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Original Research Article

Correlation between ischemic heart disease and coronary atherosclerosis: an autopsy based cross-sectional study in a tertiary care hospital

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ABSTRACT

Background: The most common cause of ischemic heart disease (IHD) is reduced blood flow due to obstructive lesions in the coronary arteries. In adults, IHD associated with coronary atherosclerosis and acquired forms of cardiomyopathy are the most common findings of autopsies. Aim and objectives were to study age and gender related prevalence of IHD in population of Sonepat district of Haryana and its association with coronary atherosclerosis in autopsy cases.
Methods: A cross sectional study was conducted from April 2019-March 2020 for a duration of one year on 140 post-mortem heart specimens received in the department of pathology at Bhagat Phool Singh government medical college for Women, Khanpur Kalan, Sonepat, Haryana. Sections from various parts of heart and from three main coronary arteries were processed and examined.
Results: In our study, 22 cases (15.71%) of chronic IHD (CIHD) and 7 cases (5%) of myocardial infarction (MI) was observed. The overall prevalence of IHD was 20.7%. All 7 cases (100%) of MI and 95.46% of CIHD revealed atherosclerosis in their coronary arteries. A highly significant statistical correlation was observed between IHD and atherosclerosis $p<0.05$ ($p=0.001$). All the cases of MI and 81.82% of CIHD were observed in more than or equal to 40 years age group.
Conclusions: The awareness regarding atherosclerosis and various preventive and screening of cardiovascular risk factors should be initiated in young population as early as second decade.

Keywords: CIHD, Coronary atherosclerosis, MI

INTRODUCTION

The human heart is a conical muscular organ situated in the middle mediastinum along with other great vessels and nerves. It weighs 250 to 360 gm which constitutes approximately 0.4-0.5% of the body weight. Cardiac myocytes require a constant supply of oxygenated blood for oxidative phosphorylation and energy generation via coronary arteries.[1] Coronary artery disease (CAD) is a major cause of disability and premature death worldwide with atherosclerosis being the major cause.[2,3]

WHO has drawn attention to the fact that CAD is our modern epidemic.[4] Globally, IHD affects around 126 million individuals (1,655 per 100,000) in 2020, which is approximately 1.72% of the world's population and nine million deaths were caused by it.[5] As per 2010 statistics from global burden of disease, 272 death per 100 000 population were due to total cardiovascular diseases of which, 178 deaths per one lac population were alone due to IHD.[5] In India, the cardiovascular disease accounted for 161,865 deaths (27%) out of the total number of 599,500 deaths due to non-communicable disease in

2015.[6] This shows an increasing trend in death due to cardiovascular diseases over the past years and is expected to rise sharply from current prevalence rate of 1,655 per 100,000 population is to 1,845 by the year 2030 which is attributed to population growth, increased longetivity and higher vulnerability because of life style changes.[6,7] Men were more commonly affected than women typically in the fourth decade and increased with age.[6]

According to an update published by American heart association on US population data in 2022, CAD was the leading cause (41.3%) of deaths attributable to cardiovascular disease followed by stroke (17.2%).[2]

IHD represents a group of pathophysiologically related syndromes resulting from MI-an imbalance between myocardial supply and cardiac demand for oxygenated blood. IHD can present as one or more of the four clinical syndromes as MI where ischemia causes frank cardiac necrosis, angina pectoris where ischemia is not severe enough to cause infarction but the symptoms nevertheless portend infarction risk, CIHD with heart failure and lastly as sudden cardiac death.[1] Most common cause of insufficient coronary supply is chronic, progressive atherosclerotic narrowing of epicardial coronary arteries, and variable degree of superimposed acute plaque change, thrombosis and vasospasm.[1]

It is not only difficult but also cost ineffective to study asymptomatic healthy population form prevalence of atherosclerosis and associated cardiac changes, thus autopsy-based studies help in gathering information on epidemiological profile and pathophysiology of heart disease. This autopsy study was conducted in Sonepat district of Haryana to find the prevalence of IHD and correlation with atherosclerosis.

METHODS

A descriptive cross-sectional study was conducted for one year (April 2019-March 2020) on autopsy specimens of heart received in the department of pathology at Bhagat Phool Singh government medical college for Women Khanpur Kalan, Sonepat. The study was approved by institutional ethical committee.

Case selection

A total of 140 autopsy specimens of heart submitted to this institute for post-mortem examination, irrespective of cause of death, were analysed for a duration of one year. The cases were medico legal and relevant clinical details including cause of death were noted from the post mortem examination report and police papers.

Exclusion criteria

Autolytic specimens, heart of children <10 years as well as fetal heart are excluded from the study.

Gross examination of heart specimens

Specimens fixed in 10% formalin were weighed, measured and grossed by inflow-outflow method. Grossly, heart was examined for location of any areas of mottling, fibrosis, rupture or any scar (Figure 1). All the chambers were examined for the presence of any pathology in endocardium and valves. Thickness of both right and left ventricular walls (RVW and LVW) and interventricular septum (IVS) were noted. All three major coronary arteries including right coronary artery (RCA), left circumflex artery (LCA) and left anterior descending artery (LAD) were traced by inserting a probe from their ostias and sectioned at 3 mm interval to examine grossly for presence of atherosclerotic plaque, calcification or thrombus. Sections from various portions of heart including any grossly pathologic areas and coronary arteries were taken and processed.

Figure 1 (A-F): Gross specimen of heart showing gray-white areas of fibrosis in apex. Gross specimen of heart showing areas of fibrosis in apex and left ventricle wall. Gross specimen of heart showing areas of mottling in LVW. Gross specimen of heart showing areas of mottling in LVW. Gross specimen of heart showing atherosclerosis in left anterior descending coronary arteryand gross specimen of heart showing left ventricle hypertrophy in transverse section.

Microscopic examination

Hematoxylin and Eosin stain sections from various portions of heart including apex, IVS, RVW and LVW as well as from major coronary arteries and other pathologically suspected area were examined by two pathologists. Microscopic assessment of atherosclerosis in major coronary vessels was done according to modified American heart association classification

(MAHA) and ischemic changes in heart were studied. These microscopic findings were correlated with available clinical details.

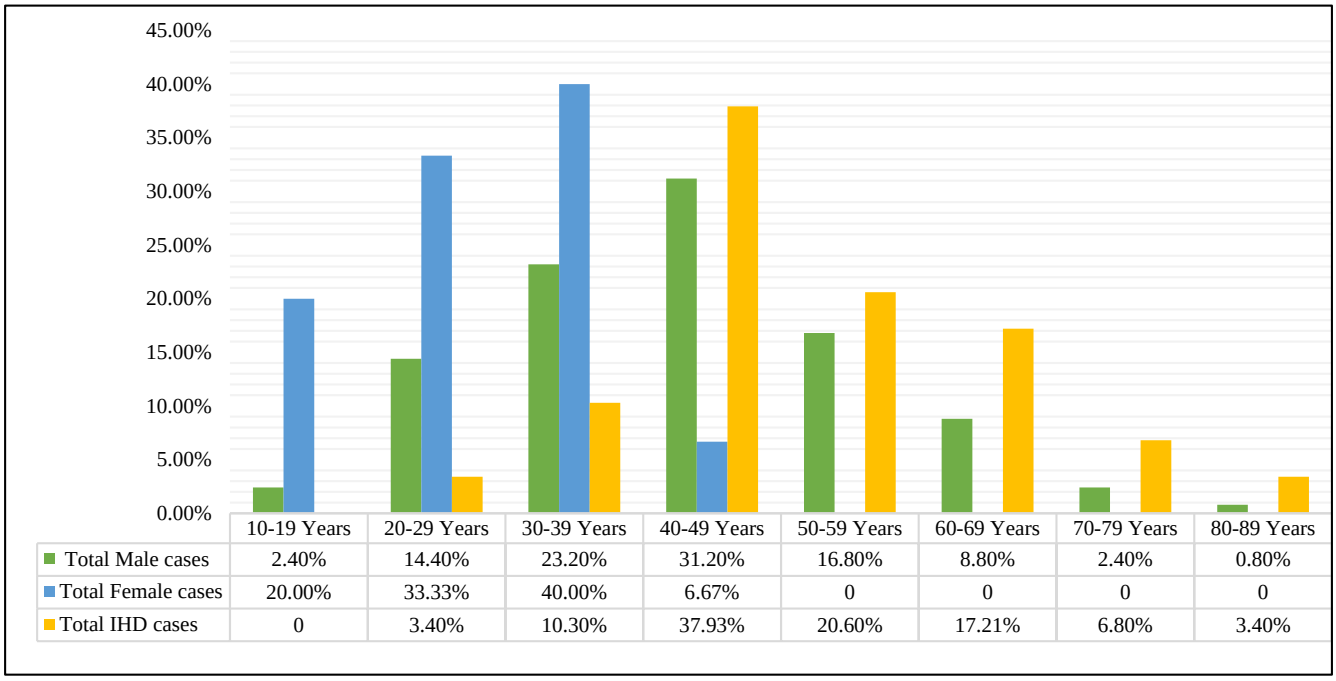
Statistical analysis

The results of the study were statistically analysed using the statistical package for the social sciences (SPSS) version 20. Data were expressed as mean ± standard deviation and range for quantitative variables, numbers and percentage.

RESULT

In this study, demographic data and histopathological findings of 140 autopsy specimens of heart were studied. As illustrated in figure 2, maximum cases were seen in the age group of 40-49 years 40 (28.58%) followed by 35 cases (25%) in 30-39 years of age group and 125 cases were male (89.29%) whereas only 15 were females (10.71%). Youngest case found in this study was 13 years old and eldest case seen was 80 years old. Mean age is 40.6±13.56 years with M:F ratio observed to be 8.3:1. The cases presented with variable causes of death. Majority of them 32 cases (22.8%) had cardiovascular signs and symptoms like chest pain, breathlessness, heart attack and heart failure. Second most common cause of death was poisoning (10.71%) followed by road side accident (8.57%) (Table 1).

Heart weight of 71.30% of male was up to 350 grams and 26.42% weighed between 351-500 gram and only 3 cases weighed more than 500 gm. Weight of heart in 86.67% female cases was less than 300 gram and only two cases (13.33%) with weight ranging between 350-500 grams were noted. Majority of cases (69.28%) were having thickness of left ventricle wall less than 1.5 cm whereas in 30% cases it was found that thickness varied from 1.6 to 2 cm and only one case revealed left ventricular thickness more than 2 cm (Figure 2).



	10-19 Years	20-29 Years	30-39 Years	40-49 Years	50-59 Years	60-69 Years	70-79 Years	80-89 Years
Total Male cases	2.40%	14.40%	23.20%	31.20%	16.80%	8.80%	2.40%	0.80%
Total Female cases	20.00%	33.33%	40.00%	6.67%	0	0	0	0
Total IHD cases	0	3.40%	10.30%	37.93%	20.60%	17.21%	6.80%	3.40%

Figure 2: Age and gender wise distribution of cases.

All three major coronary arteries were examined microscopically for atherosclerosis and categorized into three main groups namely non-atherosclerotic lesions, pathological intimal thickening (PIT) and advanced atherosclerotic lesions based on MAHA classification.

Advanced atherosclerotic lesions comprising of fibrous cap atheroma, plaque rupture, thrombosis and calcification were observed in 119 arteries (28.33%). Maximum cases of advanced lesions were observed in LCA i.e., 50 cases followed by RCA in which 39 cases were reported. In LAD least cases of advanced atherosclerotic lesions i.e., 30 cases were observed. Pathological intimal thickening (PIT) which is intermediate lesion was reported in 56 arteries (13.33%) with maximum cases observed in LAD i.e., 23 cases. Non-atherosclerotic lesions comprising of intimal thickening and intimal xanthoma were the overall most common finding observed in 150 arteries (35.72%) with maximum cases observed in RCA i.e., 54 cases followed by 49 cases in LCA and 47 cases in LAD. In our study 95 arteries (22.62%) were found to be unremarkable with maximum cases in LAD.

In terms of coronary atherosclerosis both PIT and advanced lesions were included. It was observed that

LCA is most frequently involved by atherosclerotic lesions constituting 48.47% followed by 38.57% in RCA and 37.86% in LAD. Overall prevalence of coronary atherosclerosis was 60.71%.

In our study, a total of 29 cases of IHD, of which 22 cases (15.71%) of CIHD and 7 cases (5%) of MI were reported with youngest and oldest case being 26 years and 80 years respectively. All cases were male and none of the case of IHD was female, it might be due to few cases studied. Maximum number of cases 11 cases (37.92%) of IHD were reported in the age group of 40-49 years followed by 06 cases (20.60%) and 5 cases (17.2%) in 6th and 7th decade respectively. As demonstrated in Table 2, 44.80% and 17.2% cases involved LVW and apex respectively. None of the case showed involvement of RVW.

It was observed that in all the seven cases (100%) of MI and 21 cases (95.46%) of CIHD revealed atherosclerosis in their coronary arteries while only one case of CIHD revealed non-atherosclerotic lesion. A highly significant statistical correlation was observed between ischemic heart disease and atherosclerosis with p value less than 0.05 (p=0.001). However, no significant statistical correlation was observed between IHD and the type of coronary artery lesion p>0.05 (MI and atherosclerosis with p=0.341 and CIHD and coronary atherosclerosis with p=0.104) as per illustrated in Table 3.

All the 7 cases (100%) of MI were observed in subjects with age more than or equal to 40 years. Finding of chronic ischemic heart disease was higher in older subjects (81.82%) cases than in younger individuals with age less than 40 years (18.18%). A significant statistical correlation of MI and chronic ischemic heart disease with increasing age was observed with p<0.05 (p=0.016 and p=0.005 respectively).

On evaluating the lumen both grossly and microscopically in arteries involved by progressive atherosclerotic lesions, it was observed that maximum cases had less than 40% lumen obstruction in 74 arteries (42.29%) and 40-75% obstruction reported in 63 arteries (36%) whereas >75% obstruction least commonly reported in 38 arteries (21.71%). More than 75% lumen obstruction was reported maximally in LCA followed by RCA and LAD.

It was observed that more than 75% lumen obstruction of coronary arteries was observed in 5 cases (71.43%) of MI and 9 cases (40.91%) of CIHD whereas 40-75% obstruction of lumen was reported in 2 cases of MI and 8 cases of CIHD (Figure 4). However, only 5 cases of chronic IHD and none of the case of MI revealed <40% lumen obstruction. However, no significant statistical correlation was observed between MI and CIHD with percentage of lumen obstruction p>0.05 (p=0.258 and p=0.159 respectively).

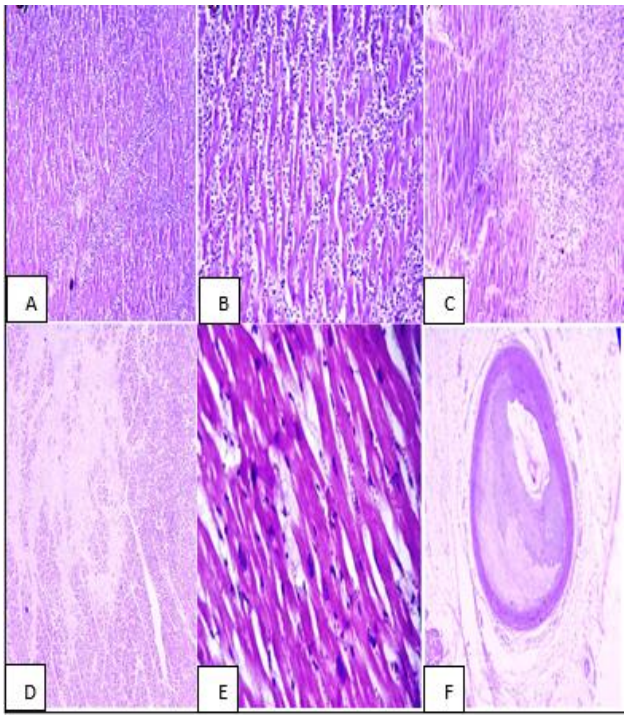


Figure 3 (A and F): Microphotograph of coagulative necrosis of cardiac myocytes along with dense neutrophilic infiltrate in MI (H and E, 100X, 200X), microphotograph of granulation tissue (in left side) with viable myocardium (right side) in case of MI (H and E, 100X), microphotograph of fibrous scar in CIHD (H and E, 40X), microphotograph of increase in both cell size and nuclear size in hypertrophied myocardium suggestive of left ventricle hypertrophy (H and E, 400X). Microphotograph of eccentric fibrous cap atheroma with 75% reduction in lumen of coronary artery (H and E, 40X).

Table 1: Clinical details.

Cause of death	Number of cases (%)
Stomachache	04 (2.85)
Cardiovascular symptoms	32 (22.80)
Pneumonia	01 (0.71)
Poisoning	15 (10.71)
Drowning	02 (1.42)
Postpartum	02 (1.42)
Road side accident	12 (8.57)
Starvation	01 (0.71)
Chronic illness	13 (9.28)
Burn	01 (0.71)
Excess alcoholism	03 (2.14)
Seizures	03 (2.14)
Suicide	01 (0.71)
Electrocution	01 (0.71)
Stroke	01 (0.71)
Unknown	48 (34.28)
Total	140 (100)

Table 2: Distribution of cases according to various location of IHD.

Anatomical location	Number of cases of IHD	Percentages (%)
LVW	13	44.80
Apex	05	17.20
IVS	02	6.88
LVW + Apex	03	10.35
LVW + IVS	02	6.88
IVS + Apex	01	3.44
LVW + IVS + Apex	03	10.35

Table 3: Association of coronary artery lesions with histological findings in heart.

Coronary artery lesions	Unremarkable		LVH		MI		CIHD	
	N	%	N	%	N	%	N	%
Unremarkable	11	10.19	01	33.33	00	00	00	00
Non atherosclerotic lesions	42	38.89	00	00	00	00	01	4.54
PIT	16	14.81	01	33.33	00	00	02	9.10
Advanced lesions	39	36.11	01	33.34	07	100	19	86.36
Total	108	100	03	100	07	100	22	100

Table 4: Association of histological findings of heart with vessel involvement.

Variables	Single vessel involvement		Double vessel involvement		Triple vessel involvement		Total	
	N	%	N	%	N	%	N	%
Unremarkable	23	41.8	14	25.4	18	32.7	55	100
LVH	01	50	01	50	00	00	02	100
MI	00	00	02	28.6	05	71.4	07	100
Chronic IHD	04	19.0	07	33.3	10	47.7	21	100
Total	28	32.9	24	28.2	33	38.8	85	100

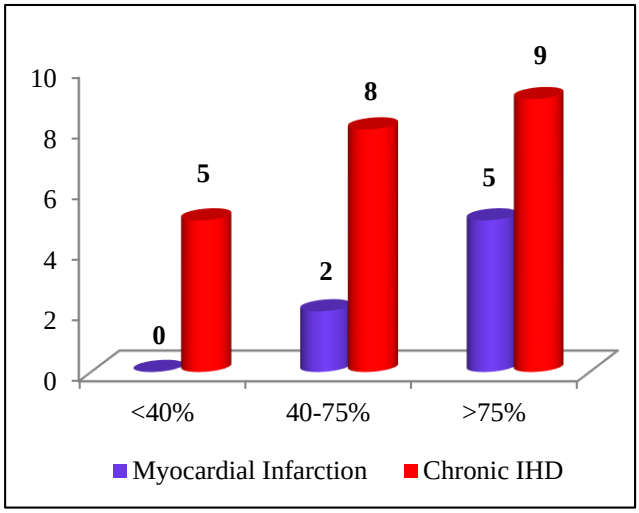


Figure 4: Association of ischemic heart diseases with percentage of lumen obstruction.

DISCUSSION

IHD is most commonly attributed by reduced blood flow due to atherosclerosis which are lipid rich intimal lesions protrude into and obstruct vascular lumen thus weaken the underlying media in the coronary arteries.[8] In developed countries, atherosclerosis peaked in mid 20thcentury and it is now advancing in developing countries like India as they are becoming affluent.[9] Incidence of CAD has doubled in Indians during the past 3-4 decades and will account for one third of all deaths in next few years. The increase in CAD prevalence in India is attributed to social and economic changes and its consequences including change in dietary habits, physical inactivity and increased incidence of diabetes and hypertension. The exact global incidence of atherosclerosis is not possible to calculate as it occurs without producing any signs or symptoms.[10] Sudden cardiac death has a much higher incidence in men than women that increases with age.[11,12]

An autopsy study gives a good measure of prevalence and distribution patterns of IHD and atherosclerotic lesions in a population and thus provide wide spectrum and better correlation with clinical details and interventions made by clinicians at the time of death of the subjects. The present study was conducted in the

department of pathology at BPS GMC (W) Khanpur Kalan, Sonepat. In this study various portions of heart and major vessels RCA, LCA and LAD of 140 autopsy heart specimens were studied to find the prevalence of IHD and its correlation with atherosclerosis and other factors.

In our study, the maximum number of cases (28.58%) were seen in 5th decade followed by 25% cases in 4th decade. Youngest case found in this study was 13 years old and eldest case seen was 80 years old. Mean age is 40.6±13.56 years. Studies conducted by Bhanvadia et al and Rani et al observed similar findings having maximum number of cases included in their study belong to age group of 40-49 years i.e., 20% and 27.8% respectively.[10,13]

In our study out of 140 cases, 125 cases (89.29%) were male whereas only 15 cases (10.71%) were female with M:F ratio of 8.3:1. Our finding were similar to many previous studies in which the frequency of male subjects was higher than female as reported by Yazadi et al, Bhanvadia et al, Rani et al and Thej et al.[9,10,12,13]

In our study, it was observed that 71.30% heart specimens of male weighed up to 350 gm and 86.67% heart specimens of female weighed less than 300 gm. A total of 28.8% specimens in males weighed more than 350 grams whereas in females, only 13.33% specimens weighed more than 300 gm. Similarly, Udhreja et al observed 75% heart weighed less than 350 gm in males and 73.9% heart weighed less than 300 gm in females whereas 25% specimens in males and 26% specimens in females were more than 350 gm and 300 grams respectively.[15]

We observed an overall prevalence of coronary atherosclerosis as 60.71%. Our findings were in concordant with studies done by Thej et al, Bhanvadia et al and Bhandari et al reported coronary atherosclerosis prevalence of 60%, 60.2% and 54% respectively.[10,14,16]

Advanced atherosclerotic lesions comprising of fibrous cap atheroma, plaque rupture, thrombosis and calcification were observed in 119 arteries (28.33%) and PIT in 56 arteries (13.33%) in our study and findings are concordant to Thej et al who reported 22.1% of advanced lesions and 28.9% of PIT.[14]

Coronary atherosclerosis in our study was observed in 48.57% of LCA similarly, Yazadi et al and Bhanvadia et al also found 42.5% and 40% involvement of LCA respectively.[9,10] Furthermore, 38.57% of RCA and 37.86% of LAD were involved by atherosclerotic lesions. Similar to our study, Porwal et al, Garg et al and Bhanvadia et al reported involvement of RCA to be 41.7%, 35.1% and 39% respectively.[10,17,18] However, LAD involvement was reported slightly higher in other studies conducted by Porwal et al and Gupta et al 49.6% and 52.38% respectively.[17,19] In most previous studies, highest frequency of atherosclerosis was observed in LAD, however in our study LCA was the most frequently involved artery. Further studies on higher number of subjects should be conducted.

A total of 29 cases of IHD were reported in our study, of which 22 cases (15.71%) of CIHD and 7 cases (5%) of MI were reported with maximum cases (37.92%) in 5th decade. All IHD cases were male and none was female, it might be due to protective effect of estrogen as well as less female subjects in the study group. MI reported in our study was concordant to Garg et al, Udhreja et al and Rani et al observed in 3%, 5.2%, and 3.09% of cases.[13,15,18] Few previous studies showed slightly higher incidence of MI by Verma et al, Marwah et al and Vyas et al found 8.5%, 15.83% and 10.8% of cases respectively.[20-22] In close concordance to our findings, Vyas et al, Udhreja et al and Rani et al also reported CIHD 13.25%, 15.2% and 13.4% cases respectively.[13,15,22] In contrast, Verma et al, Garg et al, Marwah et al and Sonawane et al observed CIHD in 21.6%, 23%, 40% and 48.27% cases respectively.[18-21,23]

Isolated involvement of LVW and apex in our study was reported in 44.80% and 17.2% cases respectively. Diffuse pattern of involvement was seen in 10.37% cases only. None of the case showed involvement of RVW. In study done by Verma et al and Shah et al most common pattern of involvement was diffuse, followed by involvement of left ventricular wall and interventricular septum.[20,24] Isolated involvement of RVW was not seen in study by Shah et al.[24]

Triple vessel involvement was most frequently observed in 38.8% cases followed by single and double vessel involvement in 32.9% and 28.23% cases respectively. Similarly, Porwal et al and Garg et al reported triple vessel involvement as the most common 40% and 44.4% in their study followed by double and single vessel involvement.[17,18]

Majority of MI cases (71.4%) showed triple vessel involvement and only two cases (28.6%) revealed double vessel involvement. No significant statistical correlation observed between IHD with number of vessel involvement $p>0.05$ ($p=0.110$). Similarly, Jha et al reported triple vessel disease was more commonly associated with MI followed by double and single vessel involvement.[25]

In our study, all the seven cases (100%) of MI and 21 cases (95.46%) of CIHD revealed atherosclerosis in their coronary arteries while only one case of CIHD revealed non-atherosclerotic lesion which might be due to vasospasm. Similarly, Jha et al reported one case of IHD without any atherosclerosis in their study.[25]

A highly significant statistical correlation was observed between ischemic heart disease and atherosclerosis with increasing age in our study with p value less than 0.05

(p=0.001). Similarly, Shah et al also observed that a significant association between increasing age and incidence of ischemic heart disease as well as between coronary atherosclerosis and MI (p<0.05).[24]

However, one case of IHD was reported in younger age of 26 years which states that now-a-days due to sedentary life style and more indulgence in smoking and alcohol as well as junk foods could results in atherosclerotic lesions at an early age of presentation which could result in ischemic changes in myocytes.

On examining the artery lumen in coronary atherosclerosis cases in our study, more than 75% obstruction was reported in 21.71% arteries with most frequently observed in LCA. No significant statistical correlation was observed between MI and CIHD with percentage of lumen obstruction p>0.05 (p=0.258 and p=0.159 respectively). Jain and Biligi (26) found critical narrowing more than 75% seen maximally in LAD and concluded that cross-sectional luminal narrowing of more than 75% is not prerequisite for luminal thrombosis, either acute or healed, or for the development of intraplaque hemorrhage. Virmani et al (27) described that sudden coronary death patients died of luminal thrombosis, at least 50% of the thrombi occurred at lesion sites with less than 75% cross sectional area stenosis by plaque.

Thus, it was concluded that MI and atherosclerosis show statistically significant correlation but even early precursors lesions of atherosclerosis could result in ischemic heart disease along with advanced lesions. Similarly, more ischemic heart disease was seen in male cases. The histopathological changes of IHD correlated in many cases with the alleged cause of death mentioned in police papers like heart attack, chest pain or heart failure. There were more chances to get the features of MI if patient presented with heart attack/chest pain whereas features of CIHD associated with coronary atherosclerosis were found in cases with some chronic illness like diabetes which could be a precipitating factor.

Limitations

The major limitation of our study was relatively lesser number of cases mainly female cases. Moreover, other relevant clinical details could not be obtained. Large number of autopsy cases to be included so that more accurate prevalence of IHD could be obtained.

CONCLUSION

This small autopsy study conducted in Sonepat district of Haryana showed relatively high overall prevalence of both ischemic heart disease and CAD. Thus, this study indicates need of substantial efforts both at individual and community levels to reduce the dreaded effects of this disease. Incorporation of healthy practices including dietary care and physical exercises, reduction of risk factors and availability of diagnostic and treatment facilities need to be augmented. Future researches targeting development of novel medical and surgical modalities for treating atherosclerosis should be promoted**.** Thus, our study will help in providing valuable data to the literature regarding the association of atherosclerotic lesion and various other factors to ischemic heart disease as well as age related prevalence of the dreadful disease.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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