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### Corresponding Author

Parth Bharatkumar Patel,  
Department of Orthopaedics,  
GMERS Medical College, Vadnagar,  
Gujarat, India  
drparthbpatel@gmail.com

### Author Designation

<sup>1,2</sup>Assistant Professor  
<sup>3</sup>Intern Doctor  
<sup>4</sup>Associate Professor

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## A Comparative Analysis Clinicoangiographic Patterns of Coronary Artery Disease in Smokers and Smokeless Tobacco Users

<sup>1</sup>Hardik Pravinkumar Modi, <sup>2</sup>Rajan Chaudhari, <sup>3</sup>Karan Chaudhari and <sup>4</sup>Parth Bharatkumar Patel

<sup>1,2</sup>Department of General Medicine, Nootan Medical College and Research Centre, Visnagar, Gujarat, India

<sup>3</sup>Department of Surgery, GMERS Medical College, Sola, Ahmedabad, Gujarat, India

<sup>4</sup>Department of Orthopaedics, GMERS Medical College, Vadnagar, Gujarat, India

### ABSTRACT

Smoking is widely recognized as a significant cardiovascular risk factor for coronary artery disease (CAD). However, its prevalence has been decreasing among the general population in recent decades due to enhanced public awareness and stricter legislation. The aim of this study was to compare the clinical and angiographic characteristics of CAD in individuals who smoke tobacco and those who use smokeless tobacco. We assessed routine reports of patients, including fasting and postprandial blood sugar levels, lipid profiles, renal function tests and liver function tests. Our final study included 246 participants out of an initial pool of 378 patients. These individuals had a history of tobacco use, either in smokeless or smoked form, without additional cardiovascular risk factors. CAD presentations were categorized into clinical patterns such as chronic stable angina, unstable angina, non-ST elevated myocardial infarction (NSTEMI) and ST elevated myocardial infarction (STEMI), based on their medical history, clinical evaluations and laboratory findings. Our findings indicated a significantly higher prevalence of female smokeless tobacco users compared to female smokers, with a  $p < 0.05$ . Among smokers, STEMI was the most common presentation, followed by NSTEMI, unstable angina and chronic stable angina. Smokeless tobacco users demonstrated a lower prevalence of fatal CAD and multi-vessel disease compared to smokers. A significant proportion of smokeless tobacco users presenting with angina or its equivalents have fatal coronary artery disease or multi-vessel disease, emphasizing the cardiovascular risks associated with smokeless tobacco use.

## INTRODUCTION

Smoking is a well-established cardiovascular risk factor for coronary artery disease (CAD) and its prevalence has been decreasing due to improved public awareness and stricter legislation<sup>[1,2]</sup>. On the other hand, the use of smokeless tobacco is also a known risk factor for CAD<sup>[3-7]</sup> and its prevalence is rising due to cultural acceptance, accessibility, affordability and insufficient awareness of its cardiovascular risks, especially among those with lower socioeconomic status. Globally, the prevalence of smokeless tobacco use (11.2%) surpasses that of smoking (8.9%), with a significant prevalence observed in South-East Asia, particularly in India, where approximately 20% of the population uses smokeless tobacco. Among Indian males aged 15-54 years, the prevalence rises to about one-third<sup>[8-10]</sup>. However, our understanding of CAD patterns among smokeless tobacco users remains limited. Both smoked and smokeless tobacco products contain nicotine, a highly addictive chemical. Nicotine absorption occurs through the lungs in smokers and through the buccal mucosa in smokeless tobacco users, with smokers experiencing a faster nicotine absorption rate and reaching peak blood nicotine levels quicker than smokeless tobacco users. Despite these differences, the peak serum nicotine concentration remains unchanged between the two groups, and regular users of smokeless tobacco often have higher basal nicotine levels than smokers<sup>[11-13]</sup>. Due to variations in tobacco consumption, administration route, absorption rate and serum nicotine levels, clinical and angiographic patterns of CAD can differ between smokers and smokeless tobacco users. To explore these differences, a case-control study was conducted on CAD patients comparing the clinical and angiographic patterns between smokeless tobacco users and cigarette smokers.

## MATERIALS AND METHODS

The study being presented is a retrospective case-control investigation. It encompassed 378 patients who sought evaluation for coronary angiography due to angina or angina-like symptoms. All patient concerns were meticulously documented, and an in-depth assessment of their cardiovascular risk factors for CAD was undertaken, including familial history, tobacco and alcohol usage history, diabetes, hypertension, chronic renal disease and dyslipidemia. Routine laboratory assessments such as fasting and post-prandial blood sugar levels, lipid profiles, renal and liver function tests were scrutinized. Ultimately, 246 patients with a history of tobacco use but devoid of additional cardiovascular risk factors were enrolled in the study. Clinical symptoms (like chest discomfort, dyspnea, palpitations, fatigue, syncope), vital signs and clinical indicators (including elevated JVP, edema, crepitation, rhonchi, S3, S4, or any murmurs) were

thoroughly recorded for each participant. Any abnormalities noted on echocardiography or electrocardiogram, such as ST-T changes, arrhythmias, mitral regurgitation, RV abnormalities, or regional wall motion irregularities, were documented. Treadmill test results were obtained for individuals suspected of chronic stable angina, while data on CKMB and Troponin levels were collected from those suspected of ACS. CAD was categorized into clinical patterns like chronic stable angina, unstable angina, NSTEMI and STEMI, based on historical, clinical and laboratory evidence. The angiography results, including lesion location, type and severity, were reported. Lesion severity was categorized as occlusive (complete occlusion), severe (>70% stenosis), borderline (50-70% stenosis), or moderate (<50% stenosis). Patients were divided into two groups based on tobacco use (smokeless or smoked) and their disease and angiographic patterns were compared using the gathered data. Statistical methods such as proportions, percentages and the Chi-square test were employed for categorical data analysis (X<sup>2</sup>). Quantitative data analysis involved mean, standard deviation, and unpaired t-tests to compare group means. Statistical significance was defined as  $p < 0.05$ , with  $p < 0.01$  indicating high significance (HS), and  $p > 0.05$  indicating lack of statistical significance (NS).

## RESULTS AND DISCUSSIONS

One hundred twenty three individuals utilized smokeless tobacco, while an equal number smoked cigarettes. In both groups, males were more prevalent than females. Among smokeless tobacco users, the majority were males, whereas in smokers, 95% were male. Interestingly, the prevalence of female smokeless tobacco users was notably higher compared to female smokers, with a  $p < 0.01$  indicating statistical significance. Chronic stable angina was the predominant pattern observed in smokeless tobacco users, followed by unstable angina, NSTEMI and STEMI. Conversely, STEMI was the most prevalent pattern among smokers, followed by NSTEMI, unstable angina and chronic stable angina (Table 1). Single valve disease was more prevalent among smokeless tobacco users, whereas multivessel disease was more common among smokers, showing a statistically significant difference with a  $p < 0.05$ . However, there was no significant difference in the prevalence of double vessel disease between the two groups (Table 2). Among smokers, occlusive lesions were detected in 58.54% of patients, whereas only 35.77% of smokeless tobacco users had occlusive lesions, indicating a statistically significant difference. On the other hand, nonconclusive lesions with severe stenosis were more frequent in smokeless tobacco users (57.72%) compared to smokers (39.84%), although this difference did not reach statistical significance based

**Table 1: CAD among smokers vs non smokers**

Type of CAD	Smokeless tobacco user		Smoker		p-value
	n	Percentage	n	Percentage	
Chronic Stable Angina	48	39.02	23	18.70	<0.01
NSTEMI	25	20.33	37	30.08	<0.05
STEMI	20	16.26	38	30.89	<0.01
Unstable Angina	30	24.39	25	20.33	0.43

**Table 2: Comparison of number of vessels affected among smokers vs non smokers**

No of vessels affected	Smokeless tobacco user		Smoker		p-value
	n	Percentage	n	Percentage	
DVD	23	18.70	25	20.33	0.29
MVD	23	18.70	39	31.71	<0.05
SVD	77	62.60	59	47.97	<0.05

**Table 3: .Comparison of severity of CAD lesions in two groups**

Severity of lesion	Smokeless tobacco user		Smoker		p-value
	n	Percentage	n	Percentage	
Below 50%	1	0.81	0	0.00	-
50-70%	7	5.69	2	1.63	0.36
Above 70%	71	57.72	49	39.84	0.21
Occlusive	44	35.77	72	58.54	0.01

on the p-value (Table 3). The research findings revealed that among smokeless tobacco users, majority were male compared to female, while among smokers also, majority were male. Notably, the prevalence of female smokeless tobacco users was significantly higher than that of female smokers<sup>[14]</sup>. This data suggests that cultural acceptance and lower awareness of the negative effects of smokeless tobacco among individuals, especially those with lower socioeconomic status, contribute to a higher frequency of female users of smokeless tobacco compared to smokers.

In terms of CAD, fatal myocardial infarctions such as ST-elevation myocardial infarction (STEMI) and non-ST-elevation myocardial infarction (NSTEMI) were more prevalent among smokers than among smokeless tobacco users<sup>[15]</sup>. Conversely, chronic stable angina was more prevalent among smokers compared to smokeless tobacco users. Angiographic analysis revealed that smokeless tobacco users had a significantly higher incidence of single-vessel disease compared to smokers, whereas multi-vessel disease was more prevalent among smokers than smokeless tobacco users<sup>[15]</sup>. Additionally, occlusive lesions were more common among smokers (58% of patients) than smokeless tobacco users. The pathophysiology of CAD in smokeless tobacco users and smokers differs due to the distinct components and absorption routes of tobacco products. Nicotine, nitrosamine and aromatic hydrocarbons in tobacco contribute to CAD pathogenesis. Nicotine stimulates the sympathetic nervous system, leading to increased heart rate, blood pressure and coronary vasospasm. Nitrosamine and aromatic hydrocarbons produce free radicals, causing endothelial dysfunction, hypercoagulability and thrombus formation in smokers<sup>[16-18]</sup>. Smokeless tobacco users may experience lower CAD risks due to antioxidant properties in some smokeless tobacco ingredients. However, smokeless tobacco still poses cardiovascular risks, including high blood pressure,

diabetes, metabolic syndrome and dyslipidemia, contributing to CAD development<sup>[19,20]</sup>. The pathophysiological processes of CAD in smokeless tobacco users and smokers overlap, with oxidized tobacco components playing a significant role in CAD progression. In summary, smokeless tobacco use has less severe cardiovascular consequences in terms of CAD compared to smoking, but it still poses significant health risks and contributes to CAD development through various mechanisms shared with smoking.

## CONCLUSION

Compared to smokers, individuals who use smokeless tobacco show a reduced prevalence of fatal coronary disease and multi-vessel disease. However, despite this observation, the impact of smokeless tobacco on the cardiovascular system cannot be disregarded, given the information provided. A significant portion of smokeless tobacco users who present with angina or angina equivalents at the cardiac catheterization lab are found to have fatal coronary artery disease, manifested as either STEMI or NSTEMI. Furthermore, approximately one-fifth of smokeless tobacco users with angina or its equivalents exhibit multi-vessel coronary artery disease.

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