Association Between Four ABCA1 gene Polymorphisms and Risk of Non-Alcoholic Fatty Liver Disease in a Chinese Han Population

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Abstract

Background: Non-alcoholic fatty liver disease (NAFLD) as a severe health problem is the leading cause of morbidity and mortality from the chronic liver disease worldwide. NAFLD is tightly associated with dyslipidemia although the etiology is still unclear. ATP binding cassette subfamily A member 1 (ABCA1) is involved in cholesterol efflux, fatty acid oxidation, and inflammation. Although some reports show that the ABCA1 polymorphisms affect the lipids metabolism and severity of clinical liver diseases, the effects of ABCA1 polymorphisms on the development of NAFLD are unknown.

Objectives: The current study was performed to investigate the association between the ABCA1 polymorphisms and the development of NAFLD and the effect of the four ABCA1 SNPs on the serum lipid levels.

Methods: The ABCA1 polymorphisms (rs1800977, rs2066714, rs2066715, and rs2230808) were determined in 265 NAFLD patients and 126 healthy controls using the sequencing and polymerase chain reaction analysis. Serum lipid profiles and liver enzymes were examined using standard clinical laboratory methods.

Results: There was a significant difference (P < 0.05) in the genotype of the ABCA1 rs1800977 G/A polymorphisms between NAFLD patients and healthy controls. No significant differences were found in genotypes and allele frequencies of the ABCA1 rs2066714T/C, rs2066715T/C, and rs2230808C/T between NAFLD patients and healthy controls. The ABCA1 rs1800977 A was independently associated with NAFLD after adjusting for the effects of age, gender, and BMI. Compared to the noncarriers in NAFLD patients, the carriers of ABCA1 rs2066714 C showed a significantly higher level of LDL (P = 0.045) and the carriers of ABCA1 rs2230808 T showed a significantly lower level of HDL (P = 0.039).

Conclusions: We first demonstrated the association between the ABCA1 polymorphisms and the risk of NAFLD in a Chinese Han population. The ABCA1 rs1800977G may be a protective factor against the development of NAFLD. The ABCA1 rs2066714 C allele could increase the serum LDL cholesterol level, and the ABCA1 rs2230808 T allele could decrease the serum HDL cholesterol level in NAFLD patients.

Keywords: Single Nucleotide Polymorphism, Non-Alcoholic Fatty Liver Disease, Polymorphism

1. Background

Non-alcoholic fatty liver disease (NAFLD) comprises a spectrum ranging from simple steatosis, non-alcoholic steatohepatitis (NASH), and fibrosis to cirrhosis. NAFLD is defined as the increased hepatic triglyceride content (HTGC) without the consumption of alcohol (1). Simple steatosis is usually benign and can progress to steatohepatitis, fibrosis, and cirrhosis, ultimately leading to the development of hepatocellular carcinoma (HCC) (2-4). NAFLD is commonly associated with obesity, insulin resistance, and hyperlipidemia, all of which are the typical metabolism syndromes (5, 6). Several population-based epidemiological studies have shown that the incidence of NAFLD in China is approximately 15% in adults and 1.3% in children and adolescents (7) while the incidence of NAFLD is 20% - 30% in Western countries (8). NAFLD is becoming a major public health problem worldwide, and is associated
with numerous pathogenesis, such as metabolic, genetic, environmental, and gut microbial factors (9).

Although abundant studies have been conducted in the fundamental and clinical features of NAFLD, the detailed pathogenic mechanism of NAFLD is still unclear. The classical "two hits" theory has been put forward as a pathogenesis of NAFLD (10). The first “hit” results in hepatic steatosis, mainly caused by obesity, type 2 diabetes mellitus, dyslipidemia, and other metabolic factors. The second “hit” leads to hepatocellular injury and liver inflammation by oxidative stress and proinflammatory cytokines (11). In recent years, a “multi-parallel hit” model has been proposed as a new pathogenesis of NAFLD due to many factors suggesting that gut-derived and adipose tissue-derived factors may react in parallel, finally resulting in the liver inflammation (12). Meanwhile, accumulated evidence suggests a link between cholesterol homeostasis and accumulation of hepatic cholesterol in the pathogenesis of steatohepatitis (13-16). Cholesterol consumption has been shown to significantly associate with the risk of cirrhosis or liver cancer in the national health and nutrition examination survey, but serum cholesterol level was not associated with the risk of cirrhosis or liver cancer (17). Furthermore, epidemiological data prove that the increased cholesterol intake contributes to the risk and severity of NAFLD (17). Caballero et al. also reported that the accumulation of hepatic free cholesterol (FC) increases the development of NASH and fibrosis in patients with NAFLD (15, 18). Although accumulated evidence suggests that the increased cholesterol level is associated with the NAFLD, the detailed mechanism of cholesterol in the development of NAFLD remains unclear. Therefore, the significant role of cholesterol in the pathogenesis of NAFLD needs further study.

The ATP binding cassette subfamily A member 1 (ABCA1) gene is located on chromosome 9 (9q31) and contains 58 exons (19, 20) (https://www.ncbi.nlm.nih.gov/gene/19). ABCA1 is a 2261-amino acid membrane protein that contains 12 transmembrane domains and mediates cholesterol efflux from cell to lipid-free apolipoprotein A-I (apoA-I) and apolipoprotein E (apoE) (21). Besides, ABCA1 is an essential regulator of high-density lipoproteins (HDL) and reverse cholesterol transport (22). In 2002, Hong et al. reported that the C254T variant in ABCA1 was associated with a reduced HDL cholesterol and familial hypoalphalipoproteinemia (FHA), suggesting that the ABCA1 polymorphism may affect the lipids metabolism (23). Recent studies have shown that the SNPs in ABCA1 might modulate plasma triglyceride and HDL cholesterol levels in HIV-infected patients (24). Although ABCA1 polymorphism is a risk factor for the lipids metabolism, a few studies have been conducted in the NAFLD patients, especially in the Chinese Han population.

2. Objectives

The aim of this study was to investigate the association between four ABCA1 SNPs and the development of NAFLD in a Chinese Han population and the effect of the four ABCA1 SNPs on the serum lipid levels.

3. Methods

3.1. Study Subjects

The study was performed in accordance with the principles of the declaration of Helsinki and its appendices (25) and approved by the ethics committee of the Qingdao municipal hospital. A written informed consent form was obtained from each patient before participation in the study.

A total of 391 unrelated Chinese Han adult subjects of both sexes, including 265 NAFLD patients diagnosed with B-type ultrasonography and 126 healthy control subjects were enrolled in this study. All subjects were recruited from the department of gastroenterology and the Medical Center of Qingdao Municipal hospital from November 2015 to August 2017. A standard study questionnaire was used to obtain the basic clinicopathological information (name, age, gender, and so on).

The diagnosis of NAFLD was performed under standard clinical evaluation conditions according to the American association for the study of liver diseases (AASLD) criteria. Hepatic steatosis was observed by B-type ultrasonography in NAFLD patients. Other causes of liver disease were excluded, including high alcohol intake (> 210/140 g/w for males/females), as confirmed by at least one family member or friend and carboxy-desialylated transferrin determination, viral and autoimmune hepatitis, hereditary hemochromatosis, and alpha-antitrypsin deficiency. Subjects with other related diseases such as type 1 diabetes mellitus and coronary atherosclerotic disease (CAD) were also excluded. The controls were confirmed as healthy by medical history, general examinations, and laboratory examinations at the same hospital.

3.2. Biochemical Analyses

Blood samples of each subject for biochemical analyses were collected into sterile tubes containing ethylene diamine tetraacetic acid after a 12-hour overnight fast. The height and body mass of each subject were obtained and approved by at least one family member or friend and carboxy-desialylated transferrin determination, viral and autoimmune hepatitis, hereditary hemochromatosis, and alpha-antitrypsin deficiency. Subjects with other related diseases such as type 1 diabetes mellitus and coronary atherosclerotic disease (CAD) were also excluded. The controls were confirmed as healthy by medical history, general examinations, and laboratory examinations at the same hospital.
(AST), γ-glutamyl transferase (GGT), and alkaline phosphatase (ALP) were measured using the standard clinical laboratory methods in the central laboratory of Qingdao municipal hospital. Glucose (Glu), triglycerides (TG), total cholesterol (TC), high-density lipoprotein (HDL), and low-density lipoprotein (LDL) were measured using routine enzymatic methods.

3.3. Genetic Analysis

Genomic DNA was extracted from peripheral blood samples using the Genomic DNA Purification Kit (BioTeke, Biotechnology, Beijing, China) following the manufacturer's instructions and stored at -20°C until use. Genotyping for the ABCA1 rs1800977G/A, rs2066714T/C, rs2066715T/C, and rs2230808C/T was performed by polymerase chain reaction (PCR) analysis using the primers shown in Table 1. Amplification was performed in a total volume of 25 µL containing 12.5 µL Taq PCR MasterMix (TaKaRa), 2 µL genomic DNA, 1 µL forward primer, 1 µL reverse primer, and 8 µL purified water on PCR amplification equipment (Labnet, United States) as follows: initial step of 95°C for 10 minutes, followed by 35 cycles: denaturation at 94°C for 1 minute, annealing at 60°C for 1 minute, and elongation at 70°C for 1 minute. All PCR products were resolved by 7% agarose gel electrophoresis at 110 V for 30 minutes and stained with ethidium bromide. The genotypes of the four sites underwent direct sequencing using the ABI Prism sequencing system ABI3730 (Foster City, CA, USA). The genotyping success rate was > 95%.

### Table 1. Primers Used for Genotyping Analysis

| SNPs       | Primer Sequences (5’ - 3’)                        | Amplicon Size, bp |
|------------|---------------------------------------------------|-------------------|
| rs1800977  | ACGTTGAGTACTTACCTGGTGGGCATTAC                   | 109               |
| rs2066714  | ACGTTGAGTGGGAGCGTGGAGAAGAGCC                    | 100               |
| rs2066715  | ACGTTGAGTGGGAGCGTGGAGAAGAGCC                    | 101               |
| rs2230808  | ACGTTGAGTGGGAGCGTGGAGAAGAGCC                    | 100               |

3.4. Statistical Analysis

Statistical analyses were performed using SPSS version 22.0 statistical software for Windows. Baseline characteristics are shown as mean ± SD. Differences in the characteristics of the study population between different groups were examined using the Student’s t-test and the χ² test. Hardy-Weinberg equilibrium between expected and observed genotype distributions was estimated by the χ² test. Genotypes and alleles were estimated by the chi-square test and DNA distributions between NAFLD patients and controls were analyzed by Pearson’s χ² test or Fisher’s exact test when appropriate. The strength of the association between the polymorphisms and NAFLD was assessed by the logistic regression analysis, adjusted for confounders (age, gender, and BMI), estimated by the odds ratio (OR) with 95% confidence interval (CI). Levels of significance were defined as P < 0.05.

4. Results

4.1. Characteristics of the Study Population

Patients in the NAFLD group (199 males, 66 females, mean age 39.73 ± 6.38 years) and control group (88 males, 38 females, mean age 38.46 ± 6.94 years) had no statistical differences in sex (P = 0.273) and age (P = 0.075). The clinical characteristics of the study participants are shown in Table 2. The patients with NAFLD had higher BMI, SBP, and DBP, higher serum levels of ALT, GGT, ALP, Glu, TG, TC, LDL, and lower serum levels of HDL than the healthy controls.

### Table 2. Demographic and Clinical Characteristics of NAFLD Patients and Healthy Controls

|                     | NAFLD Patients (n = 265) | Controls (n = 126) | PValuea |
|---------------------|--------------------------|--------------------|---------|
| BMI, kg/m²           | 26.43 ± 3.05             | 23.36 ± 2.86       | < 0.001 |
| SBP, mmHg            | 124.66 ± 14.18           | 117.37 ± 12.24     | < 0.001 |
| DBP, mmHg            | 85.00 ± 9.89             | 79.71 ± 9.84       | < 0.001 |
| ALT, U/L             | 34.09 ± 20.67            | 23.95 ± 32.37      | < 0.001 |
| AST, U/L             | 24.22 ± 9.25             | 22.82 ± 16.55      | 0.279   |
| GGT, U/L             | 43.95 ± 32.84            | 28.47 ± 21.27      | < 0.001 |
| ALP, U/L             | 70.98 ± 16.76            | 66.98 ± 18.58      | 0.034   |
| Glu, mmol/L          | 5.05 ± 1.20              | 4.50 ± 0.88        | < 0.001 |
| TG, mmol/L           | 1.98 ± 1.23              | 1.29 ± 1.05        | < 0.001 |
| TC, mmol/L           | 5.64 ± 1.06              | 5.20 ± 0.85        | < 0.001 |
| HDL, mmol/L          | 1.25 ± 0.35              | 1.40 ± 0.29        | < 0.001 |
| LDL, mmol/L          | 3.39 ± 0.75              | 2.98 ± 0.64        | < 0.001 |

Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; BMI, body mass index; DBP, diastolic blood pressure; GGT, γ-glutamyl transferase; Glu, Glucose; HDL, high-density lipoprotein; LDL, low-density lipoprotein; SBP, systolic blood pressure; TG, triglyceride; TC, total cholesterol. Values are expressed as mean ± SD and compared by Student’s t-test.

4.2. Genotypes and Allele distribution of rs1800977G/A, rs2066714T/C, rs2066715T/C, and rs2230808C/T

The genotypes distribution of each ABCA1 SNP site was in accordance with the Hardy-Weinberg equilibrium in
NAFLD patients and healthy controls as shown in Table 3. To ensure the accuracy of genotypes, we randomly selected 100 subjects for reverse sequencing. The success rate of duplicated genotyping was > 100%. As shown in Table 4, there was a significant difference in the genotype of ABCA1 rs1800977 between the NAFLD patients group and control group (P = 0.009). A strong link of the ABCA1 rs1800977 allele with NAFLD is shown in Table 5; the frequency of ABCA1 rs1800977 GA + AA genotypes was significantly lower in the NAFLD patients than in the control group (OR: 0.751; 95%CI: 0.606 - 0.931). After adjusting for gender, age, and BMI, the frequency of ABCA1 rs1800977 GA + AA genotypes was significantly lower in the NAFLD patients than in the control group (OR: 0.678; 95%CI: 0.525 - 0.876).

Table 3. Results of the Hardy-Weinberg Equilibriuma

| Gene Locus Groups | χ²   | P Value |
|-------------------|------|---------|
| rs1800977         |      |         |
| NAFLD             | 3.36 | 0.075   |
| Controls          | 3.54 | 0.060   |
| rs2066714         |      |         |
| NAFLD             | 2.01 | 0.16    |
| Controls          | 0.44 | 0.51    |
| rs2066715         |      |         |
| NAFLD             | 0.85 | 0.36    |
| Controls          | 0.0043 | 0.98 |
| rs2230808         |      |         |
| NAFLD             | 0.11 | 0.735   |
| Controls          | 3.65 | 0.059   |

aData were compared by chi-square test.

4.3. Association of the Genetic Variants in the ABCA1 Gene with Clinical Parameters in Non-Alcoholic Fatty Liver Disease Patients

To estimate whether gene polymorphisms are correlated with clinical parameters, we compared the clinical characteristics in carriers and non-carriers of the four alleles in overall series, NAFLD patients, and healthy controls. As shown in the results, in the NAFLD patients group, the carriers of rs2066714 C showed a higher serum level of LDL compared to the noncarriers (Table 6), and the carriers of 2230808 T showed a lower serum level of HDL compared to the noncarriers (Table 7). In addition, no significant difference was observed in the lipid variables (TC, TG, LDL, and HDL levels) and indices of liver damage severity (serum ALT and AST levels) between the carriers and noncarriers of rs1800977 A and rs2066715 C in overall series, NAFLD patients, and healthy controls (Data not shown).

5. Discussion

In this study, we investigated the relationship between the genetic variants of ABCA1 rs1800977, rs2066714, rs2066715, and rs2230808 and the risk of NAFLD for the first time. Previous studies have proposed that multiple factors were related to the development and progression of NAFLD such as insulin resistance, obesity, oxidative stress, and so on (26). In this study, we diagnosed the NAFLD by routine blood testing and liver ultrasonography instead of biopsy, which is regarded as the gold standard of NAFLD diagnosis. In the majority of cases, patients with NAFLD possessed elevated levels of serum lipid profiles and liver enzymes, especially ALT and GGT, which had been used as the marker of liver injury (27-29). In our study, there was a significantly higher level of serum TG, TC, LDL, ALT, GGT, and ALP in NAFLD patients compared to the healthy controls. In addition, the serum concentration of HDL was significantly lower in NAFLD patients than in healthy controls.

Accumulated evidence has shown that the ABCA1 variants were tightly associated with the abnormal metabolism of serum lipid profiles and liver enzymes (30). Recently, a report showed that the pathogenic mutations of ABCA1 (including rs9282543, rs137854496, rs374190304, rs141021096, and rs150125857) were observed in Canadians, which increased the risk of atherosclerosis compared to the patients without such mutations (31). Kolovou et al. conducted a study to investigate the association between ABCA1 gene polymorphism and the plasma lipid variables in Greek nurses; the results indicated that the R578K variant (rs2230808) of ABCA1 gene tightly affected the lipid variables; this may be helpful in assessing the risk of premature coronary heart disease and atherosclerosis (30). The association of ABCA1 R230C variant (rs9282541) with high triglyceride levels was observed in the Mexican school-age children, which confers ABCA1 R230C as a potential risk factor for the high TG syndrome (32). Although many studies of ABCA1 polymorphism have been conducted in patients with dyslipidemia, coronary heart disease, and atherosclerosis, which were tightly associated with the development of NAFLD, the effects of ABCA1 variants on NAFLD have not been reported. Our study first presented the evidence that there is a significant difference in the genotype of ABCA1 rs1800977 between the NAFLD patients and healthy controls in a Chinese Han population. However, the frequency of ABCA1 rs1800977 GA + AA genotypes was significantly lower in the NAFLD patients than in the control group. After adjusting for gender, age, and BMI, the frequency of ABCA1 rs1800977 GA+AA genotypes was significantly lower in the NAFLD patients than in the control group. These results suggest that ABCA1 rs1800977 was associated with the development
### Table 4. Distribution of Genotypes and Allele Frequencies of ABCA1 in NAFLD Patients and Controls$^{a,b}$

|                  | NAFLD       | Controls   | $\chi^2$ | P Value |
|------------------|-------------|------------|----------|---------|
| **rs1800977**    |             |            |          |         |
| Genotypes        |             |            |          |         |
| GG               | 147 (55.5)  | 52 (41.3)  | 6.892    | 0.009   |
| GA               | 93 (35.1)   | 65 (51.6)  |          |         |
| AA               | 25 (9.4)    | 9 (7.1)    |          |         |
| Alleles          |             |            | 2.986    | 0.086   |
| G                | 387 (73.0)  | 169 (67.1) |          |         |
| A                | 143 (27.0)  | 83 (32.9)  |          |         |
| **rs2066714**    |             |            |          |         |
| Genotypes        |             |            |          |         |
| TT               | 139 (52.5)  | 76 (60.3)  | 2.134    | 0.144   |
| TC               | 112 (42.3)  | 42 (33.3)  |          |         |
| CC               | 14 (5.2)    | 8 (6.4)    |          |         |
| Alleles          |             |            | 1.044    | 0.307   |
| T                | 390 (73.6)  | 194 (77.0) |          |         |
| C                | 140 (26.4)  | 58 (23.0)  |          |         |
| **rs2066715**    |             |            |          |         |
| Genotypes        |             |            |          |         |
| TT               | 90 (34.0)   | 47 (37.3)  | 0.418    | 0.518   |
| TC               | 135 (50.9)  | 60 (47.6)  |          |         |
| CC               | 40 (15.1)   | 19 (15.1)  |          |         |
| Alleles          |             |            | 0.200    | 0.655   |
| T                | 315 (59.4)  | 154 (61.1) |          |         |
| C                | 215 (40.6)  | 98 (38.9)  |          |         |
| **rs2230808**    |             |            |          |         |
| Genotypes        |             |            |          |         |
| CC               | 105 (39.6)  | 57 (45.2)  | 1.049    | 0.306   |
| CT               | 125 (47.2)  | 48 (38.1)  |          |         |
| TT               | 35 (12.2)   | 21 (16.7)  |          |         |
| Alleles          |             |            | 0.052    | 0.820   |
| C                | 335 (63.2)  | 162 (64.3) |          |         |
| T                | 195 (36.8)  | 90 (35.7)  |          |         |

$^a$Data were compared by chi-square test.  
$^b$Values are expressed as No. (%).
Table 5. Association of Genotypes with NAFLD in the Study Group^a

| rs1800977 | Unadjusted | Adjusted | OR (95% CI) | P Value | OR (95% CI) | P Value |
|-----------|------------|----------|-------------|---------|-------------|---------|
| GG        | 1          | 1        |             |         |             |         |
| GA + AA   | 0.75 (0.606 - 0.931) | 0.009 | 0.678 (0.525 - 0.876) | 0.003 |
| rs2066714  | TT         | 1        | 1           |         |             |         |
|            | TC + CC    | 1.174 (0.946 - 1.456) | 0.145 | 1.246 (0.936 - 1.657) | 0.31 |
| rs2066715  | TT         | 1        | 1           |         |             |         |
|            | TC + CC    | 1.076 (0.862 - 1.341) | 0.518 | 1.044 (0.786 - 1.386) | 0.767 |
| rs2230808  | CC         | 1        | 1           |         |             |         |
|            | CT + TT    | 1.122 (0.906 - 1.390) | 0.293 | 1.109 (0.849 - 1.448) | 0.459 |

^aThe multiple-logistic regression model was adjusted for gender, age, and BMI.

Table 6. Clinical Characteristics of ABCA1 rs2066714 C Carriers and Non-Carriers in the Study Population^b

| Overall Series | NAFLD Patients | Controls | OR (95% CI) | P Value | OR (95% CI) | P Value |
|----------------|----------------|----------|-------------|---------|-------------|---------|
| Carriers (n = 229) | Non-Carriers (n = 162) | P Value | Carriers (n = 160) | Non-carriers (n = 105) | P Value | Carriers (n = 69) | Non-Carriers (n = 97) | P Value |
| Female/Male | 42/134 | 62/153 | 0.268 | 25/101 | 41/98 | 0.070 | 17/33 | 2/55 | 0.446 |
| Age, y | 39.17 ± 6.61 | 39.50 ± 6.56 | 0.625 | 40.81 ± 6.54 | 39.38 ± 6.23 | 0.353 | 37.24 ± 6.85 | 38.32 ± 7.45 | 0.415 |
| BMI, kg/m^2 | 25.26 ± 3.43 | 25.52 ± 3.27 | 0.57 | 26.55 ± 2.76 | 26.32 ± 3.10 | 0.032 | 22.90 ± 3.01 | 23.33 ± 2.77 | 0.414 |
| SBP, mmHg | 121.69 ± 13.13 | 121.06 ± 14.97 | 0.342 | 125.47 ± 14.96 | 123.92 ± 13.43 | 0.376 | 117.00 ± 13.29 | 117.62 ± 11.58 | 0.783 |
| DBP mmHg | 82.96 ± 9.96 | 83.70 ± 10.43 | 0.471 | 85.25 ± 12.4 | 84.78 ± 9.59 | 0.700 | 79.42 ± 9.97 | 79.63 ± 9.82 | 0.917 |
| ALT, U/L | 31.81 ± 29.78 | 29.62 ± 18.62 | 0.395 | 33.56 ± 19.82 | 34.57 ± 21.47 | 0.694 | 19.67 ± 9.72 | 26.77 ± 40.52 | 0.227 |
| AST, U/L | 24.48 ± 15.14 | 22.92 ± 6.64 | 0.295 | 23.99 ± 7.05 | 24.46 ± 10.89 | 0.684 | 20.23 ± 4.49 | 24.53 ± 20.88 | 0.154 |
| GGT, U/L | 37.33 ± 28.37 | 40.94 ± 33.75 | 0.251 | 47.63 ± 37.09 | 40.61 ± 28.16 | 0.082 | 24.09 ± 12.34 | 31.55 ± 27.96 | 0.087 |
| ALP, U/L | 68.81 ± 17.2 | 70.77 ± 17.08 | 0.270 | 71.78 ± 16.28 | 70.27 ± 17.20 | 0.465 | 68.23 ± 18.88 | 66.15 ± 18.46 | 0.541 |
| Gla, mmol/L | 4.80 ± 0.95 | 4.95 ± 1.33 | 0.232 | 5.10 ± 1.34 | 5.00 ± 1.07 | 0.506 | 4.56 ± 1.25 | 4.46 ± 0.51 | 0.354 |
| TG, mmol/L | 1.72 ± 1.19 | 1.79 ± 1.25 | 0.567 | 2.07 ± 1.27 | 1.90 ± 1.18 | 0.261 | 1.11 ± 0.89 | 1.41 ± 1.14 | 0.120 |
| TC, mmol/L | 5.47 ± 0.97 | 5.52 ± 1.07 | 0.608 | 5.72 ± 1.14 | 5.56 ± 0.98 | 0.209 | 5.03 ± 0.66 | 5.32 ± 0.95 | 0.066 |
| HDL, mmol/L | 1.30 ± 0.30 | 1.29 ± 0.38 | 0.701 | 1.25 ± 0.42 | 1.24 ± 0.28 | 0.742 | 1.38 ± 0.24 | 1.42 ± 0.31 | 0.457 |
| LDL, mmol/L | 3.21 ± 0.70 | 3.32 ± 0.78 | 0.156 | 3.49 ± 0.80 | 3.31 ± 0.69 | 0.045 | 2.89 ± 0.54 | 3.04 ± 0.70 | 0.390 |

Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; BMI, body mass index; DBP, diastolic blood pressure; GGT, γ-glutamyl transferase; Gla, Glucose; HDL, high-density lipoprotein; LDL, low-density lipoprotein; SBP, systolic blood pressure; TC, total cholesterol; TG, triglyceride.

^bValues are expressed as mean ± SD and compared by Student’s t-test.

apolipoproteins of nascent HDL cholesterol in a process that contributes to the initial step of reverse cholesterol transport (36). ABCA1 polymorphisms affecting the serum levels of HDL cholesterol have been reported in many studies. Hong et al. investigated the relationship of the ABCA1 C254T variant with the serum HDL cholesterol levels in the patients with premature coronary artery disease. The results showed that the single defective allele in ABCA1 may be associated with reduced HDL cholesterol levels (23). Similar results were observed in the Mexican school-age children with a high prevalence of obesity; the study reported a tight association of R230C variant of the ABCA1 gene with the low HDL cholesterol levels (32). In this study, we observed that the serum HDL cholesterol levels were significantly lower in the NAFLD patients with ABCA1 rs2230808 T allele than in the NAFLD patients without the variant, which is in accordance with previous studies. However, there was no significant difference in the serum HDL cholesterol levels between the carriers and noncarriers of the ABCA1 rs1800977 A, rs2066714 C, and rs2066715 C
in NAFLD patients. In addition, the increased serum levels of LDL cholesterol were observed in the NAFLD patients with the ABCA1 rs2066714 C allele. The same result was also reported in Turkish adults indicating that the R219K variant (rs2230806 G > A) of ABCA1 was associated with the increased serum LDL cholesterol levels (37). No significant difference in the serum LDL cholesterol levels of NAFLD patients was observed between the carriers and noncarriers of the ABCA1 rs1800977 A, rs2066715 C, and rs2230808 T.

In summary, we investigated the association between the ABCA1 polymorphisms and NAFLD in a Chinese Han population for the first time. Our results provided preliminary evidence that ABCA1 rs1800977 is associated with the risk of NAFLD and the rs1800977 A variant may possess a protective role against the development of NAFLD. The rs2066714 C variant of ABCA1 increased the serum LDL cholesterol level and the rs2230808 T variant decreased the serum HDL cholesterol level in the NAFLD patients. Although rs1800977 showed a significant association with the development of NAFLD, the distribution of homozygote genotypes for the allele A demonstrated a higher frequency in the control group rather than in the NAFLD group. The detailed mechanism of the ABCA1 polymorphisms in the development of NAFLD and lipids metabolism remains unknown. Therefore, stronger and more validated data of ABCA1 polymorphisms in NAFLD obtained from studies with different and preferably larger populations are needed.

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Footnotes

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