Original Research Article

Clinical and angiographic pattern of coronary artery disease in smokeless tobacco users in comparison to smokers

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Received: 20-04-2021 / Revised: 09-06-2021 / Accepted: 02-07-2021

Abstract

Background: Smoking is a well-established cardiovascular risk factor for coronary artery disease (CAD), which is in a decremental trend among population over last few decades. Whereas use of smokeless tobacco is an establishing risk factor for CAD, which is in an incremental trend among population. Worldwide prevalence of use of smokeless tobacco is also higher than smoking among population. As amount of intake of tobacco, route of administration, rate of absorption, serum level of nicotine are different in both form of tobacco consumption, therefore clinical and angiographic patterns can be different in both cases.Objective:To compare and determine the difference in clinical and angiographic patterns of CAD between smokeless tobacco users and smokers.Materials and methods: Total 1848 patients attending catheterisation lab for coronary angiography with chief complain of angina or angina equivalent were enrolled in the study .Out of 1848 patients, 252 patients with history of tobacco consumption either in the form of smokeless or smoked tobacco without having any other cardiovascular risk factors for CAD were finally enrolled as study participants. Based on mode of consumption of tobacco, all study participants were categorised into two groupsi.e smokeless tobacco users group and smoker group. Data about clinical and angiographic patterns were compared between two groups.Results: Among smokers, prevalence of fatal coronary events like STEMI (32.4%), NSTEMI (29.6%) and multi vessel disease (27.7%) were significantly higher as compared to 15.2 %, 18%,19.4% cases among smokeless tobacco users respectively .On the contrary among smokeless tobacco users, prevalence of chronic stable angina (40.2%),single vessel disease(61.8%) were significantly higher as compared to 13.8%,48.1% casesamong smokersrespectively. While studying severity of lesion in patients with single vessel disease, 57.6 % patients in smoker group had occlusive(total or subtotal) lesion in comparison to 35.9% patients in smokeless tobacco user group with statistical significant P value.Conclusion: Prevalence of fatal coronary diseases, multi vessel diseases among smokeless tobacco usersis lower than that of smokers. However cardiovascular effects of smokeless tobacco can't be ignored considering above facts. More than 1/3rd of smokeless tobacco users who presents to the catheterisation lab with angina or angina equivalent had fatal coronary artery disease and around 1/5th of the smokeless tobacco users with angina or its equivalent had multi vessel coronary artery disease.

Key words: CAD, smokeless tobacco user, smoker, STEMI, NSTEMI, multi vessel disease.

Introduction

Smoking is a well-establishedcardiovascular risk factorfor coronary artery disease(CAD),which is in a decremental trend among population over last few decades due to increased awareness and strict regulations.[1-2] Whereas use of smokeless tobacco is an establishing risk factor for CAD, [3-7]which is in an incremental trend due to increased cultural acceptance, easy affordability,lesser cost and decreased awareness about its cardiovascular effects among peoples with lower socio economic status.[2]Worldwide prevalence of use of smokeless tobacco (11.2%) is also higher than smoking (8.9%)among population. [8]Burden of smokeless tobacco is quite high among people of south east ASIA, more specifically in India.Prevalence of smokeless tobacco consumption is 20% among Indian population. [9]Prevalence is much more common (around 1/3rd) among male population of India within reproductive age group(i.e15-54 years). [10]However knowledge about pattern of CAD among smokeless tobacco users is very limited.Both smokeless, smoked tobacco products containasubstancenicotine, which has very high addictive potential.Absorption of nicotine in case of smoker occurs through lungs, whereas in case smokeless tobacco users, it occurs through buccal mucosa. Rate of absorption of nicotine in case of smoking much faster than that of smokeless tobacco. [11-12] Therefore serum nicotine level peaks very fast in smokers as compared to smokeless tobacco users. [12] However peak serum nicotine remains at the same level in both cases. [12] Basal nicotine levels remains usually at a higher level in habituated smokeless tobacco user as compared to smokers. [13]As amount of intake of tobacco,route of administration, rate of absorption, serum level of nicotine are different in both modes of tobacco consumption ,therefore clinical and angiographic patterns of involvement can be different in both the cases. Hence a case control study was conducted in patient with CAD to compare and determine any difference in clinical and angiographic pattern between smokeless tobacco users and smokers.

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Material and methods

Presented study is a retrospective case control study was conducted in VIMSAR Burla between period January 2014 to January 2021.Total 1848patients attending catheterisation labfor coronary angiographywith chief complain of angina or angina equivalentwere enrolled in the study (figure 1). Concern taken from all the patients enrolled.Thorough history about cardiovascular risk factor for CAD like family history, history of consumption of tobacco, alcohol, past history of diabetes, hypertension, chronic kidney disease and dyslipidaemia elicited from the patients .Routine reports of the patients like fasting/post prandial blood sugar, lipid profile, renal function test, liver function test were studied. Out of total 1848 patients, 252 patients with history of tobacco consumption either in the form of smokeless or smoked tobacco without having any other cardiovascular risk factors were finally enrolled as study participants (figure 1). Clinical symptoms (like chest pain, dyspnoea,palpitation,fatigability, syncope), vitals, clinical signs (like raised JVP, oedema, crepitation, rhonchi, S3, S4, any murmur or abnormal heart sounds) duly noted for every patients enrolled. Any ECG abnormality (like ST –T changes,arrhythmia) ,echocardiogram-phic findings (like ejection fraction , Regional wall motion abnormality , mitral regurgitation and associated RV abnormality) were recoded . In patients with suspected chronic stable angina, treadmill test reports were collected.In patients with suspected ACS, data about CKMB/ Troponin (quantitative) were collected.Based on history, clinical,laboratory findings ,CAD in patients classified into differentclinical patterns like chronic stable angina, unstable angina, non ST elevated MI (NSTEMI) ,ST elevated MI (STEMI).Angiographic findings in patients such as site , nature and severity of lesion, were noted .Severity of lesion were further graded as occlusive(total or subtotal occlusion), severe(>70%), borderline(50-70%) andmild(<50%). Based on mode of consumption of tobacco,allpatients were categorised into two group i.e smokeless tobacco user group and smoker group (figure 1). Data about disease patterns, angiographic patterns were compared between two groups.

Statistical Analysis

Categorical data were analysed using statistical tests e.g., proportions, percentages, Chi-square test (X^2). Quantitative data were analysed with mean, standard deviation and un-paired t-test was applied to compare the means between the two groups. P value less than 0.05 was considered significant and P value less than 0.01 was taken as highly significant(HS) and P value more than 0.05 considered as non-significant(NS).

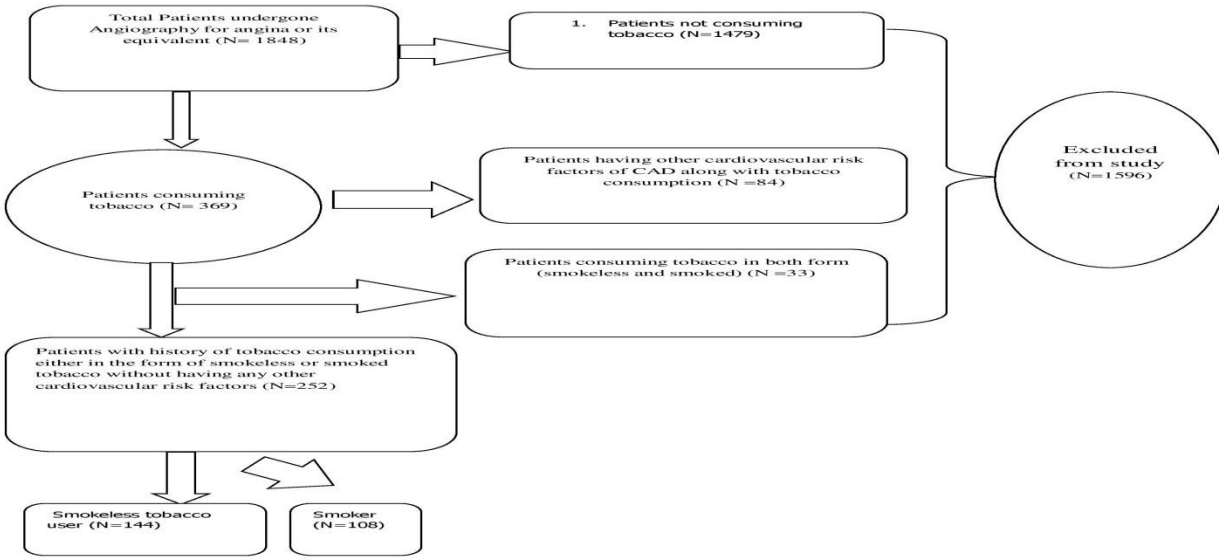

Fig 1: Flowchart showing selection of study subjects

Results

1. Out of 252 patients,144 patients were smokeless tobacco users,108 patients were smokers.In both groups males dominated female.Among smokeless tobacco users, 118(81.9%) were male and 26 (18.1%) were female, whereas among smoker, 102 (94.4%) were male and 6(5.6%) Were female. Prevalence of female i.e 26 (18.1%) among smokeless tobacco user was found to be significantly higher in comparison to 6(5.6%) among smoker group with p value = 0.0033.
2. Among smokeless tobacco users, chronic stable angina was the most common coronary artery disease pattern observed in 58(40.2%) patients,followed by unstable angina in 38(24.3%) patients,NSTEMI in 26(18 %) patients and the least common pattern i.eSTEMI in 22(15.2%) patients. Whereas among smokers,STEMIwas the most common pattern observed in 35(32.4%) patients, followed by NSTEMI in 32(29.6%) patients,unstable angina in 21(19.4%) patients and chronic stable angina in 20 (18.5%) cases(table 1,figure 2) .

Table 1: Distribution of pattern of coronary artery disease among smokers and smokeless tobacco users.

	Chronic Stable Angina	Unstable Angina	NSTEMI	STEMI
Smokeless tobacco user	58(40.2 %)	38(24.3%)	26(18.0%)	22(15.2%)
Smoker	20 (18.5%)	21(19.4%)	32(29.6%)	35(32.4%)
P Value	0.0002(HS)	0.35(NS)	0.030(S)	0.0013(HS)

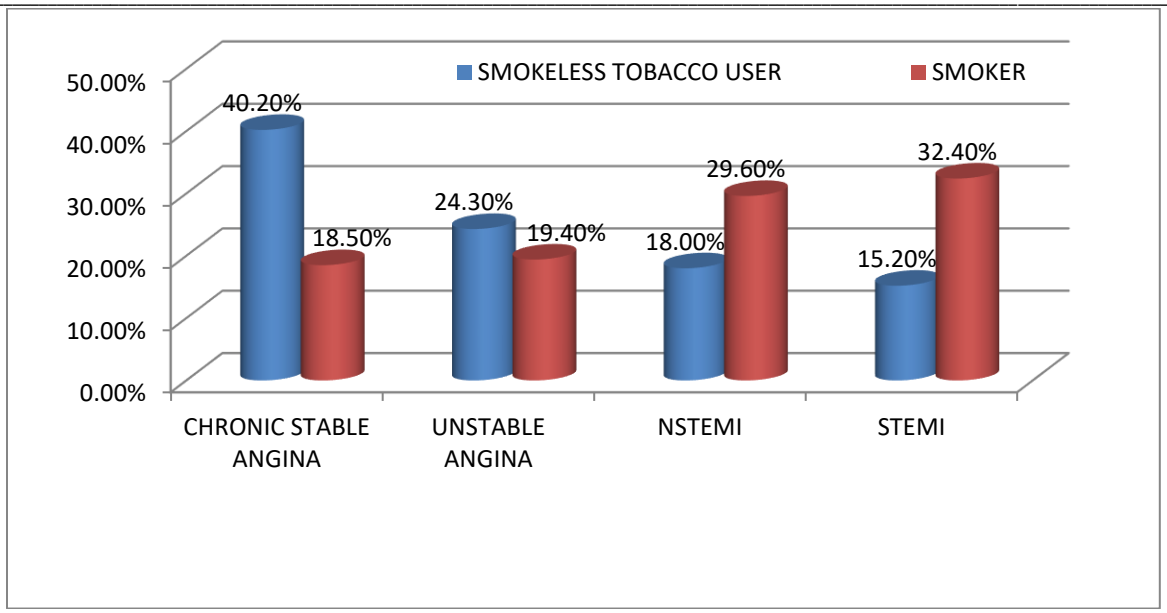

Fig 2: Distributionof pattern of coronary artery disease among smokers and smokeless tobacco users. [STEMI-ST elevated myocardial infarction, NSTEMI –non ST elevated myocardial infarction]

3)Among smokeless tobacco users, single vessel disease was more commonly observed in 89(61.8 %) cases,as compared to 52(48.1%) cases among smokers with statistical significant p value 0.03. Whereas multi vessel diseasewas more commonly observed in 34(31.4%)cases in smokers as compared to 26(18.7%) cases in smokeless tobacco users with statistical significant P value 0.028. However no significant difference was observed between two groups, while comparing prevalence of double vessel disease (table 2, figure 3).

Table 2 .Comparison of numbers of vessels effected between smoker and smokeless tobacco user group

No of vessels Effected	Smokeless tobacco user	Smoker	P value
SVD	89(61.8%)	52(48.1%)	0.03(S)
DVD	27(18.7%)	22(20.3%)	0.75(NS)
MVD	28(19.4%)	34(31.4%)	0.028(S)

[SVD-single vessel disease,DVD-double vessel disease, MVD- multi vessel disease]

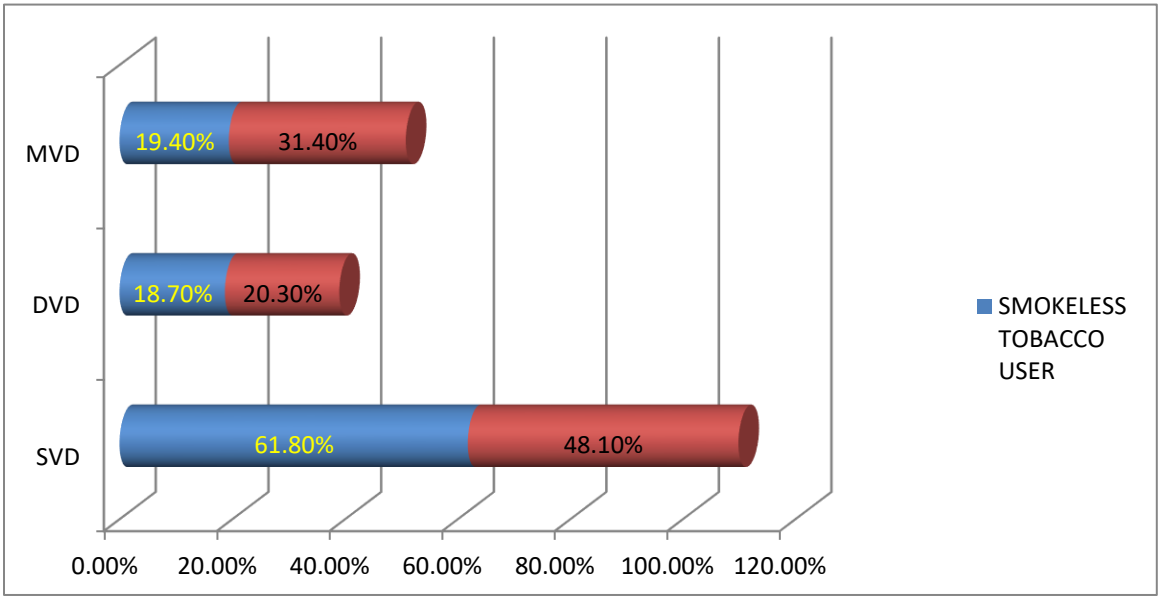

Fig 3:Comparison of nos. of vessels effected between smoker and smokeless tobacco user group [SVD-single vessel disease,DVD-double vessel disease, MVD- multi vessel disease]

4) To analyse severity of lesions,patients with single vessel lesions were taken into consideration. Among smokers, occlusive lesion more commonly observed in 30(57.6 %) patients in comparison to 32(35.9%) patients in smokeless tobacco users with statistical significant p value 0.0126 . Whereas among smokeless tobacco users, non-occlusive lesions with severe stenosis were more commonly observed in 51(57.3%) patientsin comparison to 21(40.3%) patients in smoker group without any statistical significant p value (table 3).

Table 3.Comparison of severity of lesions in CADbetween smoker and smokeless tobacco user group

Severity of lesion	Smokeless tobacco user	Smoker	P value
Occlusive	32(35.9 %)	30(57.6 %)	0.0126(s)
>70%	51(57.3%)	21(40.3%)	0.052(ns)
50-70%	05(5.6%)	01(1.9%)	0.29(ns)
<50%	01(1.1%)	0	Can't be estimated

Discussion

In present study,prevalence of female i.e 26 (18.1%) among smokeless tobacco user was found to be significantly higher in comparison to 6(5.6%) among smoker group with p value = 0.0033. It has been also observed in a study that, ratio of female to male ratio in smokeless tobacco user group is 1:2.3, [14]where as in present study,it was found to be 1:4.5.Higher prevalence of females among smokeless tobacco users as compared to smokers can be explained by thefacts as described below. In countries like India cultural acceptability for smokeless products like Pan, Gudakhu is high.Lack of knowledge about adverse effect of smokeless tobacco due lower literacy among Indian population can be also a factor for increased cultural acceptability.In present study prevalence of fatal myocardial infarction like STEMI,NSTEMI were observed in 32.4%,29.6% cases respectively among smokers ,which weresignificantly higher as compared to 15.2 %,18% cases amongsmokeless tobacco users group as depicted in table 1.On the contrary significantly higher prevalence of Chronic stable angina was observed in 40.2% cases as compared to 13.8% patients among smoker group (table 1,figure 2) . Smokeless tobacco has modest association for CAD, which may be a reason for lower prevalence of nonfatal MI in smokeless tobacco users. [15] While studying angiographic features,it was observed that multi vessel disease were observed in a significantly higher proportion (27.7%) of patients in smoker group as compared to 19.4% patientsin smokeless tobacco user group. Whereas prevalence of single vessel disease is significantly higher among smokeless tobacco users group i.e61.8% patients as compared to 48.1% patients among smokers (table2, figure 3). While studying severity of lesion in patients with single vessel disease, it was observed that, 57.6% patients in smoker group had occlusive lesion, either in the form total or subtotal occlusion in comparison to 35.9%patients in smokeless tobacco user group with statistical significant P value (table3) .Above discrepancy between smoker and smokeless tobacco user groups regarding clinical and angiographic pattern of CAD can be explained with reasons below.

1. Tobacco in any form has higher addictive potentialdue to presence of nicotine,howevertobacco specific materials like nitrosamine, aromatic hydrocarbon rather than nicotine is the main substance,which is responsible for pathophysiology for CAD .[16,17]Nicotine can increase the heart rate or blood pressure and cause acute coronary vasospasm by stimulating sympathetic system. [18]Whereasheated aerosol form of nitrosamine,aromatic hydrocarbon produces oxides of nitrogen and Carbon monoxide, many free radicals,which absorbs more easily and rapidly through alveoli of lung in to blood vessel causing endothelial dysfunction and induction of coagulation cascade leading to hypercoagulability and thrombus formation in smokers. [16,17]Inhaled butadiene, also a component of the vapour phase of smoke, which prolongs atherosclerotic process.[19] Therefore heated or burned form of nitrosamine and aromatic hydrocarbons comparatively more hazardous for cardiovascular system than non-heated or non-burnt form.
2. Carbon monoxide released from smoked gas causes hypoxia in chronic smoker, which stimulates erythropoietin stimulation leading to erythrocytosis and increased blood viscosity potentiating pro-thrombotic processes. [20]
3. Ingredient's used in smoked tobacco like cadmium, nickel,aluminium, which can catalyse oxidation of proteins in blood vessel and promotes microtubule dysfunction in endothelial cell, leading to progressive atherosclerosis. [21]
4. Fibrinolytic system in the body, which can counter the coagulation process, most often remains impaired in smokers. Smoked tobaccoproductincreases theserum levels offibrinogen or high-sensitivity C-reactive proteinand decreases plasma tissue plasminogen activators causing impairment of fibrinolytic mechanism.[22] Whereas fibrinolytic system most often remains intact in patients with smokeless tobacco users, in contrast to smokers.
5. Acrolein, a reactive aldehyde produced by endogenous lipid peroxidation in case of smoker, which modifies major protein in HDL i.eapo-lipoprotein A-I .As HDL has an important role in mobilizing cholesterol from atherosclerotic plaque,therefore malfunction of HDL leads to rapid progressivearthrosclerosis. [23]
6. Whereas in case of smokeless tobacco, ingredient's most commonly used in India were betel leaves and areca nut, which can have antioxidant property. It has been observed that antioxidant used in smokeless tobacco can have protective effect for CAD. Serum concentrations of antioxidants such as carotenes and ascorbic acid, alpha-tocopherol and lycopene do not differ between smokeless tobacco user and non-tobacco users, whereas they are reduced mostly in smokers. [24] Oral moist snuff most commonly used in western countries contains substances such as fatty acids , flavonoids and nitrates with antioxidant property and also have a protective effect for myocardial infarction.[25]

Therefore most probably due to above reasons, cardiovascular effects (in terms of coronary arterydisease) are less lethal in smokeless tobacco users as compared to smokers.However the samecan't be ignored in smokeless tobacco users considering above facts. More than 1/3rd of smokeless tobacco users who presents to the cardiac catheterisation lab with angina or angina equivalent had fatal coronary artery disease either in the form of STEMI or NSTEMI (figure 2,table 3).Around 1/5th of the smokeless tobacco userswith angina or its equivalents found to have multi vessel disease (figure 3,table2).Many studies also concluded that, smokeless tobacco is also responsible for hypertension, diabetes, metabolic syndrome, dyslipidaemia which in turn can predispose smokeless tobacco users for coronary artery disease. [26-29]Thepathophysiological mechanism of cardiovascular diseasein smokeless tobacco useris similarto that of smoker, [12]though rate of progression of disease can be different.Oxidised vapour form of nitrosamine, aromatic hydrocarbon and ingredients like cadmium ,nickel etc have a very important role in the pathogenesis of coronary artery disease ,leading to higher number of fatal coronary events with multi vessel disease in smokers. Whereas other cardiovascular risk factors, like hypertension, diabetes, dyslipidaemia,metabolic syndrome,which can arise due to use of smokeless tobacco, have an important role in pathogenesis of CAD in smokeless tobacco users. To summarise,

tobacco in any form has its devastating cardiovascular effect in the form of coronary artery disease.Strict government policies and regulations are also needed for smokeless tobacco consumption to restrict the incremental trend of using smokeless tobacco. Awareness among peoples about its harmful cardiovascular effect is extremely essential to decrease the burden of coronary artery disease in the community.

Limitation of study

Frequency,dose, duration of different form of tobacco can provide more detail information about association of tobacco with CAD. Multi centric study involving higher number of subjects, can predicts association more accurately. As present study was completely based on history elicited from the patients to derive conclusion about cardiovascular risk factor like tobacco, therefore there is chance of suppression of information's from the side of subjects , which can distracts objective of the study.

Conclusion

Prevalence of fatal coronary disease, multi vessel disease among smokeless tobacco users is lower than that of smoker. However cardiovascular effects of smokeless tobacco can't be ignored considering above facts. More than 1/3rd of smokeless tobacco users who presents to the cardiac catheterisation lab with angina or angina equivalent had fatal coronary artery disease either in the form of STEMI or NSTEMI and around 1/5th of the smokeless tobacco users with angina or its equivalents had multi vessel coronary artery disease.Therefore appropriate tobacco quitting strategies is also extremely essential for smokeless products to prevent fatal coronary events with multi vessel coronary artery disease in smokeless tobacco users.

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Conflict of Interest: Nil
Source of support:Nil