J Appl Biotechnol Rep. 2026 June;13(2):2061-2072

Journal of
Applied Biotechnology Reports

doi 10.30491/jabr.2026.587212.2020

Original Article

Impact of ABCB1 Genetic Polymorphisms on Therapeutic Response and Safety of Atorvastatin in Iraqi Dyslipidemia Patients

Sarah Alaa Fadhil [1], Noor D. Aziz [2], Shaima Jabbar [3,4*], Riyadh Mustafa Murtadha Al-Shehristani [5]

[1] The Graduate Program of The Pharmacology and Toxicology Department, Pharmacy College, Kerbala University, Karbala, Iraq
[2] Department of Clinical Pharmacy, Pharmacy College, Kerbala University, Karbala, Iraq
[3] Department of Pharmacology and Toxicology, Pharmacy College, Kerbala University, Karbala, Iraq
[4] Al-Subtain University, International Branch of Tehran University of Medical Sciences, Karbala, Iraq
[5] College of Medicine, Al-Ameed University, Karbala, Iraq

Corresponding Author: Shaima Jabbar, PhD, Assistant Professor, Department of Pharmacology and Toxicology, Pharmacy College, Kerbala University, Karbala, Iraq. Tel: +9647721012577, E-mail: shaymaa.a@uokerbala.edu.iq

Received March 28, 2026; **Accepted** June 20, 2026; **Online Published** June 30, 2026

Abstract

Introduction: Inter-individual variability in response to atorvastatin may be influenced by genetic polymorphisms affecting drug transport. The ATP-binding cassette subfamily B member 1 (*ABCB1*) gene encodes P-glycoprotein, a transporter involved in the absorption, distribution, and elimination of atorvastatin. This study investigated the association of *ABCB1* rs1045642 (C3435T) and rs2032582 (G2677T) polymorphisms with atorvastatin efficacy and hepatic safety in Iraqi patients with dyslipidemia.

Materials and Methods: A cross-sectional study was conducted on 150 Iraqi patients with dyslipidemia receiving atorvastatin monotherapy (40 mg/day) for at least six months and 100 healthy controls. Lipid profile parameters and liver enzyme activities were measured using standard biochemical methods. Genotyping of rs1045642 and rs2032582 was performed using allele-specific polymerase chain reaction. Associations between genotypes, lipid parameters, liver enzymes, and treatment response were analyzed.

Results: Patients with dyslipidemia exhibited significantly higher levels of triglycerides, VLDL-C, ALP, and AST, along with significantly lower HDL-C concentrations, compared with healthy controls (all $p < 0.05$). No significant associations were observed between rs1045642 genotypes and lipid profile parameters or achievement of the LDL-C treatment target. However, rs1045642 was significantly associated with ALT concentrations ($p = 0.0152$). In contrast, rs2032582 was significantly associated with treatment response ($P = 0.0124$), and carriers of the T allele were less likely to achieve the LDL-C target under the dominant genetic model ($p = 0.0175$). Furthermore, rs2032582 was significantly associated with ALP levels ($p = 0.0432$).

Conclusions: The *ABCB1* rs2032582 polymorphism was associated with atorvastatin treatment response, whereas rs1045642 showed no significant association with lipid-lowering efficacy. Both polymorphisms were associated with selected liver enzyme parameters, suggesting a potential role in atorvastatin disposition and hepatic handling. Further large-scale studies incorporating pharmacokinetic assessments are required to confirm these findings.

Keywords: Atorvastatin, Dyslipidemia, ABCB1, Pharmacogenetics, Lipid Profile, Hepatotoxicity

Citation: Fadhil SA, Aziz ND, Jabbar S, Al-Shehristani RMM. Impact of ABCB1 Genetic Polymorphisms on Therapeutic Response and Safety of Atorvastatin in Iraqi Dyslipidemia Patients. J Appl Biotechnol Rep. 2026;13(2):2061-2072. doi:10.30491/jabr.2026.587212.2020

Introduction

Dyslipidemia is one of the most common metabolic conditions, characterized by elevated levels of total cholesterol, low-density lipoprotein cholesterol (LDL-C), and/or triglycerides, together with reduced levels of high-density lipoprotein cholesterol (HDL-C). These abnormalities contribute to the development of atherosclerotic cardiovascular disease (ASCVD), ischemic heart disease, and stroke.[1] Dyslipidemia may result from genetic defects in lipid metabolism (primary dyslipidemia) or may occur secondary to conditions including obesity, diabetes mellitus, hypothyroidism, chronic liver or kidney diseases, smoking, alcohol abuse, and certain drugs. The pathophysiology involves the oxidation of LDL, followed by impairment of the endothelium and activation of macrophages and foam cells, contributing to atherosclerotic plaque formation.[2] Pharmacological management of dyslipidemia primarily relies on statins because of their proven efficacy in reducing cardiovascular morbidity and mortality.

Atorvastatin is one of the most frequently prescribed statins because of its potent lipid-lowering activity and favorable safety profile. It acts on 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase, thereby reducing hepatic cholesterol synthesis and increasing LDL receptor expression. Despite its established clinical benefits, considerable interindividual

variability exists in both therapeutic response and adverse effects. Increasing evidence suggests that genetic variation contributes to this variability, particularly polymorphisms affecting drug-metabolizing enzymes and membrane transport proteins involved in statin disposition.[3,4]

One such transporter is ATP-binding cassette subfamily B member 1 (ABCB1), which encodes P-glycoprotein (P-gp), an ATP-dependent efflux transporter expressed in the intestine, liver, kidney, and many other tissues. P-glycoprotein plays an important role in controlling the absorption, hepatic distribution, and biliary excretion of atorvastatin. The most extensively studied ABCB1 variants include rs1045642 (C3435T) and rs2032582 (G2677T/A), both of which have been investigated for their potential influence on statin pharmacokinetics and treatment outcomes.[5,6]

However, despite extensive investigation, the clinical significance of these polymorphisms remains highly controversial. Several studies have reported that the rs1045642 T allele is associated with enhanced statin efficacy and reduced risk of statin-induced toxicity, potentially through alterations in P-glycoprotein expression or activity and increased intracellular drug availability. In contrast, other studies have demonstrated opposing findings, linking the same variant to reduced therapeutic response or increased adverse effects. Similar inconsistencies have been reported for rs2032582, with variable associations across populations. These discrepancies may reflect ethnic differences in allele frequencies, study design variability, environmental influences, and underlying genetic architecture.[5-7] The pharmacokinetics and pharmacodynamics of atorvastatin are influenced by multiple transporters and metabolic pathways. Therefore, the contribution of ABCB1 variants should be interpreted within the broader context of other genetic and non-genetic factors that may influence statin response.[8,9]

Although pharmacogenetic studies of statin therapy have increased considerably during the past decade, most available data originate from European and East Asian populations. In contrast, pharmacogenetic information from Arab and Middle Eastern populations remains limited, particularly in Iraq, where data regarding ABCB1 polymorphisms and atorvastatin response are scarce.[10] Consequently, extrapolating findings from other ethnic groups may not accurately reflect the Iraqi population. Therefore, the present study was designed to investigate the association of *ABCB1* rs1045642 (C3435T) and rs2032582 (G2677T/A) polymorphisms with atorvastatin therapeutic response and safety among Iraqi patients with dyslipidemia.

Materials and Methods

Study Design

A cross-sectional observational study was conducted at Imam Al-Hassan Al-Mujtaba Hospital in Karbala, Iraq, from February 2025 to June 2025. The study included 150 males and females aged 30–70 years who were diagnosed with dyslipidemia and receiving atorvastatin monotherapy (40 mg/day) for at least six months. The participant recruitment steps, including assessment, inclusion and exclusion criteria, and the final study population, are shown in Figure 1. Dyslipidemia was defined as the presence of one or more of the following criteria: total cholesterol (TC) > 200 mg/dl, LDL-C > 130 mg/dl, triglycerides (TG) > 150 mg/dl, or HDL-C < 40 mg/dl in males and < 50 mg/dl in females. Demographic and clinical information, including age, body mass index (BMI), and treatment duration, were recorded using a structured questionnaire.

Inclusion and Exclusion Criteria

Eligible participants were adults aged 30–70 years diagnosed with dyslipidemia and receiving atorvastatin monotherapy (40 mg/day) for at least six months before enrollment. Healthy controls were recruited from apparently healthy individuals with no history of dyslipidemia or cardiovascular disease. Participants were excluded if they had chronic liver disease, chronic kidney disease, hypothyroidism, diabetes mellitus, malignancy, acute inflammatory or infectious diseases, pregnancy, alcohol consumption, or smoking, or if they were receiving lipid-lowering medications other than atorvastatin. Individuals with incomplete clinical data or those unwilling to provide informed consent were also excluded.

Blood Collection and Biochemical Analysis

Venous blood samples were collected from all participants after an overnight fast of 10–12 hours. Two equal blood samples were collected from each participant: one into a serum gel tube (3 ml) for biochemical analysis, and the other into an EDTA tube (2 ml) for genomic DNA isolation, the latter of which was performed only for the patient group. Serum lipid parameters, including total cholesterol (TC), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), and very low-density lipoprotein cholesterol (VLDL-C), as well as hepatic enzyme activities (AST, ALT, and ALP), were measured using enzymatic-colorimetric test kits according to the manufacturer's recommendations. All biochemical analyses were performed using an automated biochemical analyzer.

DNA Extraction, Quality Assessment, and Genotyping

Genomic DNA was extracted from peripheral whole blood samples using the FAVORGEN Blood Genomic DNA Extraction Kit according to the manufacturer's instructions. DNA concentration and purity were assessed using a NanoDrop spectrophotometer by measuring absorbance at 260 and 280 nm. DNA samples with an A260/A280 ratio between 1.8 and 2.0 were considered acceptable for downstream molecular analysis. Genotyping of *ABCB1*

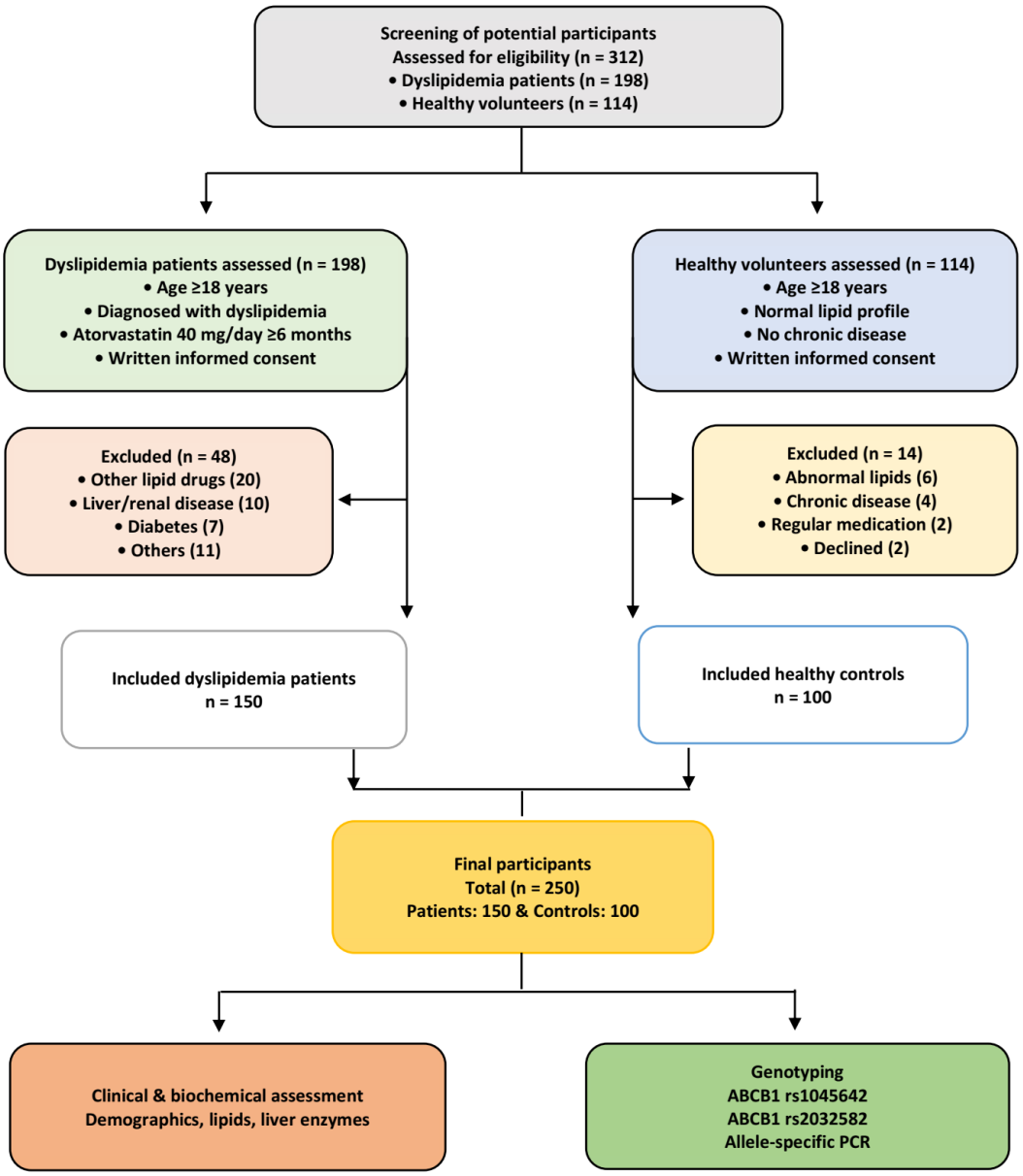

Figure 1. Flow Chart Illustrating the Participant Recruitment and Selection Process. The chart outlines the sequential steps of initial assessment, application of inclusion and exclusion criteria, and the resulting final study population, comprising 150 dyslipidemia patients and 100 healthy controls. The biochemical parameters measured in the study included the lipid profile (total cholesterol [TC], triglycerides [TG], high-density lipoprotein cholesterol [HDL-C], low-density lipoprotein cholesterol [LDL-C], and very low-density lipoprotein cholesterol [VLDL-C]) and hepatic enzymes (alkaline phosphatase [ALP], aspartate aminotransferase [AST], and alanine aminotransferase [ALT]).

rs1045642 (C3435T) and rs2032582 (G2677T) polymorphisms was performed using allele-specific polymerase chain reaction (AS-PCR). Allele-specific primers were designed using the NCBI Primer-BLAST tool based on reference genomic sequences and were synthesized commercially by Macrogen Inc. (Seoul, South Korea). To minimize genotyping errors and reduce the possibility of allele dropout, DNA quality was verified before PCR amplification, allele-specific primers were carefully designed using Primer-BLAST, and genotypes were assigned only when distinct and reproducible amplification bands were observed on agarose gel electrophoresis. Samples showing weak or ambiguous amplification patterns were re-amplified and re-evaluated. Only samples demonstrating clear, reproducible amplification after repeat testing were included in the final genetic analyses. Consequently, no unresolved or ambiguous genotypes were retained in the study dataset. Independent confirmation of genotypes by Sanger sequencing or an alternative PCR-RFLP assay was not performed.

PCR reactions were carried out in a total volume of 25 µl containing approximately 50–100 ng genomic DNA, 1× PCR buffer, 1.5–2.0 mM $MgCl_2$, 0.2 mM of each deoxy nucleotide triphosphate (dNTP), 0.2–0.4 µM of each primer, and 1 U of Taq DNA polymerase. The thermal cycling

conditions consisted of an initial denaturation at 95 °C for 5 minutes, followed by 35 cycles of denaturation at 95 °C for 30 seconds, annealing for 30 seconds (with annealing temperatures of 60 °C for rs1045642 and 58 °C for rs2032582), and extension at 72 °C for 30 seconds, with a final extension step at 72 °C for 5–7 minutes. PCR products were separated by agarose gel electrophoresis and visualized under ultraviolet illumination following ethidium bromide staining, as shown in Figure 2. Genotypes were assigned according to the presence or absence of allele-specific PCR amplification. Samples showing amplification in only one allele-specific reaction were classified as homozygous for the corresponding allele, whereas samples showing amplification in both reactions were classified as heterozygous. Only clear and reproducible amplification patterns were accepted for final genotype assignment.

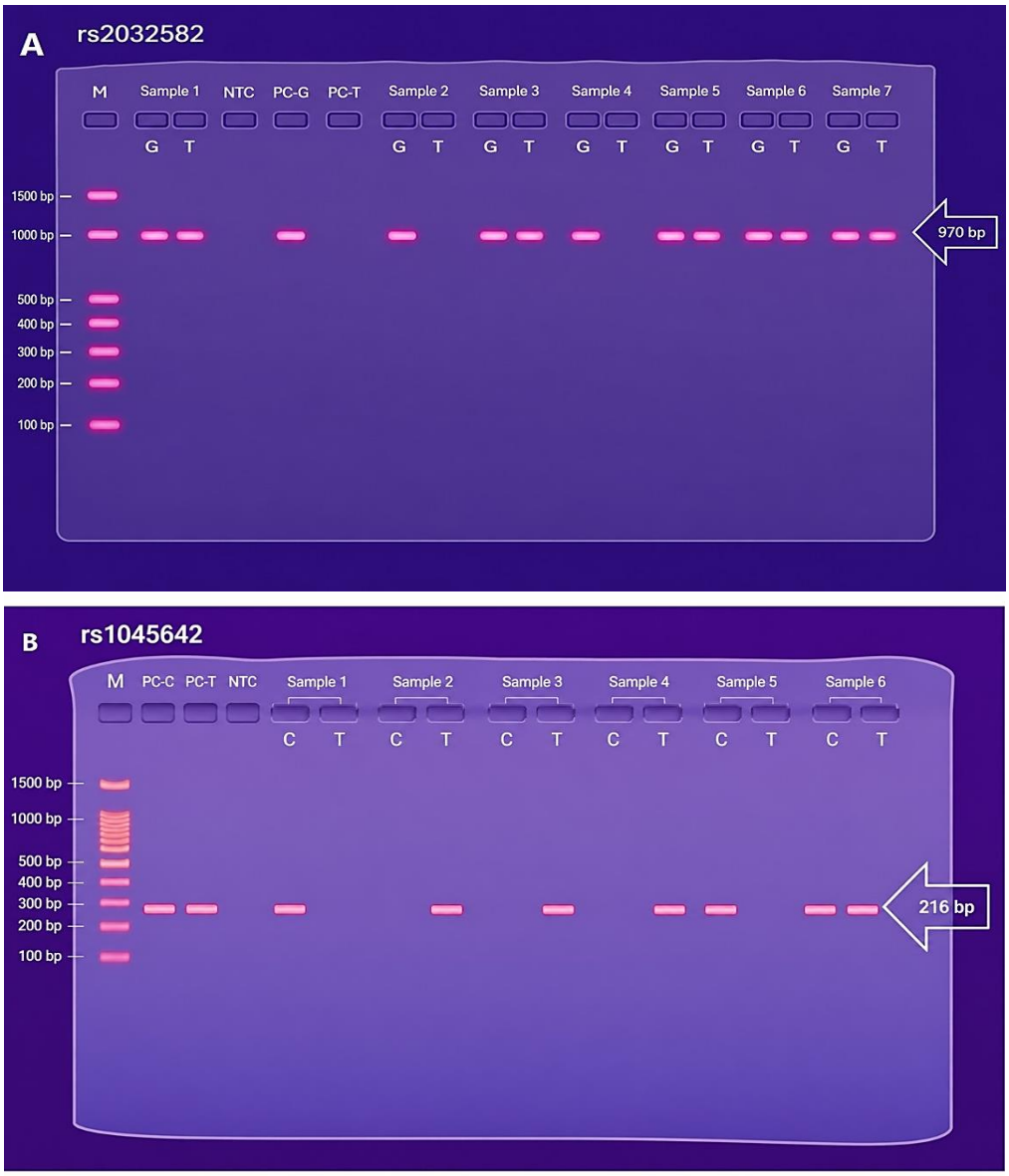

Figure 2. Representative Agarose Gel Electrophoresis of Allele-Specific PCR Products for *ABCB1* rs2032582 (G2677T) and rs1045642 (C3435T) Polymorphisms. (A) Allele-specific PCR for rs2032582 showing the expected 970-bp product. Lane M: 100-bp DNA molecular weight marker; PC-G and PC-T: positive controls for G and T alleles, respectively; NTC: no-template negative control; Lanes 1–7: representative study samples amplified with G- and T-specific primers. (B) Allele-specific PCR for rs1045642 showing the expected 216-bp product. Lane M: 100-bp DNA molecular weight marker; PC-C and PC-T: positive controls for C and T alleles, respectively; NTC: no-template negative control; Lanes 1–6: representative study samples amplified with C- and T-specific primers. PCR products were separated on agarose gel, stained with ethidium bromide, and visualized under ultraviolet illumination.

Statistical Analysis

Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS version 26, IBM Corp., Armonk, NY, USA). Variables were tested for normality using the Shapiro–Wilk test. Normally distributed data are presented as mean ± standard deviation (SD),

whereas non-normally distributed variables are expressed as median and interquartile range (IQR). We used Student's t-test or one-way ANOVA for parametric data, and the Mann–Whitney U test or Kruskal–Wallis test for non-parametric data, as appropriate. Categorical variables were compared using the Chi-square test or Fisher's exact test. Allele and genotype frequencies were calculated by direct counting. Hardy–Weinberg equilibrium was assessed using the Chi-square goodness-of-fit test. Patients were classified as responders (LDL-C < 100 mg/d) or non-responders (LDL-C ≥ 100 mg/dl). Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated to assess the association between *ABCB1* polymorphisms and treatment response under dominant and recessive genetic models. To evaluate whether the association between *ABCB1* polymorphisms and atorvastatin treatment response was independent of potential confounding variables, multivariate binary logistic regression analysis was performed adjusting for age, sex, and body mass index (BMI). Adjusted odds ratios (ORs) with 95% confidence intervals (CIs) were calculated. A two-sided $p < 0.05$ was considered statistically significant.

Results

Demographic and Clinical Characteristics of the Study Participants

A total of 250 participants were enrolled in the study, including 150 patients with dyslipidemia and 100 healthy controls, as presented in Table 1. Males constituted the majority of the dyslipidemia group (80.0%), whereas females predominated among healthy controls (56.0%), resulting in a significant difference in sex distribution between the two groups ($p < 0.0001$). Patients with dyslipidemia were significantly older than healthy controls, with a median age of 60.0 years (IQR: 52.75–65.0) compared with 43.0 years (IQR: 31.0–53.75) in the control group ($p < 0.0001$). Body mass index was significantly higher in dyslipidemia patients than in healthy controls (28.66 ± 4.18 vs. 23.46 ± 2.46 kg/m², respectively; $p < 0.0001$). Analysis according to BMI categories revealed significantly higher BMI values in dyslipidemia patients across the normal-weight, overweight, and obese subgroups compared with controls. Regarding treatment duration, most patients had received atorvastatin therapy for ≤12 months (46.0%) or 13–24 months (37.3%), whereas only a small proportion had been treated for more than 36 months.

Comparison of Lipid Profile and Liver Function Enzymes Between Healthy Controls and Dyslipidemia Patients

Table 2 describes the biochemical parameters of both the healthy control group and patients with dyslipidemia. Significant differences were found between the two groups regarding all lipid profile measurements except for ALT levels. Patients with dyslipidemia had significantly higher triglycerides and VLDL-C, but lower HDL-C, compared with the healthy control group (all $p < 0.0001$). It is worth noting that patients with dyslipidemia had significantly lower total cholesterol, LDL-C, and non-HDL-C than healthy subjects (all $p < 0.0001$). This finding is likely attributable to the effect of atorvastatin treatment, as all dyslipidemia patients had received the drug prior to assessment. Regarding hepatic enzymes, both serum ALP and AST levels were significantly higher among dyslipidemia patients than in the control group ($p = 0.0023$ and $p < 0.0001$, respectively). However, no significant difference was observed for ALT levels between the two groups ($p = 0.2756$).

Table 1. Demographic and Clinical Characteristics of the Study Participants

Genders, n (%)	**Healthy, n = 100**	**Patients, n = 150**	***p value***
Female	56 (56%)	30 (20%)	<0.0001
Male	44 (44%)	120 (80%)	
Age/Year, Median (IQR)	43.0 (31.0–53.75)	60.0 (52.75–65.0)	<0.0001
Age/Grouping, n (%)			**-**
17-26	20 (20%)	-	
27-36	17 (17%)	2 (1.3%)	
37-46	23 (23%)	14 (9.3%)	
47-56	24 (24%)	40 (26.7%)	
57-66	16 (16%)	73 (48.7%)	
67-76	-	21 (14.0%)	
BMI (kg/m), Mean ± SD	23.46 ± 2.46	28.66 ± 4.18	<0.0001
BMI categories, Median (IQR)			
Normal weight	22.23 (21.02 – 23.45)	23.31 (21.57 – 24.22)	0.0418
Overweight	25.79 (25.34 – 26.46)	27.76 (26.32 – 29.30)	<0.0001
Obese	30.48 (29.90 – 30.69)	31.99 (31.22 – 34.10)	<0.0001
Duration of statin treatment	**n (%)**	**n (%)**	**-**
≤12 months	-	69 (46%)	
13–24 months	-	56 (37.33%)	
25–36 months	-	18 (12%)	
37–60 months	-	4 (2.67%)	
>60 months	-	3 (2%)	

Data are presented as mean ± SD, median (IQR), or frequency (%). Comparisons between groups were performed using the independent t-test or Mann–Whitney U test for continuous variables, and the Chi-square test for categorical variables, as appropriate.

Table 2. Comparison of Lipid Profile and Liver Function Parameters Between Patients with Dyslipidemia and Healthy Controls

Parameters, mg/dl Median (IQR)	Healthy n = 100	Patients n = 150	*p value*
TC	179.2 (168.6 – 192.0)	138.0 (112.8 – 168.5)	<0.0001
TG	106.8 (84.85 – 125.9)	143.2 (103.9 – 207.1)	<0.0001
HDL-C	57.4 (50.23 – 62.60)	34.5 (29.00 – 40.78)	<0.0001
Non-HDL-C	123.1 (108.9 – 135.0)	103.0 (81.0 – 130.3)	<0.0001
LDL-C	101.2 (90.3 – 111.8)	66.4 (45.37 – 95.0)	<0.0001
vLDL-C	21.85 (17.80 – 26.28)	29.40 (21.15 – 44.35)	<0.0001
ALP	76.15 (66.80 – 84.38)	81.50 (69.00 – 101.00)	0.0023
AST	22.50 (19.95 – 26.20)	26.00 (22.00 – 34.50)	<0.0001
ALT	24.80 (21.23 – 28.58)	23.05 (16.00 – 31.00)	0.2756

Data are presented as median (interquartile range, IQR). TC: total cholesterol; TG: triglycerides; HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol; VLDL-C: very low-density lipoprotein cholesterol; ALP: alkaline phosphatase; AST: aspartate aminotransferase; ALT: alanine aminotransferase. Comparisons between groups were performed using the Mann–Whitney U test.

Distribution of ABCB1 rs1045642 Genotypes and Alleles in Dyslipidemia Patients

The genotype and allele distributions of the *ABCB1* rs1045642 (C3435T) polymorphism among dyslipidemia patients are presented in Table 3. The TT genotype was the most prevalent, observed in 90 patients (60.0%), followed by the CC genotype in 37 patients (24.67%) and the CT genotype in 23 patients (15.33%). At the allelic level, the T allele was more frequent than the C allele, accounting for 67.67% and 32.33% of all alleles, respectively. The genotype distribution deviated significantly from Hardy–Weinberg equilibrium ($\chi^2 = 20.00$, $p = 0.0001$).

Association Between ABCB1 rs1045642 (C3435T) Genotypes and Lipid Profile Parameters in Dyslipidemia Patients

Associations between lipid profile parameters and *ABCB1* rs1045642 (C3435T) genotypes are shown in Table 4. No significant differences were observed between the CC, CT, and TT genotypes regarding total cholesterol, triglycerides, HDL-C, LDL-C, or non-HDL-C levels ($p > 0.05$ for all comparisons). Although some variations in median lipid levels were noted among genotype groups, none reached statistical significance.

Association Between ABCB1 rs1045642 (C3435T) Genotypes and Liver Function Enzymes in Dyslipidemia Patients

The association between *ABCB1* rs1045642 (C3435T) genotypes and liver function enzymes is presented in Table 5. No significant differences were observed among genotype groups with respect to ALP or AST levels ($p = 0.2628$ and $p = 0.3287$, respectively). In contrast, ALT levels differed significantly among genotypes ($p = 0.0152$). Post-hoc analysis using Dunn's multiple-comparison test demonstrated significantly higher ALT concentrations in CC homozygotes compared with TT homozygotes, whereas the CT genotype exhibited intermediate values and did not differ significantly from either homozygous group.

Table 3. Genotype and Allele Frequencies of the *ABCB1* rs1045642 (c3435t) Polymorphism in Dyslipidemia Patients

Gene	Genotype/Allele	n	Frequency (%)
ABCB1 rs1045642 *(C3435T)*	**Genotype**		
	CC	37	24.67
	CT	23	15.33
	TT	90	60.00
	Allele		
	C	97	32.33
	T	203	67.67

Data are presented as frequencies (n) and percentages (%). Allele frequencies were calculated by direct counting. The genotype distribution showed a significant deviation from Hardy–Weinberg equilibrium ($\chi^2 = 20.00$, $p = 0.0001$).

Table 4. Association Between *ABCB1* rs1045642 (C3435T) Genotypes and Lipid Profile Parameters in Dyslipidemia Patients

Parameters, (mg/dl)	CC (n = 37) Median (IQR)	CT (n = 23) Median (IQR)	TT (n = 90) Median (IQR)	*p value*
TC	138.0 (119.0 – 176.4)	141.0 (107.0 – 170.0)	137.9 (107.7 – 163.5)	0.5549
TG	147.0 (113.5 – 197.5)	138.0 (99.0 – 189.0)	143.2 (102.4 – 214.8)	0.6562
HDL-C	31.0 (28.0 – 40.5)	36.0 (29.0 – 40.0)	35.0 (29.0 – 41.0)	0.4392
LDL-C	68.40 (40.20 – 92.00)	78.66 (46.80 – 104.60)	64.90 (45.37 – 87.75)	0.6971
Non-HDL-C	115.0 (83.5 – 139.5)	88.7 (71.0 – 128.0)	102.3 (82.8 – 124.9)	0.3317

Data are presented as median (interquartile range, IQR). Comparisons among genotypes were performed using the Kruskal–Wallis test. TC: total cholesterol; TG: triglycerides; HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol; Non-HDL-C: non-high-density lipoprotein cholesterol.

Table 5. Association Between *ABCB1* rs1045642 (C3435T) Genotypes and Liver Function Enzymes in Dyslipidemia Patients

	CC (n = 37) Median (IQR)	CT (n = 23) Median (IQR)	TT (n = 90) Median (IQR)	*p value*
ALP	84.0 (74.0 – 101.0)	84.0 (71.0 – 106.0)	78.5 (65.0 – 100.3)	0.2628
AST	30.0 (22.5 – 40.0)	29.8 (22.0 – 37.0)	26.0 (21.75 – 32.0)	0.3287
ALT	28.0 (21.0 – 35.5)[a]	21.0 (15.0 – 31.0)[ab]	21.5 (15.0 – 27.23)[b]	**0.0152**

Different superscript letters (a, b) indicate statistically significant differences between groups ($p < 0.05$) according to Dunn's multiple-comparison test following the Kruskal–Wallis test. Groups sharing the same letter are not significantly different.

Table 6. Association Between *ABCB1* rs1045642 (C3435T) Genotypes and Atorvastatin Response

Genotype	Responders	Non-responders	χ^2	*p value*
CC	29	8		
CT	16	7	0.107	0.743
TT	74	16		
Model	**Responders**	**Non-responders**	χ^2	*p value*
CC	29	8	0.107	0.743
CT+TT	90	23		
Model	**Responders**	**Non-responders**	χ^2	*p value*
CC+CT	45	15	0.833	0.361
TT	74	16		

Data are presented as frequencies (%). Responders were defined as patients achieving the LDL-C target (<100 mg/dl), while non-responders were defined as those with LDL-C ≥100 mg/dl. Comparisons between genotype groups were performed using the Chi-square test. The dominant model compared CC vs. CT+TT, and the recessive model compared CC+CT vs. TT. LDL-C: low-density lipoprotein cholesterol.

Association Between ABCB1 rs1045642 (C3435T) Genotypes and Atorvastatin Response

The association between *ABCB1* rs1045642 (C3435T) genotypes and atorvastatin response is presented in Table 6. Among the 119 responders, the TT genotype was the most frequent, followed by the CC genotype in 29 patients (19.33%) and the CT genotype in 16 patients (10.66%). Similarly, among the 31 non-responders, the TT genotype remained the most frequent, occurring in 16 patients (10.66%), followed by the CC genotype in 8 patients (5.33%) and the CT genotype in 7 patients (4.66%). No significant association was found between rs1045642 genotypes and attainment of the LDL-C treatment target ($\chi^2 = 0.107, p = 0.743$). The proportions of CC, CT, and TT genotypes were similar between responders and non-responders, indicating no significant effect of the rs1045642 polymorphism on atorvastatin response in the studied population. Additionally, analysis of possible inheritance modes, including both dominant (CC vs. CT+TT) and recessive (CC+CT vs. TT) models, revealed no significant associations ($p > 0.05$ for both).

Genotype and Allele Distributions of the ABCB1 rs2032582 (G2677T) Polymorphism

Table 7 presents the distribution of genotypes and alleles of the *ABCB1* rs2032582 (G2677T) polymorphism. The GG genotype was the most common, found in 75 subjects (50.0%), followed by the GT genotype in 45 subjects (30.0%) and the TT genotype in 30 subjects (20.0%). Allele frequency analysis showed that the G allele was the predominant allele, with a frequency of 65.0%, while the T allele had a frequency of 35.0%. The genotype distribution also deviated significantly from Hardy–Weinberg equilibrium ($\chi^2 = 13.05, p = 0.0002$).

Table 7. Genotype and Allele Frequencies of the *ABCB1* rs2032582 (G2677T) Polymorphism in Dyslipidemia Patients

Gene	Genotype/Allele	n	Frequency (%)
ABCB1 rs2032582 (G2677T)	**Genotype**		
	GG	75	50.00
	GT	45	30.00
	TT	30	20.00
	Allele		
	G	195	65.00
	T	105	35.00

Data are presented as frequencies (n) and percentages (%). Allele frequencies were calculated by direct counting. The genotype distribution showed a significant deviation from Hardy–Weinberg equilibrium ($\chi^2 = 13.05$, $p = 0.0002$).

Association Between ABCB1 rs2032582 (G2677T) Genotypes and Lipid Profile Parameters in Dyslipidemia Patients

The association between *ABCB1* rs2032582 (G2677T) genotypes and lipid profile parameters is presented in Table 8. No statistically significant differences were observed among the GG, GT, and TT genotypes for total cholesterol, triglycerides, HDL-C, LDL-C, VLDL-C, or non-HDL-C concentrations (all $p > 0.05$). Although TT homozygotes

tended to exhibit higher median TC, TG, LDL-C, and VLDL-C levels compared with GG homozygotes, these differences did not reach statistical significance. Similarly, HDL-C concentrations showed a tendency toward higher values among GT carriers; however, the observed variation among genotype groups was not statistically significant (p = 0.0775). Overall, these findings suggest that the rs2032582 polymorphism was not significantly associated with lipid profile parameters in the studied dyslipidemia patients.

Association Between ABCB1 rs2032582 (G2677T) Genotypes and Liver Function Enzymes

The association between *ABCB1* rs2032582 (G2677T) genotypes and liver function enzymes is shown in Table 9. A statistically significant difference was observed among genotype groups for ALP levels (p = 0.0432). Post-hoc analysis using Dunn's multiple-comparison test demonstrated significantly higher ALP concentrations in GT heterozygotes compared with TT homozygotes, whereas GG carriers showed intermediate values and did not differ significantly from either group. In contrast, no significant differences were detected among the three genotypes with respect to AST or ALT concentrations (p = 0.8652 and p = 0.1368, respectively). These findings suggest a possible association between rs2032582 and ALP activity, while no significant relationship was observed for AST or ALT levels.

Table 8. Association Between *ABCB1* rs2032582 G > T/A Genotypes and Liver Function Enzymes Parameters Among Patients with Dyslipidemia

Parameter (U/L)	GG (n = 75) Median (IQR)	GT (n = 45) Median (IQR)	TT (n = 30) Median (IQR)	*p value*
ALP	80.5 (66.0 – 101.0)[ab]	91.0 (77.0 – 120.0)[a]	78.5 (67.5 – 96.25)[b]	**0.0432**
AST	26.0 (21.0 – 34.0)	26.0 (23.19 – 34.0)	26.0 (19.75 – 32.88)	0.8652
ALT	23.0 (17.0 – 30.0)	18.0 (10.0 – 29.33)	22.0 (13.75 – 31.75)	0.1368

Data are presented as median (interquartile range, IQR). Comparisons among genotypes were performed using the Kruskal–Wallis test, followed by Dunn's multiple-comparison test when appropriate. Different superscript letters (a, b) indicate statistically significant differences between groups ($p < 0.05$). ALP: alkaline phosphatase; AST: aspartate aminotransferase; ALT: alanine aminotransferase.

Table 9. Association Between *ABCB1* rs2032582 (G>T) Polymorphism and Blood Lipid Profile Among Dyslipidemia Patients

Parameters, (mg/dL)	GG (n = 75) Median (IQR)	GT (n = 45) Median (IQR)	TT (n = 30) Median (IQR)	*p value*
TC	135.0 (107.0 – 159.2)	139.0 (119.0 – 186.5)	147.8 (123.9 – 178.3)	0.0749
TG	138.0 (106.0 – 190.0)	145.0 (101.7 – 212.0)	178.4 (134.5 – 244.3)	0.1617
HDL-C	32.7 (28.0 – 41.1)	38.0 (34.6–40.0)	35.6 (29.0–40.0)	0.0775
LDL-C	63.60 (43.85 – 83.80)	80.93 (53.20 – 101.0)	72.10 (54.90 – 95.00)	0.0836
vLDL-C	28.80 (21.60 – 44.20)	26.20 (20.34 – 42.40)	37.66 (27.35 – 49.30)	0.1524
Non-HDL-C	101.0 (75.0 – 128.0)	106.0 (92.0 – 131.0)	97.0 (72.25 – 137.0)	0.4057

Data are presented as median (interquartile range, IQR). Comparisons among genotypes were performed using the Kruskal–Wallis test. TC: total cholesterol; TG: triglycerides; HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol; Non-HDL-C: non-high-density lipoprotein cholesterol.

Association Between ABCB1 rs2032582 (G2677T) Genotypes and Atorvastatin Response in Dyslipidemia Patients

The association between *ABCB1* rs2032582 (G2677T) genotypes and atorvastatin response is presented in Table 10. The GG genotype was the most frequent among responders, occurring in 65 patients (43.3%), whereas the GT and TT genotypes were found in 29 (19.3%) and 25 (16.7%) patients, respectively. In contrast, among non-responders, the GT genotype was relatively more frequent, occurring in 16 patients (10.7%), compared with 10 (6.7%) for GG and 5 (3.3%) for TT. Comparison of genotype distributions revealed a statistically significant association between rs2032582 genotype and attainment of the LDL-C target (χ^2 = 8.78, p = 0.0124). Furthermore, analysis under the dominant genetic model (GG vs. GT+TT) showed a significant association (χ^2 = 5.64, p = 0.0175), indicating that carriers of the T allele were less likely to achieve the therapeutic LDL-C target compared with GG homozygotes. In contrast, the recessive genetic model (GG+GT vs. TT) did not show a significant association with atorvastatin response (χ^2 = 0.71, p = 0.399). Overall, these findings suggest that the rs2032582 polymorphism may influence atorvastatin response, with the T allele being associated with reduced treatment efficacy.

Table 10. Association Between *ABCB1* rs2032582 (G2677T) Polymorphism and Atorvastatin Response in Dyslipidemia Patients

Genotype	Responders n (%)	Non-responders n (%)	χ^2	df	*p value*
GG	65 (43.3%)	10 (6.7%)			
GT	29 (19.3%)	16 (10.7%)	8.78	2	0.0124
TT	25 (16.7%)	5 (3.3%)			
Model	**Responders n (%)**	**Non-responders n (%)**	**χ^2**	**df**	***p value***
GG	65 (43.3%)	10 (6.7%)	5.64	1	0.0175
GT+TT	54 (36.0%)	21 (14.0%)			
Model	**Responders n (%)**	**Non-responders n (%)**	**χ^2**	**df**	***p value***
GG+GT	94 (62.7%)	26 (17.3%)	0.71	1	0.399
TT	25 (16.7%)	5 (3.3%)			

Data are presented as frequencies (%). Responders were defined as patients achieving the LDL-C target (<100 mg/dl), while non-responders were defined as those with LDL-C ≥100 mg/dl. Genotype frequencies were compared using the Chi-square test. The dominant model compared GG vs. GT+TT, and the recessive model compared GG+GT vs. TT. LDL-C: low-density lipoprotein cholesterol.

Table 11. Multivariate Binary Logistic Regression Analysis for Factors Associated with Atorvastatin Treatment Response

Variable	Adjusted OR	95% CI	*p value*
rs2032582 (GT+TT vs GG)	**0.380**	**0.163 – 0.886**	**0.025**
Age	0.997	0.949 – 1.048	0.906
Sex	1.689	0.640 – 4.457	0.290
BMI	0.991	0.896 – 1.096	0.858
Variable	**Adjusted OR**	**95% CI**	***p value***
rs1045642 (CT+TT vs CC)	1.078	0.425 – 2.729	0.875
Age	0.993	0.945 – 1.044	0.796
Sex	1.551	0.601 – 4.001	0.364
BMI	0.996	0.904 – 1.098	0.943

Data are presented as adjusted odds ratios (ORs) with 95% confidence intervals (CIs), derived from multivariate binary logistic regression. The dependent variable was treatment response (responder: LDL-C <100 mg/dl; non-responder: LDL-C ≥100 mg/dl). Independent variables included genotype, age, sex, and BMI. Genotypes were analyzed under the dominant model (rs2032582: GT+TT vs. GG; rs1045642: CT+TT vs. CC). A two-sided $p < 0.05$ was considered statistically significant.

Multivariate Logistic Regression Analysis of Factors Associated with Atorvastatin Response

To determine whether the association between the *ABCB1* rs2032582 polymorphism and atorvastatin treatment response was independent of potential confounding variables, a multivariate binary logistic regression analysis was performed, including age, sex, and BMI. Under the dominant genetic model (GT+TT vs. GG), carriers of the T allele remained significantly less likely to achieve the LDL-C treatment target after adjustment (adjusted OR = 0.380, 95% CI: 0.163–0.886, $p = 0.025$). In contrast, age, sex, and BMI were not independently associated with treatment response. A similar analysis for rs1045642 showed no significant association with treatment response after adjustment (adjusted OR = 1.078, 95% CI: 0.425–2.729, $p = 0.875$), as shown in Table 11.

Discussion

The present study investigated the impact of *ABCB1* gene variations, specifically rs1045642 (C3435T) and rs2032582 (G2677T), on the efficacy and hepatic safety of atorvastatin in Iraqi patients with dyslipidemia. The findings indicate that these two polymorphisms exhibit distinct patterns of association with atorvastatin treatment outcomes. No correlation was found between rs1045642 and lipid-lowering response, whereas rs2032582 revealed a significant association with achievement of the LDL-C treatment target. However, both polymorphisms demonstrated associations with selected liver enzyme parameters, suggesting a potential influence on hepatic handling of atorvastatin. The genotype distributions of both polymorphisms deviated significantly from Hardy–Weinberg equilibrium and were characterized by a marked deficiency of heterozygous genotypes. This observation may be attributed to several factors, including non-random sampling from a hospital-based population, population stratification, regional endogamy, or potential technical limitations of allele-specific PCR. Consequently, the observed genotype–phenotype associations should be interpreted cautiously and require confirmation using larger cohorts and independent genotyping approaches.[11] Regarding lipid-lowering efficacy, no significant associations were observed between rs1045642 genotypes and serum lipid parameters or achievement of the LDL-C treatment target. These findings suggest that rs1045642 may have a limited influence on atorvastatin therapeutic response in the studied population. This observation is consistent with several previous studies that reported weak or inconsistent associations between C3435T and statin efficacy, indicating that the clinical impact of this synonymous polymorphism may be modest and influenced by other genetic and environmental factors.[7,12]

In contrast, a significant relationship was found for rs2032582. The genotype distribution differed significantly between responder and non-responder groups, and analysis under the dominant genetic model showed that carriers of the T allele were less likely to achieve the LDL-C target compared with GG homozygotes. Regional pharmacogenetic data on *ABCB1* variants and statin response remain limited and somewhat inconsistent. An Iranian study investigated *ABCB1* C3435T in relation to atorvastatin response, supporting the potential relevance of transporter polymorphisms in Middle Eastern populations.[12] Similarly, studies on Arabic populations reported associations between *ABCB1* G2677T and C3435T variants and LDL-C response to atorvastatin, which is broadly consistent with the present finding that rs2032582 was associated with achievement of the LDL-C target.[13-15] However, the direction and strength of these associations differ across studies, likely because of variations in ethnicity, baseline lipid profile, statin dose, treatment duration, sample size, and genotype distribution. Directly comparable studies from neighboring Middle Eastern countries, including Kuwait, Qatar, Bahrain, Saudi Arabia, the United Arab Emirates, and Oman, remain scarce. Therefore, the present study provides valuable pharmacogenetic data from Iraq but should be interpreted as hypothesis-generating until confirmed in larger multicenter studies across the Middle East.

Importantly, the association between the *ABCB1* rs2032582 polymorphism and atorvastatin treatment response remained statistically significant after adjustment for age, sex, and BMI in the multivariate logistic regression analysis. This finding indicates that the observed association is

unlikely to be explained solely by these demographic and anthropometric characteristics and supports an independent relationship between the rs2032582 polymorphism and atorvastatin response in the studied population. Nevertheless, because of the relatively modest sample size and the absence of pharmacokinetic measurements, these findings should be interpreted with caution and require validation in larger prospective studies. Since rs2032582 is a non-synonymous polymorphism, it has been hypothesized to influence P-glycoprotein function in previous studies. However, the present study did not evaluate P-glycoprotein activity or atorvastatin pharmacokinetics. Therefore, our findings should be interpreted as demonstrating a statistical association rather than confirming an underlying biological mechanism. Although no significant relationships were observed between rs2032582 and lipid profile parameters, the responder group analysis suggests such a possibility.[12,16,17]

Unexpectedly, HDL-C concentrations remained significantly lower in atorvastatin-treated patients than in healthy controls. Although atorvastatin therapy is generally associated with a modest increase in HDL-C, this effect is typically limited, averaging approximately 5–10%, and may not be sufficient to normalize HDL-C concentrations in patients with established dyslipidemia. The persistently reduced HDL-C levels observed in the present study likely reflect the underlying metabolic abnormalities associated with dyslipidemia, including impaired reverse cholesterol transport, insulin resistance, obesity, and chronic low-grade inflammation. In addition, variability in treatment duration, baseline HDL-C concentrations, medication adherence, lifestyle factors such as physical activity and diet, and genetic determinants of lipid metabolism may have contributed to the incomplete recovery of HDL-C despite statin therapy. Regarding hepatic safety, rs1045642 was significantly associated with ALT levels, whereas rs2032582 was associated with ALP concentrations. Because *ABCB1* encodes P-glycoprotein, an efflux transporter involved in the absorption, distribution, and biliary excretion of atorvastatin, these findings may reflect an association between genetic variation and inter-individual differences in atorvastatin disposition. However, since plasma atorvastatin concentrations and its metabolites were not measured, the underlying pharmacokinetic mechanisms could not be confirmed. Therefore, any interpretation regarding altered drug transport or hepatic exposure remains speculative and should be confirmed in future pharmacokinetic studies.[16,18] It is also important to recognize that atorvastatin pharmacokinetics and pharmacodynamics are regulated by multiple interacting genes rather than by a single transporter. In particular, the hepatic uptake transporter OATP1B1, encoded by *SLCO1B1*, plays a central role in statin disposition and has been consistently associated with both treatment efficacy and adverse effects.[19,20] Therefore, the effects attributed to *ABCB1* polymorphisms may partly reflect interactions with other pharmacogenetic determinants that were not investigated in the present study.

Finally, several limitations should be acknowledged. First, both *ABCB1* polymorphisms deviated significantly from Hardy–Weinberg equilibrium, which may reflect sampling characteristics, population stratification, or potential genotyping-related factors. Second, although samples showing weak or ambiguous allele-specific PCR amplification were re-amplified and re-evaluated before final genotype assignment, independent confirmation of genotypes by Sanger sequencing or an alternative PCR-RFLP assay was not performed because of resource limitations. Therefore, the possibility of residual genotyping error cannot be completely excluded. Third, plasma atorvastatin concentrations and its active metabolites were not measured. Consequently, the pharmacokinetic consequences of the investigated *ABCB1* polymorphisms could not be evaluated directly, and mechanistic interpretations regarding altered drug transport, systemic exposure, or hepatic handling of atorvastatin should be considered preliminary. Future studies integrating pharmacokinetic, pharmacodynamic, and pharmacogenetic analyses are needed to validate these findings. Fourth, medication adherence was not formally assessed using objective measures such as validated adherence questionnaires, pill counts, or pharmacy refill records. Therefore, some patients classified as non-responders may have exhibited suboptimal adherence to atorvastatin therapy rather than true pharmacological non-response, which could have influenced the observed associations between genotype and treatment response. Finally, although major confounding conditions were excluded, dietary habits and other environmental factors could not be completely controlled and may also have contributed to inter-individual variability in treatment response.

Conclusion

In conclusion, the present study suggests that *ABCB1* genetic polymorphisms may contribute to inter-individual variability in atorvastatin response among Iraqi patients with dyslipidemia. The rs2032582 polymorphism was significantly associated with achievement of the LDL-C treatment target, whereas rs1045642 showed no significant association with lipid-lowering efficacy. Both polymorphisms exhibited associations with selected liver enzyme parameters, suggesting a possible role in atorvastatin disposition and hepatic handling. However, these findings should be interpreted with caution because of the deviation from Hardy–Weinberg equilibrium, the absence of independent genotyping confirmation, the lack of pharmacokinetic measurements, and the possibility of residual confounding despite statistical adjustment for age, sex, and BMI. Further large-scale, multicenter studies incorporating pharmacokinetic and functional analyses are

required to validate these findings.

Authors' Contributions

SAF contributed to data collection, laboratory analysis, and manuscript drafting; NDA contributed to molecular genetic analysis and interpretation of the data; SJ contributed to study design, statistical analysis, manuscript revision, and supervision of the project. RMMAS contributed to clinical evaluation and patient recruitment. All authors read and approved the final version of the manuscript.

Ethical Approval

This study was approved by the Scientific and Ethical Committee of the College of Pharmacy, University of Kerbala, Iraq (Project No. 2024HU3; approval date: August 4, 2024). The study was conducted in accordance with the ethical principles of the 1964 Helsinki Declaration and its later amendments. Written informed consent was obtained from all participants before enrollment.

Funding

The authors did not receive any external funding for conducting this study.

Conflict of Interest Disclosures

The authors declare that they have no conflicts of interest.

Acknowledgment

The authors sincerely thank all participants who agreed to participate in this study. They also extend their gratitude to the staff of Imam Al-Hassan Al-Mujtaba Hospital and the College of Pharmacy, University of Kerbala, for their support during the course of this research.

References

1. Abera A, Worede A, Hirigo AT, Alemayehu R, Ambachew S. Dyslipidemia and associated factors among adult cardiac patients: a hospital-based comparative cross-sectional study. Eur J Med Res. 2024;29(1):237. doi:10.1186/s40001-024-01802-x
2. Nussbaumerova B, Rosolova H. Obesity and dyslipidemia. Curr Atheroscler Rep. 2023;25(12):947-55. doi:10.1007/s11883-023-01167-2
3. Park SY, Lee MK, Lim SC. Comparative drug evaluation of atorvastatin versus rosuvastatin in pharmacotherapy of Korean patients with dyslipidemia. Biomol Ther. 2008; 16(1):54-60. doi:10.4062/biomolther.2008.16.1.054
4. Ray S. Role of statins in the management of dyslipidaemia. Indian Heart J. 2024;76:S33-7. doi:10.1016/j.ihj.2023.11.267
5. Lalatović N, Ždralević M, Antunović T, Pantović S. Genetic polymorphisms in ABCB1 are correlated with the increased risk of atorvastatin-induced muscle side effects: a cross-sectional study. Sci Rep. 2023;13(1):17895. doi:10.1038/s41598-023-44792-2
6. Melhem AL, Chourasia MK, Bigossi M, Maroteau C, Taylor A, Pola R, et al. Common statin intolerance variants in ABCB1 and LILRB5 show synergistic effects on statin response: an observational study using electronic health records. Front Genet. 2021;12:713181. doi:10.3389/fgene.2021.713181
7. Su J, Xu H, Yang J, Yu Q, Yang S, Zhang J, et al. ABCB1 C3435T polymorphism and the lipid-lowering response in hypercholesterolemic patients on statins: a meta-analysis. Lipids Health Dis. 2015;14(1):122. doi:10.1186/s12944-015-0114-2
8. Bharath G, Vishnuprabu DP, Preethi L, Nagappan AS, Dhianeshwaran Isravanya RT, Bhaskar LV, et al. SLCO1B1 and ABCB1 variants synergistically influence the atorvastatin treatment response in South Indian coronary artery disease patients. Pharmacogenomics. 2022;23(12):683-94. doi:10.2217/pgs-2022-0044
9. Pratt VM, Scott SA, Pirmohamed M, Esquivel B, Kattman BL, Malheiro AJ. Medical genetics summaries. National Center for Biotechnology Information. 2012; Last Updated: December 27, 2019.
10. Saeed BN. Insight on the Side Effects of Lipid Lowering Agents (Statin) in Iraqi Patients with Ischemic Heart Diseases. Postgrad Med J. 2009;8(3):12.
11. Ningombam SS, Newmei MK, Chhungi V, Mondal PR, Devi NK, Saraswathy KN. Obesity, dyslipidaemia and candidate gene polymorphisms: a cross-sectional study among the Liangmai and Mizo tribes of Manipur, India. Ann Med. 2021;53(1):1439-47. doi:10.1080/07853890.2021.1969034
12. Behdad N, Kojuri J, Azarpira N, Masoomi A, Namazi S. Association of ABCB1 (C3435T) and ABCC1 (G2012T) polymorphisms with clinical response to atorvastatin in Iranian patients with primary hyperlipidemia. Iran Biomed J. 2017;21(2):120. doi:10.18869/acadpub.ibj.21.2.120
13. Jmel H, Romdhane L, Ben Halima Y, Hechmi M, Naouali C, Dallali H, et al. Pharmacogenetic landscape of Metabolic Syndrome components drug response in Tunisia and comparison with worldwide populations. PLoS One. 2018;13(4):e0194842. doi:10.1371/journal.pone.0194842
14. Yow HY, Hamzah S, Rahim NA, Suppiah V. Pharmacogenomics of response to statin treatment and susceptibility to statin-induced adverse drug reactions in Asians: a scoping review. Asian Biomed Res Rev News. 2023;17(3):95. doi:10.2478/abm-2023-0050
15. Rajput M, Rizvi S, Pratap PD, Raza ST, Siddiqi Z, Khare V. Pharmacokinetics and lipid-lowering efficacy affected by polymorphisms in genetic variability in statin therapy. Egypt J Med Hum Genet. 2025;26(1):160. doi:10.1186/s43042-025-00787-4
16. Chen H, Zhang H, Tao G. rs2032582 polymorphism of ATP binding cassette subfamily B member 1 affect the susceptibility of inflammatory bowel disease: a systematical meta-analysis based on 14,876 subjects. Int J Colorectal Dis. 2026;41:6. doi:10.1007/s00384-025-05045-y
17. Shahdkar M, Goorabzarmakhi MO, Shafizadeh M, Joukar F, Maroufizadeh S, Faraji N, et al. Association between dyslipidemia and elevated liver enzymes: A cross-sectional study from the PERSIAN Guilan cohort study. Endocr Metab Sci. 2025:100272. doi:10.1016/j.endmts.2025.100272
18. Rosales A, Alvear M, Cuevas A, Saavedra N, Zambrano T, Salazar LA. Identification of pharmacogenetic predictors of lipid-lowering response to atorvastatin in Chilean subjects with hypercholesterolemia. Clin Chim Acta. 2012;413(3-4):495-501. doi:10.1016/j.cca.2011.11.003
19. Lee HH, Ho RH. Interindividual and interethnic

variability in drug disposition: polymorphisms in organic anion transporting polypeptide 1B1 (OATP1B1; SLCO1B1). Br J Clin Pharmacol. 2017;83(6):1176-84. doi:10.1111/bcp.13207

20. Romaine SP, Bailey KM, Hall AS, Balmforth AJ. The influence of SLCO1B1 (OATP1B1) gene polymorphisms on response to statin therapy. Pharmacogenomics J. 2010;10(1):1-11. doi:10.1038/tpj.2009.54