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CORONARY ARTERY DISEASE IN PREMENOPAUSAL WOMEN

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Contribution

SNA & HG conceived the idea and did manuscript writing. KAH did data collection. MAKS did review and final approval of manuscript. All authors contributed equally to the submitted manuscript.

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ABSTRACT

Objective: To determine the frequency of coronary artery disease in premenopausal women.

Methodology: This cross sectional study included premenopausal women (aged 18-40 years) of any parity presenting in Cardiology Emergency Department of Chaudry Pervaiz Elahi Institute of Cardiology, Multan, from 26 July to 25th November 2018, were included in the study by non probability, consecutive sampling with chest pain and breathlessness were included in this study. These patients received standard cardiac care and underwent coronary angiography where diagnosis of CAD was confirmed.

Results: Total of 375 patients were included. Coronary artery disease (CAD) was diagnosed in 147 (39.20%) patients on coronary angiography (CAG). Diabetes was diagnosed in 81 (59.6%) patients having CAD and in 55 (40.4%) patients without CAD ($p<0.0001$). Hypertension was diagnosed in 89 (50.6%) patients with CAD and in 58 (29.1%) patients without CAD ($p<0.0001$). Mean triglycerides in CAD patients was $1.82+0.52$ mmol/L versus $1.41+0.52$ mmol/L in non-CAD patients ($p<0.0001$).

Conclusion: There is a high prevalence of coronary artery disease in symptomatic pre-menopausal women. Diabetes, hypertension and elevated serum triglyceride levels are associated with higher prevalence of CAD.

Key Words: Premenopausal women, Coronary artery disease, Diabetes, Hypertension, Triglycerides.

INTRODUCTION

Coronary artery disease (CAD) is a common cause of mortality among both genders. The risk of developing CAD is lower in females especially premenopausal as compared to males of similar age group. However the same tendency to develop CAD rises after menopause becoming almost equal between males and females at 60-65 years of age. In females above 75 years, the risk is rather more higher in females with higher chances of cardiac mortality.[1] A probable reason for this difference with agecan be the good effects of estrogen on coronary endothelium and cardiovascular system evident from the facts that the estrogen decrease after the menopausal period leads to rise in CAD.[2]

As a result of the reasons mentioned, current studies main topic of research is on females after menopause, including their risk factors and treatment strategy in females who had disease.[3,4] Among cardiology patients disease presentation with chest pain is high in young females yet, as in the past chest pain in females in ER is considered to be due to anxiety especially in young females and CAD is rare among this group.[5,6] However now there is accumulating evidence that CAD is not very rare among young female group in their menopause.[7]

Li et al. (2015) work showed that 42.11% of these young females presenting with chest pain had coronary artery disease on cardiac catheterization. Their study also showed significantly greater frequency of diabetes mellitus (68.7% vs. 28.7%; $p<0.001$), high blood pressure (62.5% vs. 36.3%; $p=0.006$) and higher lipid levels especially TGs levels among those young females with IHD (1.72 ± 0.70mmol/L vs. 1.13 ± 0.60mmol/L; $p=0.004$) in comparison to those who do not have it.[7] Similar blood pressure relation was also shown by work of Ahmad et al. [8]

Due to the results of this study, CAD is found to be a common reason of chest pain in young female group in their menopause and therefore needs standard management and diagnostic tests before diagnosing them as a case of anxiety or stress which can result in poor outcomes. The research has also depicted that diabetes mellitus, high blood pressure and higher serum TGs as probable causes in these female, presence of these risk factors also increseases the chances of IHD.[7] Due to limited research work in this issue, it needs to be explored more scientifically, most of the researches are on females after their menopause. The results of the present study will give an insight into the problem and may identify diabetes, hypertension and higher mean serum triglyceride level as probable causative factors which would help in the risk stratification

METHODOLOGY

It is cross sectional study. After approval from hospital ethical forum, premenopausal women (aged 18-40 years) of any parity presenting with chest pain and breathlessness (respiratory rate$\geq$20/minute)for less than 24 hours who subsequently undergo coronary angiography who present in the emergency department of Chaudry Pervaiz Elahi Institute of Cardiology, Multan were included in the study by non probability, consecutive sampling. Patients with other heart diseases like aortic stenosis, aortic dissection and hypertrophic cardiomyo-pathy as per echocardiographic evaluation were excluded from the study. It's descriptive cross-sectional study done in Chaudry Pervaiz Elahi Institute of Cardiology Multan between 26-July to 25-November 2018. Written informed consent was obtained. These patients received standard cardiac care and underwent coronary angiography where diagnosis of CAD was confirmed as per operational definition. Patients were looked for CAD attributing factors such as diabetes, hypertension and serum triglycerides. Patient's demographic details e.g. age and parity along with coronary artery disease and the attributing factors were recorded in the attached proforma by the candidate. All the patients were assessed clinically by a single resident (candidate himself) under supervision, all the angiographies were performed by a single surgical team and all the labs were acquired from same (hospital's lab) to eliminate bias. Confounding variables have been controlled by exclusion. Others were controlled by stratification.

All the collected data was entered and analyzed through SPSS version 21. Numerical variables age, duration of symptoms, parity and serum triglyceride level were presented by mean $\pm$SD. Categorical variables like coronary artery disease and attributing factors like diabetes and hypertension were presented by frequency and percentages. Chi-square test was applied to compare frequency of diabetes and hypertension in premenopausal women with and without CAD taking $p\leq0.05$ as significant. Independent sample t-test was applied to compare mean serum triglyceride level in premenopausal women with and without CAD taking $p\leq0.05$ as significant.

Data was stratified for age, parity and BMI (weight in kilograms/height in meters^2) to address effect modifiers. Post stratification chi-square test was applied to compare frequency of diabetes and hypertension and independent sample t-test was applied to compare mean serum triglyceride level taking $p\leq0.05$ as significant.

RESULTS

A total number of 375 female patients who presented with chest symptoms in department of emergency of the hospital were included in this study. Mean age of study patients was $29.63+5.34$ years (Figure 1).

There were 176 (46.93%) patients, who were diagnosed of having hypertension. While remaining 199 (53.07%) patients were having normal blood pressure (Figure. 2).

Diabetes mellitus was diagnosed in 136 (36.27%) patients and remaining 239 (63.73%) patients were not having diabetes mellitus (Figure. 3).

Mean serum triglyceride levels of study patients were 1.58 + 0.58 mmol/L (Fig. 7). Coronary artery disease (CAD) was diagnosed in 147 (39.20%) patients on coronary angiography (CAG) reporting (Figure. 4).

Frequency of risk factors of CAD were compared between the CAD and non-CAD patients. Regarding diabetes mellitus, diabetes was diagnosed in 81 (59.6%) patients having CAD and in only 55 (40.4%) patients without CAD. This difference was statistically significant with a $p<0.0001$ (Table 1). Regarding hypertension, hypertension was diagnosed in 89 (50.6%) patients with CAD and in 58 (29.1%) patients without CAD (Table 2).

Regarding triglycerides, mean triglyceride levels were significantly high in CAD patients as compared to non-CAD patients. Mean triglycerides in CAD patients was 1.82+0.52 mmol/L versus 1.41+0.52 mmol/L in non-CAD patients (Table 3).

Stratification of age, duration of symptoms, body mass index and parity status was done to determine the effect of these confounder variables on the frequency of hypertension, diabetes and mean serum triglyceride levels in CAD versus non-CAD patients. There was no effect of these confounders on hypertension, diabetes and serum triglyceride levels.

Figure 1: Descriptive Statistics of Age of Patients (n=375)

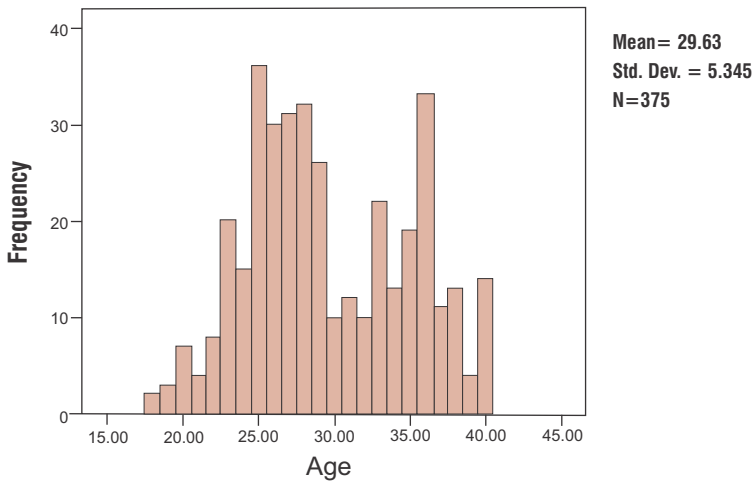

Figure 2: Frequency of Hypertension (n=375)

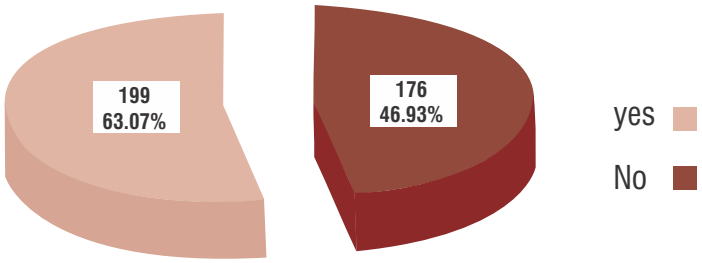

Figure 3: Frequency of Diabetes Mellitus (n=375)

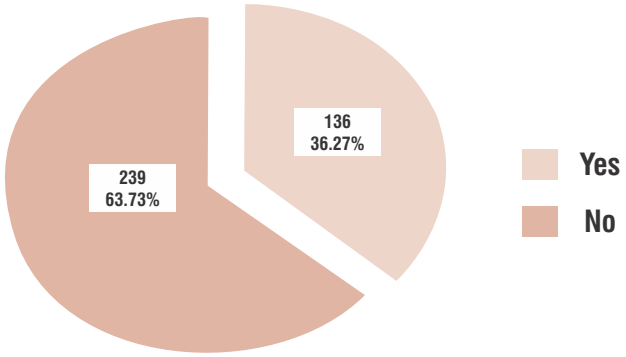

Figure 4. Frequency of Coronary Artery Disease (CAD) (n=375)

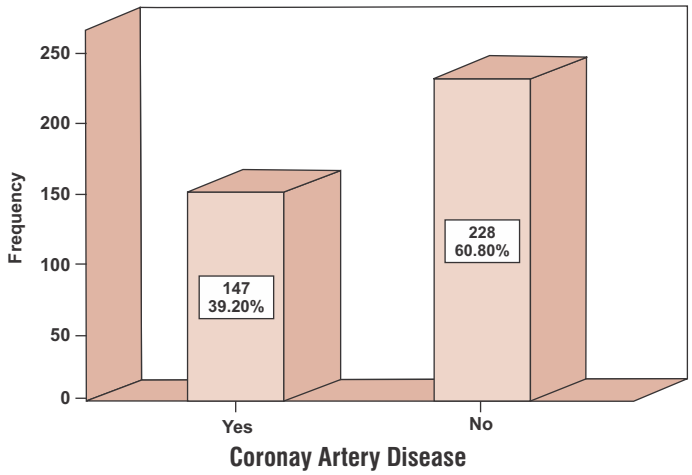

Table 1: Comparison of Frequency of Diabetes Mellitus in Coronary Artery Disease (CAD) Versus Non-Coronary Artery Disease (Non-CAD) Patients (n=375)

Diabetes Mellitus	Coronary Artery Disease		P-value
	Yes	No	
Yes	81 (59.6%)	55 (40.4%)	<0.0001
No	66 (27.6%)	173 (72.4%)	

Table 2: Comparison of Frequency of Hypertension in Coronary Artery Disease (CAD) Versus Non-Coronary Artery Disease (Non-CAD) Patients (n=375)

Hypertension	Coronary Artery Disease		P-value
	Yes	No	
Yes	89 (50.6%)	58 (29.1%)	<0.0001
No	87 (49.4%)	141 (70.9%)	

Table 3: Comparison of Frequency of Hypertension in Coronary Artery Disease (CAD) Versus Non-Coronary Artery Disease (Non-CAD) Patients (n=375)

Triglycerides	Coronary Artery Disease		P-value
	Yes	No	
Mean	1.82	1.41	<0.0001
S.D.	0.52	0.52	

DISCUSSION

Ischemic heart problems are long standing diseases caused by many different risk factors. Conventional causative factors such like high blood pressure, diabetes mellitus, abnormal lipid levels and cigarette smoking, are still the main risk factors. Multiple mechanisms attributed are that endothelial cell damage, abnormal cholesterol metabolism, inflammatory process and immune response of body immune system. Some studies indicated that high blood pressure is one of the most important risk factors to cause atherosclerotic disease in young female group in their menopause. Framingham heart study showed that systolic blood pressure (SBP) ≥ 140 mmHg is much more important risk factor of heart artery disease than diastolic pressure, the relationship is linear between rising BP and CAD.[9,11] Diabetes is considered to be a metabolic disease affecting arterial wall endothelial lining and causing atherosclerosis to develop and propagate rapidly as compared to other risk factors.

A study clarifies that patients who had both diabetes and peripheral nervous system lesion had higher incidence rate of cardiovascular events and chance of death than patients with diabetes alone.[12] This study depicted that DM and HTN both are common in young female group in their menopausewith CAD than comparison group (62.5% vs. 36.3%, 68.7% vs. 28.7%, $p < 0.05$, respectively), but there was no statistically significant differences of smoking, BMI between these two groups ($p > 0.05$).

Cholesterol disease are also the important high risk factor for development of CAD. Many researches confirmed that ischemic heart disease is a result of atherosclerosis which was a chronic inflammatory response, and LDL might be the early factor to trigger the inflammatory response.[13] Goliasch et al. found that LDL and TC were associated inyoung female group in their

menopause(less than 40 years of age) with atherosclertic process. However, this research found that HDL-C, LDL-C and TC levels were not obviously statistically significant between CAD group and comparisongroup ($P > 0.05$), except definitely high levels of TGs ($P < 0.05$), which showed that higher TG levels were possibly associated with the higher incidence rate of CADyoung female group in their menopause, and there was no significant differenceof TC and LDL levels between CAD group and control group.[14]

Dou et al. reported that non-HDLC and TC were the optimal predictable indexes for men with CAD, and triglyceride for women, which was in line with this study, which was related to the high ratio of patients with diabetes (36.27%) in this study, because abnormal blood lipid usually increased lipid protein of TG in patients with diabetes.[15] In a word, hypertension and diabetes were the major risk factors of CAD for premenopausal women, and high TG level was the independent of risk factor in women with CAD.

The Nurses' Health Study (NHS), the largest U.S. cohort study of young female group in their menopause, included 116,700 premenopausal US females age 30 to 55 years who had no known heart disease at baseline. More than 95% were followed by mail between 1976 and 1982. "In this cohort, women who had a natural (nonsurgical) menopause and who had never taken postmenopausal estrogen had no increased risk of coronary heart disease compared to premenopausal women (adjusted rate ratio 1.12; 95% CI 0.8–1.8). Women who had a natural menopause and took estrogen also showed no difference in risk. In contrast, women who reported a bilateral oophorectomy had a 2-fold increased risk if they did not use post-menopausal estrogen.[16]

These results were further endorsed in a meta-analysis of 18 published researches. The researchers concluded there was no statistically significant relationship between females after menopause and IHD.[17]

CAD symptoms of females are different from symptoms of males, and young female group in their menopausecommonly represent with indistinct symptoms, such as excessive tiredness, atypical chest pain, abdominal pain, dizziness and shortness of breath, which is sometimes misleading and ignored. It is well recognized that women especially young female group in their menopausewith IHD present more commonly with atypical symptoms as described above.[18] Almost 20% of women in the present study presented with atypical chest pain, more commonly young female group in their menopause. Almost half of women with IHD had anginal chest pain, but 83% men with IHD were diagnosed as CAD on cardiac catheterization.[19]Our research highlighted that CAD was diagnosed by invasive angiography in 39.20% young female group in their menopausewho had symptoms of the chest symptoms.

In conclusion, once female patients who had risk factors like hypertension, diabetes and abnormal blood lipid, felt chest discomfort or other atypical angina symptom, whatever menopause or not, ST-T specific change of ECG or not, they should be diagnosed distinctly.

CONCLUSION

There is a high prevalence of coronary artery disease in symptomatic pre-menopause women. Diabetes, hypertension and elevated serum triglyceride levels are associated with higher prevalence of CAD.

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