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BEYOND THE MALE PARADIGM: UNDERSTANDING THE UNIQUE ASPECTS OF CORONARY ARTERY DISEASE IN WOMEN

Arun Jacob[1], K. Jayaprakash[2] and Sowparnika Treasa Sabu[3]*

[1]Senior Resident, Department of Cardiology, Govt. Medical College- Kottayam, Kerala.

[2]Professor, Department of Cardiology, Govt. Medical College- Kottayam, Kerala.

[3]Senior Research Associate, Indian Council for Medical Research Headquarters, New Delhi.

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***Corresponding Author**
Sowparnika Treasa Sabu
Senior Research Associate, Indian Council for Medical Research Headquarters, New Delhi.

ABSTRACT

Non communicable diseases (NCDs) kill 41 million people each year, equivalent to 74% of all deaths globally. According to WHO, each year, 17 million people die from a NCD before age 70; 86% of these premature deaths occur in low- and middle-income countries. Of all NCD deaths, 77% are in low- and middle-income countries. Cardiovascular diseases account for most NCD deaths, or 17.9 million people annually, followed by cancers (9.3 million), chronic respiratory diseases (4.1 million), and diabetes (2.0 million including kidney disease deaths caused by diabetes).In 2019, worldwide 17.9 million people died as a result of CVD, which is accounting for 32% of all deaths. In 2019, out of these 17 million premature fatalities (before reaching the age of 70) owing to NCDs, 85% of these deaths were caused by strokes and heart attacks, and 38% were related to CVD.

In women, the annual mortality rate from CAD is high. According to the World Health Organization, Indians have a greater prevalence of risk factors such as diabetes mellitus and hypertension than western countries as well as early onset of CAD. This early onset of CAD among young Indians may be attributed to recent economic improvement, lifestyle changes, and an increase in the prevalence of smoking.[2]

Coronary artery disease is the biggest killer of women globally. Coronary artery disease causes 8.6 million deaths among women annually, a third of all deaths in women worldwide. India is now estimated to be the coronary artery disease (CAD) capital of the world. CAD among women especially in young women as a group is less easily recognized worldwide.

Globally, there has been a substantial rise in the proportion of women undergoing “coronary angiography” (CAG) over the last few years. The reasons for this evolutionary change may be multifactorial. As a preliminary step in the process of discerning these changes, the clinical and angiographic profiles of women undergoing CAG must be understood. There are not many studies describing the prevalence and pattern of “coronary artery disease” (CAD) in women undergoing CAG.

KEYWORDS: CAD, Angiography, Prevalence, Risk factors, Women.

INTRODUCTION

Coronary artery disease (CAD), also known as coronary heart disease (CHD) or ischemic heart disease, is a common heart condition characterized by the narrowing or blockage of the coronary arteries, which supply oxygen and nutrients to the heart muscle. CAD is typically caused by atherosclerosis, a condition in which fatty deposits, cholesterol, calcium, and other substances build up in the inner walls of the coronary arteries, forming plaques. These plaques can restrict blood flow to the heart, leading to a variety of symptoms and potentially severe complications, such as heart attacks.

Here are some key points about coronary artery disease

1. **Risk factors:** Several factors contribute to the development of CAD, including smoking, high blood pressure, high cholesterol, diabetes, obesity, a sedentary lifestyle, a family history of heart disease, and age. Managing these risk factors is crucial for preventing CAD.
2. **Symptoms:** Common symptoms of CAD include chest pain or discomfort (angina), shortness of breath, fatigue, and in severe cases, heart attacks. Some people may not experience any symptoms, a condition known as "silent" CAD.
3. **Diagnosis:** CAD is often diagnosed through a combination of methods, including a patient's medical history, physical examination, electrocardiogram (ECG or EKG), stress tests, coronary angiography, and non-invasive imaging tests like CT angiography and cardiac MRI.
4. **Treatment:** Treatment for CAD aims to relieve symptoms, slow the progression of the disease, and reduce the risk of complications. Options may include lifestyle changes, such as diet and exercise, medications (like statins, antiplatelet drugs, and beta-blockers), angioplasty with stent placement, or coronary artery bypass grafting (CABG) surgery for more severe cases.

5. **Prevention:** Preventing CAD is crucial and can involve lifestyle changes, including a heart-healthy diet, regular exercise, not smoking, managing blood pressure and cholesterol, and controlling diabetes. Reducing stress and maintaining a healthy weight also play a role in prevention.
6. **Prognosis:** The prognosis for individuals with CAD varies depending on the severity of the disease, the presence of other risk factors, and how well it's managed. With appropriate medical care and lifestyle changes, many people with CAD can live long and healthy lives.

The pathophysiology of coronary artery disease (CAD) involves a complex interplay of various factors, primarily atherosclerosis, which leads to the narrowing and blockage of coronary arteries. Atherosclerosis is a progressive, chronic inflammatory condition of the arterial walls. Here's an overview of the pathophysiology of CAD:

1. **Endothelial dysfunction:** The process begins with damage to the endothelium, the inner lining of blood vessels. Factors such as high blood pressure, smoking, high cholesterol, and diabetes can injure the endothelial cells, leading to inflammation and increased permeability.
2. **Formation of atherosclerotic plaques:** In response to endothelial injury, low-density lipoprotein (LDL) cholesterol particles can enter the arterial wall and become oxidized. Immune cells, particularly macrophages, are then recruited to the site of injury. These cells engulf oxidized LDL cholesterol, forming foam cells, which are a hallmark of atherosclerotic plaques.
3. **Plaque formation:** Over time, these foam cells, along with smooth muscle cells and connective tissue, accumulate in the arterial wall, leading to the development of a fatty streak, which is the early stage of an atherosclerotic plaque. As the process continues, the plaque can grow in size.
4. **Plaque rupture:** Atherosclerotic plaques can become unstable due to factors like inflammation, shear stress, or alterations in plaque composition. When a plaque ruptures or erodes, the contents, including lipids and debris, are exposed to the bloodstream.
5. **Thrombus formation:** The exposure of plaque contents can trigger the formation of a blood clot (thrombus) on the ruptured plaque. This thrombus can partially or completely obstruct the coronary artery, leading to reduced blood flow to the heart muscle.
6. **Ischemia and Angina:** When the coronary artery's blood flow is reduced due to plaque buildup or thrombosis, the heart muscle doesn't receive an adequate supply of oxygen and

nutrients. This can result in angina pectoris, a condition characterized by chest pain or discomfort.

7. **Myocardial Infarction (Heart Attack):** If the blood clot completely occludes the coronary artery, it can lead to a myocardial infarction (heart attack). The lack of blood flow and oxygen causes damage to the heart muscle, and the extent of damage depends on the duration and location of the blockage.
8. **Complications:** CAD can lead to various complications, such as arrhythmias, heart failure, or structural damage to the heart. In severe cases, CAD can be fatal.
9. **Chronic progression:** CAD is often a chronic, progressive condition. As atherosclerosis continues to develop in other coronary arteries, there is an ongoing risk of additional plaque formation, rupture, and clot formation.

Coronary artery disease (CAD) has several risk factors, both modifiable and non-modifiable, that can influence a person's likelihood of developing the condition. Identifying and managing these risk factors is crucial for preventing CAD. Here are some of the key risk factors for CAD:

Non-Modifiable risk factors

1. **Age:** The risk of CAD increases with age, particularly after the age of 45 for men and 55 for women.
2. **Gender:** Men tend to be at higher risk for CAD than premenopausal women. However, the risk increases for women after menopause.
3. **Family history:** If you have a family history of CAD (especially if it occurred at a young age), your risk is higher.

Modifiable risk factors

1. **Smoking:** Cigarette smoking is a significant risk factor for CAD. It damages blood vessels, reduces oxygen supply, and promotes the formation of atherosclerotic plaques.
2. **High blood pressure (Hypertension):** Elevated blood pressure forces the heart to work harder and can damage blood vessel walls, increasing the risk of CAD.
3. **High cholesterol levels:** Elevated levels of LDL (low-density lipoprotein) cholesterol, also known as "bad" cholesterol, contribute to the formation of atherosclerotic plaques. Low levels of HDL (high-density lipoprotein) cholesterol, or "good" cholesterol, can also be a risk factor.
4. **Diabetes:** People with diabetes are at a higher risk of CAD, primarily due to associated

metabolic abnormalities and damage to blood vessels.

5. **Obesity:** Excess body weight, particularly when it's concentrated around the abdomen, is a risk factor for CAD.
6. **Physical inactivity:** Lack of regular physical activity can lead to obesity, high blood pressure, and other risk factors for CAD.
7. **Unhealthy diet:** Diets high in saturated and trans fats, cholesterol, and refined sugars can contribute to elevated cholesterol levels and obesity.
8. **Metabolic syndrome:** This condition includes a cluster of risk factors, including abdominal obesity, high blood pressure, high blood sugar, and abnormal lipid profiles.
9. **Stress:** Chronic stress can indirectly affect CAD risk through behaviors like overeating, smoking, and alcohol consumption.
10. **Alcohol consumption:** Excessive alcohol intake can increase blood pressure and contribute to obesity. However, moderate alcohol consumption may have some cardiovascular benefits.
11. **Sleep apnea:** This condition, which disrupts normal sleep patterns and oxygen supply, has been associated with an increased risk of CAD.

Other risk factors

1. **Inflammation:** Chronic inflammation in the body is believed to play a role in the development and progression of atherosclerosis.
2. **High levels of homocysteine:** Elevated levels of homocysteine, an amino acid, may be associated with an increased risk of CAD.
3. **Autoimmune diseases:** Certain autoimmune diseases, such as rheumatoid arthritis and lupus, may increase the risk of CAD.

In women, the annual mortality rate from CAD is high. According to the World Health Organization, Indians have a greater prevalence of risk factors such as diabetes mellitus and hypertension than western countries as well as early onset of CAD. This early onset of CAD among young Indians may be attributed to recent economic improvement, lifestyle changes, and an increase in the prevalence of smoking.[2]

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Globally, there has been a substantial rise in the proportion of women undergoing "coronary angiography" (CAG) over the last few years. The reasons for this evolutionary change may be multifactorial. As a preliminary step in the process of discerning these changes, the clinical and angiographic profiles of women undergoing CAG must be understood. There are not many studies describing the prevalence and pattern of "coronary artery disease" (CAD) in women undergoing CAG.

It is a major cause of mortality and morbidity among women in developing countries. The onset of occurrence of CAD in women is usually significantly later than in men due to the vascular protective effect of oestrogen which helps to delay the formation of atherosclerosis. The excess in hospital CAD mortality in women compared to men almost balances their lower pre-hospital mortality. Despite their excess risk, women are only half as likely as men to receive aspirin, beta-blockers or thrombolytic therapy or to be referred for. Among Indian women, the presence of hypertension, diabetes, low levels of high-density lipoprotein and high levels of total cholesterol, triglycerides, low-density lipoprotein and Lp (a) are correlated with CAD.[18,19,20]

Compared with whites, Indian men and women have a lower prevalence of hypertension, hypercholesterolemia, obesity and smoking, but a higher prevalence of high TG, low HDL, glucose intolerance and central obesity. Prevalence of most risk factors is lower in rural than in urban India with exception of smoking/tobacco use.[21]

In addition to higher rate, it is also reported that Indian individuals may develop CAD at a very early age.[22] According to an estimate, more than half of death related to cardiovascular disease occurs in patients below the age of 50 years and one-fourth of acute myocardial infarction cases are being reported in patients under the age of 40 years. It has also been noted that the clinical presentation, risk factor profile, and coronary anatomy of young patients who develop CAD differs to those who develops CAD at an older age.[23,24,25]

Overall, these studies have indicated that patients with early onset of CAD exhibit preponderance of single vessel disease, and dominance of coronary risk factors such as hypercholesterolemia, family history of CAD, and cigarette smoking as compared to older patients.[26] However, there have been very limited data on comparison of demographic and angiographic characteristics in young patients stratified according to the type of acute coronary syndrome.[27,28]

CAD is relatively rare in subjects below 40 years of age, as it occurs in about 6–10% of them, but it has grave medical, social, psychological, and economic consequences in this age group. Sudden cardiac death, which is the most severe complication of CAD, occurs also in young subjects, and some authors believe it is one of the most common causes of mortality among young adults.[29,30,31]

Several lines of evidence suggest that the characteristics of coronary artery disease in young women may differ from those in other patients. Older surveys of hospitalized patients highlighted the rarity of symptomatic coronary artery disease in young women. The hormonal balance of premenopausal women is considered to offer partial protection against the development of coronary atherosclerosis. This concept is supported by autopsy studies demonstrating more advanced coronary atherosclerosis in women with previous oophorectomy than in control women. From 1960 to 1995, the prevalence of CAD in adults increased from 3% to 10% in urban Indians and from 2% to 4% in rural Indians with women having rates similar to men.[49]

CAD mortality in women

Women have poorer prognosis and more severe outcome than men after myocardial infarction, percutaneous coronary intervention and coronary artery bypass grafting. Women are more likely than men to die after a first MI, and for survivors, there is higher risk of recurrent MI, heart failure or death. In Framingham heart study the one-year mortality following an MI was 44% in women vs. 27% in men.[50] The overall short term and long term CAD mortality following an MI are about 40% higher in women after adjustment for age and other risk factors.

The excess in hospital CAD mortality in women compared to men almost balances their lower pre-hospital mortality. Despite their excess risk, women are only half as likely as men to receive aspirin, beta-blockers or thrombolytic therapy or to be referred for revascularization procedure. Vaccarino et al found that mortality from MI in women <50 years of age was double that of men and excess mortality in women is limited to <60 years of age.

Risk factors in women

Women, in comparison with men, tend to have a better risk factor profile at younger ages, whereas the opposite is true at older ages. Although most risk factors for CAD are similar in

men and women, gender differences have been documented, particularly for diabetes, central obesity and dyslipidemia. Among Indian women, the presence of hypertension, diabetes, low levels of high-density lipoprotein and high levels of total cholesterol, triglycerides, low-density lipoprotein and Lp (a) are correlated with CAD.[51]

Compared with whites, Indian men and women have a lower prevalence of hypertension, hypercholesterolemia, obesity and smoking, but a higher prevalence of high TG, low HDL, glucose intolerance and central obesity. Prevalence of most risk factors is lower in rural than in urban India with exception of smoking/tobacco use (Tobacco Paradox).[52]

Coronary artery disease (CAD) affects both men and women, but it can manifest differently in women, and there are some gender-specific considerations to keep in mind:

1. **Symptom presentation:** Women with CAD may not always experience the classic chest pain (angina) that men often report. Women are more likely to have atypical symptoms such as shortness of breath, nausea, vomiting, back or jaw pain, or extreme fatigue. This can make it challenging to diagnose CAD in women, and it's often misattributed to other conditions.
2. **Risk factors:** Many of the risk factors for CAD are common to both men and women, including smoking, high blood pressure, high cholesterol, diabetes, and obesity. However, some factors may be more pronounced in women, such as the link between diabetes and CAD, and the role of hormonal changes (e.g., menopause) in increasing risk.
3. **Hormonal changes:** Estrogen, which is more prevalent in premenopausal women, is thought to have a protective effect on the cardiovascular system. After menopause, when estrogen levels drop, the risk of CAD in women increases and approaches that of men. Hormone replacement therapy (HRT) has been studied as a way to mitigate this risk, but its use is a subject of ongoing research and debate.
4. **Microvascular disease:** Some women with CAD may have microvascular disease, which involves damage to the smaller arteries in the heart. This can lead to symptoms of chest pain and discomfort despite clear coronary arteries on angiography. Microvascular disease is often underdiagnosed and may require specialized testing for accurate diagnosis.
5. **Risk assessment:** Women and their healthcare providers should be vigilant in assessing risk. Women who have a family history of heart disease, especially at a young age, or

other risk factors should work closely with their healthcare team to monitor and reduce risk.

6. **Prevention:** Preventive measures for CAD are just as important for women as they are for men. This includes maintaining a heart-healthy lifestyle with a balanced diet, regular physical activity, and stress management. Women should also pay attention to their blood pressure, cholesterol levels, and blood sugar, and work with their healthcare providers to manage these risk factors.
7. **Medical care:** Women who experience symptoms of CAD should seek medical attention, and healthcare providers should consider the possibility of CAD in women, even when symptoms are atypical. Diagnostic tests, such as stress tests, angiography, and non-invasive imaging, may be used to confirm the diagnosis.
8. **Treatment:** The treatment of CAD in women often involves medications, lifestyle changes, and, in some cases, medical procedures like angioplasty and stent placement. The appropriate treatment plan depends on the severity of CAD and individual health factors.

CAD and Indian women

Coronary artery disease (CAD) is a significant health concern for Indian women, as it is for women in many parts of the world. CAD affects both genders, but it can present some unique challenges and considerations for Indian women. Here are some key points to understand:

1. **Prevalence:** CAD is on the rise among Indian women. It was traditionally considered a disease more prevalent in men, but the gap is narrowing, particularly among urban Indian women. Lifestyle changes, including dietary habits, physical inactivity, and increased stress, are contributing to this increase.
2. **Risk factors:** Indian women may have unique risk factors for CAD. These factors can include a diet high in saturated fats and trans fats, which are common in many traditional Indian dishes. Additionally, genetic factors may play a role, as South Asians, including Indians, are more prone to insulin resistance and metabolic syndrome, which increase CAD risk.
3. **Lifestyle:** Urbanization and changing lifestyles, such as sedentary jobs and reduced physical activity, have contributed to an increase in CAD risk among Indian women. Encouraging physical activity, promoting a heart-healthy diet, and addressing obesity are important measures.

4. **Early onset:** CAD can affect Indian women at a relatively young age, often in their 40s or 50s. This is a cause for concern because younger patients may have a longer duration of illness and potentially more complications over their lifetime.
5. **Delayed diagnosis:** In some cases, CAD in women may be underdiagnosed or misdiagnosed, particularly when atypical symptoms, like shortness of breath or fatigue, are present. Healthcare providers should be alert to these differences and consider CAD in the differential diagnosis for women with risk factors.
6. **Hormonal factors:** Hormonal changes, such as early menopause, can impact CAD risk. This is a significant concern, as some Indian women may experience early menopause, which may increase their risk of heart disease.
7. **Challenges in access to healthcare:** In rural and economically disadvantaged areas, access to healthcare can be a challenge, which can affect early detection and management of CAD. Public health initiatives are working to address these disparities and increase access to healthcare services.
8. **Prevention:** Preventive measures, including education on heart-healthy lifestyles, regular health check-ups, and risk factor management, are crucial. Preventing CAD in Indian women involves a multifaceted approach, addressing both individual behaviors and broader societal factors.

CONCLUSION

In conclusion, our study has shed light on the intricate landscape of coronary artery disease (CAD) in women. The findings presented in our article underscore the critical need for a nuanced understanding of CAD in women, recognizing that this condition presents unique challenges and considerations distinct from its manifestation in men. Our study has shown that CAD in women is not only prevalent but also exhibits distinctive characteristics, including atypical symptoms, early onset, and a complex interplay of risk factors influenced by lifestyle, genetics, and hormonal factors. These findings emphasize the importance of tailored approaches to CAD prevention, diagnosis, and treatment in women.

Additionally, our research highlights the necessity of gender-sensitive healthcare delivery. Medical professionals must be alert to the possibility of CAD in women, even when symptoms are not classic, and proactively engage in risk assessment and management. Furthermore, public health initiatives and educational campaigns aimed at promoting heart-

healthy lifestyles and raising awareness among women are vital for mitigating the growing burden of CAD.

Ultimately, our study reinforces the notion that CAD in women is not merely a male disease with a female face; it is a distinct entity with its own set of challenges. As we move forward, it is imperative that healthcare systems, policymakers, and the broader society acknowledge these distinctions and work collaboratively to reduce the impact of CAD on women's health. The journey to improved cardiovascular health for women must begin with knowledge, understanding, and the commitment to providing equitable and tailored care for all.

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