ORIGINAL RESEARCH

Oral Lesions and Metabolic Syndrome in Areca nut Chewers

Vasanthi V., Rooban Thavarajah, Elizabeth Joshua, Umadevi K. Rao, Kannan Ranganathan

Abstract

Background: Habitual use of Areca nut (AN) is associated with oral submucous fibrosis which is a potentially malignant disorder. The association of AN chewing with systemic disorders such as obesity, hyperglycemia, hypertension and dyslipidemia remain unclear.

Aim: This study was done to evaluate the prevalence of oral lesions and the association of AN chewing with features of metabolic syndrome (MS).

Materials and Methods: Anthropometric and biochemical investigations were performed in 50 AN chewers (cases) and 50 non-chewers (controls). Subjects were further categorized as MS positive (chewers and non-chewers) and MS negative (chewers and non-chewers) using International Diabetes Federation (IDF) classification. Chi-square and ANOVA were used to explore categorical and continuous variables respectively. $p \leq 0.05$ was considered to be statistically significant.

Results: Among AN chewers, 66% chewed AN as paan masala. Most common lesions were oral submucous fibrosis (32%) and tobacco pouch keratosis (20%). 36% of chewers had MS.

Conclusion: The present study shows difference in prevalence of metabolic syndrome among areca nut chewers and non-chewers. In addition to AN chewing, other factors could contribute to MS. Further large scale study with more parameters, on a prospective aspect may help us to better understand and address the problems of MS.

Key words: Areca nut, Oral lesions, Metabolic syndrome

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Introduction

Areca nut (AN) is the fourth (follows caffeine, nicotine, alcohol) most frequently used psychoactive substance in the world.[1] It is chewed in several forms - as an isolated raw form or in the form of quid with betel leaf, slaked lime, catechu and tobacco. The use of commercial products such as paan masala and gutkha is increasing, particularly among the younger age groups. The habit of chewing areca nut is linked to the development of oral submucous fibrosis (OSF), which is a potentially malignant disorder and cancer of oro-pharyngeal region. AN has also been documented to aggravate asthma, contribute to hypertension, obesity, type 2 diabetes, dyslipidemia, metabolic syndrome and cardiovascular diseases.[1,2]

Metabolic syndrome (MS) describes a group of disorders characterized by abdominal obesity, dyslipidemia, hyperglycemia (type 2 diabetes mellitus) and hypertension. Individuals with metabolic syndrome are five times more susceptible to type 2 diabetes and three times more liable to cardiovascular disorders.[3]

- Various criteria for the diagnosis of MS has been postulated by the following groups.[4]
- World Health Organization (1999)
- European Group for the Study of Insulin Resistance (EGIR) (1999)
- The National Cholesterol Education Program's Adult Treatment Panel III (NCEP ATP-III) (2001)
- International Diabetes Federation (IDF) (2005)
- New International Diabetes Federation (IDF) (2006)

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The New International Diabetes Federation (IDF) (2006) has defined metabolic syndrome as central obesity plus any two of the following factors.[5]

Central obesity (Waist circumference)	≥ 90 cm male ≥ 80 cm female
Raised triglycerides	≥ 150 mg/dl or specific treatment for this lipid abnormality
Reduced High Density Lipoprotein Cholesterol	< 40 mg/dl (male) < 50 mg/dl (female) or specific treatment for this lipid abnormality

Raised blood pressure	Systolic BP ≥ 130 mmHg Diastolic BP ≥ 85 mmHg or treatment for previously diagnosed hypertension
Raised fasting plasma glucose	≥ 100 mg/dl or previously diagnosed type 2 diabetes

The present study was done to evaluate the prevalence of oral lesions in AN chewers and the association of AN with MS using IDF diagnostic criteria.

Materials and Methods

Ethical approval for this study (Ethical clearance number: 20141125) was provided by the Institutional Ethical Committee on 25.11.2014.

Individuals with only history of chewing AN in any form and who does not consume alcohol or smoke tobacco were categorized as Cases. Controls were subjects without any habits. Patients with thyroid hormone imbalances and autoimmune diseases were excluded from the study. Subjects with life-style based obesity and difficulty in mouth opening due to other inflammatory conditions were also excluded from participating in the study.

A total number of 100 lorry drivers, sanitation and construction workers from various parts of Chennai were recruited after obtaining informed consent. Pre – structured case sheet was used for registering their details.

The study group comprised of

Cases = 50 (subjects with the habit of areca nut chewing for </= 20 years)

Controls = 50 (subjects without the habit of areca nut chewing)

Demographic details of the patient including name, age, gender, economic status, occupation, diet, history of habits with frequency, quantity and duration, past medical history, were recorded in the pre-structured case sheet. A thorough oral examination was done.

Blood pressure (systolic and diastolic) were recorded in mmHg using Mercury Sphygmomanometer (Diamond BPMR112 Aneroid). Systolic and diastolic values were recorded with the patient seated and the cuff tied around their upper left arm.

The following anthropometric measurements were done.

Height was measured in centimetre using standard height chart.

Weight was measured in Kilograms using Weighing scale. (Equinox weighing scale).

Waist circumference was measured in centimetre using measuring tape. The measurement was made with the patient standing, arms at the side, feet placed close together and body weight evenly distributed. Measurement was made around the

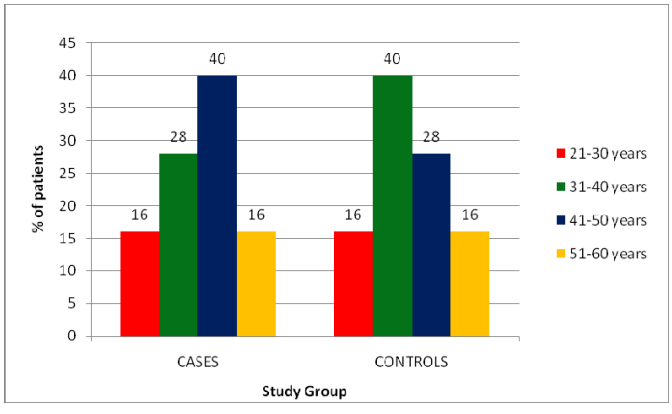
Table 1 - Age Distribution among Patients in Study Group (N=100)

Age in years	Cases (n=50) n(%)	Controls (n=50) n(%)	p-value
21-30	8(16)	8(16)	0.54
31-40	14(28)	20(40)	
41-50	20(40)	14(28)	
51-60	8(16)	8(16)	

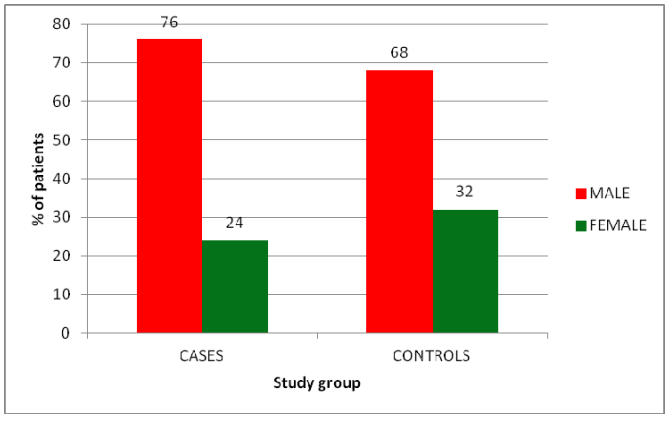
Table 2 - Gender Distribution among Patients in Study Group (N=100)

Gender	Cases (n=50) n(%)	Controls (n=50) n(%)	p-value
Male	38(76)	34(68)	0.37
Female	12(24)	16(32)	

Graph 1 - Age Distribution among Patients in study group (n=100)



Graph 2 - Gender Distribution Among Patients In Study Group (N=100)



waist at the point where the trunk bends laterally.

Hip circumference was measured in centimetre using measuring tape.

Body mass index was measured in Kg/m2 by formula –

$$\frac{\text{Weight}}{\text{Height x Height}} \text{ x10,000}$$

Waist to hip ratio was also calculated from waist and hip circumference.

Whole blood collection:

5ml of fasting morning blood was withdrawn from the antecubital vein of cases and controls, in an EDTA coated yellow sealed tube. The samples were transported within two hours for processing. The samples were centrifuged at 3000 rpm for 15 minutes. Fasting blood glucose, triglycerides, high-density lipoprotein levels were investigated.

Statistical Analysis

The predictor variables were sociodemographic factors (age, sex), AN chewing and the outcome variables were obesity, hyperglycemia, hypertension, dyslipidemia. All the data was entered and analyzed using Statistical Package for the Social Sciences (SPSS) software, version 21. Chi-square test was used to compare categorical variables. ANOVA was done to analyse continuous variables. p-value < 0.05 was considered statistically significant.

Results

The subjects were stratified into 4 groups based on age as: 21-30 years, 31-40 years, 41-50 years, 51-60 years. (Table 1, Graph 1). In cases, 76% were males and 24% were females and in controls 68% were males and 32% were females (Table 2, Graph 2).

Of chewers (n=50), 66% were paan masala chewers, 20% chewed betel quid, 14% chewed gutka.

Of 50 chewers, 32% had oral submucous fibrosis, 20% had tobacco pouch keratosis, 18% had chronic generalised periodontitis, 14% had chronic generalised gingivitis, 6% had erythroplakia, 4% had betel stains, 2% had oral squamous cell carcinoma and 2% had leukoplakia. The clinical diagnosis was confirmed histopathologically for oral submucous fibrosis and oral squamous cell carcinoma. Among 50 controls, 74% had chronic generalised gingivitis, 8% had chronic generalised periodontitis, 6% had fissured tongue, 4% had frictional keratosis, 4% had leukoedema, 2% had geographic tongue, and 2% had dental fluorosis (p=0.00). (Graph 3)

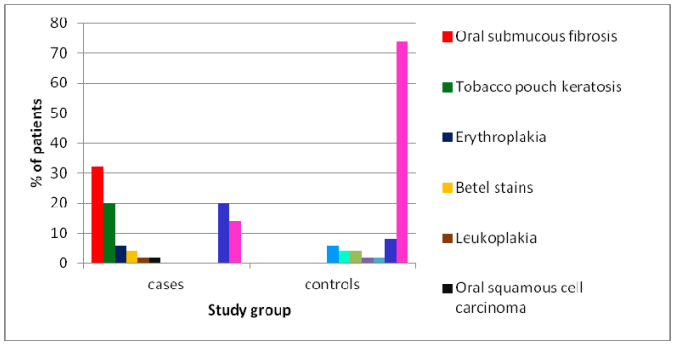
Cases {127.2(±10.6) mmHg}, {86.6(±6.8) mmHg} had higher mean systolic and diastolic blood pressure than controls {116.6(±8.7) mmHg}, {80.4(±3.4) mmHg} respectively. (p=0.00).

Waist circumference among cases {84.9(±6.1) cm} was higher than controls {83.2(±3.6) cm} with a p value of 0.09. Body mass index was higher in cases {23.97(±4.046) Kg/m2} compared to

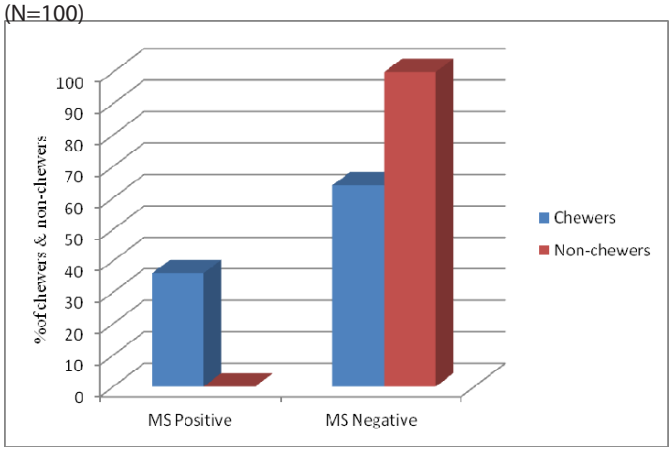
Table 3 – Mean Parameters of the Study Group

Mean Parameters	Cases(n=50) Mean±S.D	Controls (n=50) Mean±S.D	p value
Systolic blood pressure (mmHg)	127.2±10.6	116.6±8.7	0.00
Diastolic blood pressure (mmHg)	86.6±6.8	80.4±3.4	0.00
Waist Circumference (cm)	84.9±6.1	83.2±3.6	0.09
Waist to hip ratio	0.9±0.01	0.9±0.01	0.33
Body mass index (Kg/ m2)	23.9±4.1	21.7±3.1	0.00
Fasting blood glucose (mg/dL)	124.4±88.2	80.4±9.5	0.00
Triglyceride (mg/dL)	161.9±91.2	80.4±16.9	0.00
High Density Lipoprotein (mg/dL)	46.1±15.4	50.8±11.4	0.07

Graph 3 - Prevalence of Oral Lesions in the Study Group (N=100)



Graph 4 - Distribution of Metabolic Syndrome in the Study Group (N=100)



controls {21.78(±3.172) Kg/m2} (p=0.00). Cases {0.9(±0.01)} and controls {0.9(±0.01)} had similar waist to hip ratio (p=0.33).

Prevalence of hyperglycemia was higher in chewers {124.4(± 88.2) mg/dL} than non-chewers {80.4(±9.5) mg/dL} (p=0.00). The difference in triglycerides level was higher for cases {161.9(± 91.2) mg/dL} compared to controls {80.4(±16.95)mg/dl} (p=0.00).

Controls {50.8(±11.4) mg/dL} had higher high-density lipoprotein levels compared to the cases {46.1(±15.4) mg/dL} (p=0.07). (Table 3)

For further analysis, we categorized the group into MS positive chewers and non-chewers, MS negative chewers and non-chewers. (Graph 4)

Discussion

The chewing of areca nut has been associated with various oral and systemic ill effects. The deleterious oral effects of areca nut has been widely documented to range from reactive lesions, periodontitis to oral precancer and cancer.[6,7,8]

In this present study, the habit of chewing showed significant difference among the male and female. Males predominantly used paan masala as opposed to betel quid among females. This prevalence of males chewing paan masala, gutka and female chewing betel quid is consistent with earlier reports.[9]

It is reported that the arecoline, the principle alkaloid of areca nut affects the central and autonomic nervous system. The effects are dose-dependent and habit-related. The direct sympathetic effect of arecoline causes increased heart rate and vasoconstriction of blood vessels leading to elevation of blood pressure. In our study, we identified that the systolic blood pressure was significantly different between cases and controls. This is in accordance with previous studies by Tseng et al.,[10] and Heck et al.,[11].

In our study, we noticed that the mean waist circumference was higher in cases compared to controls as this is the defining criteria for metabolic syndrome. Similar observations have been previously reported by Mannan et al.,[12], Chang et al.,[13] and Lin et al.,[14]. The competitive inhibitory effect of arecoline on GABA receptors in brain, cardiovascular system and pancreas promotes increase in appetite and contributes to central obesity and increased waist circumference. Abdominal obesity is associated with insulin resistance and type 2 diabetes mellitus. Insulin resistance, hyperglycemia and cytokines released by the adipose tissue causes endothelial dysfunction, dyslipidemia and hypertension.

Our findings were consistent with those of Tung et al.,[15], Tseng et al.,[16] and Benjamin et al.,[17] with respect to fasting blood glucose levels. Nitrosated derivatives of areca alkaloids are diabetogenic. These nitroso compounds are reported to have a ring structure, similar in configuration to glucose, which binds to the islet beta cell glucose receptors and influences diabetogenecity.

Arecoline contributes to dyslipidemia by inhibiting adipogenic differentiation, inducing lipolysis in adipocytes, blocking HDL receptors and inhibiting the uptake of LDL uptake by the liver as reported earlier.[4] We observed that the difference in mean of triglyceride of cases were significantly different from controls.

To summarize, 36% of chewers were positive for metabolic syndrome. There was positive association for systolic blood pressure, diastolic blood pressure, fasting blood glucose and triglycerides among cases and controls. These are consistent with the study by Shafique et al.,[18] who reported that 17.9% of cases had metabolic syndrome. Similar association have been reported by Chung et al.,[19], and Guh et al.[20].

The prevalence of metabolic syndrome was highest in chewers (25.13%) and dose-dependent effects of betel quid chewing with metabolic syndrome has been reported by Yen et al.,[21]. In this cohort, the prevalence of metabolic syndrome was highest among chewers (36%) compared to non-chewers.

Conclusion

The results indicate that there was a significant difference in occurrence of metabolic syndrome among areca nut chewers and non-chewers. Anthropometrical and biochemical markers (other than those involved in defining metabolic syndrome) could not differentiate between areca nut chewers with and without metabolic syndrome. This suggests that other factors such as diet, lifestyle could contribute to the metabolic syndrome. Further large scale studies with more biochemical parameters will probably shed more light into the phenomenon of increased incidence of metabolic syndrome among areca nut chewers.

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