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Study of Demographic and Clinical Characteristics related to Coronary Artery Disease in an Asian Indian Population: A Case-Control Association Study

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Abstract: ***Coronary Artery Disease (CAD) is a complex, multifactorial disease. The prevalence of CAD in Asian Indians is very high as compared to other populations. Our case-control association study was carried out in the twin cities of Hyderabad and Secunderabad in the state of Telangana. A comparision was done between Controls and Cases to identify risk factors associated with CAD in our population. The study has identified a higher incidence of co-morbid conditions such as Diabetes and Hypertension in Cases as compared to Controls. Hyperlipidemia (high levels of lipids in blood), smoking, alcohol consumption and Mixed diet (vegetarian and non vegetarian) were found to be higher in Cases as compared to Controls. There is also a higher incidence of family history in Cases. Asian Indians have a propensity for premature and severe CAD.***
Keywords: Coronary Artery Disease (CAD), Asian Indian population, Atherosclerosis, Diabetes, Hypertension, Hyperlipidemia.

I. INTRODUCTION

CAD is a major public health concern in the Asian Indian population. The Global Burden of Disease study estimate of age-standardized CVD death rate is 272 per 100,000 population in India which is higher than the global average of 235 per 100,000 population [1].Heart diseases occur in Asian Indians 5–10 years earlier than in other populations around the world. The mean age for first presentation of acute myocardial infarction in Asian Indians is 53 years [2].The increasing burden of CAD in India can be explained by the steep rise in the prevalence of CAD risk factors like diabetes, hypertension, high serum lipids, smoking, abdominal obesity and physical inactivity. Rapid urbanization and changes in lifestyle that have occurred during the past two decades have led to an alarming rise in CAD risk factors in India [3].CAD is known to have a heritability of 40-60% [4]. This means that genetic factors have an equal if not more contribution to the risk of CAD. It is a complex multifactorial disorder that is caused by the interplay of Genetic and Environmental risk factors. The underlying cause of CAD is Atherosclerosis.

Atherosclerosis refers to stiffening of arteries due to deposition of lipid containing plaque on the inner side of the artery wall (Tunica intima).Atherosclerosis is an inflammatory process affecting the artery wall. It is a chronic condition that may remain asymptomatic for several decades. It is initially seen under the microscope as deposition of fatty streaks (white-yellowish lipid streaks) within the intima. Fatty streaks have been reported in adolescents. The lesion develops gradually and progresses to an Atheroma lesion or plaque. Stable plaques are generally asymptomatic. Unstable or vulnerable plaques rupture spontaneously causing thrombus (blood clot) [5]. The thrombus may block the blood flow within the artery eventually resulting in Myocardial Infarction (heart attack). Myocardial Infarction (MI) occurs due to lack of blood supply to the part of the Myocardium (Cardiac muscle) supplied by the artery. A large epidemiological case-control study, the INTERHEART (A Study of Risk Factors for First Myocardial Infarction in 52 Countries and Over 27,000 Subjects), conducted in 262 centers covering 52 countries in Asia, Europe, the Middle East, Africa, Australia, North America, and South America showed that 90% of individual attributable risk for CAD can be explained by 9 risk factors belonging to social, behavioral and physiological groups, namely: 1) low consumption of fruits and vegetables; 2) smoking; 3) alcohol consumption; 4) psychosocial factors; 5) sedentary lifestyle; 6) hypertension; 7) dyslipidemia; 8) abdominal obesity; and 9) diabetes [6].

Some of the distinctive features of CAD in the Asian Indian population are: a strong family history, distinct disease pattern, smaller coronary artery diameter, higher frequency of comorbidities like diabetes and hypertension at a much younger age and lower

thresholds of comorbidity along with elevated baseline plasma levels of inflammatory markers like interleukin-6 (IL6) and C-reactive protein (CRP) [7,8,9].Therefore there is an urgent need to reduce the burden of these risk factors to bring down the morbidities and mortality associated with the disease in this population

II. MATERIALS AND METHODS

A. Sampling methodology

The case-control association study involved 443 Controls and 218 angiographically documented CAD cases. The controls were healthy individuals unaffected with CAD recruited from the twin cities of Hyderabad-Secunderabad. The CAD cases were enrolled from KIMS (Krishna Institute of Medical Sciences), Secunderabad. The approval of the Ethical Committee of the hospital was taken before starting the study. Written informed consent was taken from all subjects before data collection. Various demographic and clinical parameters were noted by the investigators in a Data Collection Sheet (with the help of a Cardiologist in case of patients).

B. Selection criteria

1) Inclusion Criteria: Controls -healthy individuals above 40 years of age.

Cases - angiographically documented CAD cases (unstable/stable Angina, ST elevated Myocardial Infarction, Non ST elevated Myocardial Infarction) aged 30-85 years.

2) Exclusion criteria: Controls -individuals with CAD, Stroke, and Peripheral Artery disease (PAD).

a) Cases -i) patients with Stroke, PAD and Cardiomyopathies.

b) Patients with renal, hepatic, gastro intestinal disorders etc,

c) Patients with infectious diseases like HIV, Hepatitis, Tuberculosis etc.

C. Study parameters

The variables included in the study were: Age, Sex, height, weight, ABO and Rh blood groups, Systolic and Diastolic blood pressure, Diabetes and duration of Diabetes, Hypertension and duration of Hypertension, Hyperlipidemia in the last 6 months, food habits – Vegetarian or Mixed diet, Smoking habit, Alcohol consumption, Physical Exercise, Family History of CAD, and number of Coronary arteries affected in case of CAD patients.

D. Statistical analysis

Percentages among Controls and Cases have been calculated based on the total number of individuals who provided information for the various parameters. Missing information has not been included in the calculation of percentages. The data were entered in MS Excel and analysed using Excel in-built functions and further statistical processing and analysis were performed using IBM SPSS software version 20.

III.RESULTS AND DISCUSSION

A study of demographic and clinical parameters in the study population revealed a higher proportion of males, individual history of Diabetes Mellitus, Hypertension, Hyperlipidemia, Smoking habit, Alcohol consumption and Mixed diet in CAD cases as compared to Controls. However, there is a higher frequency of vegetarians (non-meat eaters), regular fruit consumers and exercisers/physically active individuals in Controls than in Cases [Table I, Fig.1and 2]. Most of these results are consistent with the risk factors that have been identified in previous studies. BMI is comparable in Controls and Cases, with Controls having a slightly higher mean value. This may be due to the fact that the average age of Controls is higher than that of Cases. There is generally an increase in BMI with age. This might also indicate that the occurrence of CAD in our population is more premature, with genetic susceptibility being a predominant risk factor so that the effect of obesity as a risk factor is obscured. Male sex has been implicated as a risk factor for CAD, especially men above 45 years of age. Men are at greater risk of heart disease than pre-menopausal women [10]. A similar trend was observed in our study population - more males are affected at a younger age as compared to females (Table I and IV).

Diabetes and Hypertension are two co-morbid conditions highly associated with CAD consistently across all populations. Table II reflects a similar trend in our study population. Patients with diabetes are 2-8 times more likely to experience future cardiovascular events such as Myocardial Infarction than age-matched and ethnically matched individuals without diabetes [11]. According to the Framingham Heart Study, even high to normal blood pressure (defined as a systolic blood pressure of 130-139 mm Hg, diastolic blood pressure of 85-89 mm Hg, or both) increased the risk of cardiovascular disease 2-fold, as compared with healthy individuals [12].Hyperlipidemia/dyslipidemia accelerates the process of atherosclerosis. The Framingham Heart Study results demonstrated a

positive correlation between cholesterol levels and CAD; alternatively, CAD was found to be less frequent in people with cholesterol levels below 150 mg/dL. A similar trend is reflected in our study (Fig.1, Table I).The proportion of Hyperlipidemics might be an underestimate in both Controls and Cases, reasons being - many normal individuals do not get a lipid profile done regularly unless indicated by a physician and generally CAD affected patients take Statins (lipid lowering drugs).Therefore the lipid profile reports were normal in many CAD patients.

Smoking is a modifiable risk factor strongly associated with CAD. The nicotine and carbon monoxide in cigarette smoke damage the arterial endothelium, setting the stage for the build-up of plaque. Cigarette smoking increases inflammation, thrombosis, and oxidation of low-density lipoprotein cholesterol (LDL-C). Recent experimental and clinical data support the hypothesis that cigarette smoke exposure increases oxidative stress as a potential mechanism for initiating atherosclerotic cardiovascular disease [13].Moderate alcohol consumption has been associated with reduced Cardiovascular disease risk, but heavy consumption has large negative medical and social consequences [14]. These findings are validated in our study (Fig.2, Table I).

The distribution of ABO and Rh blood groups in Controls and Cases is shown in Table II. The severity of CAD among Cases is given in terms of the number of vessels/coronary arteries affected (Fig 3). The severity of CAD in different age groups for both males and females is shown in Table IV. The data corroborates the fact that the disease manifests earlier in men with more severity as compared to women. In Asian Indians, CAD is known to have a strong familial component. In this population, there is a higher prevalence of premature, very severe, extensive/diffuse CAD (plaque formation occurs at several locations in the artery) that follows a malignant course with high mortality [15]. In our study population, 109 of 218 Cases (50%) showed premature CAD (disease starts at <55 years in men and <65 years in women), indicating a significant proportion of premature cases. The correlation between different demographic and clinical variables in our study population is displayed in Fig. 4.

IV. CONCLUSIONS

This study validates the role of traditional risk factors (some of which are modifiable) that predispose individuals to CAD in our population. Therefore, modifications in lifestyle such as intake of low fat, high fibre food, appropriate physical exercise, effective stress management, regular health monitoring, especially for individuals with a family history is very essential in the Asian Indian population to prevent and manage the epidemic of CAD. This study also shows a significant frequency of premature CAD in our population emphasizing the importance of identifying genetic risk factors that can help in risk prediction and disease management in affected families. Effective measures to reduce the burden of risk factors and implementation of essential long-term primary and secondary preventive medical strategies are required to fill the lacuna in the management of CAD in current clinical practice.

V. ACKNOWLEDGMENT

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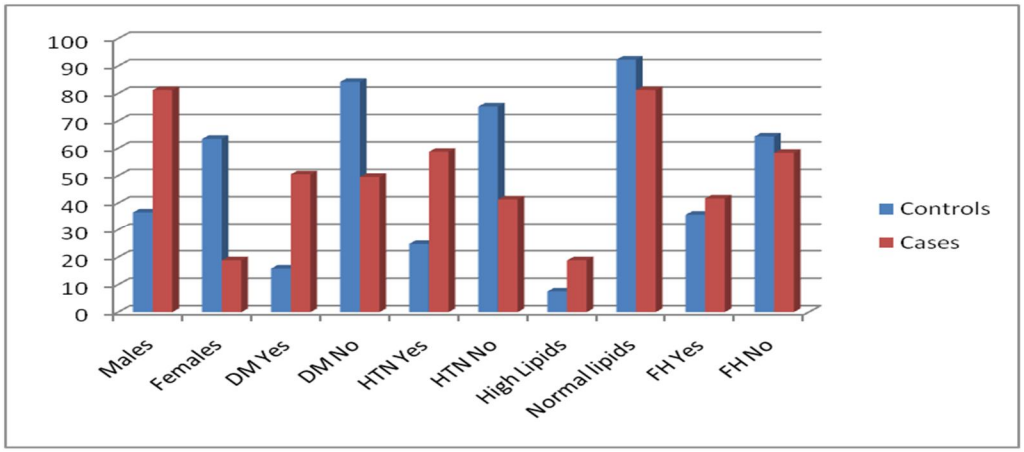

Fig. 1 Demographic Data Analysis

In the present study a higher frequency of males, individual history of Diabetes Mellitus, Hypertension, Hyperlipidemia and Family History was found in CAD patients as compared to Controls.DM – Diabetes Mellitus, HTN – Hypertension, FH – Family History

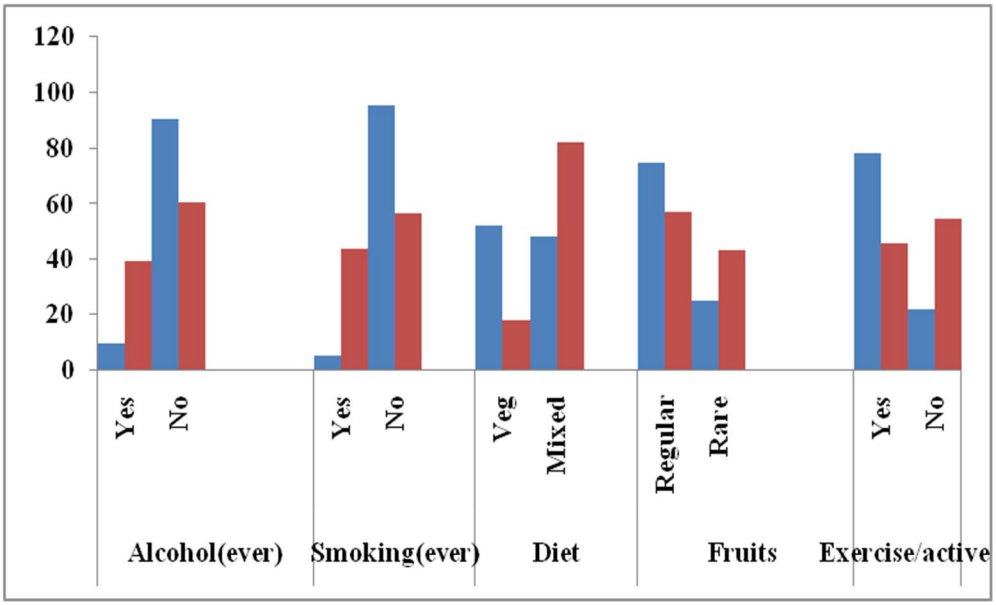

Fig. 2 Comparison of Lifestyle and Food Habits among subjects under study

In the present study, a higher frequency of individuals with alcohol consumption, smoking habit, mixed diet (veg & non-veg) was found in CAD patients as compared to Controls. Regular fruits intake and Exercise was found at a higher frequency in Controls as compared to Cases.

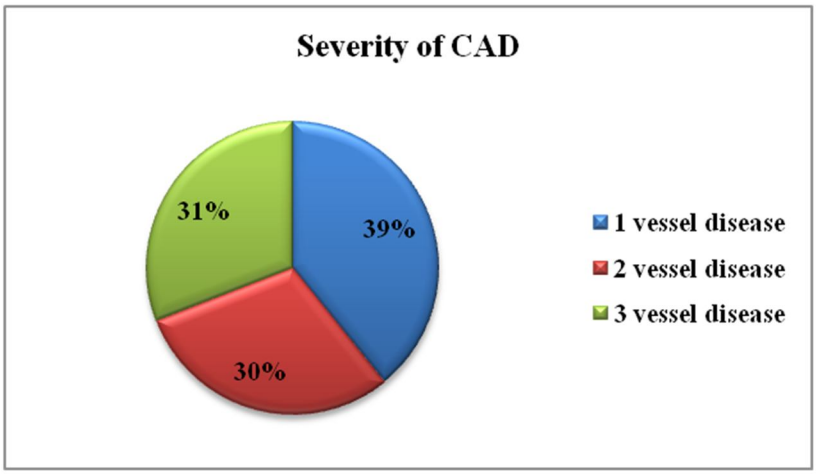

Figure 3: Pie diagram representing the percentage of vessel disease in CAD patients

		AGE	BP	FOOD	FRUITS	EXERCISE	BEVERAGES TAKEN	ALCHOHOL	NO. OF PEGS	SMOKING	Cigars/ Day	BMI	FAMILY HISTORY	VD	DIABETIC
AGE	r	1													
	SIG	.													
BP	r	-0.32	1												
	SIG	0.00	.												
FOOD	r	-0.17	-0.02	1											
	SIG	0.01	0.75	.											
FRUITS	r	-0.06	-0.03	0.07	1										
	SIG	0.36	0.63	0.29	.										
EXERCISE	r	-0.15	0.17	0.09	0.25	1									
	SIG	0.03	0.01	0.16	0.00	.									
BEVERAGES TAKEN	r	-0.15	0.02	0.06	0.02	0.12	1								
	SIG	0.03	0.73	0.34	0.82	0.07	.								
ALCHOHOL	r	0.20	-0.13	0.00	-0.06	-0.15	-0.05	1							
	SIG	0.00	0.06	0.95	0.41	0.02	0.46	.							
NO. OF PEGS	r	-0.17	-0.02	0.27	0.15	0.05	0.09	0.04	1						
	SIG	0.01	0.83	0.00	0.03	0.46	0.17	0.57	.						
SMOKING	r	0.13	-0.20	0.04	-0.06	-0.12	-0.08	0.16	0.02	1					
	SIG	0.06	0.00	0.60	0.40	0.09	0.24	0.02	0.76	.					
CIGARS/DAY	r	-0.18	0.12	0.10	0.17	0.09	0.26	-0.02	0.31	-0.12	1				
	SIG	0.01	0.09	0.15	0.01	0.16	0.00	0.74	0.00	0.07	.				
BMI	r	-0.06	-0.09	0.02	-0.06	-0.13	-0.01	0.07	0.05	0.00	0.00	1			
	SIG	0.39	0.19	0.76	0.34	0.05	0.85	0.28	0.44	0.98	0.96	.			
FAMILY HISTORY	r	0.09	-0.06	0.03	0.02	-0.01	0.02	0.04	0.06	0.07	-0.07	0.00	1		
	SIG	0.17	0.36	0.69	0.80	0.84	0.79	0.54	0.39	0.32	0.27	0.97	.		
VESSEL DISEASE	r	0.09	-0.06	0.03	0.02	-0.01	0.02	0.04	0.06	0.07	-0.07	0.00	1	1	
	SIG	0.17	0.36	0.69	0.80	0.84	0.79	0.54	0.39	0.32	0.27	0.97	0.		
DIABETIC	r	-0.23	0.27	0.03	-0.11	0.07	0.03	-0.01	0.13	0.06	0.15	-0.16	-0.19	-0.19	1
	SIG	0.00	0.00	0.64	0.09	0.30	0.65	0.85	0.06	0.39	0.03	0.02	0.01	0.01	.
		AGE	BP	FOOD	FRUITS	EXERCISE	BEVERAGES TAKEN	ALCHOHOL	NO. OF PEGS	SMOKING	Cigars/ Day	BMI	FAMILY HISTORY	VD	DIABETIC

Figure 4 Pearson's Correlation Coefficient among different Demographic and Clinical Variables

In the present study, Pearson's correlation coefficient showed significant positive correlation between- Age v/s BP, DM, lifestyle habits; Family history v/s Vessel disease; DM v/s Age, BP, Cigars/day, BMI, FH, Vessel disease.

BP –High Blood pressure/Hypertension, DM – Diabetes Mellitus, BMI – Body Mass Index, FH – Family history, VD-vessel disease/ number of vessels affected.

TABLE I
Baseline Characteristics Of The Study Population

Demographic/Clinical parameter	Controls	Cases
Age (Mean±SD)	51.8±9.8	55.9±10.7
Percentage ofMales	36.6	81.2
Percentage of Females	63.4	18.8
BMI (Mean±SD)	26±4.9	25.4±3.8
Systolic BP (Mean±SD)	121.4±6.7	125.7±18.1
Diastolic BP (Mean±SD)	80.8±5.9	76.6±10.7
Percentage of Diabetics	15.8	50.5
Percentage of Hypertensives	25	59
Percentage of Hyperlipidemics	8	19
Percentage having family history of CAD	30	39.4
Percentage of cigarette smokers (ever)	4.7	43.6
Percentage of alcoholics (ever)	9.5	39.5
Percentage of non-meat eaters	52	17.9
Percentage of regular fruit consumers	75	56.9
Percentage of regular exercisers/physically active individuals	78.4	45.5

TABLE II
ABO and RH BLOOD GROUP ANALYSIS

Subjects	ABO blood group	Rh blood group	
		+	-
Controls	A	57	6
	B	96	4
	AB	20	0
	O	155	12
Patients	A	42	8
	B	69	14
	AB	12	6
	O	57	5

The frequency of O blood group was highest in Controls (155/350 =44.3%) and frequency of B blood group was highest in Cases (69/213 =32.4%). Rh positive blood group was highly predominant in both Controls (328/350=93.7%) and Cases (180/213=84.5%).

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TABLE III
COMPARISON of DIABETES v/s HYPERTENSION among STUDY SUBJECTS

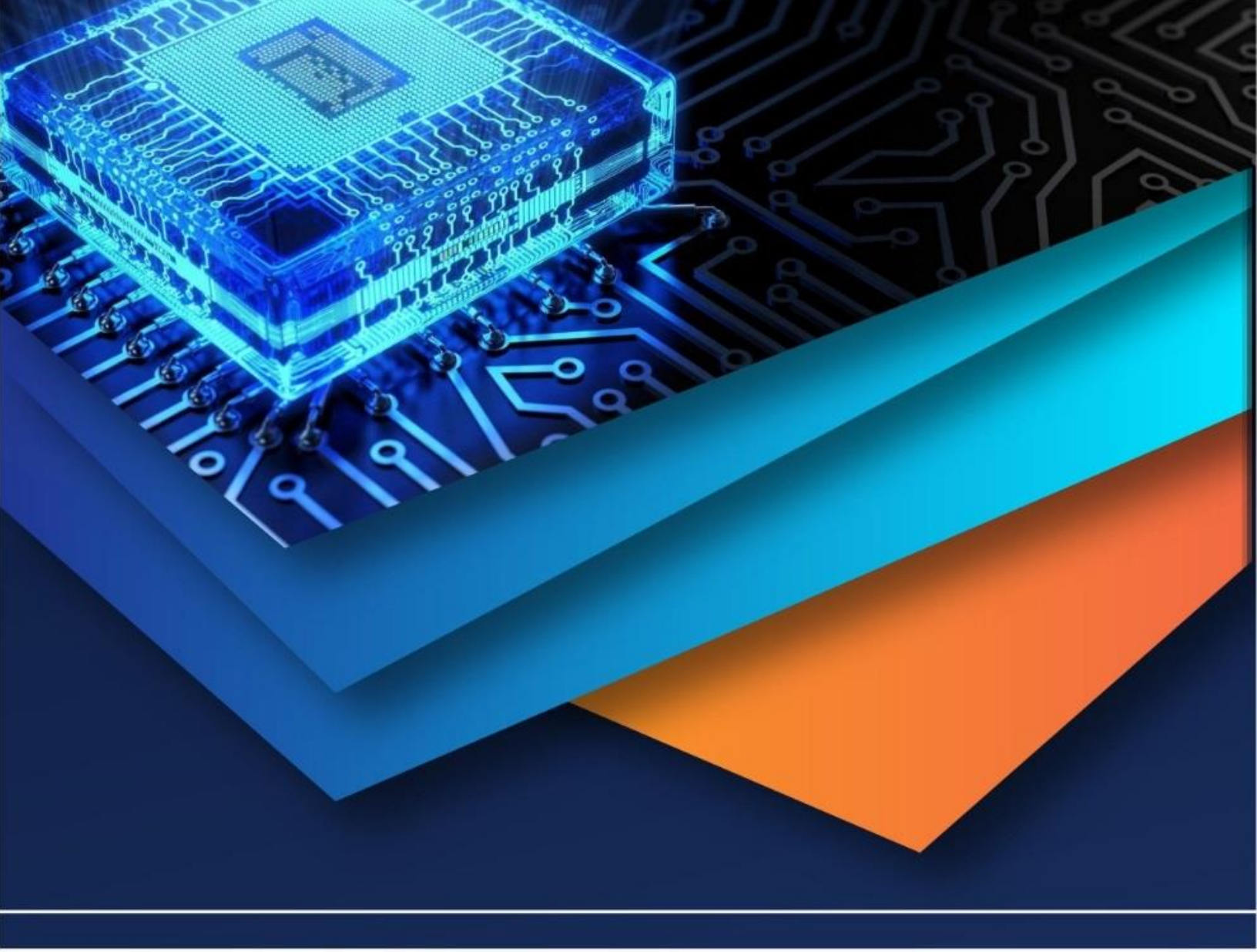
	Diabetes	HTN		Total
		Yes	No	
Controls	Yes	42	28	70
	No	68	305	373
Patients	Yes	79	31	110
	No	49	59	108

The impact of DM and hypertension on CAD was assessed in our population. The results have revealed that 79/218 (36.2%) patients had a history of both DM and HTN, whereas 42/443 (9.5%) controls had a history of both DM and HTN

TABLE IV
AGE v/s VESSEL DISEASE in MALE and FEMALE CAD PATIENTS

	AGE (years)												
	31-40		41-50		51-60		61-70		71-80		81-90		
Vessel disease	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female	Total
1	11	0	11	7	25	4	18	6	2	2	0	0	86
2	6	0	18	0	16	5	14	3	5	1	1	0	69
3	5	0	9	3	17	2	16	6	3	2	0	0	63
Total	22	0	38	10	58	11	48	15	10	5	1	0	218

Age wise distribution of CAD patients according to Vessel disease has revealed that majority of males in 51-60 yrs group and females in 61-70 yrs group had 3 vessel disease. The 3 vessel disease was more common among male CAD patients



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