control in key populations such as young adults, holding significant public health value for reducing the disease burden of gallstones.

2. Methods

2.1. Study design and population

The NHANES has been approved by the Institutional Review Board of the National Center for Health Statistics. This survey employs a complex multistage probability sampling design, integrating interview questionnaires, physical examinations, and laboratory tests to collect data. All participants have signed written informed consent. In accordance with the policies of the National Institutes of Health, analyses of de-identified data that do not involve direct interaction with participants are not classified as human subjects research and thus do not require additional Institutional Review Board review.

This study selected data from the 2017–2018 NHANES database. To ensure data validity, participants were screened as follows: First, 3,700 participants with missing gallstone-related information in the medical health questionnaire were excluded; second, 822 participants with incomplete two-day dietary recall data were excluded; additionally, 828 participants were excluded because of missing key covariates that were required for the main survey-weighted models, including marital status, educational level, family income-to-poverty ratio, race/ethnicity, and chronic disease questionnaire variables (hypertension, diabetes, asthma, arthritis, congestive heart failure, coronary heart disease, heart attack, stroke, chronic bronchitis, liver condition, and cancer). Ultimately, 3,904 participants met the inclusion criteria and constituted the final analytic sample before multiple imputation. Multiple imputation was subsequently applied only to the remaining sporadic missing values in non-key covariates,

including metabolic/obesity-related indicators (BMI and BFP), laboratory parameters (total cholesterol [Tc], serum creatinine [Scr], aspartate aminotransferase [AST], and alanine aminotransferase [ALT]), and lifestyle variables (sleep hours, sitting time, walking, smoking, and alcohol consumption). Therefore, the sample size remained 3,904 after imputation. The detailed participant screening process is shown in Figure 1.

2.2. Definition of gallstones

Consistent with previous studies, gallstone status among NHANES participants was confirmed via self-report. Specifically, trained interviewers asked participants the question: "Has a doctor or other health professional ever told you that you have gallstones?" Participants who answered "yes" were classified as having gallstones, while those who answered "no" were classified as not having gallstones.[17,18] The potential misclassification and recall bias related to self-reported gallstone status are addressed in **Section 4**.

2.3. Definition of dietary indices

2.3.1. Healthy Eating Index-2015

Healthy Eating Index-2015, a key exposure factor in this study, is a widely used dietary quality assessment tool. Detailed dietary intake data of NHANES participants were collected through two 24-h dietary recalls: The first recall was conducted through a face-to-face interview at a Mobile Examination Center, and the second was completed via telephone 3–10 days later. To fully capture differences in dietary intake across different days, the two recalls were intentionally scheduled on different days of the week, including both weekdays and weekends.

National Health and Nutrition Examination Survey provides dietary weights to correct for potential day-of-week and non-response bias: Dietary recall day 1 weight/ weighting variable was used for analyses based on the first 24-h dietary recall only, whereas the 2-day dietary recall weighting variable (WTDR2D) was used for analyses based on two complete dietary recalls. Because this study calculated dietary indices from the average intake of two 24-h dietary recalls (Day 1 total nutrient intake and Day 2 total nutrient intake), WTDR2D was used as the final dietary sampling weight in all survey-weighted analyses. Masked variance unit and masked variance unit (stratum) were incorporated to account for clustering and stratification in the NHANES complex multistage sampling design. For the single 2017–2018 cycle used in this study,

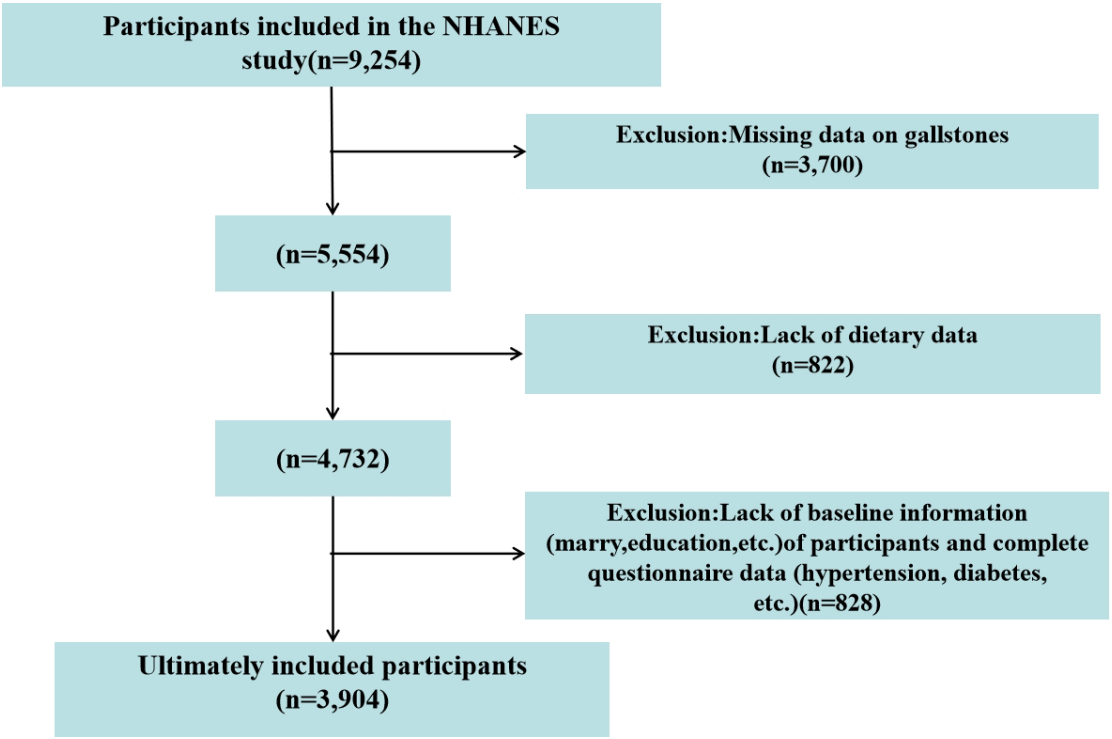


Figure 1. Participant inclusion flowchart
Abbreviation: NHANES: National Health and Nutrition Examination Survey.

WTDR2D was not divided by the number of cycles.

2.3.2. Dietary inflammatory index

Dietary inflammatory index scores were calculated based on the average data from the 24-h dietary recalls, adjusted for energy intake per 1,000 kcal. A total of 27 nutrients were included: Alcohol, vitamin A, vitamin B6, vitamin B12, vitamin C, vitamin D, vitamin E, caffeine, carbohydrates, cholesterol, total fat, dietary fiber, iron (Fe), magnesium (Mg), zinc (Zn), selenium (Se), monounsaturated fatty acids, polyunsaturated fatty acids, niacin, n-3 fatty acids, n-6 fatty acids, protein, riboflavin, saturated fat, thiamine, and β-carotene. DII scores can be calculated even if fewer than 30 nutrients are available.

The calculation process of DII is as follows: First, individual nutrient intake was standardized using the global average nutrient intake as the mean and standard deviation (SD) to obtain *z*-scores; second, *z*-scores were converted to percentiles and symmetrically adjusted to the range of −1 to +1; third, the adjusted values were doubled, subtracted by 1, and then multiplied by the specific inflammatory weight of the corresponding nutrient; finally, the sum of all weighted values was taken as the DII score.[15,19]

2.3.3. Comprehensive dietary antioxidant index

Researchers used the United States Department of Agriculture (USDA) Food and Nutrient Database for Dietary Studies to calculate participants' intake of antioxidants, micronutrients, and total energy. Based on questionnaire data, the study collected information on participants' dietary supplement intake over the past month, including dosage, frequency, and duration. Six antioxidants (manganese, selenium, zinc, vitamin A, vitamin C, and vitamin E) were selected, and their intake was standardized (i.e., data centering: each variable value minus the mean and then divided by the SD). The sum of the standardized intakes was calculated as the CDAI.[20]

2.4. Definition of covariates

Covariate data in this study were derived from the publicly available NHANES database. Participants with complete data on key variables were included, and the extracted covariates were divided into the following four categories:

- Demographic and socioeconomic factors: Age (years), gender (male/female), race/ethnicity (Mexican American, Other Hispanic, Non-Hispanic White, Non-Hispanic Black, Other Race), educational level (< High school, High school or above), marital status (living with a partner/not living with a partner), and poverty-income ratio;
- Metabolic and obesity-related indicators: BMI (kg/m^{2});
- Laboratory parameters: Tc, Scr, ALT, AST;
- Lifestyle factors, chronic diseases, and comorbidities: sleep hours, sitting time, physical activity (walking: Yes/no), hypertension, diabetes, asthma, overweight, arthritis, congestive heart failure, coronary heart disease, heart attack, stroke, chronic bronchitis, liver condition, cancer, smoking, and alcohol consumption.

2.5. Statistical analysis

First, variables with more than 20% missing values were excluded. Participants with missing key variables necessary for defining the outcome, exposures, or main adjustment set were excluded as described above. For the remaining sporadic missing values in non-key covariates, multiple imputation by chained equations was used to generate 5 complete datasets, which were then combined for analysis. The final analytic sample size was 3,904 before imputation and remained 3,904 after imputation. The Kolmogorov-Smirnov test was used to assess the normality of continuous variables. All continuous variables were expressed as mean ± SD, and between-group comparisons were performed using t-tests, supplemented by design-based Kruskal-Wallis tests to further verify between-group differences. Categorical variables were expressed as frequency (percentage), and between-group comparisons were conducted using χ^2 tests.

The three dietary indices were used as exposure factors, each divided into tertiles, with the first tertile (Q1) as the reference group. Gallstone prevalence was used as the outcome variable. Logistic regression analysis was performed using the survey package. The final survey design object included WTDR2D as the sampling weight, masked variance unit as the primary sampling unit, and masked variance unit (stratum) as the strata variable, thereby accounting for the NHANES complex sampling design.

To control for the impact of confounding factors, three gender-stratified logistic regression models were constructed:

- Model 1 (unadjusted model): No adjustment factors;
- Model 2 (partially adjusted model): Adjusted for age, education, and ethnicity based on Model 1;
- Model 3 (fully adjusted model): Adjusted for age, education, ethnicity, Tc, Scr, AST, ALT, ratio of family income to poverty, sleep hours, sitting time, hypertension, diabetes, asthma, overweight, arthritis, congestive heart failure, coronary heart disease, heart attack, stroke, chronic bronchitis, liver condition, cancer, marital status, smoking, alcohol consumption, and walking based on Model 2.

To more accurately assess the associations between the three dietary indices and gallstones, curve fitting models and threshold analysis models were used to explore potential non-linear relationships between them. Additionally, subgroup analysis was conducted to clarify whether the associations differed across population subgroups. Finally, the mediation package was used for exploratory mediation analysis of BMI and BFP, and the bootstrap method was employed to estimate the confidence intervals of the mediation effects. Because this was a cross-sectional study, these mediation analyses were interpreted as exploratory assessments of potential indirect pathways rather than evidence of temporal or causal mediation.

All statistical analyses were performed in R (version 4.4.3, R Foundation for Statistical Computing, Austria), using two-tailed tests and a p-value < 0.05 as statistically significant.

3. Results

3.1. Baseline characteristics of participants

Table 1 presents the baseline characteristics of 3,904 participants (3,478 without gallstones and 426 with gallstones) and the results of association analysis with gallstone status. The age of the gallstone group was significantly higher than that of the non-gallstone group (58.29 ± 15.35 years vs. 50.03 ± 17.43 years, $p < 0.001$). The proportion of females in the gallstone group (71.60%) was significantly higher than that in the non-gallstone group (48.68%) ($p < 0.001$). There were also significant differences in racial composition ($p < 0.001$). The BFP and BMI in the gallstone group were significantly higher than those in the non-gallstone group (both $p < 0.001$). The sitting time was significantly longer ($p = 0.041$), while the proportion of walking was significantly lower ($p < 0.001$) in the gallstone group, with no statistically significant difference in sleep hours between the two groups. Regarding dietary indicators, the DII in the gallstone group was significantly higher than that in the non-gallstone group ($p < 0.001$), the CDAI was significantly lower ($p = 0.011$), while there was no significant difference in the HEI-2015 between the two groups. There were no statistically significant differences in total cholesterol, Scr, aspartate aminotransferase, or alanine aminotransferase between the two groups. The prevalences of hypertension, diabetes, arthritis, etc., in the gallstone group were significantly higher than those in the non-gallstone group (all $p < 0.05$).

3.2. Associations between dietary indices and gallstone prevalence

Table 2 presents the gender-stratified associations between the three dietary indices (divided into tertiles, with the low tertile as the reference group) and gallstone risk in three models adjusted for potential confounders. In females: Compared to the low DII group, the risk of gallstones in the high DII group was significantly increased in Model 3 (odds ratio [OR] = 1.45, 95% confidence interval [CI]: 1.04–2.01, $p = 0.0282$); the trend test indicated that the risk of gallstones showed a significant upward trend with the increase in DII tertiles. Compared to the low CDAI group, the risk of gallstones in the high CDAI group was significantly reduced in Model 3 (OR = 0.68, 95% CI: 0.49–0.95, $p = 0.0219$); trend test suggested that the risk of gallstones showed a significant downward trend with the increase in CDAI tertiles, and this trend remained significant in Model 3 ($p = 0.0224$); continuous variable analysis of CDAI also showed a significant correlation with gallstone risk (all $p < 0.05$). For HEI-2015: Compared to the low index group, there was no significant difference in gallstone risk in the high index group in Model 3 (OR = 0.82, 95% CI: 0.59–1.13, $p = 0.2242$). In males, tertile analysis, continuous variable analysis, and trend test of the DII, HEI-2015, and CDAI all showed no significant associations between these three dietary indices and gallstone risk (all $p > 0.05$), and the results were not affected by different confounding factor adjustment models.

3.3. Results of non-linear models and threshold analysis

As shown in Table 3, after adjusting for confounding factors in Model 3, the associations between the DII, HEI-2015, CDAI, and gallstone risk were linear, with significant gender differences. In females, the critical breakpoint (K) of DII was 2.23: When DII < 2.23, there was no significant association with gallstone risk (OR = 1.01, 95% CI: 0.90–1.13, $p = 0.82$); when DII > 2.23, there was a significant positive correlation (OR = 1.24, 95% CI: 1.02–1.51, $p = 0.03$). The critical breakpoint (K) of HEI-2015 was 31.84: When HEI-2015 < 31.84, there was a significant negative correlation (OR = 0.94, 95% CI: 0.88–1.00, $p = 0.04$); when HEI-2015 > 31.84, there was no significant association (OR = 1.00, 95% CI: 0.99–1.01, $p = 0.49$). The critical breakpoint (K) of CDAI was 7.32: When CDAI < 7.32, there was a significant negative correlation (OR = 0.95, 95% CI: 0.91–0.99, $p = 0.01$); when CDAI > 7.32, there was no significant association (OR = 1.02, 95% CI: 0.92–1.12, $p = 0.71$). Combined with the curve-fitting models for females in Figure 2, the above linear association characteristics were further verified. In males, threshold analysis of the three dietary indices showed no significant associations with gallstone risk.

3.4. Results of subgroup analysis

Figure 3 presents the differences in the associations

Table 1. Participant characteristics

Gallstones	Total (*n* = 3,904)	Without gallstones (*n* = 3,478)	With gallstones (*n* = 426)	*p*
DII, mean ± SD	1.51 ± 1.91	1.47 ± 1.91	1.84 ± 1.87	<0.001
HEI-2015, mean ± SD	50.12 ± 14.17	50.17 ± 14.15	49.77 ± 14.34	0.582
CDAI, mean ± SD	0.69 ± 4.34	0.75 ± 4.39	0.19 ± 3.86	0.011
BFP, mean ± SD	36.23 ± 10.03	35.45 ± 9.88	42.60 ± 8.94	<0.001
Age, mean ± SD	50.93 ± 17.41	50.03 ± 17.43	58.29 ± 15.35	<0.001
BMI, mean ± SD	29.92 ± 7.38	29.51 ± 7.15	33.22 ± 8.35	<0.001
Tc, mean ± SD	188.96 ± 40.44	189.34 ± 40.35	185.87 ± 41.09	0.095
Scr, mean ± SD	0.91 ± 0.42	0.91 ± 0.41	0.90 ± 0.46	0.595
AST, mean ± SD	22.08 ± 11.77	22.04 ± 11.48	22.38 ± 13.98	0.570
ALT, mean ± SD	22.51 ± 16.18	22.55 ± 16.36	22.17 ± 14.70	0.643
Ratio of family income to poverty, mean ± SD	2.60 ± 1.61	2.61 ± 1.62	2.59 ± 1.53	0.855
Sleep hours, mean ± SD	7.57 ± 1.63	7.58 ± 1.62	7.44 ± 1.72	0.091
Sit time, mean ± SD	370.77 ± 611.13	360.21 ± 554.24	456.92 ± 953.12	0.041
Sex, *n* (%)				<0.001
Male	1,906 (48.82)	1,785 (51.32)	121 (28.40)	
Female	1,998 (51.18)	1,693 (48.68)	305 (71.60)	
Ethnic, *n* (%)				<0.001
Mexican American	496 (12.70)	441 (12.68)	55 (12.91)	
Other Hispanic	334 (8.56)	293 (8.42)	41 (9.62)	
Non-Hispanic White	1,479 (37.88)	1,276 (36.69)	203 (47.65)	
Non-Hispanic Black	892 (22.85)	824 (23.69)	68 (15.96)	
Other race	703 (18.01)	644 (18.52)	59 (13.85)	
Hypertension, *n* (%)				<0.001
No	2,437 (62.42)	2,225 (63.97)	212 (49.77)	
Yes	1,467 (37.58)	1,253 (36.03)	214 (50.23)	
Diabetes, *n* (%)				<0.001
No	3,189 (81.69)	2,896 (83.27)	293 (68.78)	
Yes	600 (15.37)	480 (13.80)	120 (28.17)	
Borderline	115 (2.95)	102 (2.93)	13 (3.05)	
Asthma, *n* (%)				0.038
No	3,296 (84.43)	2,951 (84.85)	345 (80.99)	
Yes	608 (15.57)	527 (15.15)	81 (19.01)	
Overweight, *n* (%)				<0.001
No	2,329 (59.66)	2,162 (62.16)	167 (39.20)	
Yes	1,575 (40.34)	1,316 (37.84)	259 (60.80)	
Arthritis, *n* (%)				<0.001
No	2,726 (69.83)	2,505 (72.02)	221 (51.88)	
Yes	1,178 (30.17)	973 (27.98)	205 (48.12)	
Congestive heart failure, *n* (%)				<0.001

(Cont'd...)

Table 1. (*Continued*)

Gallstones	Total (*n* = 3,904)	Without gallstones (*n* = 3,478)	With gallstones (*n* = 426)	*p*
No	3,770 (96.57)	3,375 (97.04)	395 (92.72)	
Yes	134 (3.43)	103 (2.96)	31 (7.28)	
Coronary heart disease, *n* (%)				<0.001
No	3,719 (95.26)	3,334 (95.86)	385 (90.38)	
Yes	185 (4.74)	144 (4.14)	41 (9.62)	
Heart attack, *n* (%)				<0.001
No	3,720 (95.29)	3,328 (95.69)	392 (92.02)	
Yes	184 (4.71)	150 (4.31)	34 (7.98)	
Stroke, *n* (%)				0.004
No	3,728 (95.49)	3,333 (95.83)	395 (92.72)	
Yes	176 (4.51)	145 (4.17)	31 (7.28)	
Chronic bronchitis, *n* (%)				<0.001
No	3,631 (93.01)	3,272 (94.08)	359 (84.27)	
Yes	273 (6.99)	206 (5.92)	67 (15.73)	
Liver condition, *n* (%)				<0.001
No	3,700 (94.77)	3,314 (95.28)	386 (90.61)	
Yes	204 (5.23)	164 (4.72)	40 (9.39)	
Cancer, *n* (%)				<0.001
No	3,496 (89.55)	3,149 (90.54)	347 (81.46)	
Yes	408 (10.45)	329 (9.46)	79 (18.54)	
Marry, *n* (%)				0.814
Living with partner	2,353 (60.27)	2,094 (60.21)	259 (60.80)	
Living without a partner	1,551 (39.73)	1,384 (39.79)	167 (39.20)	
Smoke, *n* (%)				0.002
No	2,229 (57.10)	2,015 (57.94)	214 (50.23)	
Yes	1,675 (42.90)	1,463 (42.06)	212 (49.77)	
Drink, *n* (%)				0.229
No	365 (9.35)	332 (9.55)	33 (7.75)	
Yes	3,539 (90.65)	3,146 (90.45)	393 (92.25)	
Walk, *n* (%)				<0.001
No	3,002 (76.90)	2,639 (75.88)	363 (85.21)	
Yes	902 (23.10)	839 (24.12)	63 (14.79)	
Education, *n* (%)				0.312
<High school	673 (17.24)	607 (17.45)	66 (15.49)	
High school or above	3,231 (82.76)	2,871 (82.55)	360 (84.51)	

Notes: Continuous variables are presented as mean ± SD, and categorical variables are presented as number of cases (percentage; *n* [%]); *p*-values for comparisons between groups are used to determine whether the differences are statistically significant.
Abbreviations: ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; BFP: Body fat percentage; BMI: Body mass index; CDAI: Comprehensive Dietary Antioxidant Index; DII: Dietary Inflammatory Index; HEI-2015: Healthy Eating Index-2015; Scr: Serum creatinine; SD: Standard deviation; Tc: Total cholesterol.

Table 2. Multivariate logistic regression model of dietary indicators and gallstones stratified by gender

Gender	Groups	Model 1	Model 2	Model 3
		OR (95% CI) *p*-value	OR (95% CI) *p*-value	OR (95% CI) *p*-value
Female	DII continuous	1.07 (1.00, 1.15) 0.0359	1.09 (1.02, 1.17) 0.0132	1.08 (1.01, 1.16) 0.0358
	DII groups			
	Q1 low	Reference	Reference	Reference
	Q2 middle	0.93 (0.66, 1.30) 0.6602	0.93 (0.66, 1.31) 0.6856	0.92 (0.65, 1.30) 0.6285
	Q3 high	1.35 (1.00, 1.84) 0.0515	1.48 (1.08, 2.03) 0.0137	1.45 (1.04, 2.01) 0.0282
	p for trend	0.0265	0.0060	0.0138
	HEI-2015 continuous	0.99 (0.98, 1.00) 0.1077	0.99 (0.98, 1.00) 0.0163	0.99 (0.98, 1.00) 0.1024
	HEI-2015 groups			
	Q1 low	Reference	Reference	Reference
	Q2 middle	1.00 (0.74, 1.35) 0.9955	0.92 (0.68, 1.25) 0.6042	0.94 (0.68, 1.29) 0.7043
	Q3 high	0.84 (0.62, 1.14) 0.2634	0.74 (0.54, 1.01) 0.0602	0.82 (0.59, 1.13) 0.2242
	p for trend	0.2590	0.0582	0.2217
	CDAI continuous	0.96 (0.94, 1.00) 0.0252	0.96 (0.93, 0.99) 0.0205	0.96 (0.93, 0.99) 0.0206
	CDAI groups			
	Q1 low	Reference	Reference	Reference
	Q2 middle	0.93 (0.70, 1.25) 0.6392	0.88 (0.65, 1.18) 0.4001	0.88 (0.64, 1.19) 0.3966
	Q3 high	0.70 (0.52, 0.95) 0.0221	0.69 (0.51, 0.94) 0.0204	0.68 (0.49, 0.95) 0.0219
	p for trend	0.0238	0.0210	0.0224
Male	DII continuous	1.06 (0.96, 1.17) 0.2415	1.08 (0.98, 1.20) 0.1295	1.06 (0.95, 1.18) 0.2855
	DII groups			
	Q1 low	Reference	Reference	Reference
	Q2 middle	0.94 (0.60, 1.47) 0.7879	0.99 (0.62, 1.56) 0.9539	0.98 (0.61, 1.58) 0.9354
	Q3 high	1.32 (0.85, 2.06) 0.2125	1.41 (0.89, 2.23) 0.1431	1.28 (0.79, 2.07) 0.3132
	p for trend	0.2455	0.1658	0.3367
	HEI-2015 continuous	1.00 (0.99, 1.02) 0.6374	0.99 (0.98, 1.01) 0.2444	0.99 (0.98, 1.01) 0.4666
	HEI-2015 groups			
	Q1 low	Reference	Reference	Reference
	Q2 middle	1.05 (0.67, 1.63) 0.8366	0.92 (0.58, 1.45) 0.7117	1.01 (0.63, 1.62) 0.9626
	Q3 high	1.05 (0.67, 1.66) 0.8351	0.70 (0.44, 1.14) 0.1504	0.74 (0.45, 1.22) 0.2459
	p for trend	0.8324	0.1492	0.2492
	CDAI continuous	0.97 (0.93, 1.02) 0.2695	0.98 (0.93, 1.03) 0.4175	0.98 (0.93, 1.04) 0.5728
	CDAI groups			
	Q1 low	Reference	Reference	Reference
	Q2 middle	1.12 (0.71, 1.77) 0.6207	1.07 (0.67, 1.71) 0.7801	1.12 (0.69, 1.81) 0.6591
	Q3 high	1.13 (0.71, 1.79) 0.6088	1.18 (0.73, 1.90) 0.4944	1.25 (0.76, 2.06) 0.3761
	p for Trend	0.6139	0.4926	0.3755

Notes: Model 1: Unadjusted model; Model 2: Adjusted for age, education, ethnicity; Model 3: Adjusted for age, education, ethnicity, Tc, Scr, AST, ALT, ratio of family income to poverty, sleep hours, sit time, hypertension, diabetes, asthma, overweight, arthritis, congestive heart failure, coronary heart disease, heart attack, stroke, chronic bronchitis, liver condition, cancer, marital status, smoke, drink, walk.
Abbreviations: CDAI: Comprehensive Dietary Antioxidant Index; CI: Confidence interval; DII: Dietary Inflammatory Index; HEI-2015: Healthy Eating Index-2015; OR: Odds ratio; Q: Quartiles.

Table 3. Threshold analysis of dietary indicators and gallstones

Indicators	Male	Female
DII		
Breakpoint (K)	1.53	2.23
Effect 1 for the segment < K	1.01 (0.83, 1.21) 0.95	1.01 (0.90, 1.13) 0.82
Effect 2 for the segment > K	1.15 (0.89, 1.48) 0.29	1.24 (1.02, 1.51) 0.03
Log-likelihood ratio test	0.510	0.153
HEI-2015		
Breakpoint (K)	28.00	31.84
Effect 1 for the segment < K	1.25 (0.93, 1.70) 0.14	0.94 (0.88, 1.00) 0.04
Effect 2 for the segment > K	0.99 (0.97, 1.01) 0.19	1.00 (0.99, 1.01) 0.49
Log-likelihood ratio test	0.074	0.081
CDAI		
Breakpoint (K)	8.07	7.32
Effect 1 for the segment < K	1.00 (0.94, 1.07) 0.96	0.95 (0.91, 0.99) 0.01
Effect 2 for the segment > K	0.89 (0.64, 1.24) 0.47	1.02 (0.92, 1.12) 0.71
Log-likelihood ratio test	0.447	0.247

Note: Adjusted for age, education, ethnicity, Tc, Scr, AST, ALT, ratio of family income to poverty, sleep hours, sit time, hypertension, diabetes, asthma, overweight, arthritis, congestive heart failure, coronary heart disease, heart attack, stroke, chronic bronchitis, liver condition, cancer, marital status, smoke, drink, walk.
Abbreviations: CDAI: Comprehensive Dietary Antioxidant Index; DII: Dietary Inflammatory Index; HEI-2015: Healthy Eating Index-2015.

between the DII, HEI-2015, CDAI, and gallstone risk in females across different subgroups after adjusting for confounding variables in Model 3. Interaction tests showed that, only in the association between CDAI and gallstones, age, hypertension, and arthritis were significant effect modifiers (all $p < 0.05$), while the subgroup interactions of DII and HEI-2015 were not statistically significant (all $p > 0.05$). Subgroup results showed that the negative correlation between CDAI and gallstones was more significant in populations aged < 60 years (OR = 0.94, 95% CI: 0.89–0.99, $p = 0.018$), without hypertension (OR = 0.93, 95% CI: 0.88–0.97, $p = 0.002$), without arthritis (OR = 0.93, 95% CI: 0.88–0.98, $p = 0.004$), of other races (OR = 0.88, 95% CI: 0.78–0.99, $p = 0.040$), smokers (OR = 0.94, 95% CI: 0.89–0.99, $p = 0.024$), drinkers (OR = 0.96, 95% CI: 0.93–1.00, $p = 0.040$), and those living with a partner (OR = 0.94, 95% CI: 0.90–0.99, $p = 0.016$). In contrast, there was no significant association between CDAI and gallstones in populations aged ≥ 60 years, with hypertension, or with arthritis (all $p > 0.05$). The positive correlation between DII and gallstones was stronger among those living with a partner (OR = 1.12, 95% CI: 1.02–1.24, $p = 0.021$), without hypertension, and without arthritis (all $p < 0.05$). HEI-2015 showed no significant differences in its association with gallstones across subgroups (age, race, marital status, educational level, smoking, drinking, hypertension, overweight, arthritis), and the overall association trend remained consistent.

3.5. Results of mediation effect analysis

Figure 4 and Table 4 present the results of exploratory mediation analysis of BMI and BFP in the associations between the DII, HEI-2015, CDAI, and gallstones in females after adjusting for confounding factors in Model 3. DII was significantly positively associated with gallstones in females (total effect estimates: 0.0262 and 0.0268, both $p = 0.024$), and both BMI and BFP showed significant indirect effects, with mediation proportions of 19.47% and 26.35%, respectively (both $p < 0.01$). After accounting for mediation, the direct effect of DII was not statistically significant (both $p > 0.05$). The total effect of HEI-2015 on gallstones in females was not statistically significant (both $p > 0.05$), but the indirect effects through BMI and BFP were significant (estimates: −0.0076 and −0.0093, both $p < 0.0001$), with mediation proportions of 39.42% and 45.97%, respectively. After excluding mediation, the direct effect of HEI-2015 remained non-significant (both $p > 0.05$). CDAI was significantly negatively associated with gallstones in females (total effect estimates: −0.0240 and −0.0245, both $p = 0.008$), and the indirect effects through BMI and BFP were significant but weak (estimates: −0.0026 and −0.0039, both $p < 0.05$), with mediation proportions of 10.91% and

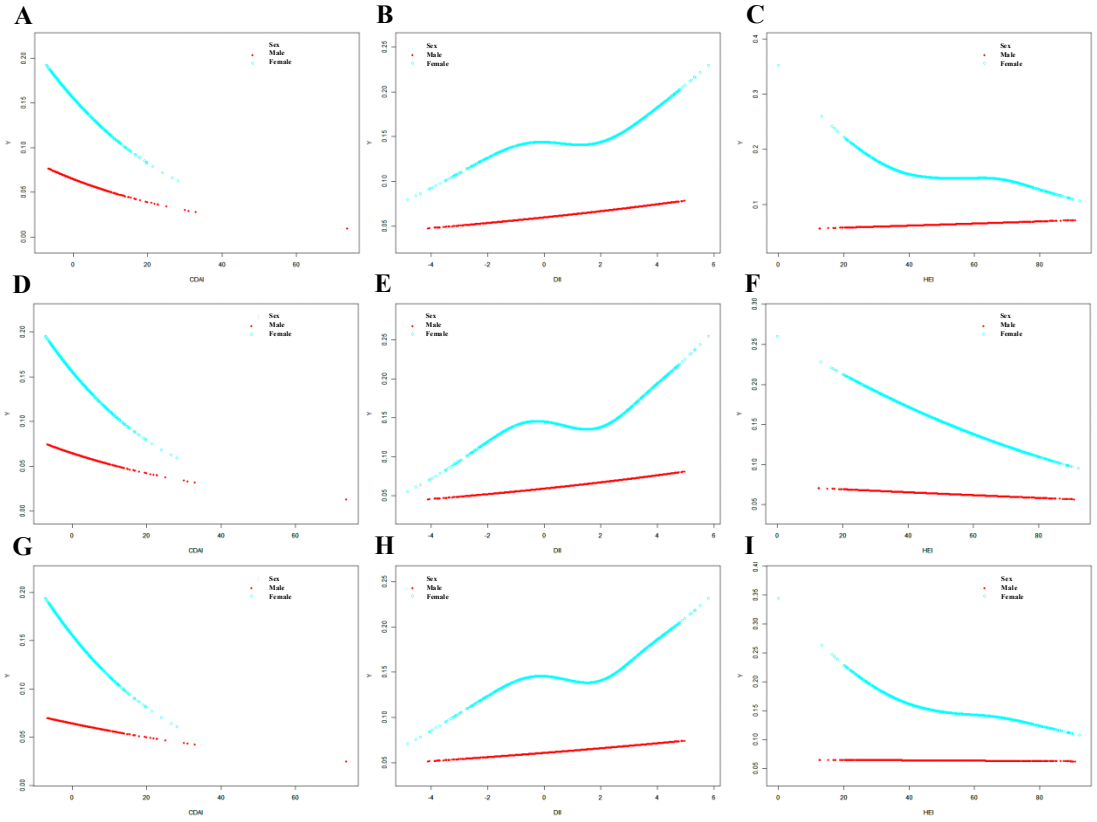


Figure 2. Curve-fitting models of dietary indices and gallstones. (A, D, G) The CDAI index of the three models. (B, E, H) The DII index of the three models. (C, F, I) The HEI-2015 index of the three models. Model 1: Unadjusted model; Model 2: Adjusted for age, education, ethnicity; Model 3: Adjusted for age, education, ethnicity, Tc, Scr, AST, ALT, ratio of family income to poverty, sleep hours, sit time, hypertension, diabetes, asthma, overweight, arthritis, congestive heart failure, coronary heart disease, heart attack, stroke, chronic bronchitis, liver condition, cancer, marital status, smoke, drink, walk.
Abbreviations: ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; BFP: Body fat percentage; BMI: Body mass index; CDAI: Comprehensive Dietary Antioxidant Index; DII: Dietary Inflammatory Index; HEI-2015: Healthy Eating Index-2015; Scr: Serum creatinine; SD: Standard deviation; Tc: Total cholesterol.

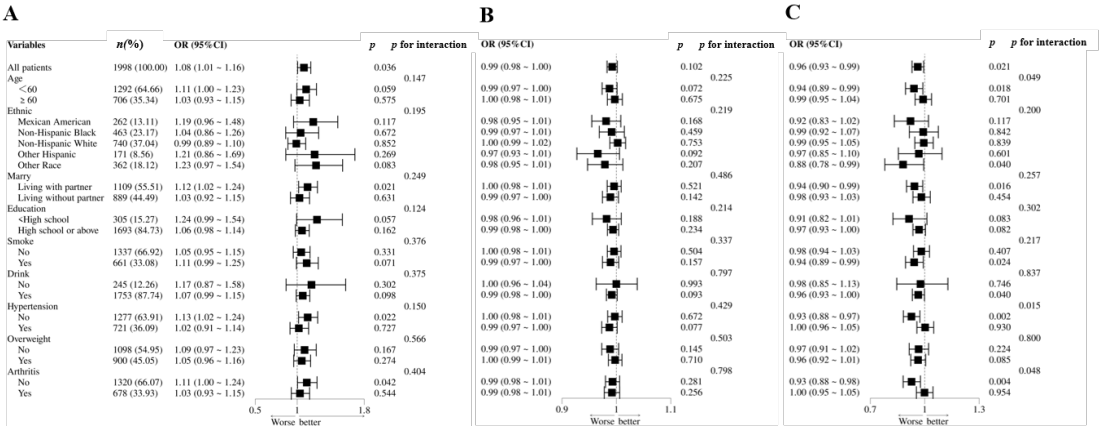


Figure 3. Subgroup analysis of three dietary indicators and gallstones in women. (A) The DII index. (B) The HEI-2015 index. (C) The CDAI index. Adjusted for age, education, ethnicity, Tc, Scr, AST, ALT, ratio of family income to poverty, sleep hours, sit time, hypertension, diabetes, asthma, overweight, arthritis, congestive heart failure, coronary heart disease, heart attack, stroke, chronic bronchitis, liver condition, cancer, marital status, smoke, drink, walk.
Abbreviations: ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; BFP: Body fat percentage; BMI: Body mass index; CDAI: Comprehensive Dietary Antioxidant Index; CI: Confidence interval; DII: Dietary Inflammatory Index; HEI-2015: Healthy Eating Index-2015; OR: Odds ratio; Scr: Serum creatinine; SD: Standard deviation; Tc: Total cholesterol.

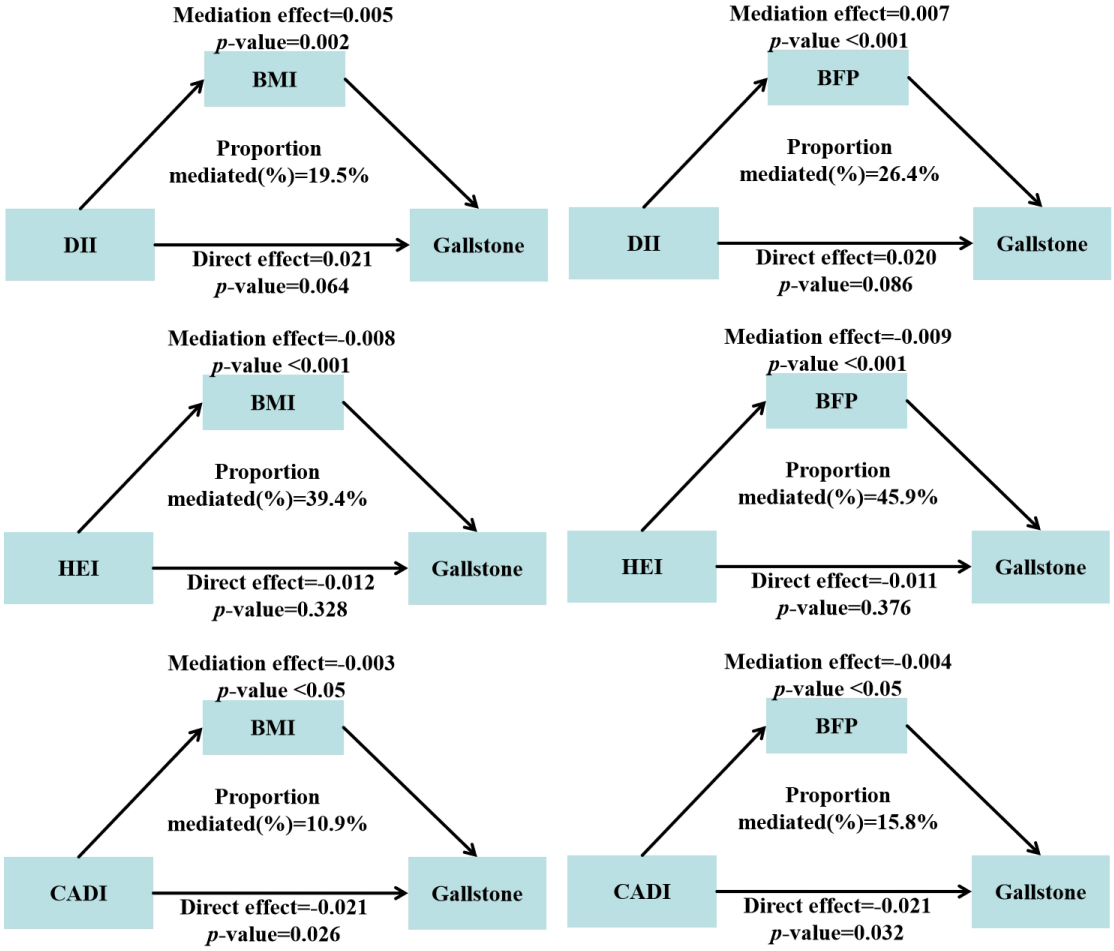


Figure 4. Mediation analysis of BMI and BFP index on the relationship between three dietary indicators and gallstones in women. Adjusted for age, education, ethnicity, Tc, Scr, AST, ALT, ratio of family income to poverty, sleep hours, sit time, hypertension, diabetes, asthma, overweight, arthritis, congestive heart failure, coronary heart disease, heart attack, stroke, chronic bronchitis, liver condition, cancer, marital status, smoke, drink, walk.
Abbreviations: ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; BFP: Body fat percentage; BMI: Body mass index; CDAI: Comprehensive Dietary Antioxidant Index; DII: Dietary Inflammatory Index; HEI-2015: Healthy Eating Index-2015; Scr: Serum creatinine; SD: Standard deviation; Tc: Total cholesterol.

15.84%, respectively. After accounting for mediation, the direct effect of CDAI remained significant (both $p < 0.05$). Given the cross-sectional design, these findings should be interpreted as exploratory evidence of potential indirect pathways rather than causal mediation.

3.6. Receiver operating characteristic results and sensitivity analysis of dietary indices for gallstone prediction

To evaluate the predictive value of dietary indices for gallstones in females, this study conducted separate prediction without adjusting variables and combined prediction ROC analysis under the fully adjusted model (Model 3). The results are shown in Figure 5 and Table 5: Without adjustment, the predictive power of CDAI, DII, and HEI-2015 alone was weak, with area under the curve (AUC) values of 0.5420, 0.5391, and 0.5236, respectively (all between 0.52 and 0.54). Among the three indices, CDAI had the best specificity (0.5600) and accuracy (0.5536), although the overall discriminatory ability remained limited. After incorporating the full set of covariates, the AUC values increased to 0.7163, 0.7157, and 0.7140, respectively (all between 0.71 and 0.72). These adjusted AUCs should be interpreted as the comprehensive predictive performance of dietary indices combined with demographic, clinical, metabolic, laboratory, lifestyle, and chronic disease variables. The improvement in predictive performance may be mainly attributable to conventional gallstone-related factors such as age, BMI, BFP, and chronic diseases rather than to HEI-2015, DII, or CDAI alone.

Table 4. The mediation analysis results of dietary indicators and gallstones

Indicator	BMI				BFP			
	Estimate	95% CI lower	95% CI upper	*p*-value	Estimate	95% CI lower	95% CI upper	*p*-value
DII								
Total effect	0.026204	0.003123	0.049956	0.024	0.026846	0.004156	0.050181	0.024
Mediation effect	0.005103	0.00211	0.008864	0.002	0.007075	0.003438	0.011273	<0.0001
Direct effect	0.021101	−0.000634	0.043966	0.064	0.019771	−0.002027	0.043324	0.086
Proportion mediated	0.194734	0.053805	0.903404	0.026	0.263544	0.084389	1.081024	0.024
HEI-2015								
Total effect	−0.019161	−0.042075	0.003783	0.112	−0.020187	−0.042807	0.002892	0.096
Mediation effect	−0.007554	−0.012038	−0.004028	<0.0001	−0.009281	−0.014231	−0.005248	<0.0001
Direct effect	−0.011607	−0.035137	0.011952	0.328	−0.010906	−0.034136	0.012855	0.376
Proportion mediated	0.394243	−2.588816	2.902178	0.112	0.459732	−2.458224	3.385252	0.096
CDAI								
Total effect	−0.024012	−0.044628	−0.005074	0.008	−0.024518	−0.045217	−0.005781	0.008
Mediation effect	−0.002621	−0.005617	−0.00022	0.034	−0.003885	−0.007111	−0.000997	0.006
Direct effect	−0.021391	−0.042776	−0.002358	0.026	−0.020634	−0.041939	−0.001645	0.032
Proportion mediated	0.109141	0.0053	0.508533	0.038	0.158436	0.035726	0.645773	0.014

Note: Adjusted for age, education, ethnicity, Tc, Scr, AST, ALT, ratio of family income to poverty, sleep hours, sit time, hypertension, diabetes, asthma, overweight, arthritis, congestive heart failure, coronary heart disease, heart attack, stroke, chronic bronchitis, liver condition, cancer, marital status, smoke, drink, walk.

Abbreviations: ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; BFP: Body fat percentage; BMI: Body mass index; CDAI: Comprehensive Dietary Antioxidant Index; CI: Confidence interval; DII: Dietary Inflammatory Index; HEI-2015: Healthy Eating Index-2015; Scr: Serum creatinine; SD: Standard deviation; Tc: Total cholesterol.

4. Discussion

Logistic regression showed significant gender differences in the associations between dietary indices and gallstones: Only in females were the DII and CDAI significantly associated with gallstones, with higher DII corresponding to higher odds and higher CDAI corresponding to lower odds. HEI-2015 had no significant overall association with gallstones in females. In males, none of the above three dietary indices was significantly associated with gallstones. In the fully adjusted model (Model 3), the odds of gallstones in the high DII group (Q3) of females were significantly higher than those in the low tertile group (Q1) (OR = 1.45, $p = 0.0282$), the odds in the high CDAI group (Q3) were significantly lower than those in Q1 (OR = 0.68, $p = 0.0219$), and there was no significant difference between the high HEI-2015 group and Q1 ($p > 0.05$). Exploratory mediation analysis indicated that both BMI and BFP showed significant indirect effects: the mediation proportions of BMI in the associations of DII, CDAI, and HEI-2015 with gallstones in females were 19.47% ($p < 0.01$), 10.91% ($p < 0.05$), and 39.42% ($p < 0.0001$), respectively; the corresponding mediation proportions of BFP were 26.35% ($p < 0.01$), 15.84% ($p < 0.05$), and 45.97% ($p < 0.0001$), respectively. Subgroup analysis further showed that age, hypertension, and arthritis moderated the association between CDAI and gallstones in females, while the association between HEI-2015 and gallstones in females showed no significant differences across subgroups. In males, none of the three dietary indices was significantly associated with gallstones.

Previous studies have reported associations between comprehensive dietary indices and gallstone prevalence or risk. Jiang and Shao[21] found that in the general population, the odds of gallstones in the highest quartile (Q4) of DII were significantly higher than those in the lowest quartile (Q1) (OR = 1.61, 95% CI: 1.08–2.39), whereas the odds of gallstones in the highest quartile (Q4) of CDAI were 34% lower than those in the lowest quartile (Q1) (OR = 0.66, 95% CI: 0.47–0.91). Wu *et al.*[11] also reported that, after adjustment for multiple confounding factors, higher DII was associated with increased odds of gallstones (continuous variable OR = 1.086), showing a non-linear relationship with a threshold of 1.842. In the present study, among females, the odds of gallstones in the high DII group (Q3) were significantly higher than those in the

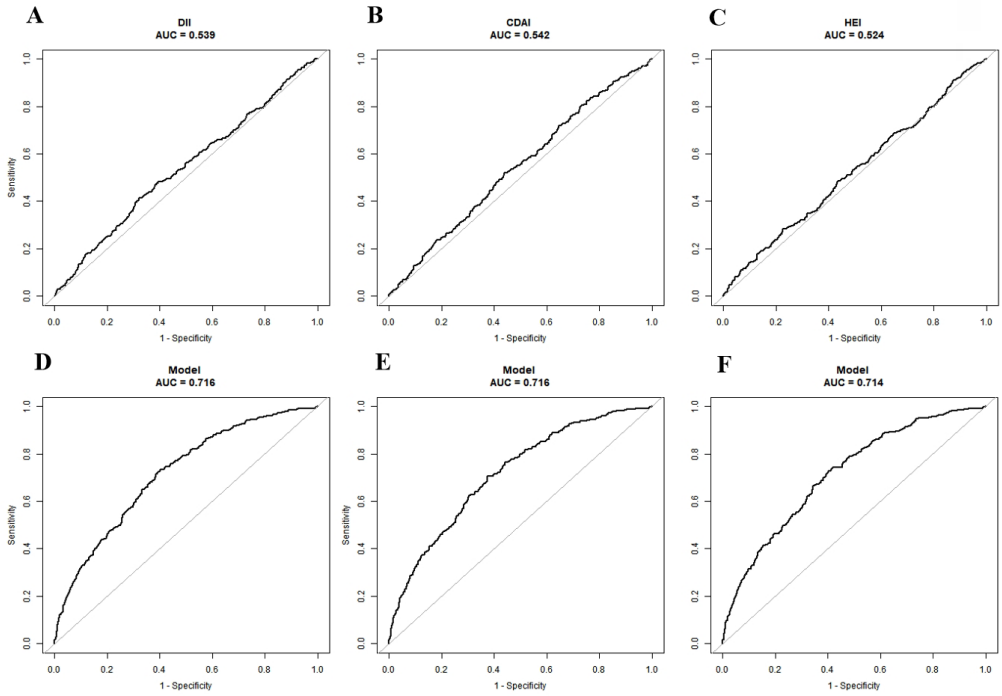


Figure 5. Receiver operating characteristic analysis of dietary indicators for predicting gallstones. (A, B, C) The predictive results of DII, CDAI, and HEI-2015 in model 1 without controlling for confounders. (D, E, F) The predictive results of DII, CDAI, and HEI-2015 in model 3 after controlling for confounders.
Abbreviations: AUC: Area under the curve; CDAI: Comprehensive Dietary Antioxidant Index; DII: Dietary Inflammatory Index; HEI-2015: Healthy Eating Index-2015.

Table 5. Receiver operating characteristic analysis results of dietary indicators for predicting gallstones

Analysis type	Dietary index	AUC	95% CI (lower–upper)	Optimal threshold	Specificity	Sensitivity	Accuracy
Unadjusted variables	CDAI	0.542	0.5074–0.5767	−0.585	0.56	0.518	0.5536
	DII	0.5391	0.5033–0.5749	2.925	0.6793	0.4131	0.6386
	HEI-2015	0.5236	0.4879–0.5594	39.925	0.7726	0.282	0.6977
Fully Adjusted Model 3	CDAI	0.7163	0.6861–0.7465	−1.7917	0.6249	0.7049	0.6371
	DII	0.7157	0.6856–0.7459	−1.8458	0.5972	0.7344	0.6181
	HEI-2015	0.714	0.6837–0.7443	−1.8874	0.5842	0.741	0.6081

Notes: Model 1: Unadjusted model; Model 3: Adjusted for age, education, ethnicity, Tc, Scr, AST, ALT, ratio of family income to poverty, sleep hours, sit time, hypertension, diabetes, asthma, overweight, arthritis, congestive heart failure, coronary heart disease, heart attack, stroke, chronic bronchitis, liver condition, cancer, marital status, smoke, drink, walk.
Abbreviations: ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; AUC: Area under the curve; BFP: Body fat percentage; BMI: Body mass index; CDAI: Comprehensive Dietary Antioxidant Index; CI: Confidence interval; DII: Dietary Inflammatory Index; HEI-2015: Healthy Eating Index-2015; Scr: Serum creatinine; SD: Standard deviation; Tc: Total cholesterol.

reference group (Q1) (OR = 1.45, 95% CI: 1.04–2.01, p = 0.0282), while the odds in the high CDAI group (Q3) were significantly lower than those in Q1 (OR = 0.68, p = 0.0219). In addition, a cohort study by Jin *et al.*[22] found that high adherence to HEI-2015 was significantly associated with a reduced risk of gallstones. In the fully adjusted model, the hazard ratio (HR) of the highest quartile (Q4) of HEI-2015 compared with the lowest quartile (Q1) was 0.89, and each 1-SD increase in HEI-2015 score was associated with a 6% lower risk. However, a case-control study by Ghorbani *et al.*[23] showed no statistically significant difference in the average HEI-2015 score between 74 female gallstone patients and 75 healthy females (case group: 57.01 ± 9.21, control group: 56.80 ± 9.52, p = 0.891). In our analysis, after controlling for potential confounding variables, there was no significant association between HEI-2015 and gallstones in either males or females. This discrepancy from previous studies may be attributed to the additional control of refined variables in this research, such as sitting time, sleep duration, chronic comorbidities like arthritis, and marital status. Meanwhile, this study found that only in females were DII and CDAI associated with gallstones, whereas none of the three indices showed significant associations in males. Combined with multi-dimensional validations including curve fitting and threshold analysis, these findings provide additional evidence regarding sex-specific diet-gallstone associations.

The study found that the risk of gallstones exhibits gender differences. Mechanistically, female sex hormones may enhance the effect of a pro-inflammatory diet on gallstone formation by altering bile composition and gallbladder contractile function. Meanwhile, a higher DII, indicating a more pro-inflammatory diet, can activate inflammatory signaling pathways, promote the release of pro-inflammatory cytokines such as interleukin-6, potentially damaging gallbladder mucosal epithelial cells and impairing their barrier function.[11,24,25] This suggests that females may be more susceptible to diet-induced systemic inflammatory responses, and chronic inflammation can facilitate cholesterol crystallization and gallbladder dysfunction, thereby increasing gallstone risk. Additionally, nutrients such as vitamins can scavenge oxidative stress products and reduce cholesterol oxidative deposition in bile[26,27]; whole grains and high-quality proteins can regulate the activity of hepatic bile acid synthase and promote bile acid secretion.[28,29]

This study has several notable strengths: First, the data were derived from the NHANES database, with 3,904 adults enrolled. The large and representative sample size laid a solid foundation for the reliability of the results. Second, the study focused on three composite dietary indices (HEI-2015, DII, and CDAI), comprehensively covering dietary quality, inflammatory potential, and antioxidant properties. Compared with single-nutrient analyses, this approach is more systematic and holistic; it also explored the association between CDAI and gallstones, supplementing evidence in this field. Third, the study adopted a rigorous design, constructing three logistic regression models (unadjusted, partially adjusted, and fully adjusted). Combined with curve fitting, threshold analysis, subgroup analysis, and exploratory mediation analyses of BMI and BFP, the study verified the characteristics of the associations from multiple dimensions. Stratified analyses of gender differences further clarified the population-specific nature of these associations. Fourth, the study comprehensively incorporated covariates such as demographic factors, metabolic indicators, and lifestyle habits, which reduced the interference of confounding factors. However, this study also has certain limitations. First, it employed a cross-sectional design, which can only reveal associations rather than establish causal relationships between dietary indices and gallstones, and reverse causality bias may exist. Accordingly, the mediation analyses of BMI and BFP should be interpreted as exploratory assessments of potential indirect pathways rather than proof of temporal or causal mediation. Second, dietary data were collected using two 24-h dietary recalls, which are prone to recall bias; moreover, two recalls cannot fully reflect long-term dietary habits, potentially leading to inaccurate dietary assessments. Third, gallstone status was confirmed by self-report. The NHANES questionnaire did not further distinguish between specific types of gallstones (e.g., cholesterol gallstones or pigment gallstones) or clarify anatomical locations such as gallbladder stones versus bile duct stones. Reliance on participants' self-reported previous diagnoses may introduce recall bias and misclassification: some participants may forget prior diagnoses or asymptomatic disease, whereas others may confuse gallstones with other biliary tract conditions. Although the standardized questionnaire enabled efficient data collection in a large nationally representative survey, the lack of imaging confirmation and detailed classification may compromise disease homogeneity. Fourth, potential confounding factors such as gut microbiota and long-term changes in dietary patterns were not included; additionally, targeted validations across different ethnic groups and age groups were not performed, which may limit the generalizability of the conclusions and necessitate further investigation in prospective studies. Finally, the ROC results should be interpreted cautiously. The three dietary indices showed weak predictive power in the unadjusted models (AUCs approximately 0.52–0.54). The AUCs of approximately 0.71 in the fully adjusted models

reflect the combined predictive ability of dietary indices plus demographic, clinical, metabolic, lifestyle, laboratory, and chronic disease variables, and the improvement in discrimination may be largely driven by conventional risk factors such as age, BMI, BFP, and chronic diseases rather than by HEI-2015, DII, or CDAI alone.

Future research directions should include the following: First, conduct prospective cohort studies with long-term follow-up to record changes in dietary patterns and gallstone incidence, thereby clarifying the causal relationship between dietary indices and gallstones and eliminating reverse causality bias. Second, optimize dietary assessment methods by combining food frequency questionnaires with biomarkers to more accurately evaluate long-term dietary inflammatory properties and dietary quality, reducing recall bias. Meanwhile, stratified intervention studies targeting specific subgroups can be carried out to improve intervention precision and further reduce the disease burden of gallstones.

5. Conclusion

This study showed that the prevalence of gallstones in the study population was 10.91%, and the associations between dietary indices and gallstones exhibited significant gender differences: statistically significant associations were observed only in females for two indices, namely the DII and the CDAI. In the fully adjusted model, compared with the reference group (Q1), females in the highest DII tertile (Q3) had significantly higher odds of gallstones (OR = 1.45, $p = 0.0282$), with a linear positive trend; conversely, females in the highest CDAI tertile (Q3) had significantly lower odds (OR = 0.68, $p = 0.0219$), with a linear negative trend. No significant overall association was found between the HEI-2015 and gallstones in females. Receiver operating characteristic analysis indicated that the unadjusted predictive power of the three dietary indices alone was weak, whereas the fully adjusted models achieved AUCs of approximately 0.71, reflecting the combined predictive ability of dietary indices and conventional demographic/clinical covariates rather than the dietary indices alone. Subgroup analysis showed that age, hypertension, and arthritis moderated the association between CDAI and gallstones in females. Exploratory mediation analysis showed that BMI and BFP had significant indirect effects in the associations between DII/CDAI and gallstones in females. Future prospective studies are needed to further verify the causal relationship and underlying mechanisms between diet and gallstones, providing more robust evidence to optimize relevant prevention and control strategies.

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Conflict of interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Author contributions

Conceptualization: Chang Chen
Data curation: Yueyu Zhang
Formal analysis: He Wang
Funding acquisition: Mengfei Cao
Methodology: Chang Chen
Supervision: Ming Jiang, Zhui Ke
Writing–original draft: Chang Chen
Writing–review & editing: Ming Jiang

Ethics approval and consent to participate

Data collection for NHANES was approved by the National Center for Health Statistics Research Ethics Review Board. This study used publicly available, de-identified NHANES data; therefore, no additional ethics approval or informed consent was required.

Consent for publication

Consent for publication was not applicable because this study used anonymized data, and no identifiable individual information is included in this manuscript.

Availability of data

Data supporting the findings of this study are available from the corresponding author upon reasonable request.

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