Journal of Rare Cardiovascular Diseases
ISSN: 2299-3711 (Print) | e-ISSN: 2300-5505 (Online)
www.jrcd.eu
RESEARCH ARTICLE

Association of cyp11b2 gene polymorphism in Diabetes and Cardiovascular disease in North Indian Population

Ambika Slathia[1], Dr Rattandeep Singh[2]*, Dr Puneet Bajaj[3], Dr Ruhi Mahajan[4]
[1]Research scholar school of biosciences and engineering lovely professional university
[2]*Prof School of Biosceinces and bioengineering lovely professional university
[3]lovely professional university
[4]Astt prof govt medical college Jammu

*Corresponding Author
Dr Rattandeep Singh

Article History
Received: 01.08.2025
Revised: 15.08.2025
Accepted: 10.09.2025
Published: 30.09.2025

Abstract: ***Objective:*** In this study, the relationship between CYP11B2 gene polymorphisms and the risk of cardiovascular disease (CVD) and type 2 diabetes mellitus (T2DM), illnesses whose incidence is rising quickly in North Indian populations, is examined. ***Background:*** An essential component of the renin-angiotensin-aldosterone system (RAAS), the CYP11B2 gene codes for the aldosterone synthase enzyme, which affects cardiovascular health, electrolyte balance, and blood pressure management. ***Methods:*** Physiometric, biochemical, and anthropometric characteristics were compared across the control, diabetes, CVD, and diabetic cardiovascular disease (DCVD) groups. PCR followed by genotyping was performed using RFLP technique. ***Results:*** The findings show that the most severe clinical phenotype is seen in DCVD patients, who have markedly higher fasting plasma glucose, HbA1c, blood pressure, LDL cholesterol, VLDL, and atherogenic index of plasma. In the groups with diabetes and DCVD, central adiposity and inadequate glycaemic control were particularly noticeable. Furthermore, there was a substantial correlation between illness states and lifestyle variables including smoking, drinking alcohol, and engaging in less physical activity. ***Conclusion:*** The results highlight how metabolic dysregulation, lifestyle variables, and genetic vulnerability (CYP11B2 _344C/T variation) all work together to increase the risk of cardiometabolic disease. This integrated approach provides important information about possible treatment and diagnostic approaches for high-risk groups.

Keywords: Hypertension, Dyslipidemia, Obesity, Insulin Resistance, Cyp11b2 gene.

INTRODUCTION

Aldosterone synthase, an essential catalyst in the renin-angiotensin-aldosterone system (RAAS), which controls blood pressure, electrolyte balance, and cardiovascular homeostasis, is encoded by the CYP11B2 gene. The development of diabetes mellitus and cardiovascular diseases may be influenced by variations in this gene, which have been linked to changed enzyme activity. Due to their common metabolic and genetic risk factors, these two non-communicable diseases pose serious worldwide health issues. A chronic metabolic disorder called diabetes mellitus is typified by persistently high blood sugar levels that are caused by deficiencies in either the action or secretion of insulin, or both. There are intricate relationships between lifestyle variables, environmental factors, and genetic predisposition in its aetiology. In 2011, there were over 366 million afflicted persons globally; by 2030, that number is expected to increase to 552 million, according to the World Health Organisation (2016). The autoimmune loss of pancreatic β-cells causes Type 1 diabetes, while insulin resistance and poor glucose utilisation are the main causes of Type 2 diabetes. The latter advances slowly and frequently go undetected until it is somewhat advanced. **Given the growing prevalence of these conditions in** North Indian populations**, exploring** CYP11B2 gene polymorphisms **may** provide valuable insights into their genetic basis and potential implications for disease prediction, prevention, and personalized treatment strategies.

Cardiovascular disease (CVD) has become much more common in developing nations during the last few decades. An estimated 8–9 million fatalities from CVD were recorded in low-income countries in 1990, which is around 70% more than the 5.3 million deaths recorded in high-income areas. As a result, rising economies now bear a greater share of the global CVD burden. One of the main side effects of type 2 diabetes mellitus (T2DM) is cardiovascular disease (CVD). By 2011, around 25.8 million people in the US had been diagnosed with type 2 diabetes, and over half of them also had associated cardiovascular diseases such coronary artery disease or stroke [1].

Between 1972 and 1975, the Indian Council of Medical Research (ICMR) carried out the country's first nationwide survey on diabetes, which found prevalence rates ranging from 1.5% to 2.8%. Subsequent research, such as the Prevalence of Diabetes in India Study (PODIS, 2004), revealed higher rates with ADA criteria of 4.7% in urban areas and 1.9% in rural areas, and WHO criteria of 5.6% and 2.7%, respectively [2,3]. Additionally, rates in major cities like Bangalore and Hyderabad ranged from 12.4% to 16.6%, according to the National Urban Diabetes Survey (NUDS) [4]. Over 170 million people worldwide suffer with diabetes, and by 2030, that number is expected to rise to 366 million

[5,6]. India presently has the highest rate of diabetes worldwide [5]. A significant risk factor for type 2 diabetes, cardiovascular disease, cancer, and sleep problems, obesity is brought on by sedentary lifestyles and increasing calorie consumption [7].

The cytochrome P450 enzyme aldosterone synthase, which is encoded by the CYP11B2 gene, catalyses the latter stages of aldosterone manufacture in the adrenal cortex's zona glomerulosa [8]. By controlling intravascular volume and vascular tone, aldosterone is essential for preserving arterial pressure and salt balance [9]. According to Tsukada, Hu and Rajan , the promoter region's i.e. 344 C to T polymorphism has been linked to increased aldosterone production and an increased risk of essential hypertension in a number of populations [10,11,12].

In this study, the relationship between CYP11B2 gene polymorphisms and the risk of cardiovascular disease (CVD) and type 2 diabetes mellitus (T2DM), illnesses whose incidence is rising quickly in North Indian populations, is examined.

MATERIAL AND METHODS

Ethical approval for the study was obtained from the Government Medical College, Jammu. Participants in the study were drawn from the North Indian population between the ages of 30 and 75. They were split into four groups: those with type 2 diabetes mellitus (T2DM), those with cardiovascular disease (CVD), those with both diabetes and cardiovascular disease (DCVD), and healthy controls. According to the American Diabetes Association's (ADA, 2022) guidelines, clinically confirmed cases of type 2 diabetes were required, as were people with a diagnosis of cardiovascular disease (CVD), such as coronary artery disease, myocardial infarction, or hypertension, as confirmed by clinical records or echocardiogram results, and healthy controls who were matched for age and sex and had no known metabolic or cardiovascular conditions.

Participants were only included if they agreed to provide written informed consent for biochemical and genetic investigations. Individuals with type 1 or gestational diabetes, secondary hypertension from pharmacological, endocrine, or renal causes, chronic kidney disease, hepatic problems, thyroid dysfunction, autoimmune illnesses, or infectious diseases were excluded.

DNA Extraction

A modified salting-out technique was used to extract genomic DNA from 400 µL of peripheral blood. In a nutshell, samples were centrifuged for two minutes at 10,000 rpm after being lysed in 1200 µL of RBC lysis solution. The resultant white blood cell pellet was reconstituted in 300 µL of WBC lysis buffer, 20 µL of 10% sodium dodecyl sulphate (SDS) was added, and it was then incubated for 30 minutes at 56°C. The mixture was treated with 150 µL of ammonium acetate, centrifuged for 15 minutes at 13,000 rpm, and the supernatant was then moved to a new tube. 50 µL of Tris-EDTA (TE) buffer was used to dissolve the DNA after it had been precipitated with two volumes of cooled ethanol, cleaned with 70% ethanol, and allowed to air dry. Before being used again, the isolated DNA was kept at -80°C.

DNA Quantification

Genomic DNA quality and concentration were evaluated using 0.8% agarose gel electrophoresis made in 1X TAE buffer with ethidium bromide (3 µL/40 mL). Five microlitres of DNA along with two microlitres of loading dye and a molecular weight marker were added to each well. DNA bands were seen when the electrophoresis was run at 100 V for 20 to 25 minutes and exposed to UV light.

Genotyping of CYP11B2 (-344C>T) Polymorphism

The CYP11B2 (-344C>T) promoter polymorphism was amplified using the following primers: Forward: 5′-CAGGAGGAGACCCCATGTGA-3′ and Reverse: 5′-CCTCCACCCTGTTCAGCCC-3′

A 10 µL reaction mixture including 50 ng of genomic DNA, 20 pmol of each primer, 1X Taq PCR buffer, 25 mM $MgCl_2$, 100 mM of each dNTP, and 0.5 U/µL of Taq DNA polymerase was used for PCR amplification. The GeneAmp PCR System 9700 (Applied Biosystems, USA) was used to conduct the reactions. The cycling settings were 95°C for 5 minutes, followed by 35 cycles of 95°C +for 30 sec., 68°C for 30 sec., and 72°C for 30 sec., with a final extension at 72°C for 7 minutes. By using 1% agarose gel electrophoresis, the amplified products were confirmed.

Restriction Fragment Length Polymorphism (RFLP) Analysis

Five units of the HaeIII restriction enzyme were used to digest the amplified 541 bp PCR products for 3.5 hours at 37°C. After being separated on a 2.5% agarose gel and stained with ethidium bromide, the digested fragments were examined under a UV lamp. In addition to smaller common pieces of 138 bp, 125 bp, and 71 bp, the T allele produced 273 bp fragments, while the C allele produced 202 bp fragments.

Statistical Analysis

The Mann Whitney U test was performed to compare Anthropometric and Biochemical parameters between the Diabetes, Cardiovascular disease and Normal participants. The chi square test was performed for categorical parameters.

RESULTS AND OBSERVATIONS:

A Mann Whitney U test was performed to compare anthropometric, biochemical, and cardiovascular parameters between the diabetes, control and CVD groups as shown in Table1 and Table 2. The mean age was comparable between the two groups (43.43 ± 14.49 vs. 45.38 ± 15.69; p = 0.276), indicating no significant difference. However, patients with CVD were significantly taller (167.32 ± 9.91 cm vs. 162.83 ± 9.61 cm; p = 0.020) and heavier (81.12 ± 22.34 vs. 73.75 ± 8.61; p = 0.010), with a higher BMI (28.74 ± 6.28 vs. 27.84 ± 2.58; p = 0.030). In contrast, waist circumference (40.39 ± 2.39 vs. 33.21 ± 2.35 cm; p = 0.040), hip circumference (42.38 ± 2.39 vs. 35.21 ± 2.35 cm; p = 0.010), and waist–hip ratio (0.95 ± 0.003 vs. 0.94 ± 0.004; p = 0.040) were significantly higher in the diabetes group, suggesting greater central adiposity. Glycaemic parameters were also elevated in diabetes patients, with fasting plasma glucose (168.14 ± 79.54 vs. 129.08 ± 31.38 mg/dl; p = 0.020) and HbA1c (7.45 ± 2.59% vs. 6.27 ± 1.01%; p = 0.050) showing significant and borderline differences, respectively. While systolic blood pressure did not differ significantly (121.53 ± 6.72 vs. 195.03 ± 24.93 mmHg; p = 0.060), diastolic blood pressure was markedly higher in the CVD group (131.55 ± 18.28 vs. 83.60 ± 4.95; p = 0.020).

Lipid profile analysis revealed that total cholesterol was higher in CVD but not statistically significant (213.28 ± 79.10 vs. 143.54 ± 23.20; p = 0.080). Triglycerides (198.15 ± 86.19 vs. 117.72 ± 19.77; p = 0.050) and HDL cholesterol (58.60 ± 18.81 vs. 28.71 ± 4.64; p = 0.050) were borderline higher in the CVD group, while LDL (118.02 ± 57.65 vs. 91.29 ± 17.95; p = 0.040) and VLDL (39.63 ± 17.24 vs. 23.54 ± 3.95; p = 0.020) were significantly elevated. Interestingly, the atherogenic index of plasma (AIP) was significantly higher in diabetes (0.61 ± 0.09 vs. 0.51 ± 0.19; p = 0.040), indicating greater atherogenic dyslipidaemia despite overall higher lipid fractions in CVD.

The comparison of diabetes patients with control individuals reveals clear differences in demographic, anthropometric, and biochemical parameters as shown in Table 2. The mean age of the diabetes group (43.43 ± 14.48) was significantly higher than that of controls (29.00 ± 4.35, p = 0.02), highlighting age as an important risk factor. Diabetic individuals were also taller (162.83 ± 9.60) compared to controls (159.85 ± 8.30, p = 0.001), and showed markedly higher mean weight (73.75 ± 8.60 vs. 57.91 ± 8.04, p = 0.04). Waist circumference (40.38 ± 2.39) and hip circumference (42.37 ± 2.39) were significantly larger in diabetics compared to controls (32.19 ± 2.31 and 34.21 ± 2.33, respectively; both p = 0.03), resulting in an elevated waist-to-hip ratio (0.95 vs. 0.94, p = 0.02). Body mass index was also higher in diabetics (27.83 ± 2.58) relative to controls (22.59 ± 1.87, p = 0.03), indicating greater adiposity.

Biochemically, diabetic patients exhibited a significantly higher fasting plasma glucose (168.13 ± 79.54 vs. 100.15 ± 6.42, p = 0.04) and HbA1c levels (7.45 ± 2.58 vs. 5.36 ± 0.25, p = 0.003), confirming poor glycaemic control. Blood pressure values were also elevated: systolic BP averaged 121.53 ± 6.72 in diabetics vs. 117.89 ± 4.70 in controls (p = 0.03), and diastolic BP was 83.60 ± 4.95 compared to 78.93 ± 2.18 (p = 0.04). Lipid parameters further showed adverse profiles among diabetics: total cholesterol was lower in diabetics (143.53 ± 23.20) compared to controls (164.64 ± 21.82, p = 0.02), yet triglycerides were reduced (117.71 ± 19.76 vs. 124.40 ± 15.56, p = 0.01), and HDL levels were significantly decreased in diabetics (28.70 ± 4.64 vs. 32.71 ± 5.11, p = 0.01). LDL levels (91.28 ± 17.94 vs. 105.96 ± 20.55, p = 0.03) and AIP (0.61 ± 0.08 vs. 0.57 ± 0.09, p = 0.03) were significantly worse in diabetics, while VLDL was elevated (23.54 ± 3.95 vs. 21.19 ± 4.10, p = 0.004).

The comparison between cardiovascular disease (CVD) patients and healthy controls demonstrates striking clinical and biochemical differences as shown in Table 2. The mean age of CVD patients was significantly higher (45.38 ± 15.69 years) compared to controls (29.00 ± 4.35 years, p = 0.03). Anthropometric measures also showed higher values in CVD, including height (167.32 ± 9.91 cm vs. 159.85 ± 8.30 cm, p = 0.04), weight (81.11 ± 22.33 kg vs. 57.91 ± 8.04 kg, p = 0.02), BMI (28.74 ± 6.28 vs. 22.59 ± 1.87, p = 0.05), waist circumference (33.21 ± 2.34 vs. 32.19 ± 2.31, p = 0.02), and hip circumference (35.21 ± 2.34 vs. 34.21 ± 2.33, p = 0.02).

Metabolic markers indicated moderate differences: fasting plasma glucose was higher in CVD (129.08 ± 31.38) compared to controls (100.14 ± 6.42, p = 0.06), and HbA1c followed a similar pattern (6.27 ± 1.00 vs. 5.36 ± 0.25, p = 0.06), though these did not reach strong significance. Blood pressure values, however, were markedly elevated in CVD, with systolic BP (195.02 ± 24.92 vs. 117.89 ± 4.70, p = 0.02) and diastolic BP (131.54 ± 18.28 vs. 78.92 ± 2.17, p = 0.01) being significantly higher.

The lipid profile showed a clear atherogenic trend in CVD: total cholesterol (213.27 ± 79.09 vs. 164.64 ± 21.82, p = 0.01), triglycerides (198.14 ± 86.18 vs. 124.40 ± 15.56, p = 0.04), LDL (118.01 ± 57.64 vs. 105.95 ± 20.54, p = 0.011), and VLDL (39.62 ± 17.23 vs. 21.19 ± 4.10, p = 0.03) were all significantly higher in CVD. Interestingly, HDL was also higher in CVD patients (58.60 ± 18.80 vs. 32.71 ± 5.11, p = 0.02), which may indicate altered lipid metabolism or medication effects. The atherogenic index (AIP) was lower in CVD (0.50 ± 0.19 vs. 0.57 ± 0.09, p = 0.03), despite worse overall lipid levels.

The comparative analysis of lifestyle parameters among control, diabetes, and cardiovascular groups reveals significant behavioural variations that correlate with disease progression as shown in Table 3 and Figure 1. In terms of smoking habits, non-smokers dominate across all groups; however, smoking prevalence increases from 12.66% in the control group to 23.44% in diabetes patients and reaches 50% among cardiovascular patients, indicating a strong association between smoking and cardiovascular risk. A similar pattern is observed in alcohol consumption, where only 9% of the control group consumes alcohol compared to 21.3% of diabetic individuals and nearly half (49.2%) of those with cardiovascular disease, suggesting that alcohol intake may aggravate both metabolic and heart-related conditions. Dietary patterns show that vegetarians are more common in the control group (56.33%), whereas non-vegetarian diets are more frequent among diabetes (53.1%) and cardiovascular (48.5%) groups, implying that diet may contribute indirectly to disease development when combined with other risk factors. Tobacco use follows the same trend, rising sharply from 5% in controls to 14.5% in diabetes and 49.2% in cardiovascular patients, further emphasizing the strong link between tobacco consumption and heart-related complications. Regarding physical activity, diabetic patients exhibit the lowest activity levels, with 48.2% reporting low physical activity compared to 32% in controls and 33.8% in cardiovascular patients, suggesting that sedentary lifestyles significantly contribute to metabolic disorders. Overall, the data indicate that unhealthy lifestyle behaviors—especially smoking, alcohol consumption, tobacco use, and physical inactivity—progressively increase from healthy individuals to those with diabetes and cardiovascular disease. This trend underscores the critical need for preventive interventions promoting healthier habits, balanced diets, and regular physical activity to mitigate the risk and progression of chronic diseases.

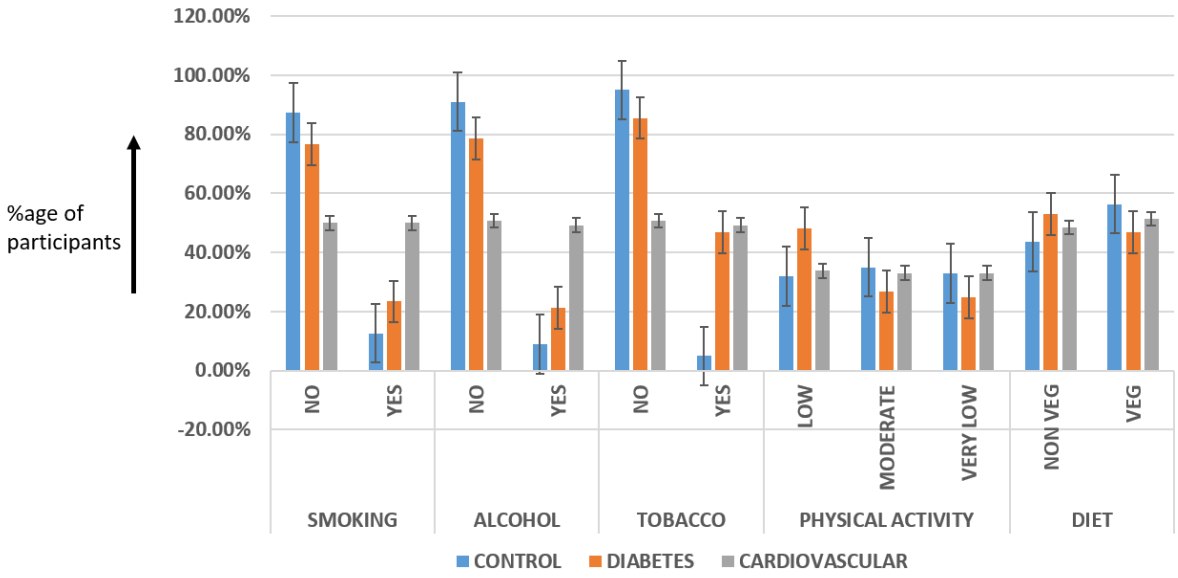

Figure 1: The Physicochemical parameters was determined between patients with control participants by using chi square test.

Table 1: The Mean ± Standard Deviation of Diabetes, CVD and Normal participants.

	GROUPS	N	Mean	Std. Deviation
AGE	DIABETES	145	43.4345	14.48745
	CVD	142	45.3803	15.69286
	CONTROL	300	29.0067	4.35083
HEIGHT	DIABETES	145	162.8324	9.60884
	CVD	142	167.3218	9.91273
	CONTROL	300	159.8530	8.30499
WEIGHT	DIABETES	145	73.7517	8.60518
	CVD	142	81.1197	22.33767
	CONTROL	300	57.9100	8.04306
WC	DIABETES	145	40.3862	2.39266
	CVD	142	33.2113	2.34545
	CONTROL	300	32.1957	2.31355
HC	DIABETES	145	42.3793	2.39232
	CVD	142	35.2113	2.34545
	CONTROL	300	34.2133	2.33509
WHR	DIABETES	145	.9528	.00335
	CVD	142	.9429	.00411
	CONTROL	300	.9408	.00561
BMI	DIABETES	145	27.8379	2.58245
	CVD	142	28.7417	6.28281
	CONTROL	300	22.5978	1.87953
FPG	DIABETES	145	168.1372	79.54450
	CVD	142	129.0845	31.38448
	CONTROL	300	100.1472	6.42236
HbA1C	DIABETES	145	7.4537	2.58712
	CVD	142	6.2705	1.00849
	CONTROL	300	5.3666	.25219
SBP	DIABETES	145	121.5310	6.72171
	CVD	142	195.0282	24.92967
	CONTROL	300	117.8933	4.70913
DBP	DIABETES	145	83.6000	4.94891
	CVD	142	131.5493	18.28443
	CONTROL	300	78.9267	2.17802
TC	DIABETES	145	143.5379	23.20232
	CVD	142	213.2796	79.09702
	CONTROL	298	164.6477	21.82128
TG	DIABETES	145	117.7172	19.76554
	CVD	142	198.1458	86.18989
	CONTROL	300	124.4033	15.56110
HDL	DIABETES	145	28.7076	4.64046
	CVD	142	58.6014	18.80781
	CONTROL	300	32.7100	5.11118
LDL	DIABETES	145	91.2869	17.94747
	CVD	141	118.0177	57.64784
	CONTROL	300	105.9593	20.54762
AIP	DIABETES	145	.6119	.08817
	CVD	142	.5080	.19452
	CONTROL	300	.5736	.09099
VLDL	DIABETES	145	23.5434	3.95311
	CVD	142	39.6292	17.23798

	CONTROL	300	21.1919	4.10952

Table 2: The statistical p value of Diabetes, CVD and Normal participants.

Parameters	D vs CVD	D vs N	CVD vs N
Age	0.276	0.02	0.03
Height	0.02	0.01	0.04
Weight	0.01	0.04	0.02
WC	0.04	0.03	0.02
HC	0.01	0.03	0.02
WHR	0.04	0.02	0.01
BMI	0.03	0.03	0.05
FPG	0.02	0.04	0.06
HbA1c	0.05	0.03	0.06
SBP	0.06	0.03	0.02
DBP	0.02	0.04	0.01
TC	0.08	0.02	0.01
TG	0.05	0.01	0.04
HDL	0.05	0.01	0.02
LDL	0.04	0.03	0.01
AIP	0.04	0.03	0.03
VLDL	0.02	0.04	0.03
Smoking	0.01	0.03	0.03
Alcohol	0.01	0.01	0.03
Diet	0.03	0.02	0.01
Tobacco	0.02	0.02	0.02
Physical Activity	0.04	0.06	0.08

Table 3: The percentage of Diabetes, CVD and Normal participants.

Parameters	CONTROL	DIABETES	CARDIOVASCULAR
Smoking NO	87.33%	76.55%	50%
YES	12.66%	23.44%	50%
Alcohol NO	91%	78.6%	50.70%
YES	9%	21.3%	49.2%
Diet NON-VEG	43.66%	53.1%	48.5%
VEG	56.33%	46.8%	51.4%
Tobacco NO	95%	85.5%	50.70%
YES	5%	46.8%	49.2%
Physical Activity LOW	32%	48.2%	33.8%
MODERATE	35%	26.8%	33%
VERY LOW	33%	24.8%	33%

DNA EXTRACTION

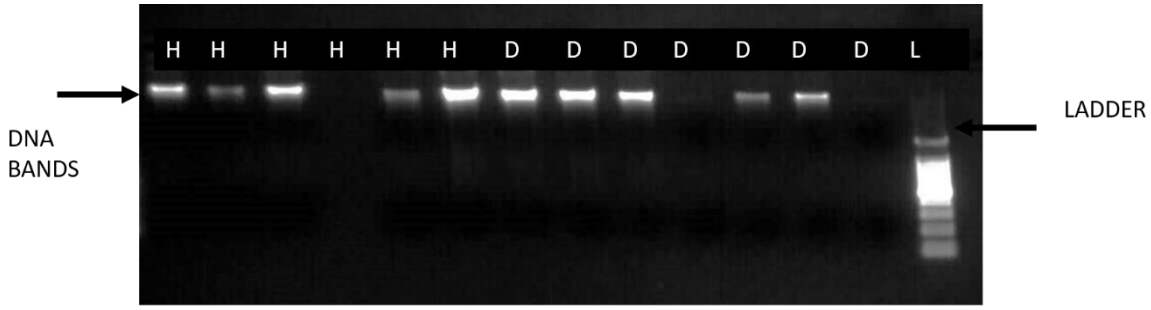

Figure 2: L: 100bp Molecular Marker, H: Cardiovascular Disease, D: Diabetes

Agarose gel electrophoresis analysis of DNA samples from patients with diabetes (D) and cardiovascular disease (H) is shown in Figure 2, with a 100 bp molecular ladder (L) acting as the size reference marker. The effective amplification of the targeted genomic areas is shown by the unique DNA bands visible in both the H and D lanes of the electrophoretic separation. The molecular ladder (L) on the extreme right exhibits a series of evenly spaced bands representing DNA fragments in 100 base pair increments, which facilitate the estimation of molecular weights of the amplified products. Overall, the gel image demonstrates clear amplification patterns and supports the comparative molecular characterization between cardiovascular and diabetic samples.

PCR AMPLIFICATION

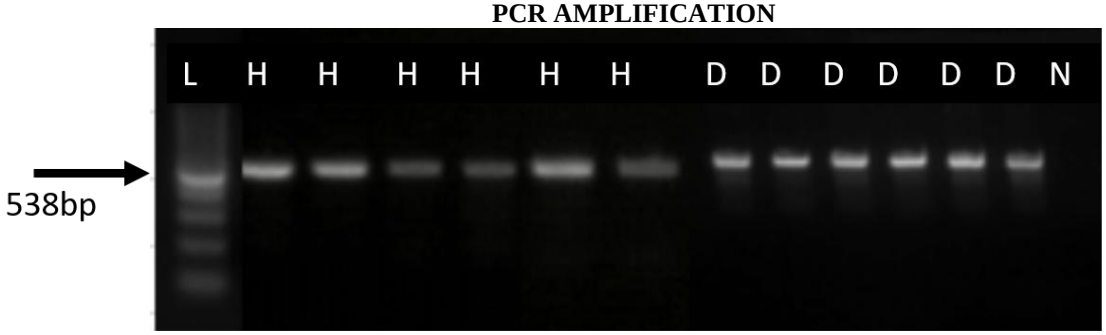

Figure 3: L: 100bp Molecular marker, PCR products (538bp) for samples, H: Cardiovascular Disease, D: Diabetes, N: Negative control

PCR **amplification products** with a target fragment size of **538 base pairs (bp) as shown in Figure 3.** The gel lanes **L** stands for the **100 bp DNA molecular marker (ladder), H** stands for **cardiovascular disease samples**, **D** stands for **diabetes samples**, and **N** for the **negative control.**

In this figure, bands appear at the **538 bp position** in all the lanes labelled **H (Cardiovascular Disease)** and **D (Diabetes),** indicating successful amplification of the target gene fragment in these samples. The intensity of the bands among these lanes appears consistent, suggesting that the PCR reaction produced comparable quantities of amplified DNA in both disease groups. The **ladder (L)** lane shows multiple bands representing standard DNA fragment sizes, which serve as a reference to confirm that the amplified products correspond to the expected 538 bp size. Importantly, the **negative control (N)** lane does not display any visible band, confirming the **absence of contamination or nonspecific amplification** in the PCR process. This validates the reliability of the experiment.

RFLP-PCR

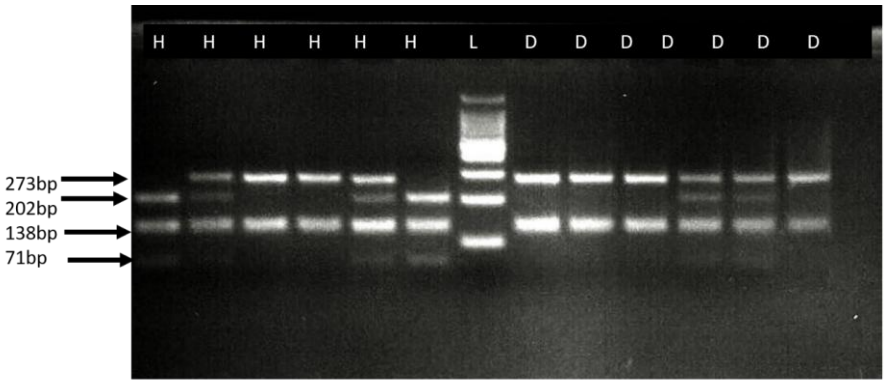

Figure 4: Digested PCR products for samples, L: 100bp Molecular marker, H: Cardiovascular Disease, D: Diabetes

Figure 4 shows the restriction enzyme–digested PCR products for cardiovascular disease (H) and diabetes (D) samples, with the 100 bp molecular marker (L) used for size reference. The digested fragments appear at approximately 273 bp, 202 bp, 138 bp, and 71 bp, confirming successful enzymatic cleavage of the amplified 538 bp product. Both cardiovascular and diabetes samples show similar band patterns, indicating the presence of specific restriction sites within the target gene. Minor variations in band intensity suggest possible genetic polymorphisms between the two groups, which may be linked to disease-related genetic differences.

DISCUSSION

The present study compared anthropometric indices and biochemical markers between control, diabetes, cardiovascular disease (CVD), and diabetic with cardiovascular disease (DCVD) groups. The findings provide important insights into how metabolic dysregulation, adiposity, hemodynamic changes, and genetic predisposition interact to increase cardiovascular risk.

Age and Population Differences

Patients with CVD (45.3 ± 15.6 years) and DCVD (60.9 ± 13.7 years) were significantly older than controls (29.0 ± 4.3 years, $p < 0.05$). This confirms that age is a strong and independent determinant of cardiovascular and metabolic disease, reflecting the cumulative effects of prolonged exposure to risk factors such as hypertension, obesity, and hyperglycemia. However, genetic studies also indicate that age interacts with polymorphisms such as the CYP11B2 _344C/T variant, where the CC genotype has been shown to increase aldosterone synthesis and accelerate vascular injury with advancing age, especially in hypertensive individuals. Thus, while age alone increases disease susceptibility, its interaction with genetic and environmental exposures amplifies the risk [13].

Anthropometric Indicators: Obesity, WC, WHR and BMI

Anthropometric measures showed a consistent pattern of central adiposity across all patient groups. WC and WHR were significantly elevated in CVD and DCVD compared to controls (CVD WC: 33.2 ± 2.3 cm vs. 32.1 ± 2.3 cm, $p = 0.02$; DCVD WC: 37.6 ± 2.3 cm vs. 32.1 ± 2.3 cm, $p = 0.02$). WHR was also higher in both groups, reflecting abdominal fat accumulation. Previous studies, including those from Brazilian and Chinese cohorts, emphasize that WC and WHR are stronger predictors of cardiovascular risk than BMI because they more closely capture visceral adiposity rather than total body fat. Visceral adipose tissue is metabolically active, secreting inflammatory mediators (IL-6, TNF-α, CRP) and adipokines such as leptin and resist in, while reducing protective adiponectin. These mediators impair insulin sensitivity, promote endothelial dysfunction, and induce vascular stiffness, thereby linking central obesity directly with CVD progression.

BMI was elevated in both diabetic and CVD groups (CVD 28.7 ± 6.2 vs. control 22.6 ± 1.8, $p < 0.05$; DCVD 26.1 ± 3.3 vs. control 22.6 ± 1.8, $p = 0.01$), indicating general overweight and obesity as important contributors. Beyond absolute BMI, recent research highlights that BMI variability over time is an independent predictor of cardiovascular risk. Frequent weight fluctuations increase visceral fat accumulation, oxidative stress, and dyslipidaemia, leading to a greater long-term risk of diabetes and atherosclerosis even in individuals with similar baseline BMI [13,14].

Glycaemic Control

Glycaemic markers were most striking in the diabetes and DCVD groups. Fasting plasma glucose was significantly elevated in diabetes (168.1 ± 79.5 vs. 100.1 ± 6.4 mg/dl, $p = 0.04$) and even higher in DCVD (196.3 ± 51.0 vs. 100.1 ± 6.4 mg/dl, $p = 0.01$). Similarly, HbA1c was markedly increased in diabetes (7.45 ± 2.5 vs. 5.36 ± 0.25, $p = 0.003$) and further elevated in DCVD (8.3 ± 1.7 vs. 5.36 ± 0.25, $p = 0.01$). Persistent hyperglycaemia induces endothelial dysfunction via advanced glycation end-products (AGEs), increases oxidative stress, and enhances LDL oxidation. These mechanisms explain why the coexistence of diabetes with CVD (DCVD group) showed the worst glycaemic and lipid derangements in our cohort [15].

Alcohol and smoking can further aggravate glycaemic control. Chronic alcohol intake impairs glycogenolysis and gluconeogenesis, leading to unstable glucose levels, while smoking reduces insulin sensitivity by stimulating adrenergic receptors and increasing sympathetic activity. These lifestyle factors, though not measured in our study, are likely contributors to the worsening metabolic profile in DCVD patients.

Blood Pressure: Hemodynamic Stress in CVD

Hypertension was the defining feature of the CVD group, with systolic blood pressure reaching 195.0 ± 24.9 mmHg compared to 117.9 ± 4.7 mmHg in controls ($p = 0.02$) and diastolic pressure at 131.5 ± 18.2 mmHg vs. 78.9 ± 2.1 mmHg ($p = 0.01$). In contrast, the DCVD group had lower SBP (163.9 ± 30.8) and DBP (101.6 ± 10.1), reflecting the possibility of antihypertensive treatment or progressive vascular damage leading to reduced compliance. Hypertension increases shear stress and promotes vascular remodelling, while neurohormonal hyperactivation of the renin-angiotensin-aldosterone system (RAAS) drives sodium retention, fibrosis, and cardiac hypertrophy. The CYP11B2 _344C/T polymorphism provides a genetic basis for this, as the CC allele has been shown to enhance aldosterone synthesis, thus potentiating hypertension and increasing the risk of adverse cardiovascular events [16].

Lipid Profile and Atherogenic Risk

Dyslipidaemia was observed across disease groups, with atherogenic patterns most pronounced in DCVD. Total cholesterol was higher in both CVD (213.2 ± 79.0 vs. 164.6 ± 21.8 mg/dl, p = 0.01) and DCVD (246.5 ± 36.4 vs. 164.6 ± 21.8, p = 0.02). Triglycerides were similarly elevated (CVD 198.1 ± 86.1 vs. 124.4 ± 15.5, p = 0.04; DCVD 220.1 ± 47.7 vs. 124.4 ± 15.5, p = 0.02). LDL was significantly increased in DCVD (162.6 ± 21.1 vs. 105.9 ± 20.5, p = 0.001), confirming the enhanced atherogenic burden. Interestingly, HDL was paradoxically higher in CVD and DCVD compared to controls, but this may reflect dysfunctional HDL particles, which lose their protective antioxidant and anti-inflammatory properties in chronic inflammatory states.

The atherogenic index of plasma (AIP) and VLDL were significantly higher in CVD and DCVD, reflecting triglyceride-rich lipoprotein excess. Central adiposity contributes directly to this pattern by increasing hepatic VLDL synthesis, reducing HDL, and promoting small dense LDL particles, which are particularly atherogenic. Obesity-driven systemic inflammation also enhances lipoprotein oxidation, further accelerating atherosclerosis [17].

Integration of Obesity, Inflammation, and Genetic Susceptibility

The combined presence of obesity, hyperglycemia, hypertension, and dyslipidemia in the DCVD group illustrates the synergistic nature of cardiometabolic risk. Obesity contributes to cardiac remodelling and subclinical organ damage by increasing preload, afterload, and fibrosis, while visceral adiposity impairs natriuretic peptide activity, depriving the heart of its natural anti-remodelling defense. Elevated BMI and WC in our data correlate with these pathophysiological mechanisms, which align with epidemiological findings showing obesity accelerates heart failure development by almost a decade.

Genetic predisposition further modifies this risk. As demonstrated in previous longitudinal studies of the Chinese EH population, the CYP11B2 _344CC genotype enhances aldosterone production, thereby increasing salt retention, blood pressure, and cardiac fibrosis independent of conventional risk factors. Such genetic factors may explain the variability in disease severity observed in our cohort despite similar anthropometric characteristics [15].

Type 2 diabetes is primarily caused by insulin resistance, which may also be a factor in the increase in BMI. Cell membranes' sensitivity to insulin is greatly reduced. This severely impairs the vital process by which insulin facilitates the passage of glucose through the cell wall for conversion to energy. Consequently, excess glucose keeps moving through the bloodstream, raising blood sugar levels that are then sent to the liver. Once there, the sugar is converted to fat and sent via the circulation to other parts of the body. This pathway leads to weight gain and obesity [14, 15]. The results of WC and HC were not found to be similar with Riaz study [18], the BMI and WHR measurements are dependent on dietary patterns and dwindling levels of physical activity. It has been hypothesised that these environmental influences, particularly in those people with metabolic genotype, reveal a hereditary vulnerability to obesity [15]. The results of TC, HDL, TG and VLDL were not found to be similar with Sheriff study [19], [15]. The LDL was statistically non-significant i.e. p>0.05 in T2DM as compared to healthy controls and similar finding was found in the research conducted by Sheriff et al [19]. According to reports, VLDL and LDL absorption in the liver is reduced in T2DM patients, which causes their amounts of these lipoproteins in the plasma to rise, especially in the postprandial period. This condition is most frequently seen in type T2DM patients who have severe insulin insufficiency or inadequate glycaemic control. Additionally, it has been stated that the lower availability of LDL receptors contributed to the restricted LDL clearance [15,16].

CONCLUSION

The present analysis demonstrates that while diabetes is primarily characterized by hyperglycaemia and central adiposity, CVD is dominated by hypertension and dyslipidaemia. When both conditions coexist (DCVD), their effects converge, producing the most severe phenotype with uncontrolled glycaemia, marked dyslipidaemia, and vascular dysfunction. These findings underscore the importance of integrating anthropometric, biochemical, lifestyle, and genetic data in cardiovascular risk stratification. Visceral adiposity, RAAS activation, and hyperglycaemia-driven vascular injury represent central mechanisms linking these conditions. The diabetic patients had significantly higher age, body mass index, central obesity markers (WC, HC, WHR), impaired glycaemic parameters (FPG, HbA1c), and adverse lipid and blood pressure profiles compared to healthy controls, with statistically significant differences ($p < 0.05$) across most variables, suggesting a strong association between diabetes, obesity, dyslipidaemia, and cardio metabolic risk.

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