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Coronary Artery disease prevalence in Patients having essential hypertension with or without Diabetes Mellitus Detected by Cardiac MIBI Scan

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ABSTRACT

BACKGROUND & OBJECTIVE: The aim of this retrospective study was to find the prevalence of coronary artery disease (CAD) in hypertensive patients with or without diabetes mellitus.

METHODOLOGY: Data of patients having essential hypertension (n=931) referred to PINUM from April 2017 to December 2018 for stress/rest cardiac MIBI scan was analyzed. This data was divided into two groups. HD group contains data of patients having hypertension with diabetes mellitus (n=456, 48.98% of total population, M:F=245:211). While data of patients having hypertension without diabetes mellitus was placed in H group (n=475, 51.02% of total population, M: F=254:221).

RESULTS: Prevalence of CAD is higher in HD group than in H group (47.8% vs. 30.1%; p<0.001). CAD is more prevalent in males than females in both groups (53.9 % vs. 40.8% in HD group, and 39.4% vs. 19.5% in H group). This difference in prevalence of CAD in HD and H groups is more marked in females (40.8% vs. 19.5%; p<0.001) than males (53.9 % vs. 39.4%; p=0.001). Prevalence of CAD in patients with typical presentation is not statistically significant in HD and H groups (72.3% vs. 68.4%; p=0.645), while in subjects with atypical presentation prevalence is significantly higher in HD group than H group (40.8% vs. 26.8%; p<0.001).

CONCLUSION: Prevalence of CAD is higher in the group of patients having essential hypertension with diabetes mellitus than the group of patients having essential hypertension without diabetes mellitus.

**KEYWORDS:** Coronary artery disease, Hypertensive, Diabetes mellitus.

INTRODUCTION

Cardiac MIBI scan is a widely used technique of nuclear medicine employed to non-invasively assess status of myocardial perfusion. It can be used as a gateway for screening patients going to cath-lab for percutaneous transluminal coronary angiography (PTCA). MPS is satisfactorily sensitive, cost effective and non-invasive and gives adequate information about cardiac perfusion abnormalities [1]. It has an edge of identifying perfusion defects due to microangiopathies, that can occur in multitude of diseases, especially essential hypertension and diabetes mellitus [2].

The burden of essential hypertension and diabetes mellitus is increasing day by day due to increasing consumption of a highly refined diet, sedentary lifestyle and multiple other risk factors. These in turn lead to a high incidence and prevalence of coronary artery disease (CAD) all over the world causing substantial morbidity, mortality and economic burden.

Essential hypertension and diabetes mellitus are known strong risk factors for CAD. It is widely observed and reported that the concomitant presence of these two risk factors substantially increases the chances of CAD. Information about status of myocardial perfusion in such a population will be highly helpful to ascertain prevalence of CAD [3]. This in turn would lead to judicious and cost-effective use of resources with better, long term patient management [4]. Little work is done using MPS for screening such a high-risk population. Cardiac catheterization, which is the gold standard for CAD diagnosis, cannot be frequently
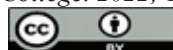
used due to its invasive nature, in a large number of patients just to find prevalence of CAD [5].

In this retrospective study, prevalence of CAD was determined in patients having essential hypertension, with or without diabetes mellitus. Data for this retrospective analysis was collected from hospital records of patients that underwent cardiac MIBI scan at PINUM from April 2017 to December 2018.

METHODOLOGY

This descriptive, cross-sectional study was done from April 2017 to December 2018 in Punjab Institute of Nuclear Medicine (PINUM), Faisalabad (ERC/2017/4/PINUM). Data of all Hypertensive patients, who were referred to PINUM for cardiac MIBI scan, was included in the study. Data of all non-hypertensive patients who were referred to PINUM for cardiac MIBI scan was excluded from this study. Data of patients with known CAD was also excluded. Standard exclusion criteria for cardiac MIBI scan was also applied. therefore, pregnant and lactating females, patients with unstable angina, patients with hypertrophic obstructive cardiomyopathy (HOCM), cerebrovascular accident (CVA) and aortic stenosis (AS) were not included in the study. This data was divided into two groups; HD group and H group. HD group contains data of patients having essential hypertension (HTN) with diabetes mellitus (DM). H group consists of data of patients having essential hypertension (HTN) without diabetes mellitus (DM).

Patients included in this study had gone through myocardial perfusion scintigraphy with different radiotracers/ pharmaceuticals, as per availability, according to hospital routine. Radiotracers used were 201Tl, 99mTc labeled MIBI (methoxy-isobutyl-isonitrile) and 99mTc labeled Tetrofosmin (myoview). Kits of MIBI and generator of 99mTc were supplied by Pakistan Institute of Nuclear Sciences and Technology (PINSTECH) Islamabad. 201Tl in the form of Thallous Chloride, and cold kits of Tetrofosmin were supplied by GE Health. Patients had gone through stress and rest Cardiac scan on separate days for 99mTc labeled radiopharmaceuticals. Stress and redistribution studies were done on the same day for 201Tl. Siemens E.CAM gamma camera was used for acquisition of all studies.

Data compilation, prevalence analysis, calculations of mean and standard deviation, etc. in different groups was done with Statistical Package for Social Sciences (SPSS) version 25. SPSS was also used for $\chi 2$ (Chi-square) test, to determine the statistical significance of the difference observed in the prevalence of CAD in HD and H group patients. A value of p<0.05 was taken as statistically significant.

RESULTS

Data of patients was quite similar regarding gender (male: 49.1% vs. 50.9%, and female: 48.8% vs. 51.1%) and age (mean + SD= 52.4 + 10.2 vs. 48.7 + 10.9 years, range: 27-80 vs. 23-80) in HD and H groups respectively. Average

duration of hypertension was 5.2+5.0 years and 5.6+5.5 years in HD and H groups respectively. Mean duration of diabetes mellitus in HD group was 7.0+5.8 years) (Table-I). Symptoms of presentation varied considerably in HD and H groups. Typical chest pain presentation was more common in males than females of HD group (62.4% vs. 37.6%) and H group (71.1% vs. 28.9%). Among the patients who presented with atypical symptoms, distribution in both genders was almost similar in HD group and H group (male: 51.3% vs. 51.9%, Female 48.7% vs. 48.1%).

No risk factor other than HTN or DM was associated in 43.2% and 54.9% of the patients in HD and H groups respectively. History of smoking was found in 13.8% of HD group and 21.9% of H group patients, while family history of CAD was observed in 24.3% of HD group and 29.3% of H group subjects (Table-II).

Out of 456 patients in HD group and 475 patients in H group, prevalence of CAD was almost 1.5 times higher in HD group (47.8%) than H group (30.1%) and $\chi 2$ test showed this difference in prevalence of CAD to be statistically significant (p = 0.0001). Out of 238 patients in HD group and 332 patients in H group, prevalence of ischemia was almost 2 times higher in HD group (31.9%) than H group (18.7%), p = 0.0001. Out of 162 patients in HD group and 270 patients in H group, prevalence of MI was 16% in HD group and 11.1% in H group (p=0.139).

Prevalence of CAD was significantly higher in patient who presented with angina as compared to those with atypical presentation in both HD and H groups. In HD group patients who presented with typical angina72.3% had CAD as compared to patients in H group 68.4% had CAD. Application of $\chi 2$ test showed that this difference of prevalence in patients with typical presentation was not statistically significant (p=0.654). However, in HD group patients with atypical presentation 40.8% had CAD as compared to patients in H group 26.8% had CAD, (p=0.0001).

In HD group patients with typical presentation 46.4% had ischemia as compared to patients in H group 33.3% had ischemia, (p = 0.443). However, in HD group patients with atypical presentation 29.5% had ischemia as compared to patients in H group 18.4% had ischemia, (p=0.003). In

Table-I: Demographic Data of the Study Population.

Total (n)		HD group	H group	All
		456	475	931
Gender	Male (n)	245	254	499
	Female (n)	211	221	432
Age (years)	Mean±SD	52.4±10.2	48.7±10.9	50.5 10.7
Duration of HTN (years)	Mean±SD	5.2±5.0	5.6±5.5	5.4 5.2
Duration of DM (years)	Mean±SD	7.0±5.8	Not applicable	7.0
			Not applicable	5.8

HD group patients with typical presentation 33.3% had MI as compared to patients in H group 25% had ischemia, (p = 0.679). However, in HD group patients with atypical presentation 15.5% had MI as compared to patients in H group 10% had MI, (p=0.095).

Prevalence of CAD increases with increasing age in both groups. In HD group, prevalence of CAD was 25%, 44.8%, 49.5% and 64.3% in patients with age; less than 36 years, 36-50 years, 51-65 years and greater than 65 years respectively. In H group patients, CAD was found in 13.2%, 25.7%, 40.28% and 45.5% subjects with age; less than 36 years, 36-50 years, 51-65 years and greater than 65 years

respectively. Prevalence of ischemia and MI behaved with a trend similar to that of CAD, i.e., prevalence increases with increasing age.

Table-II: Associated Risk Factors in HD and H Groups.

Risk factors for CAD	HD group	H group
No other risk factor	197 (43.2%)	261 (54.9%)
Smoking	63 (13.8%)	104 (21.9%)
Family history of CAD	111 (24.3%)	139 (29.3%)
Hyperlipidemia	68 (15%)	44 (9.3%)
Obesity	129 (28.3%)	131 (27.6%)

Table-III: Coronary artery disease in HD and H Groups.

Variables		Group		Total	Total	p-value
		HD	H			
Coronary artery disease	Yes	218(23.42%)	143(15.36%)	361(38.78%)		<0.001
	No	238(25.56%)	332(35.66%)	570(61.22%)		
	Total	456(48.98)	475(51.02%)	931 (100%)		
Ischemia	Yes	76(13.33%)	62(10.88%)	138(24.21%)		<0.001
	No	162(28.42%)	270(47.37%)	432(75.79%)		
	Total	238(41.75%)	332(58.25%)	570 (100%)		
Myocardial infarction	Yes	26(6.02%)	30(6.94%)	56(12.96%)		0.139
	No	136(31.48)	240(55.56%)	376(87.04%)		
	Total	162(37.50%)	270(62.50%)	432 (100%)		

Table-IV: Coronary artery disease in HD and H Groups according to symptoms of presentation.

Symptoms	Variables		Group		Total	p-value
			HD	H		
	Coronary artery disease	Yes	73	26	99	0.654
		No	28	12	40	
		Total	101	38	139	
Typical Angina	Ischemia	Yes	13	4	17	0.443
		No	15	8	23	
		Total	28	12	40	
	Myocardial infarction	Yes	5	2	7	0.679
		No	10	6	16	
		Total	15	8	23	
Atypical Presentation	Coronary artery disease	Yes	145	117	262	<0.001
		No	210	320	530	
		Total	355	437	792	
	Ischemia	Yes	62	59	121	0.003
		No	148	261	409	
		Total	210	320	530	
	Myocardial infarction	Yes	23	26	49	0.095
		No	125	235	360	
		Total	148	261	409	

DISCUSSION

In this retrospective analysis, prevalence of CAD was estimated in essential hypertensive (HTN) patients with and without diabetes mellitus (DM) by using SPECT cardiac

MIBI scan. Our study showed a statistically significant difference in prevalence of CAD between HD and H groups, prevalence being almost 1.5 times more in HD group than H group (47.8% vs. 30.1%, p<0.001). Difference in prevalence of ischemia was almost 2 times higher in HD group than H

groups. This high prevalence of CAD in HD than H group highlights the importance of diabetes mellitus as a major risk factor for CAD, as shown by different other research workers in their work correlating different CAD risk factors with the likelihood of CAD [6,7]. Diabetes mellitus has been found as an independent risk factor for CAD, irrespective of the fact whether other risk factors are present or absent [8] Our results are similar to those of Lacourciere et al [9]. They conducted MPS in 1116 hypertensive patients without known coronary artery disease (CAD), and found CAD in 28.9% of patients. In their study the prevalence of CAD was higher in hypertensive patients with diabetes mellitus (DM) than without diabetes mellitus (35.9% vs. 23.9%; odds ratio, 1.79; 95% confidence interval, 1.38-2.33; p<0.0001). Their reported prevalence is somewhat less than that of our study, and is most likely related to different set of population. Although many studies had been conducted to determine the prevalence of CAD in diabetic patients, only few studies are available which compare the prevalence of CAD in hypertensive subjects with and without diabetes mellitus. Reported prevalence of CAD in diabetic subjects in various studies markedly varies due to different set of population and criteria used by different researchers [10].

In hypertensive subjects without diabetes mellitus, who are on adequate treatment, reported prevalence of CAD is almost similar to that of non-hypertensive subjects, as shown by Elhendy et al in their study. They compared the prevalence and extent of stress induced myocardial perfusion abnormalities in 350 patients without known CAD, including 146 hypertensive patients, by using dobutamine stress 99mTc myocardial perfusion SPECT imaging. They reported prevalence of CAD in hypertensive and non-hypertensive subjects to be 28% vs. 31% in patients with low, 38% vs. 33% in patients with intermediate and 60% vs. 58% in patients with high pretest probability of CAD, respectively. They found that treated HTN patients without known CAD have a similar prevalence and severity of myocardial perfusion abnormalities, compared with normotensive patients with similar clinical characteristics [11].

The risk of cardiovascular events in patients with diabetes is twofold to fourfold greater than individuals of same age and sex without diabetes [12]. Patients of hypertensive diabetes had a higher risk of cardiovascular events, the risk of myocardial infarction was 12.2 times greater and the risk of stroke was 6.1 times greater than non-diabetic hypertensive patients [13].

In our study we found that prevalence of CAD in males was significantly higher than that in females of both HD and H groups. In males, prevalence was slightly higher in HD group than H group, while in females it was almost 2 times higher in HD group than that of H group. The results of study of Manfirini et al showed that women had more traditional risk factor of cardiovascular disease as compared to male counterparts and women also had greater risk of developing cardiovascular events than males [14].

In our study, we found that prevalence of CAD was significantly higher in patient who presented with angina as compared to those with atypical presentation in both HD and H groups. In patients with typical presentation, we found almost similar prevalence of CAD in HD and H groups in males and females. Similar prevalence of CAD in patients with typical presentation in HD and H groups shows that when patient develops typical angina, then extent of prevalence is not dependent on the presence or absence of diabetes mellitus or gender. Observed almost 2 times higher prevalence of CAD in patients with atypical presentation of HD group than H group is due to blunt pain perception caused by autonomic neuropathy in diabetic subjects. As a result of this reduced pain perception, myocardial ischemia or infarction may go unrecognized, resulting in high rates of silent coronary events and events with atypical presentation. Other causes of more common atypical presentation in diabetics include increased pain threshold, increased β-endorphin levels, impairment of pain pathways, smaller ischemic regions in comparison with painful angina, psychological factors and transient platelet micro aggregates [15].

Nesto et al studied 50 consecutive patients with diabetes and 50 consecutive patients without diabetes (irrespective of hypertension), all with ischemia, on exercise. Tl scintigraphy and found that only 14 patients with diabetes compared with 34 patients without diabetes had angina during exertional ischemia. He concluded that absence of angina is an unreliable index of myocardial ischemia in diabetic patients with coronary artery disease [16]. Aslam et al [17] conducted myocardial perfusion scintigraphy in 266 diabetic subjects who were either asymptomatic or having atypical presentation, and found CAD in 52.6 % subjects (inducible ischemia in 40.6% and MI in 12% subjects). In totally asymptomatic subjects of their study, this prevalence of CAD was 46.1%, while in other subjects with atypical presentation CAD was present in 61.4% subjects. Prior et al [18] also found silent stress induced perfusion defects in diabetic patients, at a rate almost similar to that in patients with a history of chest pain. However, these two researchers did not separate the typical angina patients from patients with atypical chest pain.

In our study, we found that prevalence of CAD increases with increasing age in both HD and H groups. Prevalence of ischemia and MI behaved with a trend similar to that of CAD, i.e. prevalence increases with increasing age. We found that although prevalence of CAD increases with increasing age in both groups, this increase was more marked in HD group than H group. It is explainable on the basis that rate of atherosclerosis increases with increasing age, and progression of atherosclerosis is more rapid in patients with diabetes mellitus than those without diabetes [19].

Our study documented that prevalence of CAD increases with increasing age in all the groups based on clinical presentation in both HD and H groups and is due to increasing rate of atherosclerosis as the age advances [20]. With the exception of HD subjects with age less than 36 years, prevalence of CAD was higher in patients with typical presentation than subjects with atypical presentation in all other subgroups

based on age and clinical presentation in both HD and H groups. This study showed that there is no statistically significant difference in CAD prevalence between HD and H group patients who presented with typical presentation and have age between 36 and 50 years. This comparison could not be done in typical presentation patients with age greater than 65 years because there was no patient in H group of this category. In subgroup of patients who have atypical presentation, prevalence of CAD was higher in HD group than H group subjects of all ages and is explainable on the basis of blunt pain perception in diabetics. In subgroup of patients with age less than 36 years and typical presentation, number of patients was very small in both HD (n=3) and H groups (n=4), and hence results should not be compared, although higher prevalence of CAD was noted in group H than HD group.

CONCLUSION

This study concludes that there is high prevalence of coronary artery disease in hypertensive subjects with diabetes mellitus (HD group) than those hypertensive patients without diabetes mellitus (H group). Prevalence of CAD increases with increasing age and also male predominance. So, we recommend that further extensive studies are needed with larger study populations, preferably conducted at multiple centers to accurately find the prevalence of CAD in different subgroup of patients based on risk factors for CAD. Confirmation and correlation with other modalities like PTCA, CT angiography, MR angiography, etc. should also be done.

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Owais Bin Qadeer Gill: Conception and design, revising it critically for intellectual content, final approval.

Talal Abdul Rehman: Acquisition of data, interpretation of data, final approval.

Hafiz Amjad Hussain: Conceived and designed the analysis. Proof reading of the manuscript.

Muhammed Shahzad Afzal: Acquisition of data, analysis of data, drafting the article, final approval.