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Original Research Article

Impact of smokeless tobacco products on myocardial infarction and stroke and it's prognostic significance

Rajesh Ranjan Behera*, Rajesh Padhi

Department of Medicine, Institute of Medical Sciences and SUM Hospital, Sikhsha 'O' Anusandhan University, Bhubaneshwar, Odisha, India

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***Correspondence:**
Dr. Rajesh Ranjan Behera,
E-mail: ranjanrajesh608@gmail.com

ABSTRACT

Background: The use of smokeless tobacco (SLT) predates smoking and its effects on the health of the individuals is very much similar tobacco smoking. The present study was done with the aim to find out independent prognostic significance of ST products on disease outcome like myocardial infarction and stroke.
Methods: This prospective study was done on the patients attending to the Department of Internal Medicine, Institute of Medical Sciences and SUM Hospital, Bhubaneswar with complaints suggesting of coronary artery disease and stroke during the period from July 2016 to June 2018. The exposure of risk factors and confounding factors are detailed and collected from the patients by using predesigned questionnaire. All the data was analysed by using SPSS version 20.
Results: During the study period a total of 423 patients were included in the study. Mean average age of the participants was 56.58±11.23 years. Male preponderance was seen in the study. Out of total patients, myocardial infarction was noticed in 49 and stroke in 64 patients. SLT was used by 323 (76.4%) users. Among SLT both gutkha and pan was most commonly used (55.6%). Among them hypertension and diabetes were seen in 193 and 184 patients respectively. Risk of incidence of CVA and stroke was found to be more among SLT users compared to non-users.
Conclusions: SLT is considered to be an important etiological factor for the incidence of myocardial infarction and stroke. There is an urgent need to increase clinical interventions and awareness in public to decrease SLT addiction.

Keywords: Cerebrovascular accident, Myocardial infarction, Smokeless tobacco

INTRODUCTION

Use of tobacco collectively considered preventable reason of premature death, fatality and melancholy among adults universally. Most predominant form of tobacco use is tobacco smoking and, in most countries, promotive as well as preventive actions against tobacco use is focused towards the tobacco smoking. Tobacco use nearly causes death in about 6 million people per year, and the current statistics shows that its use will cause about 8 million death by the end of 2030.[1]

Apart from smoking there are many other forms of tobacco known as smokeless tobacco (SLT) which is prevalent in many countries. In India, SLT products are more commonly used in different forms like dry and wet snuff, zarda, gutkha, pan etc. Whatever may be the form but it has been proved through research that use of

tobacco adversely affect the health of individual and may affect those who are not using it but in contact with it.[2-4] Products of ST and other tobacco products induces cancer in oral, oesophagus, pharyngeal, pancreatic and stomach.[5] Some studies have confirmed that those who are addicted to ST die of Cardio Vascular Disease (CVD), circulatory diseases, reproductive results in connection with pregnancy as either low birth weight and stillbirths.[6,7] In western countries, several studies are carried out to examine the presence of harmful CAD and CVD such as myocardial infraction, ischemic heart disease, and stroke by intake of ST products.[6] In India myocardial infarction (MI) and stroke are major cause of mortality and long-term morbidity. Among many changeable risk factors for coronary artery diseases (CAD), use of tobacco in any form is well recognized. However, risk of CAD due to use of SLT products such as tobacco chewing and their outcome is not well known, even though use of smokeless tobacco is very common in southwest Asia. In Odisha, use of SLT products (like, "Gutkha", "Khaini" and "Gudakhu" among others) is a common occurrence among adult population without any gender difference. So, in this study author aimed to study the association of long-term use of these SLT products with risk and outcome of MI and stroke.

METHODS

This was a prospective study conducted over a period of 2 years from July 2016 to June 2018. All the patients attending to the Department of Internal Medicine, Institute of Medical Sciences and SUM Hospital, Bhubaneswar with complaints suggesting of coronary artery disease and stroke were selected for the study. Patients of age greater than 18 years and willing to participate in the study were included. Exclusion criteria were currently smoking patients, patient with emergency condition or terminally ill, patients with oral and other malignancies and patients with renal and multi-organ failure.

To measure the exposure of risk factors and confounding factors a structured interview was conducted. Initially, a semi analytical, pre-tested survey questions format was used to recruit eligible CAD, stroke and controls into the study. The questionnaire included different risk factors like age, smoking, residence, CAD and cerebro-vascular disease status. Different data pertaining to socio-demographic information, other known coronary heart disease risk factor, a detailed history of ST use had asked to the patients recruited into the study after taking a written informed consent. Laboratory investigation findings like complete blood count, urea, creatinine, sodium and potassium level, fasting and post-prandial blood glucose levels were also noted down. For the study purpose, leaf of betel and nuts of areca alone was not enclosed as ST, as tobacco was not present in these products. In case of a patient use ST with leaf of betel or nuts of areca then this was a subject for current ST user. In case of a patient not using ST for last 1 year, then subject called as past ST user. If a patient has no history of ST using or not taking ST now, then called never ST user.

The data collected was entered in Microsoft Excel 2007 and further analysed in SPSS version 20. All the categorical variable was expressed in term of number and percentages. The association between categorical variable was evaluated using Chi-squared test/Fischer exact test. All the quantitative variables were expressed as mean and variance. The difference in mean in two groups was obtained by using t-test. $P \leq 0.05$ contemplated statistically significant.

RESULTS

During the study period a total of 423 patients were included in the study. Table 1 describes the socio-demographic and clinical characteristics of the study group.

Table 1: Socio-demographic and clinical characteristics of the study group.

Variables	Number (n=423)	Percentage (%)
Age in years		
<40	10	2.4
40-60	267	63.1
>60	146	34.5
Gender		
Male	234	55.3
Female	189	44.7
Residing area		
Urban	265	62.6
Rural	158	37.4
Type of smokeless tobacco		
Gutkha and pan	235	55.6
Pan	52	12.3
Gutkha	36	8.5
No	100	23.7
Clinical condition		
Myocardial infarction	49	11.6
Cerebro-vascular accident	64	15.1
No abnormality (NA)	310	73.3
Co-morbidities		
Hypertension	193	45.6
Diabetes	184	43.5

Mean average age of participants was 56.58±11.23 years. Male subjects are more (234, 55.3%) compared to females (189, 44.7%). higher proportion of the population (62.6%) belonged to urban area while only 37.4% belonged to rural population. From the total 323 (76.4%) of study subjects used some form of smokeless tobacco products while 100 subjects did not use any form of tobacco. Out of 323 users of ST, 235 (55.6%) subjects used both gutkha and pan, 52 (12.3%) subjects used only

pan while 36 (8.5%) subjects used only gutkha. Out of total study subjects, 49 (11.6%) suffered from myocardial infarction while 64 patients suffered from cerebro-vascular accident. Associated co-morbid conditions were hypertension noted in 193 (45.6%) patients and diabetes mellitus in 184 (43.5%) population.

Table 2: Association of socio-demographic and clinical factors with myocardial infarction (MI) among study population.

Variables		MI present	MI absent	Odds ratio	95% CI	P value
		N (%)	N (%)			
SLT user	Yes	42 (85.7)	223 (71.9)	2.341	1.10-5.40	0.041
	No	7 (14.3)	87 (28.1)			
Age	<50 years	9 (18.4)	127 (41.0)	1.138	1.05-1.22	<0.0001
	≥50 years	40 (81.6)	183 (59.0)			
Gender	Male	26 (53.1)	173 (55.8)	0.895	0.489-1.63	0.719
	Female	23 (46.9)	137 (44.2)			
Geography	Urban	21 (42.9)	207 (66.8)	1.15	1.04-1.274	0.001
	Rural	28 (57.1)	103 (33.2)			
Hypertension	Present	49 (100.0)	192 (61.9)	1.41	1.28-1.56	<0.001
	Absent	0 (0)	118 (38.1)			
Diabetes	Present	49 (100.0)	184 (59.4)	1.389	1.26-1.52	< 0.001
	Absent	0 (0)	126 (40.6)			

Table 3: Association of hemodynamic, haematological and biochemical parameters with MI among study population.

Variables		Diagnosis category	N	Mean	SD	P value
Haemodynamic parameters	Systolic blood pressure	MI	49	150.98	27.737	0.761
		NA	310	152.34	29.193	
	Diastolic blood pressure	MI	49	86.65	16.255	0.483
		NA	310	88.43	16.446	
	Pulse rate	MI	49	80.20	18.042	0.995
		NA	304	80.22	18.846	
Haematological parameters	Hemoglobin	MI	44	13.35	11.840	0.704
		NA	287	12.75	9.578	
	Total leucocyte count	MI	49	7.25	0.530	0.952
		NA	310	7.26	1.284	
	Neutrophils	MI	45	80.39	11.349	0.031
		NA	291	75.70	13.854	
	Lymphocyte	MI	44	14.06	8.712	0.070
		NA	287	16.87	9.702	
	Monocytes	MI	46	2.69	5.883	0.423
		NA	295	2.07	4.774	
	Eosinophils	MI	44	2.34	3.083	0.198
		NA	282	3.52	5.933	
	Basophils	MI	45	0.34	0.239	0.170
		NA	287	0.66	1.540	
Biochemical parameters	Sodium	MI	48	131.83	7.603	0.603
		NA	305	130.30	20.209	
	Potassium	MI	48	4.68	4.532	0.280
		NA	305	10.47	36.984	
	Urea	MI	49	26.67	14.385	0.639
		NA	303	27.68	13.965	
	Creatinine	MI	49	6.60	21.785	0.403
		NA	303	4.36	16.596	
	Fasting blood sugar	MI	47	121.98	48.384	0.210
		NA	303	136.71	78.110	
	Post-prandial blood sugar	MI	43	185.53	65.416	0.553
		NA	282	193.33	82.148	

Table 4: Association of socio-demographic and clinical factors with cerebrovascular accident (CVA) among study population.

Variables	CVA present N (%)	CVA absent N (%)	Odds ratio	95% CI	P-value
SLT user					
Yes	58 (90.6)	223 (71.9)	3.771	1.57-9.05	0.002
No	6 (9.4)	87 (28.1)			
Age					
<50 years	10 (15.6)	127 (41.0)	3.745	1.24-7.63	<0.0001
≥50 years	54 (84.4)	183 (59.0)			
Gender					
Male	35 (54.7)	173 (55.8)	0.956	0.557-1.64	0.870
Female	29 (45.3)	137 (44.2)			
Geography					
Urban	37 (57.8)	207 (66.8)	0.682	0.394-1.18	0.170
Rural	27 (42.2)	103 (33.2)			
Hypertension					
Present	63 (98.4)	192 (61.9)	14.1	12.8-35.6	<0.001
Absent	1 (1.6)	118 (38.1)			
Diabetes					
Present	64 (100.0)	184 (59.4)	1.508	1.36-1.66	< 0.001
Absent	0 (0)	126 (40.6)			

Table 2 shows the association of different factors with myocardial infarction (MI) among study population. Those who had a myocardial infarction (N=49) among them 85.7% (N=42) were SLT users while less proportion i.e. 71.9% were SLT users in non-myocardial infarction group. This difference was statistically significant with odds ratio of 2.342 and 95% CI 1.10-5.40 (P value=0.041).

Similarly, author found statistically significant association of myocardial infarction with age groups, geographical residency, hypertension and diabetes.

Correlation of hemodynamic, haematological and biochemical parameters with myocardial infarction among study population was seen in Table 3. No significant association was noted between blood pressure parameters and rate of pulsation in patients with presence or absence of myocardial infarction (Table 3).

Among all other haematological parameters the difference in mean neutrophil count in patients with and without MI was found to be statistically significant (P=0.031).

Other parameter like TLC, lymphocyte counts, monocyte and other parameters of complete blood count did not show any statistical significance. Difference in mean sodium and potassium levels sin MI and non-MI patients were found to be not significant (p>0.05). No significant correlation was noted between biochemical parameters and presence or absence of MI (p>0.05).

Table 4 describes the correlation of socio-demographic parameters with cerebrovascular accident (CVA/stroke) among study population. Out of 64 patients diagnosed with CVA, 58 were SLT users and among 310 patients without CVA, 223 were SLT users. This difference was statistically significant with odds ratio of 3.71 and 95% CI 1.57–9.05 (p=0.002).

Similarly, analytical implication association of cerebro-vascular events with age groups, hypertension, and diabetes was statistically significant (p<0.05) but no significant difference was observed for geographical residency and gender.

The correlation of hemodynamic and biochemical parameters with cerebrovascular accident (CVA/stroke) among study population was presented in Table 5. No significant association was found between the associated parameters and the number of patients with or without affecting CVA (P>0.05).

Figure 1 presents the ECG and non-contrast CT scan findings in study population. Most common ECG abnormality noticed in study group was left ventricular hypertrophy followed by ST depression in V1 to V6.

Among the CVA patients 27 (42%) had left side infarction on the NCCT while 37 (58%) patient had right side infarction. From the Figure 2, it was evident that the risk of incidence of CVA and stroke was more among SLT users compared to non-users.

Table 5: Association of hemodynamic, haematological and biochemical parameters with CVA among study population.

Variables	Diagnosis category	N	Mean	SD	P value
Haemodynamic parameters					
Systolic blood pressure	CVA	64	150.33	32.579	0.624
	NA	310	152.34	29.193	
Diastolic blood pressure	CVA	64	87.77	17.020	0.771
	NA	310	88.43	16.446	
Pulse rate	CVA	62	80.03	19.067	0.943
	NA	304	80.22	18.846	
Biochemical parameters					
Sodium	CVA	63	125.83	34.112	0.165
	NA	305	130.30	20.209	
Potassium	CVA	63	14.65	44.156	0.431
	NA	305	10.47	36.984	
Urea	CVA	61	27.59	13.804	0.962
	NA	303	27.68	13.965	
Creatinine	CVA	61	1.61	3.249	0.199
	NA	303	4.36	16.596	
Fasting blood sugar	CVA	63	147.16	89.023	0.347
	NA	303	136.71	78.110	
Post-prandial blood sugar	CVA	61	201.00	83.708	0.510
	NA	282	193.33	82.148	

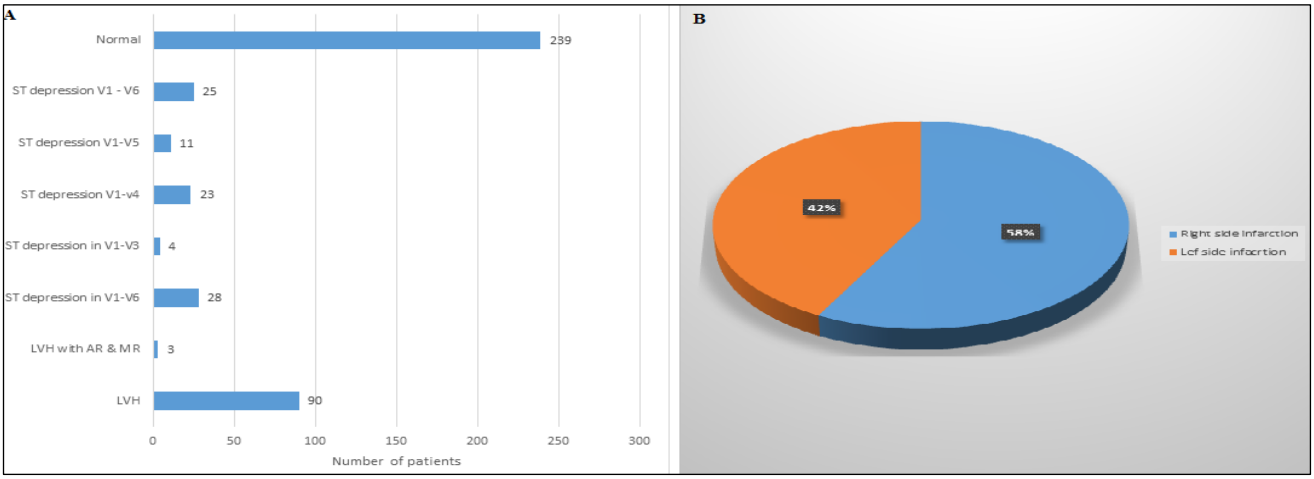

Figure 1: ECG abnormality and non-contrast CT scan findings in study population.

Table 6: Association of diabetes and hypertension with ST users.

Variables		ST user N (%)	ST nonuser N (%)	Odds ratio	95% CI	P-value
Hypertension	Present	193 (59.8)	0 (0)	1.769	1.58-1.98	<0.001
	Absent	130 (40.2)	100 (100)			
Diabetes	Present	184 (57.0)	0 (0)	1.719	1.54-1.91	<0.001
	Absent	139 (43.0)	100 (100)			

Out of 323 SLT users, hypertension and diabetes was seen in 193 and 184 patients respectively with significant association (p<0.001) with odds ratio of 1.769 and 1.719 respectively. As shown in Table 7, no significant

association was observed between ST users and hemodynamic, hematological and biochemical parameters among study population.

DISCUSSION

Smokeless tobacco (SLT) was used in many forms without combustion, results in possessing high percentage of free nicotine, total nicotine and various carcinogens.[8] The mode of use of SLT depends on its available forms, culture, geography and individual preferences. In India, ST products are used in different forms such as mishri, gul, mawa, snus, areca nut, slaked lime preparations, paan masala and paan with tobacco.[8,9] In present study, pan and gutkha was the most commonly used form (55.6%).

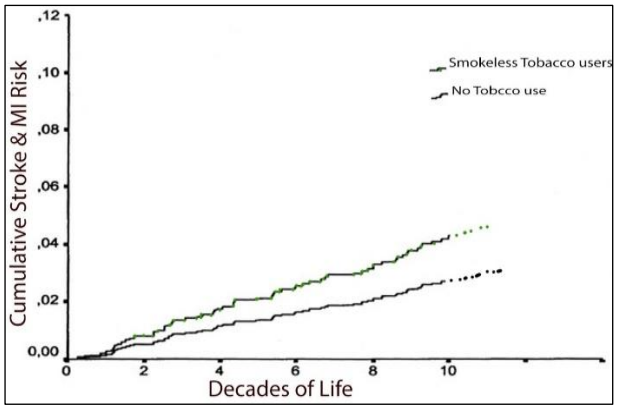

Figure 2: Cumulative risk of stroke and MI among ST user's vs non-users of tobacco (Kaplan-Meier curve).

Table 7: Association of hemodynamic, haematological and biochemical parameters with use of ST among study population.

Variables	ST users	N	Mean	SD	P value
Haemodynamic parameters					
Systolic blood pressure	Yes	323	151.81	29.397	0.934
	No	100	152.09	30.003	
Diastolic blood pressure	Yes	323	88.14	16.425	0.961
	No	100	88.05	16.752	
Pulse	Yes	317	80.25	18.849	0.909
	No	98	80.00	18.483	
Haematological parameters					
Hemoglobin	Yes	300	12.68	9.379	0.816
	No	93	12.95	10.379	
Total leucocyte count	Yes	323	7.24	1.270	0.729
	No	100	7.19	1.260	
Neutrophil	Yes	304	75.96	13.888	0.971
	No	94	75.90	14.257	
Lymphocyte	Yes	300	16.75	9.781	0.933
	No	93	16.65	9.729	
Monocyte	Yes	308	2.08	4.703	0.777
	No	95	1.92	4.285	
Eosinophil	Yes	294	3.54	5.875	0.887
	No	91	3.44	5.574	
Basophil	Yes	300	0.64	1.509	0.773
	No	93	0.69	1.615	
Biochemical parameters					
Sodium	Yes	318	129.56	22.342	0.695
	No	98	130.56	20.801	
Potassium	Yes	318	10.62	36.865	0.855
	No	98	9.85	33.603	
Urea	Yes	316	27.53	13.873	0.966
	No	97	27.60	14.315	
Creatinine	Yes	316	4.29	16.283	0.859
	No	97	3.96	15.732	
Fasting blood sugar	Yes	316	136.37	76.745	0.903
	No	97	137.47	79.276	
Post-prandial blood sugar	Yes	295	194.04	80.871	0.871
	No	91	192.47	80.251	

The prevalence of ST consumption in India was 20%.[3] The rate of consumption was higher in males compared to females.[4] This was in accordance with the results of this study. Lesser cost, easy availability, misconceptions about its useful health effects are important contributing factors of its higher consumption rate. Usage of these products was higher in rural area compared to urban.[4] In contrast to this, more of this study population addicted to SLT belongs to urban area.

Nicotine in tobacco products was involved in initiation of various pathological mechanisms which include platelet activation, endothelial dysfunction, accelerated atherogenesis, cardiac arrhythmias, cellular inflammation, relative insulin resistance and dyslipidemia, all of them contributing to cardiovascular disease.[10]

In this series, MI was seen in 49 (11.6%) and stroke in 64 (15.1%) patients. Previous studies found a significant association of SLT consumption with incidence of adverse cardiovascular diseases.[6]

In the present study, association between ST and CVD showed that those who had cerebrovascular events among them 90.6% were ST user while 71.9% were ST users in non-cerebrovascular events group. This difference was statistically significant (P=0.002). Similarly, author found statistically significant association of cerebro-vascular events with age groups, hypertension and diabetes.

Moreover, author also found those who had myocardial infarction among them 85.7% were ST user while 71.9% were ST users in non-myocardial infarction group. This difference was statistically significant (P=0.041). These findings were in accordance with the observations of Piano in western population.

Very few studies were done to assess the role of SLT on CVD outcomes and mortality. The results of these studies provided conflicted responses. In a meta-analytical study done by Boffetta P et al, eight studies evaluated the risk of fatal MI and five studies evaluated the incidence of fatal stroke by the consumption of SLT.[11] Of them, three studies showed increased risk for cardiovascular deaths (fatal myocardial infarction and stroke) when compared to non-users of SLT, while others did not show any significant difference in outcomes.

In another study, by Gupta BK et al, a significant greater prevalence of tachycardia, hypertension, low HDL, hypertriglyceridemia, hypercholesterolemia and diabetes was observed in SLT users when compared to non SLT users.[12] Similar observation was noticed in this study but did not found any significant association of these parameters between SLT users and non-users.

This study was probably the first study from Eastern India on clinical symptomology of cardiovascular diseases due to SLT. Author hypothesize the incidence of CVD in SLT users of this study might be due to accelerated cerebrovascular atherogenesis and cellular inflammation.

CONCLUSION

To conclude, the results suggest that SLT significantly increase liability towards CAD and stroke and becomes the predominant cause of mortality and morbidity in study population. Hence, implementing wide range of population and community-based policy interventions are necessary for control of SLT.

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