

# Betel-quid use and its effects on symptoms of schizophrenia and extrapyramidal symptoms among a group of patients in a tertiary care hospital in Sri Lanka

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## Abstract

### Background

There is limited research regarding the prevalence of betel quid use and its effects on symptoms of patients with schizophrenia. Available studies suggest an association between betel chewing and positive symptoms among males with schizophrenia.

### Aims

This study aimed to compare the prevalence of betel quid chewing between patients with and without mental illness, and to explore the association between betel quid use, symptoms of schizophrenia and side effects of psychotropic medication.

### Methods

A cross sectional descriptive study was carried at outpatient clinics at a tertiary care hospital in Sri Lanka. A structured interview schedule was administered to all participants.

### Results

Out of 1000 participants, 20.9% chewed betel quid

(95%CI: 18.4% - 23.4%). The rate of betel chewing among patients with and without a mental illness was 20.7% (95% CI: 17.0% - 24.4%) and 21.0% (95% CI: 17.6% - 24.5%) respectively and there was no significant difference between the two groups. There was no statistically significant difference between the occurrence of positive or negative symptoms and extrapyramidal side effects in patients with schizophrenia who did and did not chew betel. Female gender ( $p=0.004$ ) and betel quid chewing (0.002) were associated with more anticholinergic side effects.

### Conclusions

There was no association between betel quid usage and the occurrence of positive or negative symptoms of schizophrenia or extrapyramidal side effects.

**Key words:** schizophrenia, betel quid, positive symptoms, negative symptoms, extrapyramidal side effects.

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## Background

Betel consumption has been traditionally associated with cultural practices in South Asian, South East Asian and Asian Pacific regions (1,2). Betel is chewed either alone or more often as a quid with additives such as areca nut, slaked lime, tobacco, cloves, or cardamom. The ingredients and preparation of the betel quid may vary from region to region. In Sri Lanka betel leaf (*Piper betle*) is usually consumed in a quid of varied combinations with ingredients such as slaked lime, tobacco, areca nut (*Areca catechu*) (3). Areca nut is the primary ingredient in the quid and chewing tobacco may or may not be added according to preference.

Population based rural and urban surveys in Pakistan and India conducted during the last twenty-five years, report that 20-40% of the population aged fifteen years and over were betel quid or areca nut chewers (2). A prevalence study conducted in 1995 in Palau reported that 72% of the males and 80% of the females chewed betel quid, and of these, 80% had incorporated tobacco in their quid (4). According to the National Oral Health Survey of 1994-1995 carried out in Sri Lanka, the prevalence of betel chewing was 40.5% among those aged between 35-74 years, while it was 33.78%, among those between the aged 35-44 years (5). Another study among the villagers in the Central Province of Sri Lanka



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reported that 54% of males and 42% of females used betel quid regularly (6). A 2007 study in two districts in Sri Lanka reported a marked difference in the prevalence of betel quid chewing between urban and rural populations – 17.6% and 1.7% in the rural and urban district, respectively (7).

An Indian study on the prevalence of areca nut use among psychiatric patients showed that 24% of the study sample had recent use and 10% had dependence (8). However, prevalence studies related to betel quid and areca nut use among mentally ill patients in Sri Lanka are sparse. A preliminary study conducted at North Colombo Teaching Hospital, Ragama, reported that a higher proportion of patients with schizophrenia chewed betel compared with control subjects (9).

Burton-Bradley first referred to the psychotropic effects of areca nut among chronic users in Papua New Guinea (10). Research on patients with mental illness and areca nut or betel quid use has been mainly in relation to patients with schizophrenia (11, 12). Research evidence supports the high prevalence of betel chewing amongst patients with schizophrenia compared to the normal population (11). Sullivan et al, in 2007 suggested a therapeutic relationship between areca chewing and positive symptoms among male schizophrenic patients in Palau, but could not demonstrate an association between betel use and extrapyramidal symptoms (11). Some authors suggest that patients with schizophrenia chew betel as a measure to self-medicate their symptoms, but there is also increasing research evidence contradicting the self-medication hypothesis (11, 13). On the other hand, arecoline, which is an ingredient of the areca nut, is a potent muscarinic receptor agonist. Recent neurobiological research hypothesizes the possible mechanisms involving muscarinic receptors in the causation of some of the symptoms of schizophrenia (13). Therefore, it is important to understand the basis of the association between schizophrenia and betel chewing, which may have therapeutic and etiological implications with regards to this disorder. This study aimed to compare the prevalence of betel quid chewing between patients with and without mental illness, and to explore the association between betel quid use, symptoms of schizophrenia and side effects of psychotropic medication.

## Methods

### Study design

This was carried as a cross sectional study, conducted from January 2014 to December 2014.

### Sample

Patients attending medical, surgical and psychiatry outpatient clinics of North Colombo Teaching Hospital

during the study period, who were aged 18 years and over, were considered eligible for inclusion in the study. Patients who were less than 18 years of age, who were grossly psychotic or severely physically ill were excluded.

### Outcome measures and tools used in the study

A structured interview schedule administered to all participants, by an interviewer conversant in all three languages (Sinhalese, Tamil and English), was used to gather demographic data, and factors related to medical, surgical illness, and substance use. The psychiatric diagnoses of patients recruited from the psychiatry outpatient clinics were confirmed by perusal of patient diagnoses cards and/or by a clinical interview conducted by a consultant psychiatrist based on ICD 10 criteria. In patients diagnosed to have schizophrenia, the Positive and Negative Syndrome Scale (PANSS) and the Liverpool University Neuroleptic Side Effect Rating Scale (LUNCERS) were used to measure symptoms of schizophrenia and the side effects due to psychotropic respectively (15, 16).

### Quantification of the amount of betel used

During the interviewer-conducted structured interview schedule, participants were asked regarding the number of betel quid they chewed per day. They were also asked to show how much areca was included per quid using a betel/areca tray made available to them during the interviews and the amount chosen by each subject was weighed.

### Ethics

All participants were provided information about the study. Only those who gave written informed consent were included in the study. Ethical approval for the study was granted by Ethical Review Committee, University of Kelaniya, Sri Lanka.

### Analysis

Demographic data were summarized using means with standard deviations and counts with percentages. The prevalence of betel quid chewing was estimated for the whole study sample, as well as for those with and without mental illness. Group comparisons were done using the two-sample t test. Linear models were used to investigate the variables associated with EPSE and anticholinergic side effects. A p value of 0.05 was considered as significant. R programming language version 3.5.1 was used for the analysis.

## Results

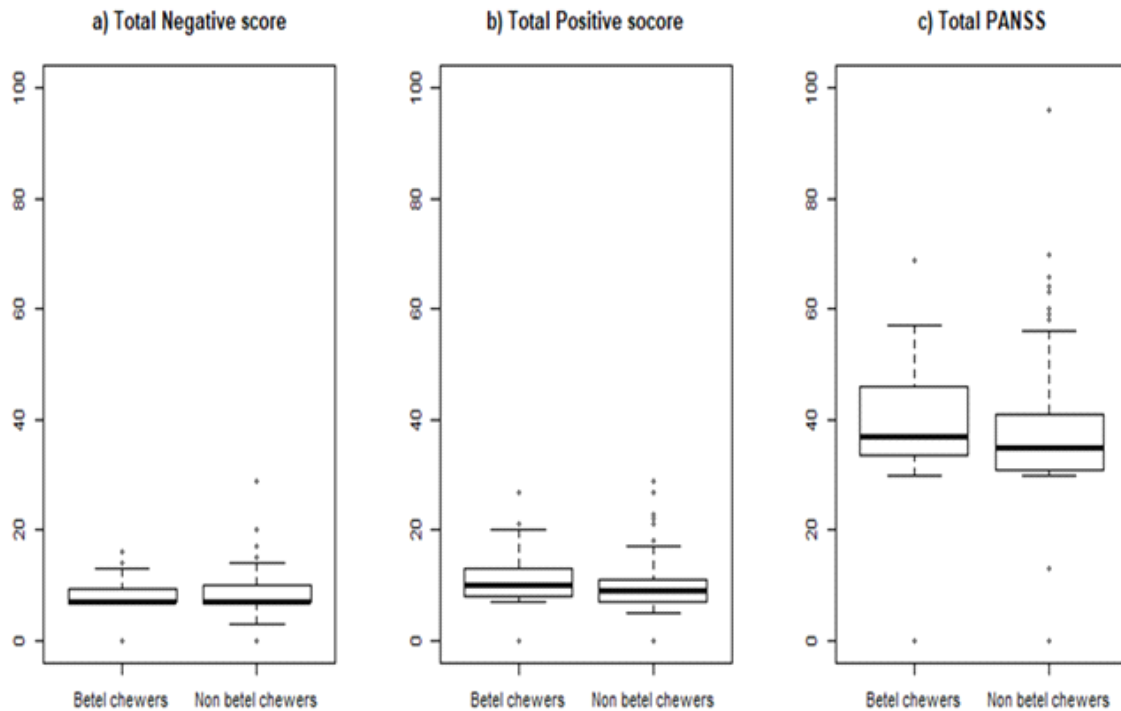
A total of 1,000 patients attending outpatient clinics in the North Colombo Teaching Hospital, Sri Lanka, were included in the study, of whom 502 (50.3%) were attending medical clinics, 462 (46.2%) were attending psychiatry clinics and 35 (3.5%) surgical clinics. Of the total study sample 410 (41.0%) were males (Table 1). The diagnoses of patients recruited from the psychiatry clinic included schizophrenia, schizoaffective disorder, bipolar affective disorder, depression, cannabis induced psychosis, and alcohol use disorders. Of the total study participants, 209 (20.9%) chewed betel quid (95% CI: 18.4% - 23.4%). The rate of betel quid use was 20.7% (95% CI: 17.0% - 24.4%) among patients with mental illnesses and 21.0% (95% CI: 17.6% - 24.5%) among other patients who were attending medical or surgical clinics. There was no significant difference in the prevalence of betel quid chewing between those with and without mental illnesses.

Betel quid chewing was reported among 38 (80.9%) of the males with a diagnosis of schizophrenia ( $p < 0.01$ ). There was no significant difference in the total positive, negative scores or total scores of the PANSS, in patients with schizophrenia who did and did not chew betel quid (Figure 1, Table 2). Betel quid chewers with schizophrenia had more anticholinergic side effects ( $p = 0.04$ ) compared to those patients with schizophrenia who did not chew betel quid.

According to the fitted models, in participants with schizophrenia, only the age of patients showed a significant association with extra pyramidal side effects (EPSE). Increasing age was associated with higher scores when EPSE were assessed using the LUNCERS ( $p = 0.025$ ). Anticholinergic side effects were significantly associated with female gender ( $p = 0.004$ ) and betel chewing (0.002) (Table 3).

Table 1. Demographic characteristics of the total study participants

	Psychiatric patients (n=463)	Non-psychiatric patients (n=537)	P value
Mean age (SD)	45.1 (13.7)	60.5 (13.4)	<0.001
Males (%)	310 (57.5)	227 (42.3)	0.414
Educational level			
Primary	44 (9.7)	98 (18.7)	<0.001
Secondary	312 (68.7)	356 (67.8)	
Tertiary	98 (21.6)	71 (13.5)	
Employed (%)	181 (39.2)	275 (51.4)	<0.001
Marital status			
Single	156 (33.7)	32 (6.0)	<0.001
Married	293 (63.3)	505 (94.0)	
Separated/Divorced	14 (3.0)	0 (0.0)	
Living status			
Own/relatives home	453 (98.1)	526 (98.7)	0.299
Residential home	3 (0.6)	0 (0.0)	
Homeless	6 (1.3)	7 (1.3)	
<b>Betel quid use</b>			
Yes	96 (20.7)	113 (21.0)	0.967
No	367 (79.3)	424 (79.0)	
1-5 quids/day	77 (80.2)	99 (84.2)	0.373
6-10 quids/day	14 (14.6)	16 (14.0)	
10+ quids/day	5 (5.2)	2 (1.8)	



**Figure 1. Distribution of a) total negative score, b) total positive score and c) total PANSS score between betel chewers and non-betel chewers among schizophrenia patients.**

Table 2. PANSS score, EPSE and anticholinergic side effects among patients with schizophrenia and use of betel quid			
	Patients with schizophrenia who chewed betel quid (n=47)	Patients with schizophrenia who didn't chew betel (n=104)	P value
Mean age (SD)	46.0 (13.9)	45.2 (13.0)	0.737
Males	38 (80.9)	34 (32.7)	<0.001
<b>Total PANSS score</b>	38.1 (13.3)	36.6 (14.2)	0.545
<b>Total positive score</b>	10.9 (5.3)	9.7 (5.0)	0.222
High consumption (10+quids/day)	15.5 (10.1)		0.392
Low consumption (>10 quids/day)	10.4 (4.6)		
<b>Total negative score</b>	8.4 (3.3)	8.4 (3.8)	0.907
High consumption (10+quids/day)	7.7 (1.0)		0.217
Low consumption (>10 quids/day)	8.4 (3.4)		
<b>EPSE</b>	1.6 (1.9)	1.0 (1.7)	0.088
High consumption (10+quids/day)	1.2 (1.2)		0.593
Low consumption(>10 quids/day)	1.6 (2.0)		
<b>Anticholinergic side effects</b>	3.0 (2.2)	2.1 (2.3)	0.040

Table 3. Parameters estimate of the linear models for extra pyramidal side effects and anticholinergic side effects in patients with schizophrenia

Dependent variable	Independent variables	Estimate	Standard error	T value	P value
EPSE	Intercept	0.096	0.519	0.185	0.853
	Age	0.024	0.011	2.264	0.025
Anticholinergic SE	Intercept	1.357	0.347	3.910	<0.001
	Female gender	1.170	0.403	2.906	0.004
	Betel quid chewing	1.3766	0.4343	3.170	0.002

## Discussion

The prevalence of betel quid in the total study population was 20.9%. The prevalence of betel chewing among patients with and without mental illness was similar. In a previous study conducted among the general population in Sri Lanka the prevalence of betel chewing was reported as 17.6% in rural and 1.7% in urban areas, whereas another study reported that nearly 53% of the rural community in Sri Lanka chewed betel, specially estate workers, labourers, and drivers (7, 17). De Silva et. al., reported that betel chewing was more prevalent among older people in Sri Lanka (7).

We could not elicit a significant difference in betel chewing among different age groups. However, we found that betel chewing was significantly more prevalent among males and also among those who had a lower level of education. We did not find a significant association between betel quid chewing and economic status of the patient.

Arecoline, the major alkaloid released from areca nut, which is one of the constituents of betel quid, is reported to function as a partial muscarinic agonist and has been hypothesized to have beneficial effects on both positive and negative symptoms of schizophrenia (11). Sullivan et al. reported that patients with schizophrenia who chewed betel quid had lower scores on both the negative and positive scales of the PANSS, but there were no differences in extrapyramidal symptoms or tardive dyskinesia (11,15). A review done by Coppola reported that males with a high consumption of betel quid had significantly lower positive symptoms compared to low consumers or non-betel users (18). However, a study done in Nepal among patients with schizophrenia did not find a significant difference in the PANSS scores

among betel chewers and non-chewers (19). Deahl described two patients with chronic schizophrenia who were on depot antipsychotics, who developed severe extrapyramidal symptoms in the context of a period of heavy betel nut consumption (20). Deahl had hypothesized that this is due to the antagonistic effect of arecoline (active ingredient of areca) on the anticholinergic agent, procyclidine (20).

In this study, we did not find a significant difference in the positive scores of PANSS, in patients with schizophrenia, who did and did not chew betel quid. Similarly, among our study participants, betel quid chewing did not have a significant impact on the extra pyramidal symptoms, in patients with schizophrenia. However occurrence of anticholinergic side effects showed a significant association with gender and betel chewing.

## Study Limitations

We did not have access to the patients' clinical records and most of the patients were not aware of the names or doses of the psychotropic medication they were on; therefore, we could not investigate the effects of psychotropics on the PANSS as a confounding factor, which is a limitation. Betel quid chewed by some of the participants of our study sample contained tobacco as an ingredient, which may have an effect on the symptoms of schizophrenia. This and other psychoactive substances which some of the patients used may have had an effect on the PANSS score.

## Conclusions

There was no significant difference in the prevalence in betel quid chewing between those with and without a

mental illness. There was no association between betel quid use and symptoms of schizophrenia or extra pyramidal side effects. The possible effect of betel quid chewing on symptoms of schizophrenia and side-effects of psychotropic medication should be explored further, preferably in a longitudinal study. This is particularly important in Sri Lanka, given the relatively high prevalence of betel quid use among patients with schizophrenia in this country.

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## Conflicts of interest

None declared.

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