

To investigate the clinical characteristics of CAD in individuals who use smokeless tobacco and smoke

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ABSTRACT

Background: Tobacco use has been widely recognised as a significant contributor to the development of coronary artery disease (CAD), a condition that has exhibited a downward trend in prevalence among the general population in recent years, largely attributable to heightened awareness and stringent regulatory measures. This study aims to investigate the clinical and angiographic characteristics of coronary artery disease in individuals who use smokeless tobacco in comparison to those who smoke.

Material and methods: The study presented is a retrospective case-control study that was carried out in the department of cardiology of JAH group of hospitals Gwalior, M.P. from August 2020 to April 2022. Of the entire sample size of 1348 patients, a subset of 120 individuals with a history of tobacco use, either in the form of smokeless or smoked tobacco, and without any other known cardiovascular risk factors, were selected to participate in the study. A comparative analysis was conducted between two groups to examine the disease patterns and angiographic patterns.

Results: Among the sample of 120 patients, 70 individuals reported using smokeless tobacco while 50 individuals reported smoking. The prevalence of single vessel disease was found to be higher among users of smokeless tobacco, with 43 cases (61.43%) exhibiting this condition, as compared to 25 cases (50%) among smokers. This difference was statistically significant, with a p value of 0.04. The prevalence of multi vessel disease was found to be higher in smokers, with 30% of cases exhibiting this condition, compared to smokeless tobacco users, where only 18.57% of cases showed multi vessel disease. This difference was statistically significant, with a P value of 0.03. No statistically significant difference was detected between the two groups in terms of the prevalence of double vessel disease.

Conclusion: A significant proportion of individuals who utilise smokeless tobacco and present to the cardiac catheterisation lab with symptoms of angina or angina equivalent exhibit fatal coronary artery disease, manifesting as either ST-segment elevation myocardial infarction (STEMI) or non-ST-segment elevation myocardial infarction (NSTEMI).

Keywords: Smokeless, Smoked, Tobacco, STEMI

Introduction

The World Health Organisation has identified non-communicable diseases as a significant health priority for the next two decades, particularly in developing countries, due to the rising number of fatalities associated with these conditions.[1-3] Cardiovascular disease is widely acknowledged as the primary and predominant cause of mortality in numerous countries. The prevalence of mortality caused by cardiovascular disease witnessed an increase from 10% to 30% throughout the 20th century. Coronary artery disease (CAD) is widely acknowledged as the primary etiological factor for cardiovascular disease, accounting for a significant proportion of mortality rates. Specifically, CAD has been linked to 2 out of 10 deaths, and it is projected that the number of CAD-related deaths will

increase from 17.3 million in 2012 to 23.6 million in 2030. The incidence of cardiovascular disease is on the rise in developing nations. The coronary arteries are accountable for providing oxygenated blood to the cardiac muscle and arise from the aorta, specifically above the aortic valve. Various diagnostic tests are employed in the identification of cardiovascular disease. Angiography is considered the optimal technique for detecting coronary artery disease (CAD). Coronary artery disease (CAD) is primarily attributed to smoking and physical inactivity, although hypertension, dyslipidemia, and certain ethnic factors are also associated with the development of CAD. Several studies have investigated the incidence of cardiovascular risk factors in diverse populations. However, inconsistent findings have been documented due to the multifactorial nature of CAD, which encompasses risk factors such as age, gender, family history, genetic predisposition, hypertension, diabetes mellitus, smoking, and elevated blood cholesterol levels.[4-6]

Tobacco use has been widely recognised as a significant contributor to the development of coronary artery disease (CAD), a condition that has exhibited a downward trend in prevalence among the general population in recent years, largely attributable to heightened awareness and stringent regulatory measures. The use of smokeless tobacco has been identified as a contributing risk factor for coronary artery disease (CAD). This trend is on the rise due to factors such as increased cultural acceptance, affordability, lower cost, and decreased awareness of its cardiovascular effects among individuals with lower socioeconomic status. The global prevalence of smokeless tobacco use is higher (11.2%) than that of smoking (8.9%) among the general population. The prevalence of smokeless tobacco usage is notably elevated among individuals residing in Southeast Asia, particularly in India, resulting in a significant burden. The Indian population exhibits a smokeless tobacco consumption prevalence of 20%. The prevalence of the condition is notably higher, approximately one-third, among the male population of India within the reproductive age group, specifically individuals aged 15 to 54 years. The current body of research on the prevalence of coronary artery disease (CAD) among individuals who use smokeless tobacco is lacking. Both smokeless and smoked tobacco products contain nicotine, a highly addictive substance. The absorption of nicotine in individuals who smoke is facilitated through the lungs, whereas in the case of smokeless tobacco users, it occurs through the buccal mucosa. The rate of nicotine absorption is significantly higher in individuals who smoke as compared to those who use smokeless tobacco. [7-10]

Material and methods

The study presented is a retrospective case-control study that was carried out in the department of cardiology of JAH group of hospitals Gwalior (mp) from August 2020 to April 2022. The study included a total of 1348 patients who underwent coronary angiography in the catheterisation lab and presented with symptoms of angina or angina equivalent. Apprehension was expressed by all of the patients who were registered. A comprehensive medical history is obtained from patients to identify cardiovascular risk factors for coronary artery disease (CAD). These risk factors include but are not limited to family history, tobacco and alcohol consumption, past medical history of diabetes, hypertension, chronic kidney disease, and dyslipidemia. The study analysed routine patient reports, including measurements of fasting/postprandial blood sugar, lipid profile, renal function, and liver function. Of the entire sample size of 1348 patients, a subset of 120 individuals with a history of tobacco use, either in the form of smokeless or smoked tobacco, and without any other known cardiovascular risk factors, were selected to participate in the study. The clinical presentation of patients, including chest pain, dyspnea, palpitations, fatigue, and syncope, were carefully documented along with vital signs and clinical indicators such as elevated jugular venous pressure, edema, crepitation, rhonchi, S3, S4, and any abnormal heart sounds or murmurs. This was done for all patients who were included in the study. All electrocardiogram abnormalities, such as ST-T changes and arrhythmias, as well as echocardiographic findings, including ejection fraction, regional wall motion abnormality, mitral regurgitation, and associated right ventricular abnormality, were documented. Treadmill test reports were gathered from individuals who were suspected to have chronic stable angina. Quantitative data on CKMB/Troponin were gathered in individuals with suspected ACS. Drawing from historical, clinical, and laboratory data, coronary artery disease (CAD) can be categorised into distinct clinical presentations, including chronic stable angina, unstable angina, non-ST elevated myocardial infarction (NSTEMI), and ST elevated myocardial infarction

(STEMI). The study recorded angiographic observations pertaining to the location, type, and extent of lesions in patients. The severity of the lesion was classified into four categories: occlusive (total or subtotal occlusion), severe (>70%), borderline (50-70%), and mild (<50%). The patients were classified into two distinct groups based on their mode of tobacco consumption, namely the smokeless tobacco user group and the smoker group. A comparative analysis was conducted between two groups to examine the disease patterns and angiographic patterns.

Statistical Analysis

The analysis of categorical data was conducted through the utilisation of statistical tests such as proportions, percentages, and the Chi-square test (X²). The quantitative data was subjected to analysis using measures of central tendency such as mean and standard deviation. Additionally, an unpaired t-test was utilised to compare the means of the two groups. A significance level of 0.05 was utilised to determine statistical significance, while a P value of less than 0.01 was deemed highly significant (HS). Conversely, P values greater than 0.05 were classified as non-significant (NS).

Results

Among the sample of 120 patients, 70 individuals reported using smokeless tobacco while 50 individuals reported smoking. Males were the dominant gender in both groups. The study found that the majority of smokeless tobacco users were male (78.57%), while a smaller proportion were female (21.43%). Similarly, among smokers, a significantly higher percentage of males (96%) were observed compared to females (4%). The study revealed a statistically significant difference in the prevalence of female individuals, specifically 15 (21.43%), among smokeless tobacco users compared to 2 (4%) among smokers, with a p-value of 0.002.

Table 1 age and gender of the participants

	Smokeless tobacco user=70	%	Smoker=50	%	P value
Gender					
Male	55	78.57	48	96	
Female	15	21.43	2	4	0.002
Age					
Below 25 years	6	8.57	3	6	
25-35	25	35.71	18	35	0.36
35-45	20	28.57	15	30	
45-55	12	17.14	10	20	
above 55	7	10	4	8	

The study found that within the population of smokeless tobacco users, the prevalent pattern of coronary artery disease was chronic stable angina, observed in 30 individuals or 42.86% of the sample. Unstable angina was the second most common pattern, present in 17 individuals or 24.28% of the sample, followed by NSTEMI in 12 individuals or 17.14%. The least common pattern observed was STEMI, present in 11 individuals or 15.71% of the sample. The study findings indicate that STEMI was the predominant pattern observed among smokers, with 17 (34%) patients exhibiting this pattern. This was followed by NSTEMI, which was observed in 14 (28%) patients, while unstable angina was observed in 10 (20%) patients and chronic stable angina was observed in 9 (18%) cases, as presented in Table 2.

Table 2: coronary artery disease among smokers and non smokers

	Smokeless	%	Smoker	%	P value
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	tobacco user				
Chronic Stable Angina	30	42.86	9	18	0.001
Unstable Angina	17	24.28	10	20	0.63
NSTEMI	12	17.14	14	28	0.03
STEMI	11	15.71	17	34	0.001

The prevalence of single vessel disease was found to be higher among users of smokeless tobacco, with 43 cases (61.43%) exhibiting this condition, as compared to 25 cases (50%) among smokers. This difference was statistically significant, with a p value of 0.04. The prevalence of multi vessel disease was found to be higher in smokers, with 30% of cases exhibiting this condition, compared to smokeless tobacco users, where only 18.57% of cases showed multi vessel disease. This difference was statistically significant, with a P value of 0.03. No statistically significant difference was detected between the two groups in terms of the prevalence of double vessel disease, as shown in Table 2.

Table 3 .Comparison of numbers of vessels

No of vessels Effected	Smokeless tobacco user	Percentage	Smoker	percentage	P value
DVD	14	20	10	20	0.44
SVD	43	61.43	25	50	0.04
MVD	13	18.57	15	30	0.03

The severity of lesions was analysed by considering patients with single vessel lesions. The incidence of occlusive lesions was found to be higher among smokers, with 28 out of 50 patients (56%) exhibiting this condition. In comparison, only 25 out of 70 smokeless tobacco users (35.71%) showed occlusive lesions. This difference was statistically significant, with a p value of 0.01. In comparison to the smoker group, the non-occlusive lesions with severe stenosis were more frequently observed among smokeless tobacco users, with 58.57% of patients exhibiting such lesions. However, the difference between the two groups was not statistically significant, as indicated by the p value in Table 4.

Table 4. Comparison of severity of lesions in CAD

Severity of lesion	Smokeless tobacco user	%	Smoker	%	P value
Occlusive	25	35.71	28	56	0.01
Above 70%	41	58.57	19	38	0.21
50-70%	3	4.28	3	6	0.36
below 50%	1	1.43	0	0	-

Discussion

The addictive potential of tobacco is primarily attributed to the presence of nicotine, although the main substance responsible for the pathophysiology of coronary artery disease (CAD) is not nicotine, but rather tobacco-specific materials such as nitrosamine and aromatic hydrocarbon. [11-14]The stimulation of the sympathetic system by nicotine can lead to an increase in heart rate or blood pressure and the occurrence of acute coronary vasospasm. The heated aerosol form of nitrosamine and aromatic hydrocarbon generates oxides of nitrogen and carbon monoxide, along with numerous free radicals. These substances are absorbed more efficiently and quickly through the alveoli of the lungs and into the bloodstream, resulting in endothelial dysfunction and the initiation of the coagulation cascade. This ultimately leads to hypercoagulability and the formation of thrombi in smokers. [15-16] Butadiene, when inhaled, is a constituent of smoke's vapour phase and has the potential to extend the atherosclerotic process.[17] The heated or burned forms of nitrosamine and aromatic hydrocarbons are deemed to be more perilous for the cardiovascular system when compared to their non-heated or non-burnt counterparts. The emission of carbon monoxide from smoked gas induces hypoxia in

individuals who smoke habitually. This hypoxia triggers the stimulation of erythropoietin, which results in erythrocytosis and heightened blood viscosity, thereby enhancing pro-thrombotic processes. The utilisation of certain components in smoked tobacco, such as cadmium, nickel, and aluminium, has been found to induce protein oxidation in blood vessels and cause microtubule dysfunction in endothelial cells. This process ultimately contributes to the development of atherosclerosis. The fibrinolytic system, responsible for counteracting the coagulation process within the human body, is frequently found to be compromised in individuals who smoke. The consumption of smoked tobacco products has been found to elevate the serum levels of fibrinogen or high-sensitivity C-reactive protein, while simultaneously reducing the plasma tissue plasminogen activators. This can result in the impairment of the fibrinolytic mechanism.[18] In contrast to smokers, it is often observed that the fibrinolytic system remains intact in individuals who use smokeless tobacco. Acrolein is a reactive aldehyde that is generated through endogenous lipid peroxidation in individuals who smoke. This compound has been observed to modify a key protein in high-density lipoprotein (HDL), namely apolipoprotein A-I. The role of HDL in the mobilisation of cholesterol from atherosclerotic plaque is significant. Consequently, any malfunction of HDL can result in the rapid and progressive development of atherosclerosis. [19] In the context of smokeless tobacco, it is noteworthy that betel leaves and areca nut are the most frequently utilised ingredients in India. These components are known to possess antioxidant properties. Studies have indicated that the utilisation of antioxidants in smokeless tobacco may confer a protective effect against coronary artery disease (CAD). The levels of antioxidants, namely carotenes, ascorbic acid, alpha-tocopherol, and lycopene, in the serum do not exhibit significant differences between individuals who use smokeless tobacco and those who do not. However, smokers tend to experience a decrease in these antioxidant levels.[20] The consumption of oral moist snuff, prevalent in western countries, typically involves the intake of various substances, including fatty acids, flavonoids, and nitrates, which possess antioxidant properties. Additionally, these substances have been found to confer a protective effect against myocardial infarction. [21] The current investigation revealed a statistically significant difference in the prevalence of female individuals, specifically 15 (21.43%), among smokeless tobacco users as compared to 2 (4%) among smokers, with a p-value of 0.002. A study has indicated that the proportion of females to males in the smokeless tobacco user group is 1:2.3.[22] In contrast, the current study found the ratio to be 1:3.67. The greater incidence of females among users of smokeless tobacco in comparison to smokers can be elucidated by the following factors. Smokeless products such as Pan and Gudakhu are widely accepted in countries such as India due to their cultural significance. The increased cultural acceptability of smokeless tobacco in India may be attributed, in part, to lower levels of literacy among the population, which has resulted in a lack of awareness regarding its adverse effects. In the current investigation, The study revealed that within the population of smokeless tobacco users, the predominant manifestation of coronary artery disease was chronic stable angina, observed in 30 individuals, accounting for 42.86% of the sample. This was followed by unstable angina in 17 individuals (24.28%), NSTEMI in 12 individuals (17.14%), and the least frequently observed pattern, STEMI, in 11 individuals (15.71%). The study findings indicate that STEMI was the predominant pattern observed in 34% of smokers, followed by NSTEMI in 28% of smokers, unstable angina in 20% of smokers, and chronic stable angina in 18% of cases. Smokeless tobacco exhibits a modest correlation with coronary artery disease (CAD), which could potentially explain the reduced incidence of nonfatal myocardial infarction (MI) among smokeless tobacco consumers.[23] During the examination of angiographic features, it was noted that individuals who use smokeless tobacco had a higher incidence of single vessel disease, with 43 cases (61.43%) exhibiting this condition. This is in contrast to smokers, where 25 cases (50%) were observed to have single vessel disease. The statistical analysis revealed a significant p value of 0.04. The prevalence of multi vessel disease was found to be higher in smokers (30%) compared to smokeless tobacco users (18.57%), with a statistically significant p-value of 0.03. No statistically significant difference was observed between the two groups when comparing the prevalence of double vessel disease. The incidence of occlusive lesions was found to be higher among smokers, with 28 out of 50 patients (56%) exhibiting this condition, as compared to smokeless tobacco users, where only 25 out of 70 patients (35.71%) had occlusive lesions. This difference was statistically significant, with a p-value of 0.01. In comparison to the smoker group, non-occlusive lesions with severe stenosis were more frequently observed in 58.57%

of smokeless tobacco users, although the difference was not statistically significant ($p > 0.05$) in the sample of 41 patients. In contrast, only 38% of smokers exhibited these types of lesions.

Hence, it is highly likely that the aforementioned factors contribute to the comparatively lower fatality rate of cardiovascular consequences, specifically coronary artery disease, among individuals who use smokeless tobacco in comparison to those who smoke. Nevertheless, the aforementioned facts cannot be disregarded in individuals who use smokeless tobacco. The study findings indicate that a significant proportion of individuals who utilise smokeless tobacco and exhibit symptoms of angina or angina equivalent upon presentation to the cardiac catheterisation lab have succumbed to fatal coronary artery disease, as evidenced by STEMI or NSTEMI occurrences. Approximately 20% of individuals who utilise smokeless tobacco and exhibit symptoms of angina or its related equivalents have been identified as having multi-vessel disease. Numerous studies have also determined that smokeless tobacco usage is associated with hypertension, diabetes, metabolic syndrome, and dyslipidemia, all of which may increase the risk of coronary artery disease among smokeless tobacco users. [24-25]

Conclusion

The incidence of fatal coronary disease and multi-vessel disease is comparatively lower among individuals who use smokeless tobacco in comparison to those who smoke. Nevertheless, the cardiovascular implications of smokeless tobacco cannot be disregarded in light of the aforementioned facts. A significant proportion of individuals who utilise smokeless tobacco and present to the cardiac catheterisation lab with symptoms of angina or angina equivalent exhibit fatal coronary artery disease, manifesting as either ST-segment elevation myocardial infarction (STEMI) or non-ST-segment elevation myocardial infarction (NSTEMI). Specifically, over one-third of such individuals demonstrate this outcome. Additionally, approximately one-fifth of smokeless tobacco users with angina or its equivalents exhibit multi-vessel coronary artery disease. Hence, it is imperative to implement suitable cessation techniques for smokeless tobacco users in order to avert lethal coronary incidents associated with multi-vessel coronary artery disease.

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