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Platelet Receptor Gene Polymorphisms and Acute Coronary Syndrome: Insights from *Integrin Subunit Alpha-2* (C807T) and *Integrin Subunit Beta-3* (rs5918) Variants in an Indian Population.

(ITGA2 (C807T) and ITGB3 (rs5918) Gene Variants in Acute Coronary Syndrome)

Sanchita srivastava[1], Syed Tasleem Raza[2] , Saliha Rizvi[1], Irshad Ahmad Wani[3], Zeba Siddiqi[4], Ale Eba[1], Farzana Mahdi[5]

1. Department of Biotechnology, Era's Lucknow Medical College and Hospital Era Univeristy, Lucknow India.
2. Department of Biochemistry, Era's Lucknow Medical College and Hospital, Era Univeristy, Lucknow India.
3. Cardiology Unit, Department of Medicine, Career Institute of Medical Science and Hospital, Lucknow India.
4. Cardiology Unit, Department of Medicine, Era's Lucknow Medical College and Hospital, Lucknow India.
5. Department of Personalized and Molecular Medicine, Era University, Lucknow, India.

Address of Correspondence:

Dr. Syed Tasleem Raza, Professor, Department of Biochemistry, Era's Lucknow , Medical College and Hospital, Lucknow, India- 226003.

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Use of AI-assisted tools:

Artificial intelligence (AI)-assisted tools (ChatGPT; OpenAI Large Language Model) were used only for language refinement, grammar correction, and improvement of readability. AI was not used for data analysis, interpretation, scientific content generation, or drawing conclusions.

Ethical approval

All procedures involving human participants were conducted in accordance with the ethical standards of the institutional and national research committees, and with the 1964 Helsinki Declaration and its later amendments. Ethical approval was obtained from the Institutional Ethical/Review Committee of Era's Lucknow Medical College and Hospital, Era University, Lucknow, India (ethical code: **ELMC & H/R Cell/2024/33**).

Consent to participate

All participants voluntarily agreed to take part in the study. Written informed consent was obtained from **all subjects** prior to enrollment.

Consent for publication

All authors reviewed the study findings and approved the final version of the manuscript for publication.

Authors' contributions

- **Sanchita Srivastava (SS):** Performed laboratory experiments, data collection.
- **Syed Tasleem Raza (STR):** Conceptualization, study design, supervision, manuscript review.
- **Saliha Rizvi (SR):** Study design, data interpretation, manuscript drafting.

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- **Irshad Ahmad Wani (IAW):** Clinical assessment, patient recruitment, verification of clinical diagnoses.
- **Zeba Siddiqi (ZS):** Clinical data acquisition, patient evaluation.
- **Ale Eba (AE):** Laboratory assistance, data management.
- **Farzana Mahdi (FM):** Study supervision, critical manuscript revision, project guidance.

All authors read and approved the final manuscript.

Data availability

All relevant data supporting the findings of this study are included within the manuscript. Additional information can be provided by the corresponding author upon reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Abbreviations

ACS – Acute Coronary Syndrome
ADP – Adenosine Diphosphate
A260/A280 – Absorbance Ratio at 260 nm and 280 nm
BMI – Body Mass Index
bp – Base Pair
CAD – Coronary Artery Disease
CC – Homozygous Wild-Type Genotype (C/C)
CI – Confidence Interval
CT – Heterozygous Genotype (C/T)
DBP – Diastolic Blood Pressure
DNA – Deoxyribonucleic Acid
ECG – Electrocardiography
EDTA – Ethylenediaminetetraacetic Acid
GPIa/IIa – Glycoprotein Ia/IIa (Integrin α2β1 Receptor)
HWE – Hardy–Weinberg Equilibrium
HR – Heart Rate
ITGA2 – Integrin Subunit Alpha-2 Gene
ITGB3 – Integrin Subunit Beta-3 Gene
LD – Linkage Disequilibrium
LDL – Low-Density Lipoprotein
HDL – High-Density Lipoprotein
MspI – A Type II Restriction Endonuclease
NSTEMI – Non–ST-Elevation Myocardial Infarction
OR – Odds Ratio
PCR – Polymerase Chain Reaction
PCR-RFLP – Polymerase Chain Reaction–Restriction Fragment Length Polymorphism
RFLP – Restriction Fragment Length Polymorphism
SBP – Systolic Blood Pressure
SD – Standard Deviation

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STEMI – ST-Elevation Myocardial Infarction
Taq DNA Polymerase – Thermus aquaticus DNA Polymerase
TT – Homozygous Mutant Genotype (T/T)
UA – Unstable Angina
VLDL – Very Low-Density Lipoprotein

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KEYWORDS

Acute Coronary Syndrome; ITGA2; ITGB3; Gene Polymorphism; Platelet Receptors; Genetic Susceptibility; PCR-RFLP; Cardiovascular Risk

ABSTRACT:

Background: Acute Coronary Syndrome (ACS) is a major cause of morbidity and mortality worldwide. Genetic variations influencing platelet adhesion and aggregation may contribute to individual susceptibility. This study investigated the association of ITGA2 (C807T) and ITGB3 (rs5918) polymorphisms with ACS risk and evaluated their distribution among different ACS subtypes.

Methods: A case–control study was conducted involving 150 ACS patients and 150 age- and sex-matched controls. Genotyping of ITGA2 and ITGB3 polymorphisms was performed using PCR-RFLP. Clinical, biochemical, and genetic variables were compared using Chi-square and unpaired t-tests. Odds ratios (ORs) with 95% confidence intervals (CIs) were calculated to assess the strength of genetic associations. A p-value < 0.05 was considered statistically significant.

Results: Unstable Angina (36.7%), STEMI (32.7%), and NSTEMI (30.7%) were the predominant ACS presentations. The CT and TT genotypes of ITGA2 were significantly higher in ACS cases, conferring increased risk (CT: OR = 2.19; TT: OR = 4.55). The T allele of ITGA2 also showed a strong association with ACS (OR = 2.17). Similarly, the TT genotype and T allele of ITGB3 were significantly associated with elevated ACS susceptibility (TT: OR = 2.48; T allele: OR = 1.57). In contrast, the C alleles of both genes appeared protective. No significant differences in genotype distribution of either gene were observed among ACS subtypes (STEMI, NSTEMI, UA).

Conclusion: ITGA2 and ITGB3 polymorphisms show a significant association with overall ACS susceptibility, with the T allele representing a key genetic risk marker. However, these genetic variants do not influence the type of ACS presentation. These findings underscore the potential role of platelet receptor gene variants in ACS pathogenesis and highlight their relevance for cardiovascular risk profiling.

Background

Acute coronary syndrome (ACS) is a critical clinical condition characterized by symptoms resulting from myocardial ischemia due to coronary artery obstruction, primarily caused by atherosclerotic plaque rupture or erosion (1,2). ACS encompasses three main entities: unstable angina, ST-segment elevation myocardial infarction (STEMI), and non-ST-segment elevation myocardial infarction (NSTEMI) (3). Diagnosis typically relies on electrocardiographic changes and biochemical markers, such as high-sensitivity cardiac troponins, to differentiate between these subtypes (4,5). The clinical presentation often includes chest discomfort, dyspnea, and other symptoms, with management strategies focusing on symptom relief, myocardial salvage through revascularization, and prevention of long-term complications (6). Given its significant morbidity and mortality impact, particularly in low- and middle-income countries, a multidisciplinary approach to treatment is essential (7).

The ITGA2 gene polymorphism C807T has been associated with an increased risk of developing acute coronary syndrome (ACS) through its influence on platelet function. Studies indicate that the T allele of the C807T polymorphism correlates with higher glycoprotein Ia/IIa receptor density on platelets, which enhances platelet aggregation, particularly in response to agonists like adenosine diphosphate (ADP) and arachidonic acid (8,9). In a case-control study, the frequency of the T allele was significantly higher in ACS patients compared to healthy controls, suggesting a genetic predisposition to ACS among T allele carriers (9). Furthermore, the TT genotype was linked to a 2.9-fold increased risk of ACS compared to C allele carriers, particularly in individuals with additional cardiovascular risk factors (10,11). These findings

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underscore the importance of the ITGA2 C807T polymorphism in identifying patients at higher risk for ACS and potentially guiding more aggressive antithrombotic treatment strategies (9,11).

The impact of the ITGB3 rs5918 variant on the risk of acute coronary syndrome (ACS) appears to be inconclusive based on current research. One study indicated a significant association between the rs5918 polymorphism and coronary artery disease (CAD), suggesting that individuals with this variant may have an increased risk, with odds ratios indicating a notable susceptibility in both dominant and recessive models (12). However, a systematic review and meta-analysis found no significant role for the rs5918 variant in CAD, reporting pooled odds ratios that did not support a strong association (13). Additionally, research on patients with recurrent myocardial infarction did show an association with ITGB3 polymorphisms, but the specific contribution of rs5918 was not definitively established (14). Furthermore, a study focusing on premature CAD patients found no significant differences in the frequency of the rs5918 variant between those with and without myocardial infarction, suggesting it may not be a critical risk factor in this population (15). Overall, while some studies suggest a potential link, the evidence remains mixed, indicating a need for further investigation.

Thus, this study aimed to determine whether functional polymorphisms in *ITGA2* and *ITGB3* serve as genetic risk markers for the development of Acute Coronary Syndrome in Indians.

Material and methods

Study Setting

This hospital-based case–control study was conducted at the Cardiology Unit, Department of Medicine, Era's Lucknow Medical College and Hospital, Era University, Lucknow, India, a tertiary-care center that caters to a wide population from both urban and rural regions. The clinical setting provided access to patients with acute coronary syndrome (ACS) as well as suitable healthy controls for comparison.

Study Participants

A total of 150 patients with confirmed ACS (including STEMI, NSTEMI, and unstable angina) and 150 age- and sex-matched healthy controls without a history of cardiovascular disease were enrolled. Cases were recruited consecutively at the time of hospital admission after confirmation of ACS diagnosis based on clinical presentation, electrocardiography (ECG), cardiac biomarkers, and angiographic evidence. Controls were selected from the same hospital population, primarily consisting of individuals attending routine health check-ups, ensuring comparability while excluding cardiovascular disease history. The study protocol was reviewed and approved by the Institutional Ethical/Review Committee of Era's Lucknow Medical College and Hospital, Lucknow (Reference no. ELMC&H/R-Cell-/2019/24). Written informed consent was obtained from all participants prior to enrollment.

Sample Collection and DNA Extraction

Peripheral venous blood samples (5 mL) were collected from each participant in EDTA-coated vacutainer tubes. Samples were stored at –20 °C until further processing. Genomic DNA was extracted using the standard phenol–chloroform method. DNA quality and concentration were measured spectrophotometrically at A260/A280, and integrity was verified by agarose gel electrophoresis.

Genotyping of *ITGA2 (C807T)* Polymorphisms

Genotyping of the ITGA2 C807T polymorphism was performed using the PCR–restriction fragment length polymorphism (PCR-RFLP) method. The target region was amplified using the forward primer 5′-CCTTAAAGCTACCGGCCCATGT-3′ and reverse primer 5′-TTGGCCTATTAGCACCAAAACTTACC-3′. PCR amplification was carried out with an initial denaturation at 95°C for 2 minutes, followed by 35 cycles consisting of denaturation at 95°C for 30 seconds, annealing at 57°C for 30 seconds, and extension at 72°C for 30 seconds. A final extension was performed at 72°C for 5 minutes. The amplified products were resolved on a 2% agarose gel. For RFLP analysis, the 288-bp PCR products were digested with the Hpy188I restriction enzyme. As the resulting 44-bp fragment may not be visible on a 2% agarose gel, genotype determination was based on the presence or absence of the 244-bp digested fragment relative to the 288-bp undigested product, as illustrated in Figure 1.

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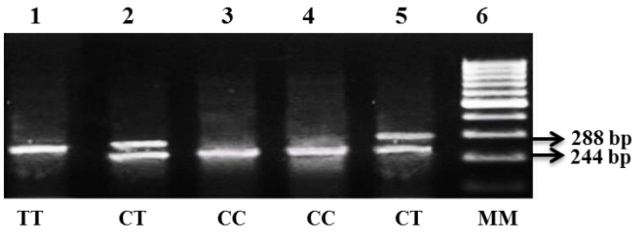

Figure 1: Lane 1 shows the TT genotype with a 288 bp band, Lanes 2 and 5 show the CT genotype, Lanes 3 and 4 show the CC genotype, and Lane 6 contains the molecular ladder.

Genotyping of *ITGB3 (rs5918)* Polymorphisms

Genotyping of the ITGB3 rs5918 polymorphism was carried out by PCR using the forward primer 5′-CTTAGCTATTGGGAAGTGGTAGG-3′ and reverse primer 5′-ACTGACTTGAGTGACCTGGGAG-3′. Each 25 µL PCR reaction contained 2.5 µL of 10× buffer, 2.0 µL of 2.5 mmol/L dNTPs, 20 pmol of each primer, 2.0 µL of template DNA, and 1.25 U of Taq DNA polymerase, with the final volume adjusted using sterile distilled water. PCR cycling conditions included an initial denaturation at 94°C for 5 minutes, followed by 35 cycles of denaturation at 94°C for 30 seconds, annealing at 65°C for 45 seconds, and extension at 72°C for 45 seconds, with a final extension at 72°C for 5 minutes. The PCR amplicons were digested with the MspI restriction enzyme (New England BioLabs, UK) at 37°C for 3 hours, and the resulting fragments were separated on 8% polyacrylamide gels stained with ethidium bromide.

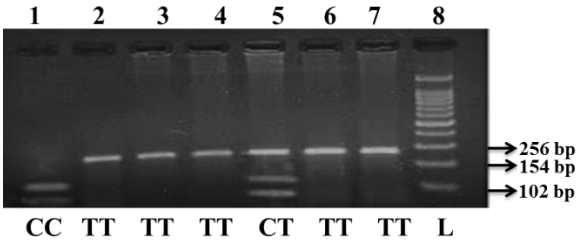

Figure 2: The **RFLP analysis of the ITGB3 gene** was carried out by digesting the PCR-amplified product, producing distinct banding patterns corresponding to different genotypes. Lane 1 (CC) showed two fragments of 154 bp and 102 bp**,** indicating complete digestion of the PCR product. Lane 2 (TT) displayed a single undigested fragment of 256 bp**,** characteristic of the homozygous TT genotype. Lane 5 (CT) revealed three fragments of 256 bp, 154 bp, and 102 bp**,** representing the heterozygous condition where both alleles are present.

Statistical Analysis

Statistical analysis was performed using appropriate descriptive and inferential methods to compare clinical, biochemical, and genetic variables between Acute Coronary Syndrome (ACS) cases and controls. Categorical variables—including age group, sex, BMI categories, and genotype and allele frequencies of the ITGA2 (C807T) and ITGB3 (rs5918) polymorphisms were summarized as frequencies and percentages, and intergroup comparisons were evaluated using the Chi-square test. Continuous variables such as vital parameters (SBP, DBP, HR), lipid profile (HDL, LDL, VLDL, triglycerides, total cholesterol), and BMI were expressed as mean ± standard deviation (SD), and group differences were assessed using the unpaired t-test. The strength of association between specific genotypes/alleles and ACS was estimated using odds ratios (ORs) with 95% confidence intervals (CIs). A p-value < 0.05 was considered statistically significant for all analyses.

Results

The present study examined the clinical characteristics and genetic profiles of ACS patients in comparison with healthy controls to evaluate the potential role of platelet receptor gene polymorphisms in disease susceptibility. The results are presented in a structured manner, beginning with the distribution of ACS subtypes, followed by detailed comparisons of ITGA2 (C807T) and ITGB3 (rs5918) genotypes and alleles between cases and controls. Finally, the variation of these genetic markers across different ACS subtypes STEMI, NSTEMI, and Unstable Angina—is explored to assess their influence on clinical presentation.

Table 1: Distribution of Acute Coronary Syndrome (ACS) Cases by Clinical Presentation

Variable		Case (ACS)	
		N (150)	%
ACS	STEMI	49	32.7%
	NSTEMI	46	30.7%

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	UA	55	36.7%

The distribution of Acute Coronary Syndrome (ACS) subtypes demonstrated a relatively even representation across the study cohort. Among the 150 ACS cases, Unstable Angina (UA) emerged as the most frequent clinical presentation, accounting for 55 cases (36.7%). ST-Elevation Myocardial Infarction (STEMI) constituted 49 cases (32.7%), while non–ST-Elevation Myocardial Infarction (NSTEMI) comprised 46 cases (30.7%). Although all three ACS categories were well represented, UA showed a modest predominance. This pattern reflects the heterogeneous nature of ACS presentations and underscores the clinical variability with which patients may present, emphasizing the importance of comprehensive diagnostic evaluation in acute cardiac care.

Table 2: Intergroup Comparison of ITGA2 Genotypes and Alleles between ACS Cases and Controls

ITGA2		Case (ACS)		Control		Significance		OR (95% CI)
		No.	%	No.	%	chi sq	p-value	
Genotype	CC	64	42.7%	97	64.7%	Ref.		
	CT	68	45.3%	47	31.3%	10.10	**0.002**	2.19 (1.35-3.57)
	TT	18	12.0%	6	4.0%	10.52	**0.001**	4.55 (1.71-12.07)
Allele	C	196	65.3%	241	80.3%	17.06	**<0.001**	0.46 (0.32-0.67)
	T	104	34.7%	59	19.7%	17.06	**<0.001**	2.17 (1.50-3.14)

The distribution of ITGA2 genotypes and alleles showed significant differences between ACS cases and controls, indicating a meaningful genetic association. The CC genotype, used as the reference, was considerably more common among controls (64.7%) than cases (42.7%), suggesting a protective effect. In contrast, the CT genotype was markedly higher in ACS cases (45.3% vs. 31.3%) and showed a significant association with disease risk ($\chi^2 = 10.10$, $p = 0.002$; OR = 2.19, 95% CI: 1.35–3.57). The TT genotype also demonstrated a strong risk relationship, being three times more frequent in cases (12.0%) than controls (4.0%) ($\chi^2 = 10.52$, $p = 0.001$; OR = 4.55, 95% CI: 1.71–12.07). Allelic analysis supported these genotype-based findings. The C allele was significantly enriched in controls (80.3%) and showed a protective association (OR = 0.46, 95% CI: 0.32–0.67), whereas the T allele was more common in ACS cases (34.7% vs. 19.7%), conferring over a twofold increase in risk ($\chi^2 = 17.06$, $p < 0.001$; OR = 2.17, 95% CI: 1.50–3.14). Collectively, these results demonstrate a robust association between ITGA2 polymorphism and ACS susceptibility. The CT and TT genotypes, as well as the T allele, significantly elevate ACS risk, while the C allele appears protective. These findings underscore the potential role of ITGA2 genetic variation in the pathogenesis of ACS and its relevance in cardiovascular risk stratification.

Table 3: Intergroup Comparison of ITGB3 Genotypes and Alleles between ACS Cases and Controls

ITGB3		Case (ACS)		Control		Significance		OR (95% CI)
		No.	%	No.	%	chi sq	p-value	
Genotype	CC	38	25.3%	56	37.3%	Ref.		
	CT	75	50.0%	72	48.0%	2.58	0.108	1.54 (0.91-2.59)
	TT	37	24.7%	22	14.7%	7.20	**0.007**	2.48 (1.27-4.84)

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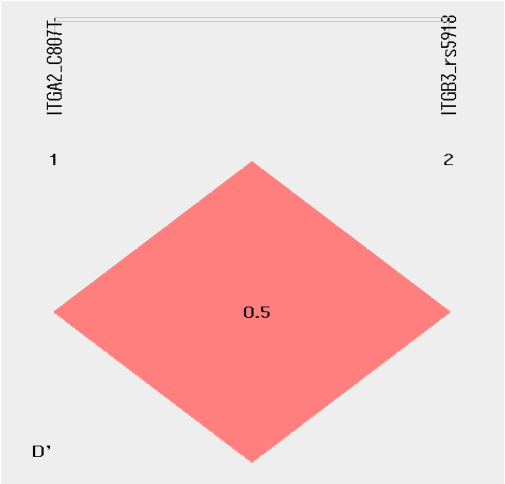
Allele	C	151	50.3%	184	61.3%	7.36	**0.007**	0.64 (0.46-0.88)
	T	149	49.7%	116	38.7%	7.36	**0.007**	1.57 (1.13-2.17)

Analysis of ITGB3 polymorphism demonstrated notable differences between ACS cases and controls. The CC genotype was more common among controls (37.3%) than cases (25.3%), suggesting a protective role. The CT genotype showed no significant association with ACS ($\chi^2 = 2.58$, $p = 0.108$; OR = 1.54, 95% CI: 0.91–2.59). In contrast, the TT genotype was significantly overrepresented in ACS cases (24.7% vs. 14.7%), indicating a 2.5-fold increased risk ($\chi^2 = 7.20$, $p = 0.007$; OR = 2.48, 95% CI: 1.27–4.84). Allelic analysis aligned with these observations. The C allele was more frequent in controls (61.3%) and showed a protective association ($\chi^2 = 7.36$, $p = 0.007$; OR = 0.64, 95% CI: 0.46–0.88). Conversely, the T allele was significantly elevated in ACS cases (49.7% vs. 38.7%) and conferred a higher risk of ACS (OR = 1.57, 95% CI: 1.13–2.17). These findings highlight the TT genotype and T allele of ITGB3 as important genetic contributors to increased ACS susceptibility.

Table 4: Comparison of ITGB3 and ITGA2 Genotypes Among Different ACS Subtypes

Genes		ACS						Significance	
		STEMI		**NSTEMI**		**UA**			
		No.	%	No.	%	No.	%	chi sq.	p-value
ITGB3	CC	11	22.4%	12	26.1%	15	27.3%	1.691	0.792
	CT	27	55.1%	24	52.2%	24	43.6%		
	TT	11	22.4%	10	21.7%	16	29.1%		
ITGA2	CC	19	38.8%	20	43.5%	25	45.5%	2.263	0.687
	CT	26	53.1%	19	41.3%	23	41.8%		
	TT	4	8.2%	7	15.2%	7	12.7%		

The distribution of ITGB3 and ITGA2 genotypes across ACS subtypes (STEMI, NSTEMI, and UA) showed no statistically significant differences, with all p-values exceeding 0.05. ITGB3 genotypes (CC, CT, TT) were similarly distributed across the three ACS categories ($\chi^2 = 1.691$, $p = 0.792$), indicating no subtype-specific pattern. Likewise, ITGA2 genotypes demonstrated comparable frequencies among STEMI, NSTEMI, and UA patients ($\chi^2 = 2.263$, $p = 0.687$). These findings suggest that neither ITGB3 nor ITGA2 polymorphisms influence the clinical presentation of ACS, and their effects, if present, do not appear to differentiate between STEMI, NSTEMI, or Unstable Angina in this cohort.



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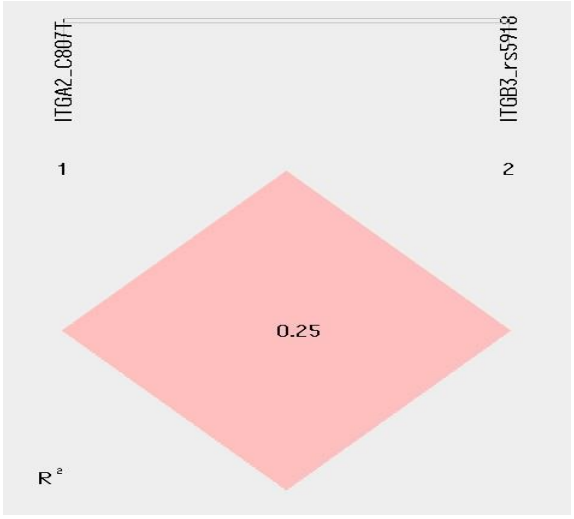

Figure 3: Linkage disequilibrium (LD) plot showing the relationship between ITGA2 (C807T) and ITGB3 (rs5918) polymorphisms. The red diamond represents the LD strength between the two loci, with a D′ value of 0.5 indicating moderate linkage disequilibrium. This suggests partial but not strong allelic association, implying that ITGA2 and ITGB3 variants segregate largely independently despite both contributing to platelet adhesion and aggregation pathways. The moderate LD supports the study's findings that each polymorphism independently increases susceptibility to Acute Coronary Syndrome (ACS), without influencing specific ACS subtypes.

Discussion

The findings of this study provide important insights into the genetic determinants of Acute Coronary Syndrome within the Indian population. By analyzing two key platelet receptor genes **ITGA2** and **ITGB3** the study evaluates their contributions to ACS risk and examines whether these polymorphisms influence the pattern of clinical presentation.

In the present study, the ITGA2 CC genotype appeared in 42.7% of ACS cases and 64.7% of controls—a 22% difference indicating strong protection. This case frequency is almost identical to that reported in the Indonesian Javanese cohort by Ningrum et al. (2021) (16) (41%) and closely matches the CC frequencies noted in Chinese ischemic stroke cohorts studied by Lu et al. (2014) (17) and Zhang et al. (18) (2016) (42–46%). In contrast, large Caucasian datasets such as the European venous thromboembolism cohort examined by Kvasnicka et al. (2015) (19) reported CC frequencies of only 34–36%, roughly 6–8% below our ACS cases and nearly 30% lower than our Indian controls. These comparisons suggest that the Indian population maintains a significantly higher reservoir of the protective CC genotype than many Western cohorts.

The CT genotype in our ACS cases (45.3%) showed a 14% elevation relative to controls (31.3%). Comparable CT frequencies have been reported in Asian populations, including the Javanese cohort of Ningrum et al. (2021) (16) (51%), the Jordanian aspirin-response cohort of Al-Azzam et al. (2013) (20) (47–50%), and Chinese cohorts investigated by Chen et al. (2011) (21) and Lu et al. (2014) (17) (39–45%). In contrast, Liakhotska (2017) (22) reported a CT frequency of only 21% among Ukrainian PCI responders less than half of our ACS proportion—highlighting marked regional variation. Although Caucasian stroke or CAD cohorts evaluated by Cole et al. (2003) (23) and Rath et al. (2017) (24) show CT frequencies of 46–48%, no case–control differences were observed. Therefore, the CT elevation in our study (45.3% vs. 31.3%) is among the most pronounced globally.

The TT genotype demonstrated the clearest disease-linked disparity, occurring in 12% of ACS cases versus 4% of controls a threefold difference. Similar TT frequencies have been reported across East and Southeast Asian groups, including Japanese subjects in Fujiwara et al. (2007) (25) (13.6%), Chinese cohorts in Lu et al. (2014) (17) (8–18%), and Indonesian participants in Ningrum et al. (2021) (16) (8%). Some Caucasian cohorts, such as those examined by Martínez et al. (2009) (26) or Rath et al. (2017) (24), show TT rates as high as 17%, while Eastern European clinical datasets reported by Filippova et al. (2020) (27) exhibit TT frequencies up to 53%, yet none demonstrated the clear case–control separation seen in our ACS cohort. Thus, while TT frequencies in Indians fall within global ranges, the differential between cases and controls is substantially sharper.

At the allele level, the T allele occurred in 34.7% of ACS cases but only 19.7% of controls—a 15% excess. This mirrors T-allele levels seen in Chinese ischemic stroke cohorts reported by Lu et al. (2014) (20) (30–40%) and Indonesian samples described by Ningrum et al. (2021) (16) but exceeds levels from Caucasian

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controls in the meta-analysis by Wu et al. (2014) (28) (17–25%). Our control T-allele frequency (19.7%) aligns with values reported in Jordanian (Al-Azzam et al., 2013) (20) and Japanese (Fujiwara et al., 2007) (25) cohorts. Conversely, the protective C allele in our controls (80.3%) is markedly higher than the 55–70% control frequencies commonly reported worldwide.

Taken together, although Indian genotype and allele distributions fall within global ranges, the case–control differences are markedly larger in our study than in most international cohorts. While several Asian studies resemble our overall allele profile, the effect sizes particularly the CT and TT risk gradients relative to the CC protective genotype are considerably more pronounced in Indians. These findings support the conclusion that the ITGA2 C807T polymorphism exerts a stronger, ethnicity-dependent genetic influence on ACS susceptibility in the Indian population compared with Western, Middle Eastern, and Eastern European cohorts.

In the present study, the ITGB3 (rs5918) polymorphism showed a strong association with ACS, with the TT genotype observed in 24.7% of cases versus 14.7% of controls (OR = 2.48). The CT genotype was comparable between cases and controls (50.0% vs. 48.0%), while the protective CC genotype was significantly reduced among ACS cases (25.3% vs. 37.3%). At the allele level, the risk-associated T allele was markedly higher in cases (49.7%) than controls (38.7%) (OR = 1.57), whereas the C allele was correspondingly lower in cases (50.3%) than in controls (61.3%). These differences 10% for TT and 11% for the T allele—reflect a strong and quantifiable genetic signal, exceeding the effect sizes commonly reported in platelet-receptor polymorphism studies and emphasizing the pathogenic relevance of the αIIbβ3 (GPIIIa) pathway in the Indian population.

When compared with earlier global investigations—most of which examined ITGA2 C807T—the strength of association observed in our ITGB3 results is substantially greater. For instance, the Indonesian cohort studied by Ningrum et al. (2021) (16) reported TT = 8%, CT = 51%, and CC = 41%, but found no disease association. Similarly, Caucasian stroke cohorts examined by Cole et al. (2003) (23) showed TT ≈ 17%, CT ≈ 48%, CC ≈ 34%, yet without significant thrombotic correlation. Chinese ischemic stroke studies by Zhang et al. (2016) (18) and Lu et al. (2014) (17) reported TT frequencies of 8–18% and CT values of 39–45%, but again noted no consistent association with vascular events. Jordanian data from Al-Azzam et al. (2013) (20) and Pakistani data from Mukarram et al. (2016) (29) reported TT frequencies of only 6–14% in aspirin-response cohorts, while Ukrainian findings by Liakhotska (2017) (22) and European PCI cohorts studied by Verschuren et al. (2013) (30) showed TT ranges from 12% to over 50% in certain subgroups, yet none demonstrated the clear case–control separation seen in our ACS cohort (24.7% vs. 14.7%). Furthermore, large-scale meta-analyses by Wu et al. (2014) (28), Liu et al. (2017) (31), and Weng et al. (2013) (32), encompassing over 2,500 cases and 2,600 controls, concluded that ITGA2 exhibits only weak or non-significant associations with ischemic outcomes. In contrast, the markedly higher effect sizes in our ITGB3 findings—reflected in elevated TT and T-allele frequencies and correspondingly higher odds ratios—indicate that the rs5918 variant exerts a stronger, more consistent, and potentially population-specific genetic risk for ACS than the widely studied ITGA2 C807T polymorphism

Conclusion

This study demonstrates a significant association between ITGA2 (C807T) and ITGB3 (rs5918) gene polymorphisms and susceptibility to Acute Coronary Syndrome (ACS). The CT and TT genotypes and the T allele of both ITGA2 and ITGB3 were found to be strongly associated with increased risk of ACS, whereas the C allele of each gene exhibited a protective effect. However, neither polymorphism showed any relationship with the clinical presentation of ACS, as genotype distributions did not differ significantly among STEMI, NSTEMI, and Unstable Angina subtypes. Collectively, these findings highlight the potential contribution of platelet receptor gene variants to ACS pathogenesis and support their role as genetic markers of increased cardiovascular risk. Further research in larger, diverse populations is warranted to validate these results and explore their utility in risk prediction, personalized prevention, and therapeutic decision-making.

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