

Psychiatric Morbidity Among Patients With Oral Submucous Fibrosis: A Controlled Study

Jigna V Raja¹, Puja Rai², Naveen C Kumar³, Mubeen Khan⁴, H Chandrashekar⁵

¹MDS. Senior Lecturer, Department of Oral Medicine and Radiology, Dr Syamala Reddy Dental College Hospital and Research Centre, Bangalore, Karnataka, India. ²MDS. Senior Lecturer, Department of Oral Medicine and Radiology, Maharana Pratap College of Dental Sciences, Gwalior, Uttar Pradesh, India. ³MD, DPM. Assistant Professor, Department of Psychiatry, National Institute of Mental Health and Neurosciences (NIMHANS), Bangalore, Karnataka, India. ⁴MDS. Professor and Head, Department of Oral Medicine and Radiology, Government Dental College & Research Institute, Bangalore, Karnataka, India. ⁵MD. Professor and Head, Department of Psychiatry, Bangalore Medical College and Research Institute, Bangalore, Karnataka, India.

Abstract

Aim: The study aimed to evaluate the association between oral submucous fibrosis (OSF) and psychiatric morbidity in a controlled manner.

Methods: Matched patients were divided into three groups: Those with areca nut chewing habits with OSF (Group 1; n=50); those with areca nut chewing habits without OSF (Group 2; n=50); those without areca habits and with dental problems other than OSF (Group 3; n=50). The Mini International Neuropsychiatric Interview was used to assess psychiatric morbidity. Dependence to areca products was also assessed.

Results: Sixteen (32%) Group 1 patients had psychiatric morbidity compared to one (2%) in Group 2 and two (4%) in Group 3 ($P<0.001$). Further, psychiatric morbidity was significantly higher among patients with advanced stages of OSF. In Groups 1 and 2, 49 (98%) and 47 (94%) patients, respectively, had dependence on areca products.

Conclusion: This study has suggested the association of substantial psychiatric morbidity among patients with OSF. In addition to mandatory psychiatric management of these patients, future research should be targeted at a prospective evaluation of a cause and effect relationship as well as at psychiatric interventions.

Key Words: Oral Submucous Fibrosis, Chronic Disorder, Psychiatry, Areca, Dependency

Introduction

In many countries including India, Pakistan, Malaysia, China, Canada, South Africa, Sri Lanka, and other South East Asian countries, the use of areca nut in its various forms is very popular and has led to the development of a unique generalised fibrosis of the oral tissues called oral submucous fibrosis (OSF). OSF is a chronic, progressive, pre-malignant and crippling condition affecting the oral mucosa and oropharynx. It is associated with a juxta-epithelial inflammatory reaction followed by a fibro-elastic change of the lamina propria, with epithelial atrophy leading to stiffness of the oral mucosa [1]. The resultant trismus and inability to eat cause significant debilitation and also increase the chances of developing oral malignancies, with frequencies ranging from 7% to 13% [2]. OSF has

become a serious concern to the health care providers as it largely affects the younger age group.

During recent years, the important interrelationship between chronic physical illnesses and psychiatric disorders has been studied extensively [3-5]. It is suggested that individuals with chronic somatic diseases are at a relatively higher risk of developing psychological distress than physically healthy people. Psychological distress may manifest itself in many different ways, from having to make an extra effort to cope with illnesses, through emotional symptoms such as grief or anxiety that naturally accompany a fearful situation, to a clear-cut psychiatric disorder [3]. Numerous studies show an association between psychiatric morbidity and chronic disorders such as cardiovascular dis-

Corresponding author: Dr Jigna V Raja, Department of Oral Medicine and Radiology, Dr Syamala Reddy Dental College Hospital and Research Centre, 111/1, SGR College Main Road, Munnekolala, Marathalli Post, Bangalore-560037, Karnataka, India; e-mail: jigna.vr@gmail.com, jigna_ad@yahoo.com,

eases, cancers, asthma, arthritis, chronic obstructive pulmonary disease, diabetes mellitus, temporomandibular disorders, burning mouth syndrome, oral lichen planus and recurrent aphthous stomatitis [3-7]. However, literature on psychiatric morbidity in OSF remains scarce. A recent preliminary study on this aspect found that OSF is associated with considerable psychological morbidity when compared to control patients who had dental diseases other than OSF and had no areca/tobacco habit [8]. In that study, the mean (SD) scores on the 28 item General Health Questionnaire (GHQ) for patients and control groups were 48.2 (18.1) and 24.2 (6.5), respectively ($P < 0.001$). The GHQ is a screening instrument that only gives an indication for the presence of psychiatric morbidity. In the current study, we improved the methodology by incorporating a standardised structured instrument that was used to assess the psychiatric morbidity (Mini International Neuropsychiatric Interview; MINI) [9]. Patients with areca/tobacco use but without OSF were also recruited to the control group in order to ascertain the contribution of OSF per se towards the presence of psychiatric morbidity.

Aims

1. To study the psychological morbidity among patients with oral submucous fibrosis.
2. To study the psychological correlates of areca nut use among patients with and without oral submucous fibrosis.

Methods

Setting

The study was conducted in the Department of Oral Medicine and Radiology of the Government Dental College and Research Institute, a tertiary health care centre in Bangalore, South India. This institute caters for patients in and around Bangalore city. On an average, 5 to 15 patients with OSF come for consultation to this institute every month.

Subjects

All patients aged between 18 and 70 years who visited the outpatient department were invited to participate in the study. Patients were divided into the following three groups:

- Group 1: Those with an areca nut chewing habit and a diagnosis of OSF which had been made according to the following

WHO criteria [10]: history of intolerance to spicy food; inability to open the mouth wide; altered oral mucosal appearance (pale pink, mottled, whitish or opaque whitish), loss of elasticity with the resultant tightening feeling or firm fibrous bands in the buccal and labial mucosa.

- Group 2: Those with an areca nut chewing habit but without OSF.
- Group 3: Those with other dental problems in the form of pulp and periapical pathologies, gingivitis, pericoronitis, partial edentulism and malocclusion with no areca nut or tobacco habits.

The patients in the three groups were matched for age, gender and socioeconomic status.

Patients with a history of having psychiatry consultations were excluded from the study, as were those with co-existing temporomandibular joint disorders, facial neuralgias, atypical facial pain, atypical odontalgia, bruxism, salivary gland disorders, chronic advanced periodontitis and viral infections that could have had a bearing on the psychiatric disorders. Previous studies have identified a complex mutual relationship between psyche and systemic diseases such as asthma, arthritis, cardiovascular diseases, chronic lung disease, neurological disease, diabetes, migraine, obesity and HIV/AIDS [3,4], hence patients with any such systemic compromises were not included in the study. As there is emerging literature on psychiatric co-morbidity in patients with different dermatological disorders such as urticaria, lichen simplex chronicus, atopic dermatitis, psoriasis, alopecia areata, and pruritus [11] and oral mucosal disorders such as burning mouth syndrome, oral lichen planus and recurrent aphthous stomatitis [7], patients with these were excluded. Also, mucocutaneous diseases such as lupus erythematosus, pemphigus, pemphigoid and erythema multiforme, which have a psychosomatic basis, were excluded from the study.

Epidemiological data have suggested that the prevalence of psychiatric morbidity in the general Indian population is around 7% [12]. It was expected that this percentage would be found in the control sample (Group 3). It was also expected that about a third of patients with OSF would have a psychiatric diagnosis. To detect this difference (i.e., a difference of about 23%) with an alpha of 0.05, a sample of 45 patients in each group would have a power of 80%. Expecting inappropriate or no response in about five in each group, the sample

size of each group was increased to 50. Hence, this sample had 80% power to detect a difference of about 23%.

In Group 1, 62 subjects with OSF were originally interviewed, of whom 12 dropped out from the final data analysis. These patients were those who did not provide complete sociodemographic details, information on pattern of use of areca nut and its products, or those who consented for the screening by the dentist in the dental setting but were apprehensive of visiting the psychiatrist for further confirmation of the findings. These issues were found in the other groups also. In Group 2, 56 patients were interviewed among whom six did not qualify. A total of 67 subjects participated in Group 3. Among these, detailed examination of teeth revealed extrinsic stains typical of past/current smokeless tobacco and areca nut use in seven patients, hence they were excluded. Furthermore, ten patients were not considered because of lack of information provided. Thus, for the final analysis, 50 patients were included.

Assessments

The assessment for clinical and functional staging devised by Haider *et al.* (2000) [13] was followed. In this system, categorisation is as follows:

Clinical staging:

1. Faucial bands only.
2. Faucial and buccal bands.
3. Faucial, buccal and labial bands.

Functional staging:

- A. Mouth opening: ≥ 20 mm.
- B. Mouth opening: 11-19 mm.
- C. Mouth opening: ≤ 10 mm.

In addition, the following clinical staging as given by Khanna *et al.* (1995) [14] was also recorded: *Group I (very early cases)*: Burning sensation in the mouth, acute ulcerations, recurrent stomatitis, normal mouth opening.

Group II (early cases): Limitation of mouth opening present, soft palate and faucial pillars are the areas primarily affected, buccal mucosa mottled, fibrosis seen.

Group III (moderately advanced cases): Trismus evident, pale buccal mucosa firmly attached to the underlying tissue, vertical fibrous bands palpable in premolar area, inability to blow out or whistle, fibrous bands radiating from pterygomandibular raphe or anterior faucial pillar on the soft palate.

Group IVa (advanced cases): Severe trismus, thickened fauces which is shortened and firm on

palpation, limited tongue movements, circular bands felt on palpation around the entire mouth.

Grade IVb (advanced cases with premalignant and malignant changes): In addition to clinical signs of advanced OSF, leukoplakia and carcinoma are seen.

Version 5 of the Mini-International Neuropsychiatric Interview (MINI-Plus) [9], a brief structured instrument, was used to assess all the subjects for the presence of psychiatric disorders included in the fourth edition of the *Diagnostic and Statistical Manual (DSM-IV)* [15] and the tenth version International Classification of Diseases of the World Health Organization (ICD-10) [16]. The MINI-Plus employs different time frames for various disorders: current, past, or lifetime. Psychometric examination of the MINI-Plus shows acceptable test-retest and inter-rater reliability. Validation and reliability studies comparing the MINI-Plus to the Structured Clinical Interview for DSM-III-R Patient Edition (SCID-P) and the Composite International Diagnostic Interview (CIDI; a structured interview developed by the World Health Organization for lay interviewers for ICD-10) showed that the instrument has acceptably high validation and reliability scores and could be obtained in a much shorter period of time (mean 18.7 ± 11.6 min, median 15 min) than the above instruments [17,18]. The MINI-Plus screening was administered by the first (JVR) and the second (PR) authors. The screening instrument consisted of 45 questions each pertaining to a particular psychiatric disorder. The third (CNK) and (HC) fifth authors held four one-hour training sessions in its use and administration. However, because no calibration of such training was performed, patients who failed the screening (patients who answered yes to any of the screening questions in the instrument) were further interviewed by a consultant psychiatrist (CNK) using the MINI-Plus.

A separate pro forma was used to collect details regarding areca nut use. Age of initiation, type of preparations of areca nut used, frequency of use, duration of each chew, quantity used (number of pouches of processed areca nut preparations or number of units of unprocessed areca preparations) and co-morbid use of other substances were recorded. Along with these details, the reason(s) for starting the habit, maintaining factors and effect after substance use were documented. The questionnaire also incorporated issues of substance use disorders modified for areca nut from the ICD-10 and DSM-

IV to determine the presence of dependent use of areca products. The domains assessed were:

1. Craving: a strong desire or sense of compulsion to take the substance.
2. Tolerance: the need for significantly increased amounts of the substance to achieve intoxication or the desired effect, or a markedly diminished effect with continued use of the same amount of the substance.
3. A physiological withdrawal state when substance use is reduced or ceased, as evidenced by the characteristic withdrawal syndrome for the substance, or by use of the same (or closely related) substance with the intention of relieving or avoiding withdrawal symptoms.
4. Impaired capacity to control substance-taking behaviour in terms of its onset, termination, or levels of use, as evidenced by the substance being often taken in larger amounts or over a longer period than intended, or by a persistent desire or unsuccessful efforts to reduce or control substance use
5. Salience: a great deal of time spent in activities necessary to obtain the substance, use the substance, or recover from its effects; preoccupation with substance use, as manifested by important alternative pleasures or interests being given up or reduced because of substance use.
6. Persistent substance use despite clear evidence of harmful consequences as evidenced by continued use when the individual is actually aware, or may be expected to be aware, of the nature and extent of harm. Three (or more) of the domains 1–6 occurring any time in the same 12-month period were required for a diagnosis of areca and areca/tobacco dependence according to DSM-IV or ICD-10 criteria.

The withdrawal syndrome related to areca use was identified using the constructed items taken from Amphetamine Withdrawal Questionnaire (AWQ) by Srisurapanont *et al.* (1999) [19] and from the Hughes–Hatsukami Scale for Tobacco Withdrawal [20]. These scales have been previously used by Benegal *et al.* (2008) [21] to assess areca nut dependence and are short, reliable and valid scales with satisfactory internal consistency and test–retest reliability. The domains assessed for

withdrawal were craving, dysphoria, anhedonia, increased appetite, fatigue, agitation/anger/irritability, anxiety/feeling tense, increased sleep, vivid, unpleasant dreams and slowing of movement over the previous 24 hours, angry/irritable/frustrated, anxious/tense, depressed, restless/impatient.

The Fagerstrom Tolerance Questionnaire [22] was also used to assess the nicotine dependence syndrome. This is a commonly used paper and pencil test with six simple questions to assess addiction to nicotine. The Alcohol Use Identification Test (AUDIT) [23] was used to identify persons with hazardous and harmful patterns of alcohol consumption. The AUDIT was developed by the World Health Organization as a simple method of screening for excessive drinking and to assist in brief assessment. The AUDIT also helps to identify alcohol dependence and some specific consequences of harmful drinking.

Ethical aspects

The study was performed after approval from the institutional review board (approval protocol number: GDCRI/ACM/PG/Ph.D/1/2009-10) and each patient was recruited only after giving written informed consent.

Statistical analysis

Statistical analysis was conducted using statistical software (Statistical Package for the Social Sciences Version 13.0; SPSS Inc, Chicago, IL, USA). Discrete variables were analysed using the chi-square test; continuous variables were analysed using the analysis of variance (ANOVA) test.

Results

Details of OSF disease

Table 1 describes the socio-demographic characteristics of the study group. Mean duration (SD) of oral problems in OSF patients was 7.5 (10.9) months, with burning sensation in the mouth being the first symptom in 44 (88%) patients. Most patients were in the clinical stage 2 (26; 52%) and functional stage B (20; 40%). Twenty-two (44%) and 11 (22%) patients had a severe clinical (stage 3) and functional compromise (stage C), respectively. Categorisation according to Khanna *et al.* (1995) [14] revealed two (4%) cases in group IVb (advanced stage with premalignant and malignant changes), 22 (44%) patients in group IVa (advanced cases), 17 (34%) in group III (moderately advanced cases), one (2%) in group II

(early case) and eight (16%) were in group I (very early stage).

Results of the MINI-Plus interview

Table 2 shows the findings of the MINI-Plus interview. The results presented in Table 3 revealed psychiatric morbidity to be significantly higher among patients with advanced stage of OSF. Moreover, patients with a longer duration of oral

problems had more psychiatric co-morbidity (10.2 ± 14.4 months among patients with psychiatric morbidity compared to 6.3 ± 8.8 months among patients with no psychiatric morbidity). However, the findings did not reach statistical significance ($P=0.2$). The duration of the habit of chewing areca products had no significant bearing on the presence of psychiatric morbidity ($P=0.06$), but the frequency of use of areca products was significantly high-

Table 1. Comparison of socio-demographic details between the groups

	Group 1 (N=50) n (%)	Group 2 (N= 50) n (%)	Group 3 (N=50) n (%)	t/df	P value
Mean age (SD)	34.3 (11.03)	34.6 (7.5)	31.3 (8.3%)	2 (2.152)	0.1
Mean years of education (SD)	7.4 (5.2)	6.7 (5.1)	7.7 (4%)	2 (0.505)	0.6
Gender males	43 (86)	41 (82)	47 (94%)	2	0.2
Married	34 (68%)	39 (78%)	30 (60%)	4	0.2
Unskilled labour	41 (82%)	42 (84%)	44 (88%)	4	0.7
Urban domicile	44 (88%)	41 (82%)	46 (92%)	2	0.3
Hindu religion	33 (66%)	37 (74%)	38 (76%)	2	0.5

Table 2. Findings of MINI interview

	Group 1 (N= 50) n (%)	Group 2 (N= 50) n (%)	Group 3 (N=50) n (%)	t/df	P-value
Positive findings with MINI	16 (32%)	1 (2%)	2 (4%)	2	<0.001
Major depressive episode:					
Lifetime	13 (26%)	1 (2%)	2 (4%)	2	<0.001
Current	10 (20%)	1 (2%)	2 (4%)		0.002
Dysthymia					
Lifetime	8 (16%)	1 (2%)	1 (2%)	2	0.005
Current	8 (16%)	1 (2%)	1 (2%)		
Risk of suicide:					
Low	5 (10%)		1 (2%)	2	0.001
Moderate	4 (8%)	1 (2%)	1 (2%)		
High	2 (4%)				
Hypomanic episodes	6 (12%)	0	0	2	0.002
Social phobia	5 (10%)	0	1 (2%)	2	0.03
Alcohol abuse and dependence	3 (6%)	0	0	2	0.04
Lifetime alcohol abuse and dependence	4 (8%)	0	0	2	0.02
Generalised anxiety disorder	10 (20%)	0	2 (4%)	2	<0.001
Antisocial personality disorder:					
Before 15 yrs of age	9 (18%)	0	0	2	<0.001
After 15 yrs of age	12 (38%)	0	0	2	<0.001
Adjustment disorders	3 (6%)	0	0	2	0.05

er ($P=0.03$) among patients with psychiatric morbidity (13.4 ± 9.4 units in patients with positive MINI-Plus findings vs. 8.2 ± 5.7 units in negative MINI-Plus patients). When psychiatric morbidity in patients using areca nut alone ($n=6$; 18.2%) was compared to those taking both areca nut and tobacco ($n=11$; 18.6%), there was no difference ($P=0.6$).

Table 3. Positive findings from MINI interview compared with severity of OSF disease

Staging of OSF	Positive findings on MINI n (%)	Df	P-value
Haider <i>et al.</i> (2000) classification			
Clinical staging:			
Stage 1	0	2	0.009
Stage 2	4 (15.4%)		
Stage 3	12 (54.5%)		
Khanna <i>et al.</i> (1995) classification			
Functional staging:			
Stage A	4 (21.1%)	2	0.04
Stage B	5 (25%)		
Stage C	7 (63.6%)		
Group I	0	4	0.01
Group II	0		
Group III	3 (17.6%)		
Group IVa	11 (50%)		
Group IVb	2 (100%)		

Areca nut and tobacco dependence

Mean duration (SD) of use of areca/tobacco products was 8.3 (6.8) years and mean (SD) number of pouches or units of areca preparations used was 9.8 (7.4) per day. The duration of chewing the content of each pouch ranged between three minutes and one hour. In Group 1 (patients with OSF), 20 (40%) were using areca nut preparations without tobacco (areca quid without tobacco, pan masala) and 30 (60%) were using areca with tobacco (Gutkha, areca quid with tobacco). In Group 2 (patients without OSF), 14 (28%) subjects indulged in chewing areca without tobacco whereas 36 (72%) chewed areca nut with tobacco. The majority of patients in Groups 1 (34; 68%) and 2 (37; 74%) started the habit due to peer pressure, followed by stress—18 (36%) in Group 1 and 15 (30%) in Group 2—and depression, with 15 (30%) in Group 1 and 13 (26%) in Group 2 (*Figure 1*). Depression was the foremost maintaining factor among both groups, with 40 (80%) in Group 1 and 36 (72%) in Group 2 (*Figure 2*). Mood elevation—47 (94%) in Group 1 and 49 (98%) in Group 2—and stress relief—43 (86%) in Group 1 and 39 (78%) in Group 2—were the main effects after taking the substance (*Figure 3*). Dependence on areca products was present in both groups, with 49 (98%) of patients in Group 1 and 47 (94%) in Group 2 meeting ICD-10 and DSM-IV criteria for dependence. A significant difference was noted among Group 1 and Group 2 with regard

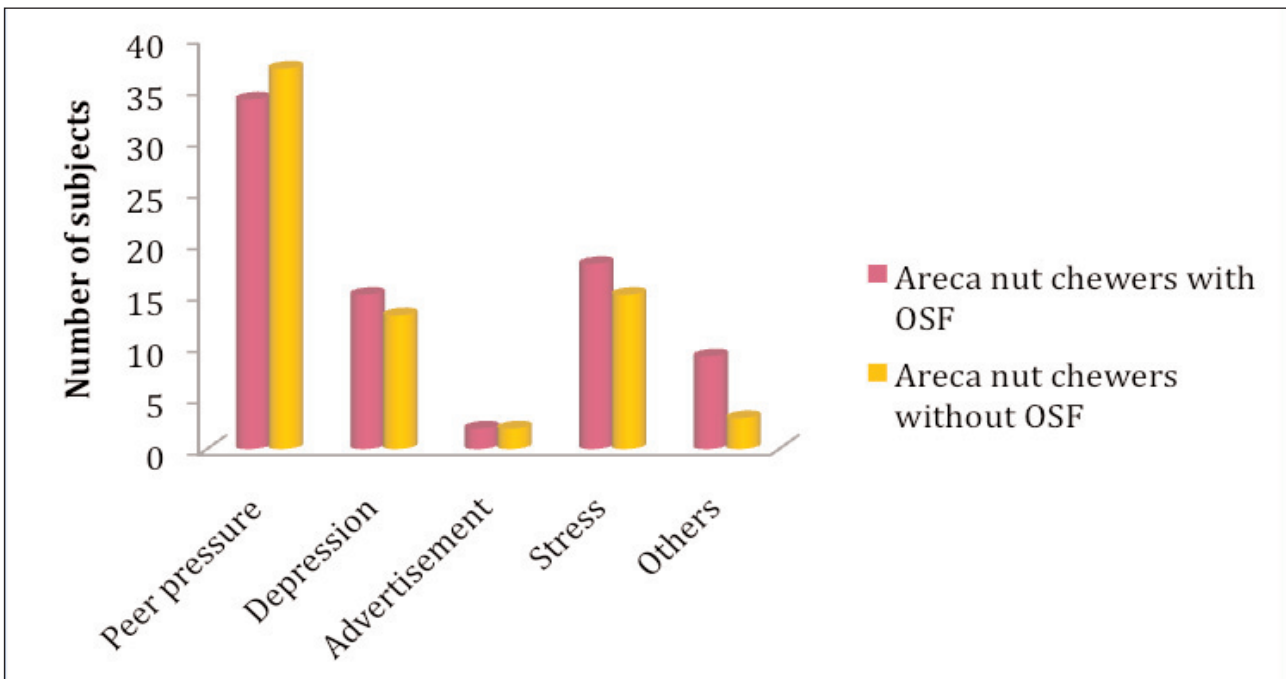


Figure 1. Reason for starting the areca products chewing habit.

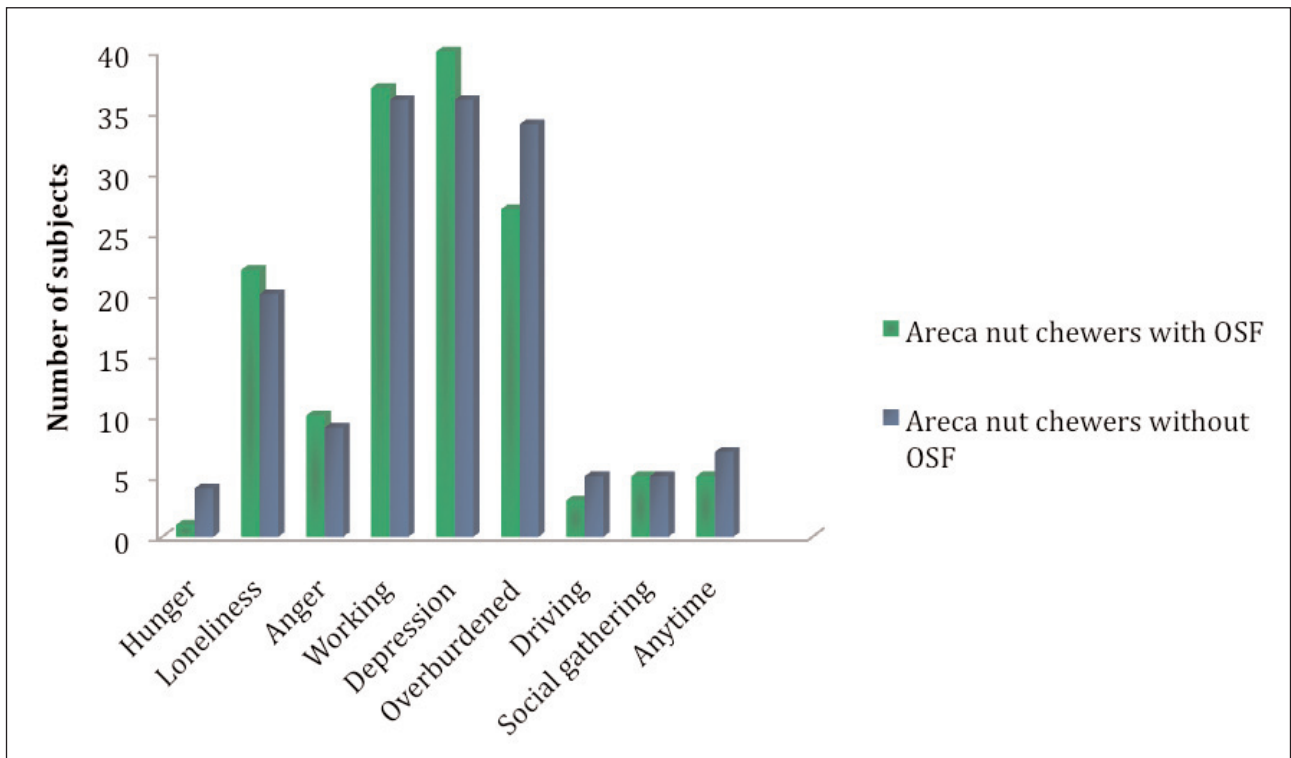


Figure 2. Maintaining factors for areca products chewing habit.

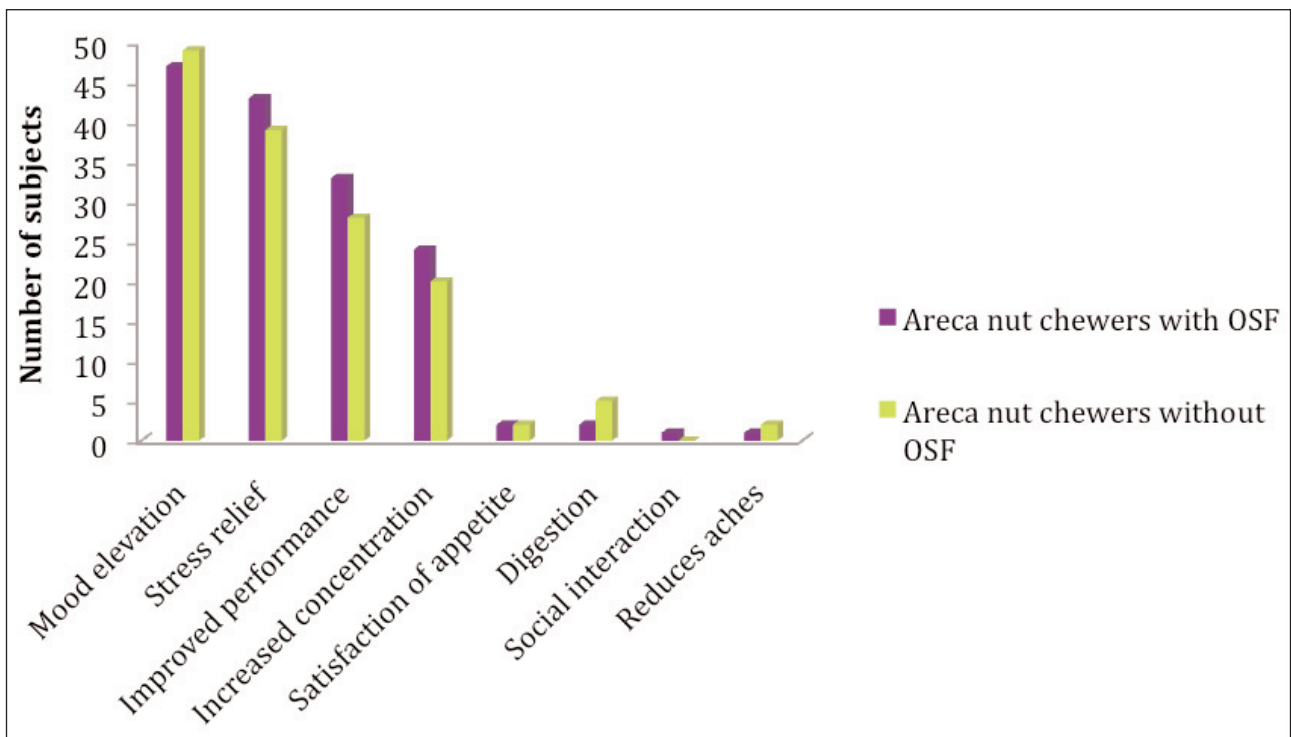


Figure 3. Effect after chewing of areca products.

to knowledge about the harmful use, number of unsuccessful attempts to quit the habit, craving as reason to restart the habit, and severity of withdrawal symptoms (Table 4).

Discussion

This study has established an association between psychiatric morbidity and OSF. The main strength of the study is that psychiatric morbidity was assessed using a structured standardised instrument

Table 4. Comparison of dependence on areca nut products between Groups 1 and 2

	Group 1 (N=50) n (%)	Group 2 (N=50) n (%)	t/df	P-value
Craving	49 (98%)	47 (94%)	1	0.307
Tolerance	48 (96%)	45 (90%)	1	0.240
Knowledge of harmful use	41 (82%)	29 (58%)	1	0.009*
Loss of control	45 (90%)	43 (86%)	1	0.538
Unsuccessful attempts	38 (76%)	33 (66%)	1	0.271
Number of unsuccessful attempts	3.8 (4.3%)	2.2 (2.2%)	2.4	0.011*
Reason to restart the habit:				
Peer pressure	10 (26.3%)	9 (27.3%)	1	0.928
Craving	32 (84.2%)	6 (15.8%)	1	0.047*
Depression	16 (42.1%)	21 (63.6%)	1	0.59
Any other	16 (48.5%)	1 (3%)	1	0.07
Severity of withdrawal symptoms	3.8 (2.6%)	3.3 (1.7%)	0.854	0.05*

*denotes significant difference

by a consultant psychiatrist. A significantly higher number of patients with OSF had psychiatric morbidity when compared to those with no OSF. This observed psychiatric morbidity might be either antecedent or subsequent to the onset of OSF. Psychological factors such as stressful life events and negative affective states (anxiety, depression) might have led to compromised functioning of the immune system in these individuals, as suggested by the results of previous psychoneuro-immunological studies [24,25]. Moreover, these patients are more prone to indulge in substance abuse [26]. This was demonstrated in our patients as increased frequency of areca use when compared to those without psychiatric morbidity ($P=0.03$). It could also be due to chronicity of the condition and significant debilitation such as limited mouth opening, eating, swallowing, speaking difficulties and burning sensation in the mouth associated with the disease process. The current study found that as the clinical and functional staging of the disease worsens, the chance of having psychiatric morbidity increased. This finding is similar to that of three previous studies [3,8,27].

Although there remains a dilemma as to whether psychiatric morbidity is a cause or an effect of OSF, either way, the findings may have major clinical implications and OSF may require intervention from mental health professionals in addition to routine management. It is imperative for

oral clinicians managing patients with OSF to identify patients with mental disorders and promptly refer them to psychiatrists.

The issue of dependence on areca is again established, reinforcing an earlier observation in the preliminary study [8]. This remains a burning issue as the habit is particularly prevalent in younger population groups. In the current study, although most areca nut chewers used areca nut with tobacco, dependence was equally present in exclusive areca nut chewers and chewers of areca along with tobacco ($P=0.6$). Such dependence has been suggested in earlier studies [20,28-31], implying that the problem is a major public health concern. However, large-scale population-based studies are required to confirm areca nut as a product of substance abuse.

Furthermore, it was interesting to note that dependence was more severe in Group 1 compared to Group 2 patients in certain domains (*Table 4*). It is well known that substance abuse and dependence severity is higher among those with other psychiatric disorders [32]. Thus the finding reinforces the possibility of psychiatric morbidity among patients with OSF. This could mean that patients with OSF have more difficulty in quitting the habit and may require aggressive psychiatric management when compared to those without the disease. It also suggests that if patients with an areca nut habit with severe dependence are identified early and if intervention is provided, the possibility of OSF disease

occurrence among them may be averted.

Because the study was conducted at a tertiary care institute that remains a referral centre for severe cases of oral mucosal diseases, the possibility of biased clinical sampling cannot be ruled out. Moreover, patients with psychiatric illnesses may not visit a dentist often and hence the prevalence of psychiatric morbidity in the healthy controls of our study might be underrepresented. This suggests the need for future epidemiological studies with larger samples representative of the population groups.

Conclusions

- There was significant psychiatric morbidity in patients with OSF enrolled in this study. This strongly suggests the need for mandatory psychological assessment and treatment of patients with the condition along with the routine management.
- The study results also suggest that patients with OSF present with higher dependence on areca nut products than those without the disease and hence require aggressive intervention programmes. Also, an attempt at prompt recognition and treatment of those patients with dependence on an areca nut habit may ultimately help in the prevention of OSF in them.
- Further epidemiological studies in different population groups can give an additional insight into the intriguing association of mental disorders with OSF disease and

dependence on areca nut and its products.

Acknowledgement/funding

The study was a non-funded project and the minor expenses incurred were met by contributions from the authors.

Contributions of each author

- JVR contributed to the design of the work, collection of the data, analysis, and the writing of the manuscript.
- PR contributed to the conception and design of the work and collection of the data.
- CNK contributed to the design of the study, trained authors JVR and PR for data collection, carried out psychiatric assessments, interpreted the data, and contributed to the writing of the manuscript.
- MK contributed in the intellectual content, conception and design of the work, and provided guidance throughout the project.
- HC contributed to the intellectual content, conception and design of the work, trained authors JVR and PR for data collection, and provided guidance throughout the project.

Statement of conflict of interest

In the opinion of the authors, there was no conflict of interests.

References

1. Arakeri G, Brennan PA. Oral submucous fibrosis: an overview of the aetiology, pathogenesis, classification, and principles of management. *British Journal of Oral and Maxillofacial Surgery*. 2012 Oct 26. doi:pii: S0266-4356(12)00525-6.10.1016/j.bjoms.2012.08.014. [Epub ahead of print]
2. Angadi PV, Krishnapillai R. Evaluation of PTEN immunoeexpression in oral submucous fibrosis: role in pathogenesis and malignant transformation. *Head Neck Pathology*. 2012; **6**: 314-321.
3. Verhaak PF, Heijmans, MJ, Peters L, Rijken M. Chronic disease and mental disorder. *Social Science & Medicine*. 2005; **60**: 789-797.
4. Chapman DP, Perry GS, Strine TW. The vital link between chronic disease and depressive disorders. *Preventing Chronic Disease*. 2005; **2**: 1-10.
5. Katon W, Lin EH, Kroenke K. The association of depression and anxiety with medical symptom burden in patients with chronic medical illness. *General Hospital Psychiatry*. 2007; **29**: 147-155.
6. Slade GD, Diatchenko L, Bhalang K, Sigurdsson A, Fillingim RB, Belfer I, et al. Influence of psychological factors on risk of temporomandibular disorders. *Journal of Dental Research*. 2007; **86**: 1120-1125.
7. Soto-Araya M, Rojas-Alcayaga G, Esguep A. Association between psychological disorders and the presence of oral lichen planus, burning mouth syndrome and recurrent aphthous stomatitis. *Medicina Oral*. 2004; **9**: 1-7.
8. Mubeen K, Kumar CN, Puja R, Jigna VR, Chandrashekhar HC. Psychiatric morbidity among patients with oral submucous fibrosis. A preliminary study. *Journal of Oral Pathology and Medicine*. 2010; **39**: 761-764.
9. Sheehan DV, Lecrubier Y, Sheehan KH, Amorim P, Janavs J, Weiller E, et al. The Mini-International Neuropsychiatric Interview (M.I.N.I.): the development and validation of a structured diagnostic psychiatric interview for DSM-IV and ICD-10. *Journal of Clinical Psychiatry*. 1998; **59** (Suppl 20): 22-33.
10. Kramer IR, Pindborg JJ, Bezroukov V, Infirri JS. Guides to epidemiology and diagnosis of oral mucosal diseases and conditions. World Health Organization. *Community Dentistry and Oral Epidemiology*. 1980; **8**: 1-26.

11. Picardi A, Pasquini P. Toward a biopsychosocial approach to skin diseases. *Advances Psychosomatic Medicine*. 2007; **28**: 109-126.
12. Reddy MV, Chandrashekar CR. Prevalence of mental and behavioural disorders in India: A meta-analysis. *Indian Journal of Psychiatry*. 1998; **40**: 149-157.
13. Haider SM, Merchant AT, Fikree FF, Rahbar MH. Clinical and functional staging of oral submucous fibrosis. *British Journal of Oral & Maxillofacial Surgery*. 2000; **38**: 12-15.
14. Khanna JN, Andrade NN. Oral submucous fibrosis: a new concept in surgical management: Report of 100 cases. *International Journal of Oral Maxillofacial Surgery*. 1995; **24**: 433-439.
15. American Psychiatric Association (APA). Diagnostic and Statistical Manual of Mental Disorders. 4th ed, text revision. Washington, DC: APA; 2000.
16. *The ICD-10 Classification of Mental and Behavioural Disorders; Clinical Description and Diagnostic Guidelines*. Geneva: World Health Organization; 1992.
17. Sheehan DV, Lecrubier Y, Harnett-Sheehan K, Janavs J, Weiller E, Bonora I, *et al*. Reliability and validity of the MINI International Neuropsychiatric Interview (M.I.N.I.): According to the SCID-P. *European Psychiatry*. 1997; **12**: 232-241.
18. Lecrubier Y, Sheehan D, Weiller E, Amorim P, Bonora I, Sheehan K, *et al*. The M.I.N.I. International Neuropsychiatric Interview (M.I.N.I.). A short diagnostic structured interview: reliability and validity according to the CIDI. *European Psychiatry*. 1997; **12**: 224-231.
19. Srisurapanont M, Jarusuraisin N, Jittiwutikan J. Amphetamine withdrawal: Reliability, validity and factor structure of a measure. *Australian and New Zealand Journal of Psychiatry*. 1999; **33**: 89-93.
20. Hughes, JR, Hatsukami D. Signs and symptoms of tobacco withdrawal. *Achieves of General Psychiatry*. 1986; **43**: 289-294.
21. Benegal V, Rajkumar RP, Muralidharan K. Does areca nut use lead to dependence? *Drug and Alcohol Dependence*. 2008; **97**: 114-121.
22. Fagerstrom KO, Schneider NG. Measuring nicotine dependence: a review of the Fagerstrom Tolerance Questionnaire. *Journal of Behavioral Medicine*. 1989; **12**: 159-182.
23. Piccinelli M, Tessari E, Bortolomasi M, Piasere O, Semenzin M, Garzotto N, *et al*. Efficacy of the alcohol use disorders identification test as a screening tool for hazardous alcohol intake and related disorders in primary care. A validity study. *British Medical Journal*. 1997; **314**: 420-424.
24. Andersen BL. Biobehavioral outcomes following psychological interventions for cancer patients. *Journal of Consulting and Clinical Psychology*. 2002; **70**: 590-610.
25. Segerstrom SC, Miller GE. Psychological stress and the human immune system: A meta-analytic study of 30 years of inquiry. *Psychological Bulletin*. 2004; **130**: 601-630.
26. Chandra PS, Carey MP, Carey KB, Jairam KB. Prevalence and correlates of areca nut use among psychiatric patients in India. *Drug and Alcohol Dependence*. 2003; **69**: 311-316.
27. Hansen MS, Fink P, Frydenberg M, Oxhøj M, Sondergaard L, Eriksen M. Mental disorder in medical inpatients and the association to severity of illness, self rated physical disability and health perception. *Psychosomatics*. 2001; **42**: 41-47.
28. Winstock A. Areca nut-abuse liability, dependence and public health. *Addiction Biology*. 2002; **7**: 133-138.
29. Winstock AR, Trivedy CR, Warnakulasuriya KA, Peters TJ. A dependency syndrome related to areca nut use: some medical and psychological aspects among areca nut users in the Gujarat community in the UK. *Addiction Biology*. 2000; **5**: 173-179.
30. Oakley E, Demaine L, Warnakulasuriya S. Areca (betel) nut chewing habit among high-school children in the Commonwealth of the Northern Mariana Islands (Micronesia). *Bulletin of the World Health Organization*. 2005; **83**: 656-660.
31. Bhat SJS, Blank MD, Balster RL, Nichter M, Nichter M. Areca nut dependence among chewers in a South Indian community who do not also use tobacco. *Addiction*. 2010; **105**: 1303-1310.
32. Regier DA, Farmer ME, Rae DS, Locke BZ, Keith SJ, Judd LL, *et al*. Comorbidity of mental disorders with alcohol and other drug abuse. Results from the Epidemiologic Catchment Area (ECA) Study. *Journal of the American Medical Association*. 1990; **264**: 2511-2518.