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ORIGINAL RESEARCH

An Exploration of Alanine Aminotransferase (ALT) and Aspartate Aminotransferase (AST) Platelet Ratio Index (APRI) Scores with Dysglycemia and Diabetic Retinopathy: The Beichen Eye Study

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Background and Purpose: Liver metabolism is closely linked to glucose levels. Studies have shown that the aspartate aminotransferase to platelet ratio index (APRI), as a marker of liver fibrosis, is associated with type 2 diabetes mellitus (T2DM). However, the existing evidence remains insufficient to establish this association definitively. Furthermore, no prior studies have investigated the potential relationship between APRI and diabetic retinopathy (DR). This study aimed to investigate the association of alanine aminotransferase (ALT) and aspartate aminotransferase (AST) to platelet ratio index (APRI) scores with dysglycemia and DR.

Methods: This cross-sectional study analyzed data from 5828 participants aged 50 and older. All participants underwent laboratory blood tests, ophthalmological examinations, and interviews using questionnaires. Multiple linear regression models and receiver operating characteristic (ROC) curves explored the association between ALT and AST APRI scores and dysglycemia. Binary logistic regression was used to analyze the association between ALT and AST APRI scores and DR. Analyses were conducted for males and females separately to examine sex-specific effects.

Results: In the multiple linear regression models, ALT and AST APRI scores were associated with fasting blood glucose after adjusting various potential confounders in the whole population or subgroup analysis (all $P < 0.05$). ALT APRI score was superior to AST APRI score in the discrimination of hyperglycemic participants. In the univariate analysis, the ALT and AST APRI scores were associated with DR in the female participants with diabetes ($P = 0.043$, $P=0.022$). However, binary logistic regression models found no evident significant association between the ALT and AST APRI scores and DR in the female participants with diabetes (all $P>0.05$).

Conclusion: ALT and AST APRI scores are potential markers for the diagnosis of hyperglycemia, and ALT APRI score is superior to AST APRI score. ALT and AST APRI scores are not independent risk factors for DR.

Keywords: APRI score, alanine aminotransferase, aspartate aminotransferase, dysglycemia, diabetic retinopathy

Introduction

Type 2 diabetes mellitus (T2DM) is a group of chronic metabolic disorders characterized by elevated blood glucose levels. Globally, T2DM affects approximately 25% of people over 65 years, and its prevalence is increasing.[1] Poor glycemic control is related to a higher risk of developing macrovascular and microvascular complications in diabetes. Diabetic retinopathy (DR) is the most common microvascular complication of DM[2] and the leading cause of visual loss in working-age adults worldwide,[3] which can lead to serious public health problems.[4] Studies have shown

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that T2DM is related to liver diseases.[5] As the primary organ for storing glucose in the form of glycogen and endogenous glucose, the liver plays a crucial role in maintaining glucose homeostasis.[6] Hence, the condition of the liver can impact the glycemic status. The liver enzymes, particularly alanine aminotransferase (ALT) and aspartate aminotransferase (AST), are important indicators of liver health. The ALT/AST ratio is also used to indicate general health. A secondary analysis of a retrospective cohort study indicated that the AST/ALT ratio was inversely associated with the risk of T2DM.[7] Recent studies have revealed that the AST/ALT ratio was also an independent risk factor for diabetic retinopathy in type 2 diabetes mellitus.[8] Thus, liver injury markers have the potential to predict the risk of type 2 diabetes and microvascular complications of type 2 diabetes.[8,9]

The AST to Platelet Ratio Index (APRI), a non-invasive liver fibrosis score, has recently been used as a hepatic inflammation marker.[10] One study demonstrated that the APRI score could predict the progression from prediabetes to diabetes.[11] In another retrospective study, the APRI score also showed potential in diagnosing and managing hyperglycemic conditions.[12] The APRI score has also been clinically accepted as a marker for non-alcoholic fatty liver disease (NAFLD).[13] It has been reported that NAFLD is associated with an increased prevalence of proliferative/laser-treated retinopathy in type 2 diabetic patients.[14] However, the relationship between the APRI score and diabetic retinopathy has almost never been explored. It is crucial to further explore the role of the APRI score in dysglycemia and diabetic retinopathy because of its non-invasiveness and convenience. Furthermore, few studies have tested ALT's clinical practicality in calculating the APRI score index instead of AST, although ALT is also an essential marker of hepatocellular injury. For these reasons, the study aimed to determine whether ALT and AST APRI scores are associated with the risk of hyperglycemia and diabetic retinopathy (DR). As estrogen affects liver metabolism and glycemic status,[15] the role of gender was also considered in this study.

Methods

The Study Design and Population

The Beichen Eye Study is a population-based, cross-sectional study of people aged 50 years and older recruited between June 2020 and February 2022 from 4 towns and 12 villages in the urbanized areas of Beichen District, north of Tianjin. For this study, communities were selected using a multi-stage random sampling procedure. In accordance with the Declaration of Helsinki, the study was approved by the Ethics Committee of Tianjin Medical University Eye Hospital (Approval No. 2019ky-22), and written informed consent was obtained from all participants. Participants with complete data from laboratory blood tests, ophthalmological examinations, and questionnaires were included. Participants with incomplete data were excluded. When exploring the association between ALT and AST APRI scores and DR, we also excluded participants without diabetes mellitus and participants with other ocular diseases, such as glaucoma, uveitis, keratitis, and macular degeneration. Study design is summarized in a flow diagram (Figure 1).

Examination

All participants underwent assessments of height, weight, waist circumference, and body mass index (BMI). The waist circumference was measured using a sagittal waist measuring ruler (Holtain Ltd, UK). Questionnaires acquired demographic characteristics, medical history, and lifestyle of the participants. Total cholesterol (TC), triglycerides (TG), high-density lipoprotein (HDL), low-density lipoprotein (LDL), fasting blood glucose (FBG), and other routine blood indices were measured with the automatic hematology analyzer. Aspartate aminotransferase (AST), alanine aminotransferase (ALT), total bilirubin (TBIL), and other biochemical indicators were detected by an automated biochemical analyzer (AU5800 Automatic Biochemical analyzer, Beckman Coulter). Ophthalmologic examination included assessment of vision acuity test, optometry examination, intraocular pressure measurement, slit-lamp examination, direct ophthalmoscope, dilated fundus examination, fundus photography, optical coherence tomography (OCT) and optical coherence tomography angiography (OCTA). The diagnosis and staging of DR were made by two trained fundus doctors on the basis of fundus photographs. Discrepant results were assessed by a senior retinal ophthalmologist for final evaluation. The diagnosis and staging of DR were based on the International Clinical Diabetic Retinopathy (ICDR) classification criteria: no DR, mild non-proliferative DR (NPDR), moderate NPDR, severe NPDR, and proliferative DR (PDR). The examination process of the participants in this study were referred to the literature 16.[16]

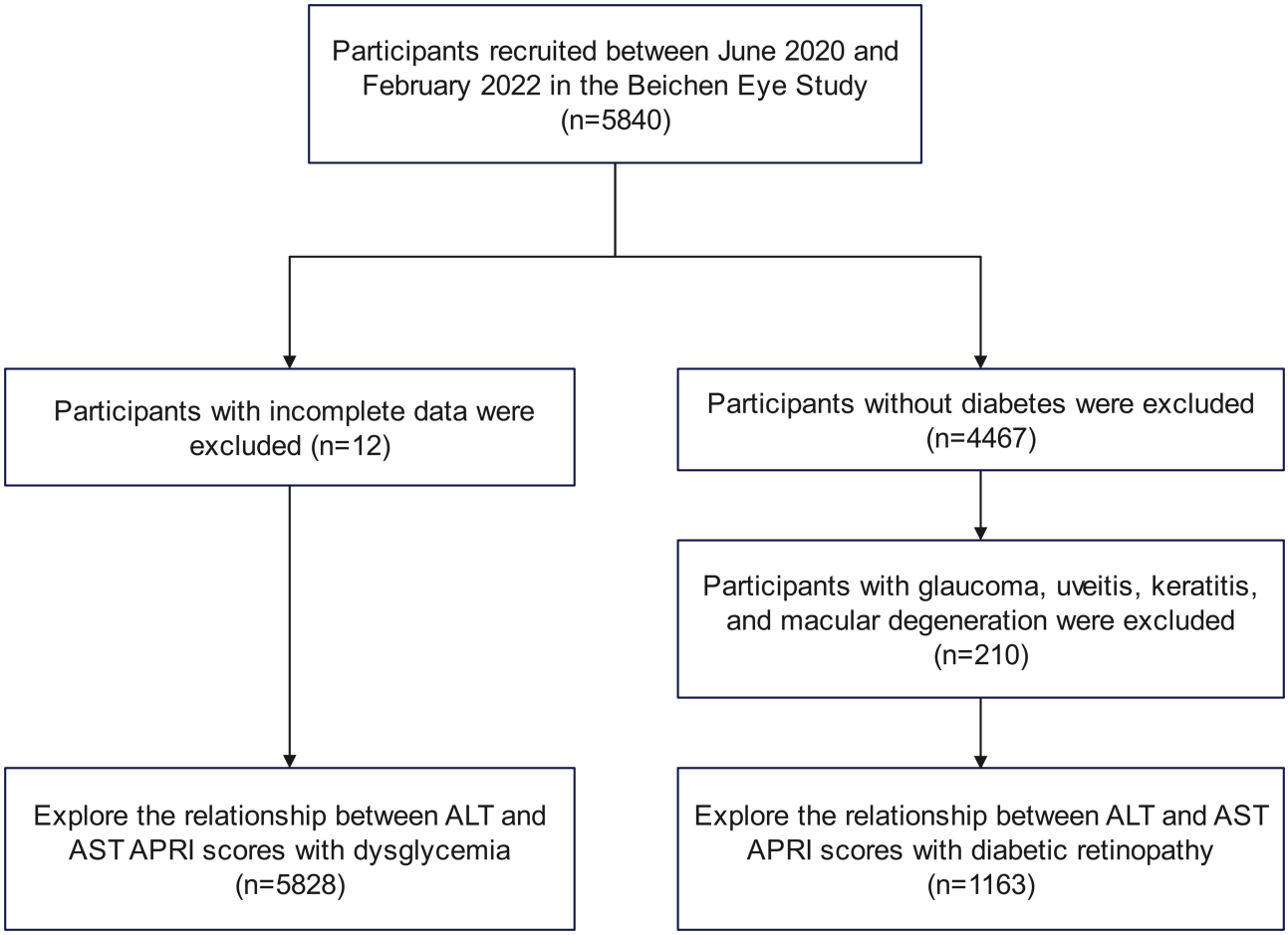

Figure 1 Participants selection and study flow diagram.

Data Collection

The AST APRI score was calculated using the formula "AST/upper limit of normal/platelet count [10^9/L]" × 100.[17] Similarly, the ALT APRI score was calculated using the formula "ALT/upper limit of normal/platelet count [10^9/L]" × 100. The upper normal limit used in the study was 40 U/L for both AST and ALT. The APRI score equal to or greater than 0.5 was considered a high APRI score (H-APRI).[18] To explore the relationship between ALT and AST APRI scores with dysglycemia, we divided this population into three groups: normoglycemia (NG) group, impaired fasting glycemia (IFG) group, and hyperglycemia (HG) group. Normoglycemia was defined as FBG < 6.1 mmol/L. Impaired fasting glycemia was defined as 6.1≤ FBG ≤ 6. 9 mmol/L.[19] Hyperglycemia was defined as FBG ≥ 7.0 mmol/L. To explore the relationship between ALT and AST APRI scores and diabetic retinopathy, enrolled participants were categorised into non-DR and DR groups.

Statistics

Statistical analysis data was conducted with SPSS (IBM, USA. Version 25). All quantitative data were non-normally distributed and presented as medians (interquartile range [IQR]). The differences among the three groups were compared using the Kruskal–Wallis test, while the two groups were compared using the Wilcoxon rank-sum test. The counting data were expressed as count (percentage) and processed using a chi-square test. Multiple linear regression models were used for continuous variables, and binary logistic regression models were used for categorical outcomes. The area under the curve (AUC) of the receiver operating characteristic (ROC) was used to compare the diagnostic performance across various models. $P<0.05$ was indicated as a statistical difference.

Results

Association Between ALT and AST APRI Scores with Dysglycemia

Study Population Characteristics

Baseline characteristics of the study population are presented in Table 1. A total of 5828 participants were enrolled in this study, 2077 males (35.64%) and 3751 females (64.36%). The median age of participants was 63 years (interquartile range 58–67 years). There were 4862 participants in the NG group, 354 in the IFG group, and 612 in the HG group. No statistically significant correlations were observed between age, current smoking, TC, LDL, PLT count, AST, TBIL, ALB, CRE, and UA among the 3 groups (all $P > 0.05$). Significantly, the IFG group was the oldest. The NG group had the lowest proportion of males, current drinkers, and hypertension, but there were no statistical differences between the IFG and HG groups. The HG group showed the highest levels of TG, WBC, RBC, and ALT, followed by the IFG and NG groups. Conversely, HDL was highest in the NG group and lowest in the HG group.

Simple Correlation Analysis

We evaluated the associations between ALT and AST APRI scores with dysglycemia in Figure 2 and found that ALT APRI scores in both groups IFG and HG displayed statistically significant differences from the NG group ($P < 0.0001$). However, the ALT APRI scores cannot clearly separate the IFG and HG groups (Figure 2A). Similar results were found for both males and females ($P < 0.0001$) (Figure 2B and C). For the AST APRI scores, there were statistically significant differences between the NG and IFG groups ($P < 0.01$) (Figure 2D). Nevertheless, the difference vanished when males/females were analyzed separately (Figure 2E and F). The ALT/AST APRI scores were divided into two levels, normal APRI score (N-APRI) and high APRI score (H-APRI). For ALT APRI scores, FBG were significantly different between the N-APRI group and H-APRI group ($P < 0.0001$) (Figure 3A). And the results were unaffected by gender (Figure 3B and C). For AST APRI scores, there was statistically significant difference in FBG between the two groups ($P < 0.001$) (Figure 3D). Interestingly, this result also held for the male population but not females. (Figure 3E and F).

Table 1 Baseline Characteristics of the Study Participants

Characteristic	NG (n=4862)	IFG (n=354)	HG (n=612)	P value
Age [years, M (IQR)]	63.00 (10.00)	64.00 (10.00)	63.00 (9.00)	0.003
Male (N, %)	1666 (34.30%)	155 (43.80%)	256 (41.80%)	< 0.001
BMI [kg/m^{2,} M (IQR)]	25.80 (4.49)	26.88 (4.50)	26.81 (4.23)	< 0.001
Current Smoking (N, %)	949 (19.52%)	74 (20.90%)	140 (22.88%)	0.132
Current Drinking (N, %)	888 (18.26%)	87 (24.58%)	151 (24.67%)	< 0.001
Hypertension history (N, %)	2034 (41.83%)	226 (63.84%)	375 (61.27%)	< 0.001
TC [mmol/L, M (IQR)]	5.30 (1.30)	5.20 (1.60)	5.30 (1.60)	0.835
TG [mmol/L, M (IQR)]	1.38 (0.85)	1.63 (0.99)	1.70 (1.22)	< 0.001
HDL [mmol/L, M (IQR)]	1.12 (0.35)	1.06 (0.32)	1.03 (0.30)	< 0.001
LDL [mmol/L, M (IQR)]	3.00 (1.02)	3.00 (1.18)	3.00 (1.20)	0.843
WBC count [×106/μL, M (IQR)]	5.79 (1.85)	6.29 (2.11)	6.51 (2.14)	< 0.001
RBC count [×106/μL, M (IQR)]	4.59 (0.56)	4.66 (0.53)	4.72 (0.55)	< 0.001
PLT count [×106/mL, M (IQR)]	247.00 (73.00)	242.00 (71.75)	244.00 (79.00)	0.036
AST [U/L, M (IQR)]	19.00 (7.00)	19.00 (8.00)	19.00 (8.00)	0.489
ALT [U/L, M (IQR)]	17.00 (10.00)	20.00 (14.00)	21.00 (14.00)	< 0.001
TBIL [μmol/L, M (IQR)]	13.20 (6.90)	13.20 (7.30)	13.10 (7.10)	0.810
ALB [mg/dL, M (IQR)]	45.30 (3.40)	45.60 (3.70)	45.10 (3.80)	0.079
CRE [mmol/L, M (IQR)]	59.20 (19.00)	59.40 (20.70)	58.60 (19.55)	0.120
UA [μmol/L, M (IQR)]	302.00 (101.00)	314.50 (107.00)	306.50 (106.00)	0.117
ALT APRI score	0.17 (0.12)	0.22 (0.18)	0.22 (0.18)	< 0.001
AST APRI score	0.19 (0.09)	0.21 (0.10)	0.20 (0.12)	< 0.001

Abbreviations: NG, normoglycemia; IFG, impaired fasting glycemia; HG, hyperglycemia; M, median; IQR, interquartile range; BMI, body mass index; TC, total cholesterol; TG, triglycerides; HDL, high-density lipoprotein; LDL, low-density lipoprotein; WBC, white blood cell; RBC, red blood cell; PLT, platelet; AST, aspartate aminotransferase; ALT, alanine aminotransferase; TBIL, total bilirubin; ALB, albumin; CRE, creatinine; UA, uric acid.

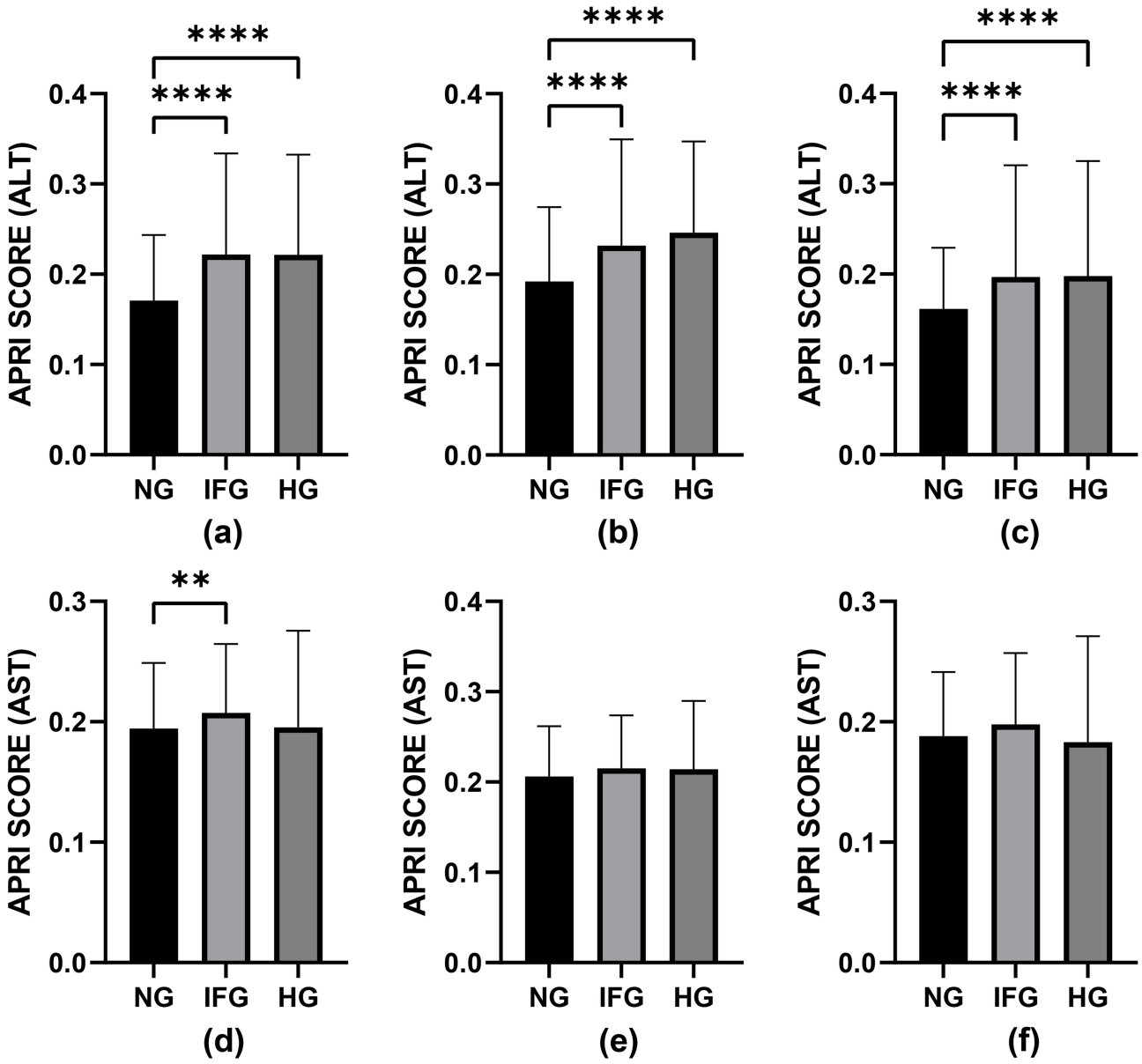

Figure 2 Comparative Changes of APRI Scores According to FBG. Median with interquartile range of the ALT APRI score of participants with NG, IFG and HG in (**a**) both genders, (**b**) males and (**c**) females. Median with interquartile range of the AST APRI score of participants with NG, IFG and HG in (**d**) both genders, (**e**) males and (**f**) females. ** $p < 0.01$, and **** $p < 0.0001$.

Multiple Linear Regression Model Analysis

Multiple linear regression analysis was conducted using FBG as a dependent variable. ALT and AST APRI scores were each included as independent variables in different models together with age, BMI, current drinking, hypertension history, triglycerides, high-density lipoprotein, white blood cell count, red blood cell count in all participants. Multiple linear regression analysis was also performed within each gender. In the four models, ALT APRI score was determined as significant variable associated with FBG in the model 1, model 2, model 3, and model 4 ($P < 0.001$). A consistent result was observed in both males and females. AST APRI score was also found to be a significant variable associated with FBG in all models ($P < 0.001$). The results remained largely similar when males and females were analyzed separately ($P < 0.05$). Table 2 and Table 3 show the results of different multiple linear regression models.

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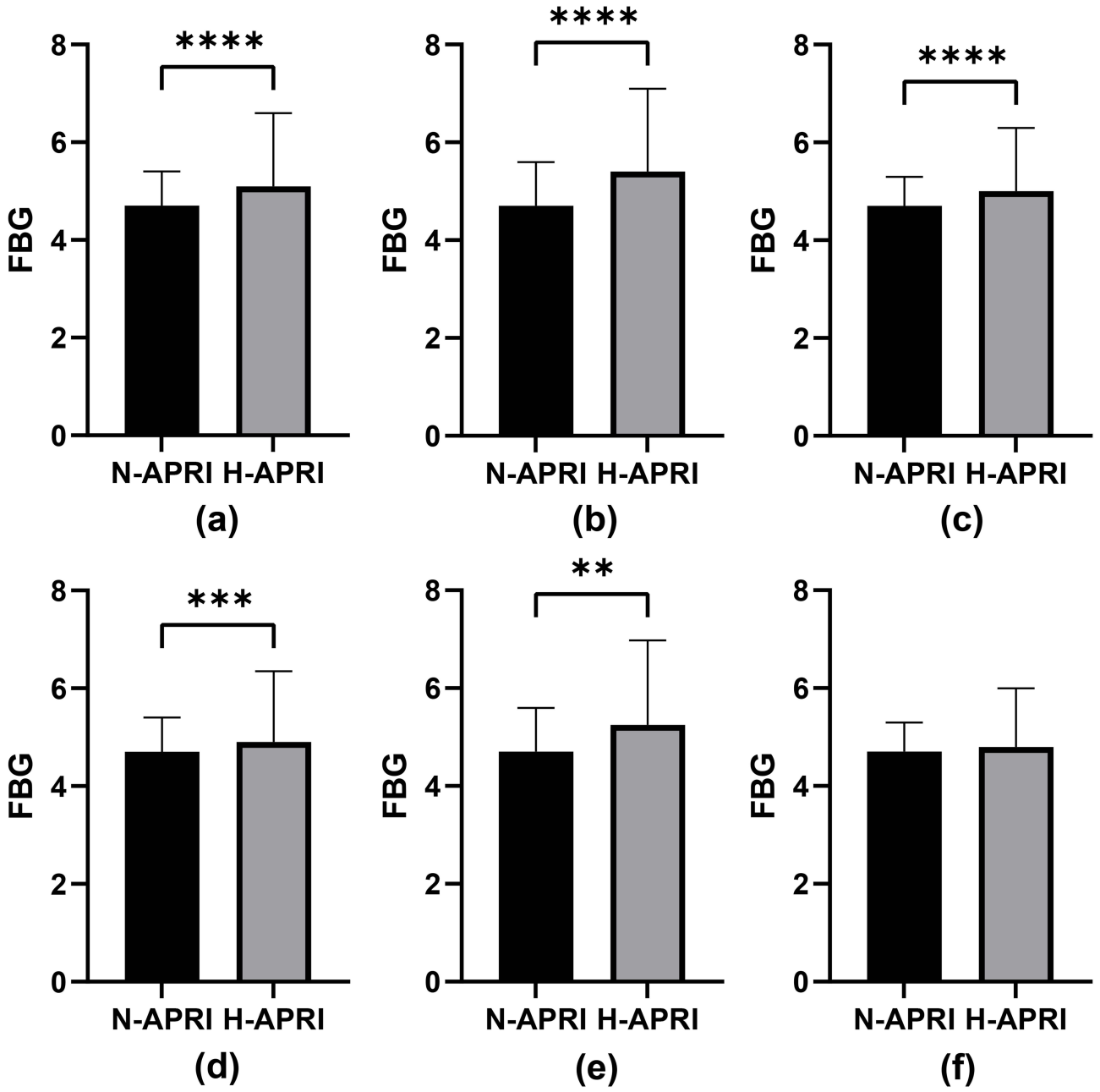

Figure 3 Comparative changes of FBG according to APRI scores. Median with interquartile range of FBG concentrations in the normal ALT APRI score (N-APRI) and high ALT APRI score (H-APRI) groups in (**a**) both genders, (**b**) males and (**c**) females. Median with interquartile range of FBG concentrations in the normal AST APRI score (N-APRI) and high AST APRI score (H-APRI) groups in (**d**) both genders, (**e**) males and (**f**) females. ** $p < 0.01$, *** $p < 0.001$ and **** $p < 0.0001$.

ROC Curve Analysis for Different Models

The ROC curve analysis was used to evaluate the ability of model 1 (ALT /AST APRI scores), model 2, model 3, and model 4 to identify participants with HBG. The results showed that model 4, adjusted for ALT/AST APRI scores, exhibited a high discriminating value for HBG (AUC 0.703, 95% CI: 0.683–0.724, $P < 0.001$, cut-off 0.081; AUC 0.690, 95% CI: 0.669–0.712, $P < 0.001$, cut-off 0.90). Results were similar in both males (AUC 0.665, 95% CI: 0.628–0.701, $P < 0.001$, cut-off 0.153; AUC 0.650, 95% CI: 0.613–0.687, $P < 0.001$, cut-off 0.85) and females (AUC 0.729, 95% CI: 0.703–0.754, $P < 0.001$, cut-off 0.081; AUC 0.716, 95% CI: 0.690–0.742, $P < 0.001$, cut-off 0.917). Figure 4 illustrates these results.

Table 2 Multiple Linear Regression of Different Models of APRI Score (ALT)

	B value	SE	β value	t value	95% CI	R^2value	F	P value
Model 1	1.147	0.118	0.126	9.703	0.915–1.379	0.016	94.152	<0.001
Model 2	1.166	0.118	0.128	9.862	0.934–1.398	0.018	52.849	<0.001
Model 3	1.033	0.118	0.114	8.777	0.802–1.263	0.037	45.727	<0.001
Model 4	0.990	0.118	0.109	8.397	0.759–1.222	0.060	41.633	<0.001
Male								
Model 1	1.467	0.229	0.140	6.405	1.018–1.917	0.019	41.026	<0.001
Model 2	1.501	0.230	0.143	6.515	1.049–1.953	0.019	21.444	<0.001
Model 3	1.409	0.229	0.135	6.161	0.961–1.858	0.036	16.186	<0.001
Model 4	1.358	0.231	0.129	5.873	0.904–1.811	0.047	12.228	<0.001
Female								
Model 1	0.975	0.136	0.116	7.151	0.707–1.242	0.013	51.142	<0.001
Model 2	0.988	0.136	0.118	7.255	0.721–1.255	0.015	30.394	<0.001
Model 3	0.851	0.136	0.101	6.259	0.584–1.117	0.036	29.154	<0.001
Model 4	0.828	0.134	0.099	6.177	0.565–1.091	0.083	38.111	<0.001

Notes: Model 1 was unadjusted. Model 2 was adjusted for age on top of model 1.Model 3 was adjusted for BMI, current drinking, hypertension history on top of model 2. Model 4 was adjusted for triglycerides, high-density lipoprotein, white blood cell count, red blood cell count on top of model 3.
Abbreviations: SE, standard error; CI, confidence interval.

Table 3 Multiple Linear Regression of Different Models of APRI Score (AST)

	B value	SE	β value	t value	95% CI	R^2value	F	P value
Model 1	0.637	0.142	0.059	4.477	0.358–0.917	0.003	20.045	<0.001
Model 2	0.620	0.142	0.057	4.353	0.341–0.899	0.004	13.641	<0.001
Model 3	0.564	0.141	0.052	4.003	0.288–0.840	0.027	33.209	<0.001
Model 4	0.699	0.141	0.065	4.955	0.423–0.976	0.052	36.261	<0.001
Male								
Model 1	0.744	0.233	0.070	3.187	0.286–1.201	0.004	10.156	0.001
Model 2	0.742	0.233	0.070	3.178	0.284–1.199	0.004	5.266	0.002
Model 3	0.722	0.231	0.068	3.132	0.270–1.174	0.022	10.440	0.002
Model 4	0.811	0.232	0.077	3.490	0.355–1.266	0.037	9.658	<0.001
Female								
Model 1	0.521	0.181	0.047	2.884	0.167–0.875	0.002	8.319	0.004
Model 2	0.494	0.181	0.045	2.730	0.139–0.848	0.004	7.757	0.006
Model 3	0.421	0.179	0.038	2.353	0.070–0.772	0.028	22.234	0.019
Model 4	0.666	0.178	0.060	3.748	0.318–1.014	0.077	35.214	<0.001

Notes: Model 1 was unadjusted. Model 2 was adjusted for age on top of model 1.Model 3 was adjusted for BMI, current drinking, hypertension history on top of model 2. Model 4 was adjusted for triglycerides, high-density lipoprotein, white blood cell count, red blood cell count on top of model 3.
Abbreviations: SE, standard error; CI, confidence interval.

Association Between ALT and AST APRI Scores with Diabetic Retinopathy

Study Population Characteristics

The baseline parameters of the two groups are shown in Table 4. There were 828 participants in the non-DR group, and 335 participants in the DR group. Statistically significant correlations were observed between age, sex, duration of diabetes, FBG, HbA1c, TC, TG, ALT, AST, and UA in the two groups (all $P < 0.05$). The remaining indices were not significantly different between the two groups (all $P > 0.05$).

Simple Correlation Analysis

Figure 5 presents the comparison of ALT and AST APRI scores in the non-DR and DR groups. The same comparison was performed separately by gender. The ALT and AST APRI scores were not statistically comparable

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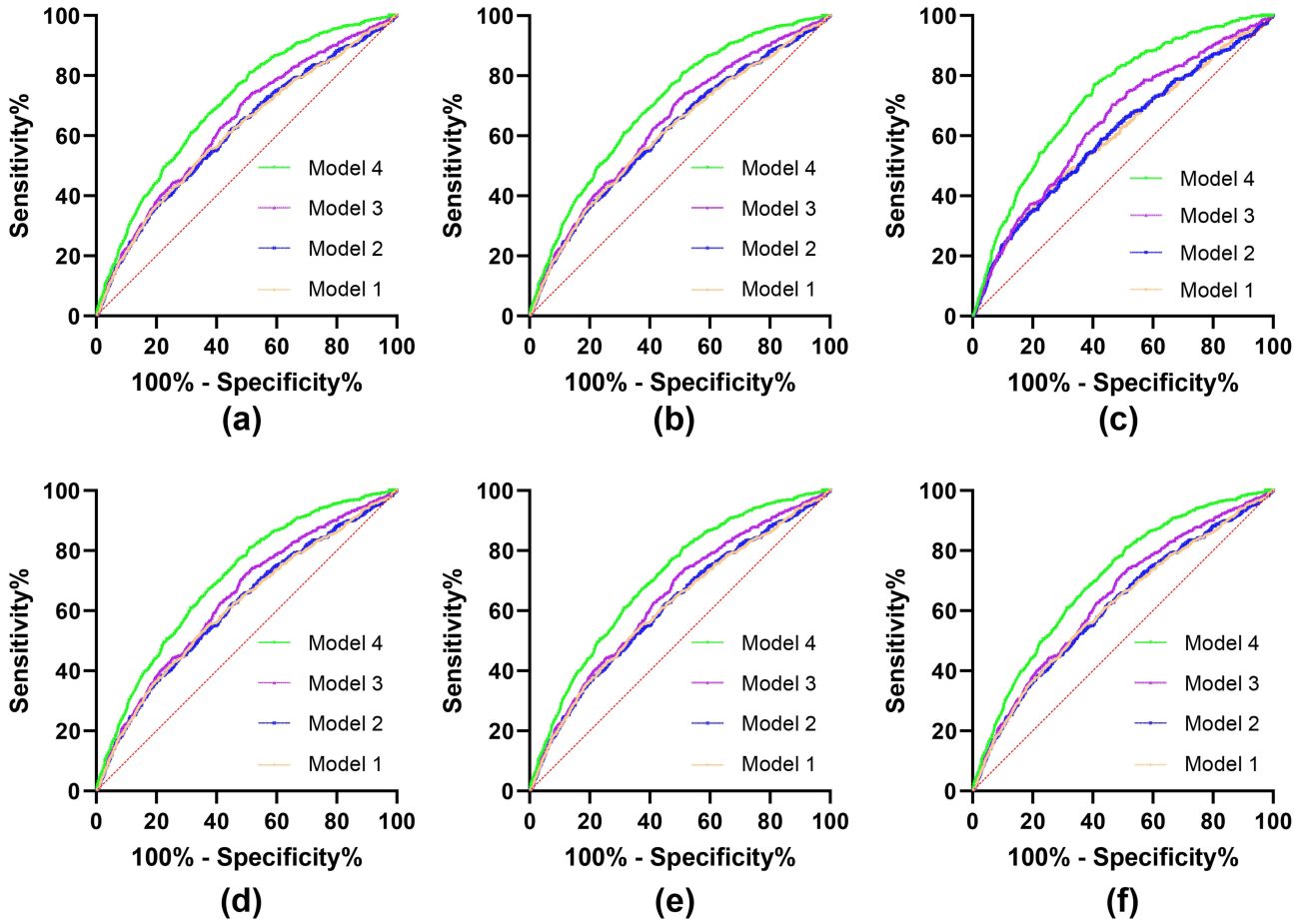

Figure 4 ROC curves for different models in predicting HBG. ROC curves for model 1 (ALT APRI scores), model 2, model 3, and model 4 in predicting HBG in (**a**) both genders, (**b**) males, and (**c**) females. ROC curves for model 1 (AST APRI scores), model 2, model 3, and model 4 in predicting HBG in (**d**) both genders, (**e**) males and (**f**) females. Model 1 was unadjusted. Model 2 was adjusted for age on top of model 1. Model 3 was adjusted for BMI, current drinking, hypertension history on top of model 2. Model 4 was adjusted for triglycerides, high-density lipoprotein, white blood cell count, red blood cell count on top of model 3.

between the two groups. The same result was found in the male population (P>0.05). However, in the female population, it can be noticed that ALT and AST APRI scores were negatively correlated with DR in the non-DR and DR groups (P = 0.043, P=0.022).

Table 4 Baseline Characteristics of the Study Participants

Characteristic	Non-DR (n=828)	DR (n=335)	P value
Age [years, M (IQR)]	63.00 (9.00)	62.00 (9.00)	0.034
Male (N, %)	317 (38.30%)	150 (44.80%)	0.041
BMI [kg/m^2, M (IQR)]	26.82 (4.56)	26.81 (4.53)	0.654
Current Smoking (N, %)	162 (19.60%)	63 (18.80%)	0.767
Current Drinking (N, %)	165 (19.90%)	83 (24.80%)	0.068
Hypertension history (N, %)	529 (63.90%)	216 (64.50%)	0.850
Duration of diabetes [years, M (IQR)]	5.00 (9.00)	10.00 (14.00)	< 0.001
FBG [mmol/L, M (IQR)]	6.60 (2.10)	7.50 (3.00)	< 0.001
HbA1c [%, M (IQR)]	7.00 (1.30)	7.60 (1.90)	< 0.001
TC [mmol/L, M (IQR)]	5.20 (1.60)	5.00 (1.40)	0.185
TG [mmol/L, M (IQR)]	1.64 (1.09)	1.59 (1.14)	0.072

(*Continued*)

Table 4 (Continued).

Characteristic	Non-DR (n=828)	DR (n=335)	P value
HDL [mmol/L, M (IQR)]	1.04 (0.32)	1.02 (0.29)	0.609
LDL [mmol/L, M (IQR)]	2.99 (1.14)	2.84 (1.23)	0.283
WBC count [×106/μL, M (IQR)]	6.38 (2.09)	6.27 (2.02)	0.319
RBC count [×106/μL, M (IQR)]	4.69 (0.55)	4.73 (0.58)	0.112
PLT count [×106/mL, M (IQR)]	245.00 (77.00)	243.00 (75.00)	0.691
AST [U/L, M (IQR)]	19.00 (7.00)	17.00 (7.00)	0.001
ALT [U/L, M (IQR)]	20.50 (13.00)	19.00 (12.00)	0.033
TBIL [μmol/L, M (IQR)]	13.40 (7.03)	13.10 (8.00)	0.268
ALB [mg/dL, M (IQR)]	45.40 (3.60)	45.30 (3.40)	0.829
CRE [mmol/L, M (IQR)]	58.30 (20.12)	59.50 (22.00)	0.301
UA [μmol/L, M (IQR)]	313.00 (106.00)	303.00 (108.00)	0.014
ALT APRI score	0.22 (0.18)	0.22 (0.16)	0.155
AST APRI score	0.20 (0.11)	0.19 (0.12)	0.099

Abbreviations: M, median; IQR, interquartile range; BMI, body mass index; FBG, fasting blood glucose; HbA1c, hemoglobin A 1c; TC, total cholesterol; TG, triglyceride; HDL, high-density lipoprotein; LDL, low-density lipoprotein; WBC, white blood cell; RBC, red blood cell; PLT, platelet; AST, aspartate aminotransferase; ALT, alanine aminotransferase; TBIL, total bilirubin; ALB, albumin; CRE, creatinine; UA, uric acid.

Binary Logistic Regression Model Analysis

The binary logistic regression analysis did not show a statistically significant difference in ALT and AST APRI scores between the non-DR and DR groups in female diabetic participants after adjustment for factors statistically significant in univariate analysis (all P>0.05). A consistent result was observed in both males and females. This indicated that ALT and AST APRI scores were not independent risk factors for DR. Table 5 illustrates these results.

Discussion

Chronic hyperglycemia is one of the major characteristics of type 2 diabetes. As the liver is the main glucose-regulating organ, the health of the liver and glycemic status are closely linked.[6] APRI score, calculated by AST and PLT, is a liver function indicator that reflects liver fibrosis.[20] Given its low cost and high accessibility, it is of great significance to explore the role of APRI score in predicting dysglycemia and DR. In the current study, we also analyzed and compared the ALT APRI and AST APRI scores. The results revealed that ALT and AST APRI scores were associated with fasting blood glucose after adjusting for various potential confounders. This association remained when sex was analyzed separately. However, they were not independent risk factors for DR. We also found that the ALT APRI score was more sensitive to recognizing hyperglycemia than the AST APRI score. These findings suggest that the ALT and AST APRI scores may have potential for diagnosing hyperglycemia and that the ALT APRI score was superior to the AST APRI score.

The findings are consistent with a study conducted on the Saudi Arabian population.[12] We have thoroughly validated these results within the Chinese population, accounting for potential confounding variables. In a cross-sectional study, Carlo et al identified the potential utility of APRI score in predicting cardiovascular risk. Their research also indicated that elevated APRI levels were prevalent among individuals with high glycemia.[18] This is in agreement with our study's findings as well. Furthermore, a multi-center study from the USA has concluded that indices of liver fibrosis may serve as predictors for pre-diabetes, which also corroborates our results.[11]

Insulin resistance is one of the pathogenesis of type 2 diabetes.[21] It has been shown that a high degree of hepatic fibrosis might be correlated with insulin resistance.[22] Insulin resistance causes the release of fatty acids to increase in hepatocytes, leading to hepatic lipid deposition[23] and lipid peroxidation[24] and subsequently to the formation of fibrosis. Additionally, previous studies indicate that liver fibrosis would impair the synthetic and metabolic functions of the liver,[25] subsequently affecting glucose levels. These indicate that liver fibrosis and glucose levels have mutual effects, and the above speculation still needs to be verified by further prospective studies.

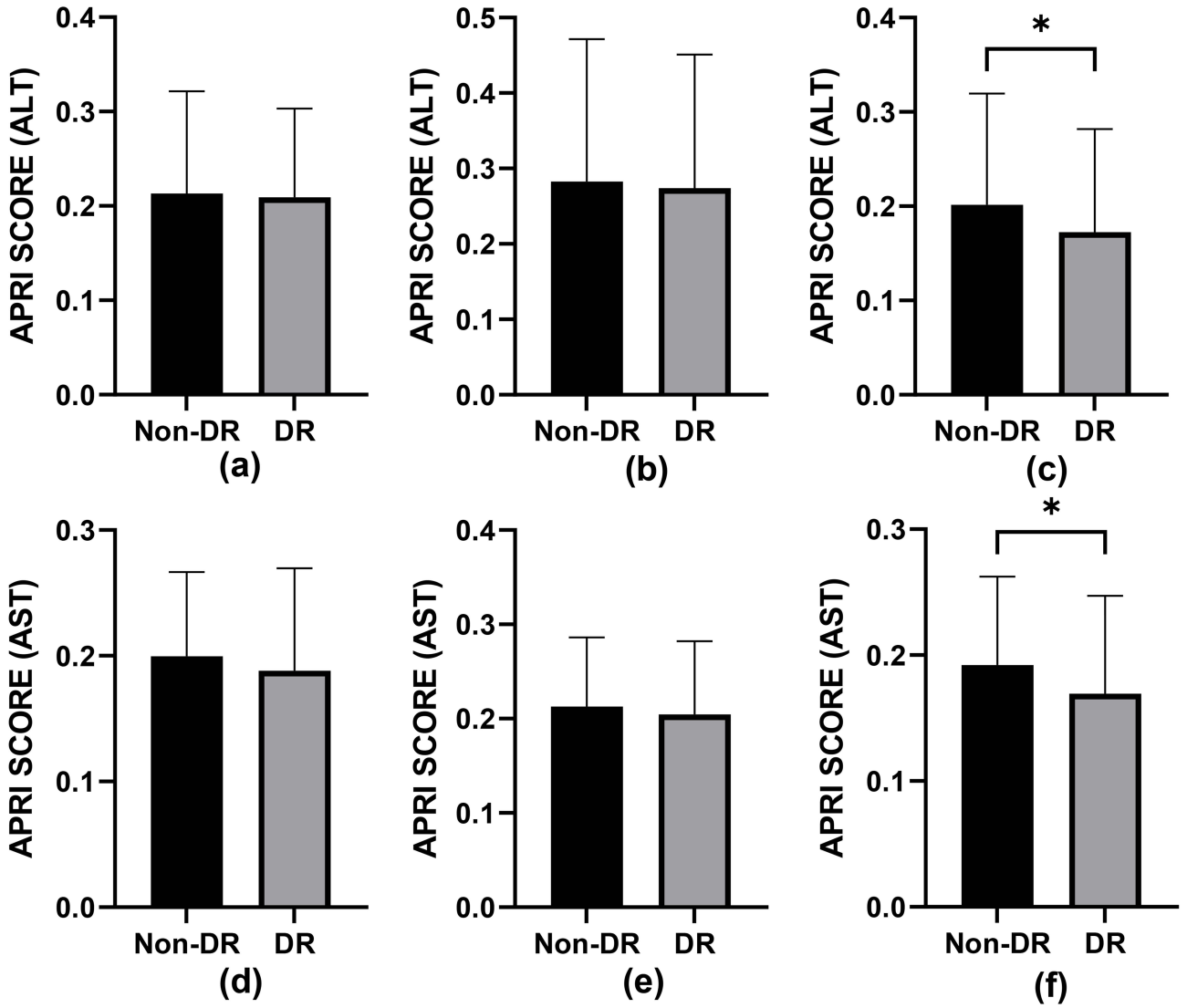

Figure 5 Comparative changes of APRI scores in the non-DR and DR groups. Median with interquartile range of the ALT APRI score of participants in two groups in (**a**) both genders, (**b**) males and (**c**) females. Median with interquartile range of the AST APRI score of participants in two groups in (**d**) both genders, (**e**) males and (**f**) females. * $p < 0.05$.

In our study, ALT APRI score is superior to AST APRI score in identifying HG. The distribution of ALT and AST could be associated with it. The ALT primarily exists in the liver, but AST exists in various tissues. ALT is a specific marker for the accumulation of fat in the liver and plays an important role in the insulin sensitivity of the liver[26,27] and it has been demonstrated to be an independent risk factor for T2DM.[26] In addition, the results showed that the ROC curve analysis was larger in females than in males. This seems to be related to the fact that different genders have different energy metabolism and susceptibility to pathophysiological conditions, such as T2DM.[28] It has been reported that women are usually less likely than men to develop fatty liver due to higher levels of oestrogen.[29] In addition, women have higher levels of leptin and adiponectin, which also contribute to the development of peripheral insulin resistance.[30] Furthermore, the sample size of the female group is almost double that of the male group, so the efficiency of the female statistical test is relatively higher, which may be one of the reasons for the gender differences in the results.

In this study, univariate linear regression analysis showed an association between ALT and AST APRI scores and DR in the female population, but we were not able to find the same association by using binary logistic regression analysis. This may be due to the mediation of other influencing factors. The small sample size of the DR population may also be one of the reasons for this results.

Table 5 Binary Logistic Regression of Different Models of APRI Score

	ALT APRI Score			AST APRI Score		
	OR	**95% CI**	**P value**	**OR**	**95% CI**	**P value**
Model 1	0.784	0.407–1.512	0.468	0.910	0.407–2.032	0.818
Model 2	0.750	0.387–1.450	0.392	0.932	0.419–2.075	0.863
Model 3	0.957	0.454–2.111	0.957	1.290	0.533–3.122	0.573
Male						
Model 1	0.772	0.263–2.263	0.637	1.321	0.321–5.433	0.699
Model 2	0.688	0.231–2.049	0.501	1.329	0.322–5.495	0.694
Model 3	0.631	0.185–2.158	0.463	1.269	0.265–6.078	0.765
Female						
Model 1	0.740	0.317–1.731	0.488	0.717	0.254–2.029	0.531
Model 2	0.719	0.307–1.685	0.448	0.738	0.263–2.074	0.565
Model 3	1.214	0.445–3.312	0.704	1.289	0.421–3.949	0.657

Notes: Model 1 was unadjusted. Model 2 was adjusted for age on top of model 1.Model 3 was adjusted for Duration of diabetes, fasting blood glucose, hemoglobin A 1c, uric acid.
Abbreviations: OR, odds ratio; CI, confidence interval.

This study also has several limitations. First, due to the cross-sectional design of the study, cause-and-effect conclusions could not be made. In addition, the participants of this study are the elderly aged 50 years and older in China Tianjin Beichen, so there may be some age bias and race bias.

Conclusion

In summary, this study found that the ALT and AST APRI scores were associated with FBG. ALT and AST APRI scores may have potential in the diagnosis and management of hyperglycemic conditions. Due to the limitations of the study design, we could not prove causality. Further large-scale prospective studies in diverse populations are needed in the future.

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Disclosure

The author(s) report no conflicts of interest in this work.

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