Demographic and Clinical Profile of Oral Submucous Fibrosis: A Retrospective Study

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Aims: Assessment of risk factors and the role of habit variables such as duration and frequency in the severity of OSMF and to ascertain the association of gender predilection for different habits and severity of OSMF.
Study design: Descriptive retrospective study.
Place and Duration of Study: Department of Oral Medicine and Radiology, Rural Dental College, Pravara Institute of Medical Sciences (Deemed University), Loni Bk. between January 2012 and December 2019.
Methodology: This descriptive retrospective study of 1790 OSMF patients was carried out at the tertiary level dental hospital in the rural population of Western Maharashtra. The clinicodemographic data including details of habits was collected for a period of 8 years.
Results: The average age of the patient in the study was 32.8 years, with 16.5:1 M:F ratio.Significantly higher proportions of females (69.6%) were illiterate and belonged to low socioeconomic status.There was a statistically significant increase for areca nut chewing (OR=0.135(0.054-0.342), P < 0.0001), gutkha chewing (OR=22.32(10.421-47.817), P < 0.0001), tobacco chewing (OR= 0.111(0.04-0.308), p<0.0001), smoking habits (OR=30.791(7.472-126.89), P < 0.0001) and alcohol (OR=12.692(3.077-52.347, p < 0.0001) in males when compared with females.The maximum patients were seen in stage II (37%) and stage III (34%), followed by stage I (18.73%) and stage IV (10.3%) and the severity of OSMF was more in subjects who had the habits for longer duration.
Conclusion: There was a definite gender predilection for various habits and their variables (frequency, duration), educational and socioeconomic status, clinical features and disease severity. Significant correlation was also found between habit variables (duration, frequency) and severity of the disease.

Keywords: Areca nut, clinical grading, gender, gutkha, oral submucous fibrosis, oral cancer

1. INTRODUCTION

Schwartz in 1952 first described Oral Submucous Fibrosis (OSMF) as “Atropica idiopathica mucosae oris” while Jens J. Pindborg in 1966 described it as “an insidious, chronic disease that affects any part of the oral cavity and sometimes the pharynx. Although occasionally preceded by, or associated with, the formation of vesicles, it is always associated with a juxta-epithelial inflammatory reaction followed by fibroelastic change of the lamina propria and epithelial atrophy that leads to stiffness of the oral mucosa and causes trismus and an inability to eat”.[1] Along with the features mentioned above, OSMF, a potentially malignant disorder (PMD) is also characterized by clinical features such as progressive reduction of mouth opening, reduced tongue movement, blanching and leathery texture of the oral mucosa, depapillation of the tongue, and shrunken uvula.[2,3]
Areca nut-chewing, in any formulation, has been considered the main etiological agent even though multifactorial etiopathogenesis has been reported.[1] The disease has shown predominance towards Asian population and more exclusively in Indian population which could be attributed to the areca nut chewing habit in these regions. Prevalence of OSMF in Indian rural population has been reported ranging up to 0.4%.[4] Illiteracy, lack of awareness

of ill effects of various habits, lower socioeconomic status and peer-pressure plays an important role in development of OSMF in rural population. The premalignant lesions caused by gutkha, areca nut, tobacco and related products can be reversed by quitting the habits at an earlier stage and by early diagnosis and proper treatment. Thus, it proves the importance of identifying the high-risk group and educating them about ill-effect of areca nut, tobacco, along with early diagnosis, treatment and prevention of debilitating diseases caused by these habits. These observations justified our surge for the present study to assess the risk factors and clinical presentations of OSMF in the rural population. The role of critical components of a habit such as duration, frequency, and chewing time in the clinical grading of OSMF and its gender specificity is lacking in the present scenario of evidence-based dentistry.[5,6]Thus, this study was also carried out to correlate these habit factors to the clinical grading of OSMF, in addition to its demographic and clinical profile in this rural population of western Maharashtra.

2. MATERIAL AND METHODS / EXPERIMENTAL DETAILS / METHODOLOGY

An Observational Descriptive retrospective study of 1790 patients with a clinically diagnosed OSMF was carried out in the Department of Oral Medicine and Radiology, after approval from institutional ethical committee. The data was collected for a period of 8 years from January 2012 to December 2019, from the detailed case records of these patients. Patients with a clinical diagnosis of OSMF, in the age group of 15 to 90 years were selected. Patients with known history of systemic disorders causing limitation of mouth opening like anemia and scleroderma and patients with a history of previous treatment for OSMF were excluded from the study. Data was collected in the context of details of demographics, involved habits, sites of lesion, signs and symptoms, clinical grading etc.

The OSMF patients were divided in five categories based on age groups (Group I: ≤19years, group II: 20-29 years, group III: 30-39 years, group IV: 40-49 years, group V: ≥50 years) and duration of the habit (Group A:up to 5 years, group B:6-10 years, group C:11-15 years, group D:16-20 years and group E:more than 20 years) and into four groups according to their frequencies of habits per day (Group 1: upto 5 times/day, group 2: 6-10 times/day, group 3: 11-15 times/day, and group 4: more than 16 times/day). The different types of habits such as chewing of Gutkha, Areca nut, Pan masala, Betel quid, Smokeless tobacco, Smoking and Alcohol were recorded in detail in terms of duration and frequency. The patients were divided into single & multiple habits. The clinical grading into four stages according to their clinical presentation of the disease was done using Khanna and Andrade (1995) classification.[7] The data was collected and recorded in tabulated format in excel sheet. All statistical analyses were performed using Systat version 12 software. Descriptive measures like mean values and standard deviations for continuous variables and percentage for categorical variables were calculated. The OSMF cases were classified by gender for comparison purposes. Estimation of odds ratio (OR)along with 95% confidence intervals was made for comparing risk of OSMF by gender. Tests of significance like unpaired t-test for comparing means and Chi-square test of association were performed for comparing percentages of two independent samples (male vs. females). A value of $P < 0.05$ was considered statistically significant.

3. RESULTS AND DISCUSSION

3.1 Demographics

In the present study males were predominant, out of 1790 patients, 1688 (94.30%) were male. The male to female ratio was 16.5:1. The youngest patient was 15years of age whereas the oldest patient was 88 years old. Majority (68.3%) of the OSMF cases belonged to 20-39 years of age group. The average age of the patient in the study was 32.8 years.

The mean age for males (n = 1688) was 32.2 ± 11.3 (range 15–84) years and for females (n = 102) it was 42.9 ± 15.4 (range 15–88) years. Thus, occurrence of OSMF in younger age group (<30 years) was significantly higher in males as compared to females (P = 0.0001). 69.6% of females with OSMF had a low socioeconomic status which was a significant observation when compared to males (14.9%). Similarly, proportion of illiterate females was also significantly higher (69.6%) when compared with illiterate men (12.8%).[Table 1]

Table 1. Demographics of OSMF patients

Study Variable	Male (n=1688)		Female (n=102)		Total (n=1790)		Test of significance
	No.	%	No.	%	No.	%	
Age group (years)							
10-19	97	5.7	2	2	99	5.5	
20-29	725	43	16	15.7	741	41.4	
30-39	455	27	26	25.5	481	26.9	*P<0.0001
40-49	260	15.4	23	22.5	283	15.8	
>50	151	8.9	35	34.3	186	10.4	
Education							
Illiterate	216	12.8	71	69.6	287	16	
Non-Graduate	805	47.7	31	30.4	836	46.7	*P<0.0001
Graduate	539	31.9	0	0	539	30.1	
Postgraduate	128	7.6	0	0	128	7.2	
Socio Economic Status							
Lower	251	14.9	71	69.6	322	18	
Lower Middle	769	45.6	23	22.5	792	44.2	*P<0.0001
Middle	574	34	8	7.8	582	32.5	
Upper Middle	93	5.5	0	0	93	5.2	
Upper	1	0.1	0	0	1	0.1	

** Indicates P value as derived by Fishers exact test.*

3.2 Habits

Out of 1790 patients, 61.56% (n = 1102) patients had multiple (more than one) habits, 37.71% (n = 675) patients had exclusive habits (only one habit), while 0.7% (n = 13) patients did not give history of any habit.

3.2.1 Exclusive habits

Table 2 shows the risk distribution of OSMF cases having exclusive habits (n =675). Females have shown statistically significant predilection for exclusive gutkha chewing habit [OR = 0.094 (0.049-0.180), P =0.0001] when compared with males, followed by tobacco chewing habit [OR=0.560(0.295-1.063), P=0.08] which however was not statistically significant. Significant predilection for exclusive areca nut [OR =12.788(5.321-30.732) P =0.0001] was found more in males as compared to females.

Table 2. Sex wise Risk Distribution with Single Risk Factor of OSMF

Risk Factors	Male (N=631) n (%)	Female (N=44) n (%)	OR (95% CI)	P value
Areca nut				
Yes	422 (66.9)	6 (13.6)	12.788(5.321-30.732)	<0.0001
No	209 (33.1)	38 (86.4)		
Guthka				
Yes	54 (8.6)	22 (50)	0.094 (0.049-0.180)	<0.0001
No	577 (91.4)	22 (50)		

Tobacco (Non smoked)				
Yes	153 (24.2)	16 (36.4)	0.560(0.295-1.063)	0.076
No	478 (75.8)	28 (63.6)		
Smoking				
Yes	2 (0.3)	--	-	-
No	629 (99.7)	--		

3.2.2 Multiple habits

Table 3 shows the risk distribution of OSMF patients with multiple habits (n =1102). There was a statistically significant predilection for areca nut chewing (OR=0.135(0.054-0.342), P < 0.0001), gutkha chewing (OR=22.32(10.421-47.817), P < 0.0001), tobacco chewing (OR= 0.111(0.04-0.308), P<0.0001), smoking habits (OR=30.791(7.472-126.89), P < 0.0001) and alcohol (OR=12.692(3.077-52.347), p < 0.0001) in males when compared with females.

Table 3. Sex wise Risk Distribution with Multiple Risk Factors of OSMF

Risk Factors	Male (N=1045) n (%)	Female (N=57) n (%)	OR(95% CI)	P value
Areca nut				
Yes	611 (58.5)	52 (91.2)	0.135(0.054-0.342)	<0.0001
No	434 (41.5)	5 (8.8)		
Guthka				
Yes	820 (78.5)	8 (14)	22.32(10.421-47.817)	<0.0001
No	225 (21.5)	49 (86)		
Tobacco (Non smoked)				
Yes	621 (59.4)	53 (93)	0.111(0.04-0.308)	<0.0001
No	424 (40.6)	4 (7)		
Smoking				
Yes	552 (52.8)	2 (3.5)	30.791(7.472-126.89)	<0.0001
No	493 (47.2)	55 (96.5)		
Alcohol				
Yes	330 (31.6)	2 (3.5)	12.692(3.077-52.347)	<0.0001
No	715 (68.4)	55 (96.5)		

Table 4 shows the gender-wise distribution of signs/symptoms in OSMF cases at first presentation. Vesicles /ulcerations [OR= 0.605(0.383-0.956),P= 0.03] and shrunken uvula [OR =0.616(0.408-0.929),P 0.02] were found to be significantly more prevalent in females when compared with males.

Table 4. Symptoms and Sex wise Risk Distribution

Symptoms	Male (n=1688)		Female (n=102)		OR (95% CI)	P value
	No.	%	No.	%		
Burning Sensation	1367	81	89	87.3	0.622(0.343-1.127)	0.118
Vesicles Ulceration	302	17.9	27	26.5	0.605(0.383-0.956)	**0.031**
Reduced Mouth Opening	1362	80.7	83	81.4	0.956(0.573-1.597)	0.895
Restricted Tongue Movement	623	36.9	43	42.2	0.803(0.535-1.204)	0.288
Shrunken Uvula	480	28.4	40	39.2	0.616(0.408-0.929)	**0.021**
Xerostomia	374	22.2	28	27.5	0.752(0.480-1.179)	0.215

3.3 Clinical grading

Out of 1790 patients, 335 cases (18.7%) were of stage I, 662(37%) patients were having stage II OSMF,608(34%) cases had stage III while 185(10.3%) patients had stage IV OSMF. Prevalence of OSMF was also recorded based on age groups. It was more (41.4%) in group II (age 20-29 years) patients while it was least (5.53%) in group I (≤ 19 years) patients. The stage I OSMF was more prevalent in group I patients and stage II OSMF was more prevalent in group V (above 50 years) patients. The highest prevalence of stage IV (14.4%) OSMF was in group IV (40-49 years) patients whereas the stage III (36.4%) OSMF had highest prevalence in group II (20-29 years) patients. By applying Chi square test significant association was found between age group and clinical staging of OSMF ($P < 0.001$) [Table 5].

Table 5. Association between age groups and clinical grading of OSMF

Stage	Age Groups					Total
	Group I (≤ 19)	Group II (20-29)	Group III (30-39)	Group IV (40-49)	Group V (≥50)	
I	28(28.3)	149 (20.1)	85(17.7)	46(16.3)	27(14.5)	335(18.7)
II	35(35.4)	255 (34.4)	185(38.5)	110(38.9)	77(41.4)	662(37.0)
III	30(30.3)	270(36.4)	161(33.5)	86(30.4)	61(32.8)	608(34.0)
IVA	5 (5)	64 (8.6)	40 (8.3)	30 (10.6)	20 (10.7)	159 (8.8%)
IVB	1 (1)	3 (0.4)	10 (2)	11 (3.8)	1 (0.5)	26 (1.5%)
Total	99(100.0)	741(100.0)	481(100.0)	283(100.0)	186(100.0)	1790(100.0)

**Chi Square=37.573, df=16, P=0.0017*

Table 6 depicts the gender-wise distribution of clinical grading of OSMF, where 32.35% females were affected with stage III and stage II OSMF, each, while 37.26% males had stage II and 34.06% had stage III OSMF. Stage I OSMF was present in 18.84% males and 16.67% females whereas stage IV OSMF was seen in 18.63% females and 9.83% males.
In the present study 26 cases (25 male, 1 female) were of squamous cell carcinomas (IVB) which accounts for 1.5% malignancy potential in our study. One hundred and fifty-nine (141 male, 18 female) patients (8.8%)were having other precancerous lesion associated with OSMF (IVA). By applying Chi square test significant association was found between gender and clinical staging of OSMF (P < 0.001). [Table 6]

Table 6. Association between genders and clinical grading of OSMF

Stage	Male		Female		Total
	No. (%)		No (%)		
I	318 (94.9)	18.8%	17 (5.1)	16.6%	335 (100%)
II	629 (95)	37.3%	33 (5)	32.4%	662 (100%)
III	575 (94.5)	34.1%	33 (5.5)	32.4%	608 (100%)
IVA	141 (88.6)	8.3%	18 (11.4)	17.7%	159 (100%)
IVB	25 (96.2)	1.5%	1 (3.8)	0.9%	26 (100%)
Total	1688	100%	102	100%	1790

**Value of x^2 =10.472, df = 4, significant, p=0.03*

3.4 Duration and frequency of the habits

Table 7 shows prevalence of OSMF based on duration of the habits. Duration of habit was divided in 5 groups. A higher prevalence was recorded in Group A (up to 5 years) [719 (40.2%)] followed by Group B (6-10 years) [417 (23.3%)], Group C (11-15 years) [256 (14.3%)], Group E (more than 20 years) [202 (11.2%)] and Group D (16-20 years) [196 (11%)]. This prevalence was statically significant (P < 0.0001). [Table 7]

Table 7. Association between duration of habit and clinical grading of OSMF

Stage	Duration of the habits					Total
	Upto 5 years	6-10 years	11-15 years	16-20 years	> 20 years	
I	147	78	44	39	27	335
II	255	150	102	64	90	662
III	250	150	81	67	61	608
IVA	65	33	20	23	18	159
IVB	2	6	9	3	6	26
Total	719	417	256	196	202	1790

**Value of x^2 =31.971, d.f.=16, significant, p=0.01*

Frequency of habit was divided in four groups. Prevalence of OSMF was more in Group 2 (6-10 times/day) [612 (34.2%)] and group 3(11-15 times/day) [543 (30.3%)]in comparison to group 1 (up to 5 times/day) [368 (20.6%)] and Group 4 (more than 16 times/day) [267 (14.9%)]. The prevalence was statistically significant (P < 0.0001) [Table 8].

Table 8. Association between habit frequencies and clinical grading of OSMF

Stage	Frequencies of the habits				Total
	Upto 5 times	6-10 times	11-15 times	≥16 times	
I	60 (16.3%)	122 (19.9%)	105 (19.3%)	48 (18%)	335(18.7)
II	130 (35.3%)	210 (34.3%)	215 (39.6%)	107 (40.1%)	662(37.0)
III	132 (35.9%)	215 (35.1%)	176 (32.4%)	85 (31.8%)	608(34.0)
IVA	46 (12.5%)	58 (9.5%)	34 (6.3%)	21 (7.9%)	159 (8.8%)
IVB	0 (0%)	7 (1.2%)	13 (2.4%)	6 (2.2%)	26 (1.5%)
Total	368 (20.6%)	612 (34.2%)	543 (30.3%)	267 (14.9%)	1790(100.0)

**Value of x^2 =26.740, d.f.=12, significant, p=0.0084*

3.5 Discussion

Prevalence of OSMF has been estimated to range from 0.1 to 30% based on geographical location, sample size, and sampling methodology.[8]The prevalence of OSMF in India, having a broad age range of 11 to 60 years, has been estimated to range from 0.2–2.3% in males and 1.2–4.6% in females.[3,8]

The present study showed a higher prevalence of OSMF in males (16.5:1), which is similar to the studies reporting a varying but higher male prevalence with male: female ratio ranging from 2.4:1 to 40:1.[5,9-14] Biradar et al in their study reported all were male patients.[15] However, few studies have reported female preponderance.[16-18]The higher involvement of males in all studies, reflects their easy access to the abusive habits when compared with females.

In the present study, the youngest patient was 15 years of age whereas the oldest patient was 88 years old. The average age of the patient in the study was 32.8 +11.8 years, which is in the similar range with previous studies. [5,19, 20] Majority of the OSMF cases (68.3%) belonged to 20-39 years of age group. This is in consistent with the earlier studies by Sirsat and Khanolkar,[21] Sinor et al,[16] Ahmad et al [2] and Shah et al.[20] During the recent years, with the arrival of attractive and convenient packaging in the forms of sachet, beguiling advertisements linking it to the social status and most importantly easy availability has led to an increase in consumption of gutkha and pan masala among the younger population, which is also noted in the present study.[2]

Most of the OSMF patients (62.2%) in the present study belonged to lower middle and lower socioeconomic class. Shiau and Kwan[22] and Ramanathan et al [23] also made a similar observations with most cases from Indian population being from low socioeconomic group of

the society. McGurk and Crag [24] studied Asian community settled in United Kingdom and they found that most of the OSMF patients were from a low or middle-income group. The reason might be attributed to poor nutritional quality of food with low vitamins, iron and use of more spices and chillies to make the food tasty, coupled with lack of health consciousness.[2]

Apart from areca-nut chewing being considered as the main causative agent, other contributory risk factors for etiopathogenesis of OSMF includes chewing of smokeless tobacco, high intake of chillies, toxic levels of copper in foodstuffs, vitamin deficiencies, malnutrition resulting in low levels of serum proteins, anaemia and genetic predisposition.[8] Areca-nut consumption is estimated to be by 10-20% of World's population in different forms.[8] Areca-nut chewing in its various forms is widely prevalent in the India, giving rise to an increased prevalence of OSMF, from an estimated 2,50,000 cases in 1980 to an estimated 5 million people in 2002.[5] Moreover, recent data suggests that prevalence of OSMF in India has increased from 0.03% to 6.42%.[25] A marked increase in incidence has been observed after the widespread marketing of commercial products known as Gutkha (mixture of tobacco and areca-nut), sold in single-use packets.[8]

In present study, areca nut chewing and the use of tobacco for teeth cleaning were proportionately higher in females which are attributable primarily to the local cultural practices and easy availability of areca nut and tobacco. Inversely, gutkha chewing and tobacco smoking was more prevalent in males. Seedat and Van Wyk[26] from South Africa and Hazare et al [5] from India had similar observations in their studies. In various epidemiological studies on OSMF, the investigators found a strong association between gutkha, areca nut chewing and OSMF and pointed that these habits led to OSMF. [2,5,10,12,14,16,27] In the present study, 13 patients (0.7%) reported no history of any habits.

Burning sensation of oral mucosa (81.34%) and inability to open the mouth wide due to fibrotic bands, were the chief complaints in the present study, which can be considered as the diagnostic signs of the disease.[5,11,28]

In present study, majority of patients were seen in stage II (37%) and stage III (34%) OSMF, followed by stage I (18.73%) and stage IV (10.3%) OSMF. These findings are in consistent with the study by Srivastva et al.[14] Kumar et al [12] found stage II was more prevalent followed by stage IV, III and stage I in their study whereas in the study conducted by Hazare et al [5], majority of OSMF (48.3%) cases were in grade III followed by grade II. The less prevalence of stage I in the present study as well as in various other hospital-based studies may be due to the fact that in the early cases significant changes, especially limited mouth opening, are not seen, and unless there are any significant symptoms or dysfunction of affected part/organ, patients usually do not approach the doctor. A population screening study by Nigam et al.[10] revealed majority of patients in asymptomatic stage, stage I OSMF was more prevalent.

In the present study, posterior one-third of oral cavity involving both buccal mucosa, retromolar area and soft palate were predominantly affected, which is similar to the observations from two studies from Maharashtra state. Contrary to these findings, a study from Kerala state, reported labial mucosa to be significantly affected, which represents a regional variation with respect to various chewing habits practised in different parts of India.[5]

Although the prevalence based on duration and frequency of habit was variable in the present study, a generalized observation made was that 59.8% of the patient had habit duration for more than 5 years and 79.4% of the patient had frequency of more than 5 times in a day. As most of the patient were in stage II and stage III OSMF, it led us to conclude that the severity was more in subjects who were chewing for longer duration and frequencies. These findings were in accordance with the previous studies. [11,12]

3.5.1. Malignant transformation of OSMF

Patients with OSMF have been reported with higher risk of developing oral squamous cell carcinoma (OSCC), compared to other PMDs.[8] In the present study 26 cases (25 male, 1

female) were of squamous cell carcinomas (IVB) which accounts for 1.5% malignancy potential. In 1970, a 17-year follow up study reported malignant transformation in 7.6% of OSMF cases.[29] Studies with smaller follow up periods also have reported malignant transformation rates ranging from 1.9 to 9%, depending on diagnostic criteria and duration of follow up.[8]A recent study from India has reported malignant transformation in 25.77% of OSMF cases indicating the alarming malignant potential of OSMF.[30]

We can conclude from the present study that habit variables in the form of duration, frequency, have increased significance in correlation to severity of clinical grading of OSMF. It was also found that there is a marked difference in the habits, their frequency and duration, signs and symptoms and disease severity in females when compared with males seeking dental care for OSMF at tertiary level, in the Western Indian rural population.

Limitations of the present study includes that since it was a retrospective study, control group was not there and there were a smaller number of females in the study. Also amount/quantity of gutkha/areca nut, its duration in the mouth, style of chewing gutkha-swallowing/spitting and association of prevalence and severity of OSMF with different types of habits were not included. Hence, a well-designed, large, multicentric, prospective study including matched control groups is recommended.

4. CONCLUSION

In conclusion, primary prevention for a potentially malignant disorder such as OSMF needs to be improved at national, state, and individual levels and should involve education of the public regarding the ill effects of areca nut and tobacco along with harsher laws and punishments to restrict the sale of gutkha and similar products. More focus should be on early diagnosis since many patients come so late to diagnosis that interventions are of limited efficacy and despite the efforts taken cure is almost impossible. Further, having multiple habits such as chewing tobacco or areca-nut products, imbibing unhealthy amounts of alcohol, abusing other drugs, and often having dietary deficiencies increases the risk of co-morbidities such as metabolic syndromes, respiratory, gastrointestinal/liver, and cardiovascular diseases. [8,31] Depending on their dominant symptoms, patients may seek consultation/treatment by either a primary care physician (PCP) or an oral physicians/dentist. Thus, an interdisciplinary approach that may help in early diagnosis of OSMF/potentially malignant disorders and OSCC, with integrated management of both oral and systemic symptoms, improving long term prognosis, reducing suffering and improving quality of life is crucial. Hence all health care professions must work together as a team with the primary goal of prevention.

ACKNOWLEDGEMENTS

COMPETING INTERESTS

Authors declares that no competing interests exist.

AUTHORS' CONTRIBUTIONS

'Author 1' designed the study, performed the statistical analysis, wrote the protocol, and wrote the first draft of the manuscript. 'Author 2' and 'Author 3' managed the analyses of the study and drafting of manuscript. 'Author 4', "Author 5' and 'Author 6' managed the literature searches. All authors read and approved the final manuscript."

ETHICAL APPROVAL (WHERE EVER APPLICABLE)

Institutional ethical committee approval was taken for the study.

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