ISSN 0973-2063 (online) 0973-8894 (print)

Bioinformation 22(10): 6509-6516 (2026)

©Biomedical Informatics (2026)

BIOINFORMATION
Discovery at the interface of physical and biological sciences

BIOMEDICAL INFORMATICS

www.bioinformation.net

Volume 22(10)

Research Article

Received October 1, 2026; Revised October 31, 2026; Accepted October 31, 2026, Published October 31, 2026

DOI: 10.6026/973206300226509

SJIF 2026 (Scientific Journal Impact Factor for 2026) = 8.478
2022 Impact Factor (2023 Clarivate Inc. release) is 1.9

Declaration on Publication Ethics:
The author's state that they adhere with COPE guidelines on publishing ethics as described elsewhere at https://publicationethics.org/. The authors also undertake that they are not associated with any other third party (governmental or non-governmental agencies) linking with any form of unethical issues connecting to this publication. The authors also declare that they are not withholding any information that is misleading to the publisher in regard to this article.

Declaration on official E-mail:
The corresponding author declares that lifetime official e-mail from their institution is not available for all authors

License statement:
This is an Open Access article which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly credited. This is distributed under the terms of the Creative Commons Attribution License

Comments from readers:
Articles published in BIOINFORMATION are open for relevant post publication comments and criticisms, which will be published immediately linking to the original article without open access charges. Comments should be concise, coherent and critical in less than 1000 words.

Disclaimer:
Bioinformation provides a platform for scholarly communication of data and information to create knowledge in the Biological/ Biomedical domain after adequate peer/editorial reviews and editing entertaining revisions where required. The views and opinions expressed are those of the author(s) and do not reflect the views or opinions of Bioinformation and (or) its publisher Biomedical Informatics. Biomedical Informatics remains neutral and allows authors to specify their address and affiliation details including territory where required.

Edited by P Kangueane
Citation: Rai *et al.* Bioinformation 22(10): 6509-6516 (2026)

Long-term outcomes of unani and allopathic therapy in oral submucous fibrosis

Arpita Rai[1,*], Shama Parveen[2], Mohammad Fazil[3], Gulam Rabbani[4], Zeya Ul Haque[1], Tannu Kumari[1] & Ansul Kumar[5]

[1]Department of Oral Medicine and Radiology, Dental Institute, Rajendra Institute of Medical Sciences (RIMS), Ranchi, Jharkhand, India; [2]Department of Biological sciences, Centre for Interdisciplinary Research in Basic Sciences, Jamia Millia Islamia, New Delhi, India; [3]Department of Literary and Historical Research, Ansari Health Centre, Jamia Millia Islamia, New Delhi, India; [4]Community Health Centre, CHC-Karra, Khunti, Jharkhand, India; [5]Departmentof Cardio Thoracic Vascular Surgery (CTVS), Rajendra Institute of Medical Sciences (RIMS), Ranchi, Jharkhand, India; *Corresponding author

Affiliation URL:
https://rimsranchi.ac.in/
https://jmi.ac.in/

ISSN 0973-2063 (online) 0973-8894 (print)
Bioinformation 22(10): 6509-6516 (2026)
©Biomedical Informatics (2026)

Author contact:
Arpita Rai - E-mail: arpita.dirims@gmail.com; Phone: +91 9871743893
Shama Parveen - E-mail: shamp25@yahoo.com; Phone: +91 9818286423
Mohammad Fazil - E-mail: fazildr@yahoo.com; Phone: +91 9818345757
Gulam Rabbani - E-mail: rabbani120186@gmail.com; Phone: +91 9931072295
Zeya Ul Haque - E-mail: zeya486@gmail.com; Phone: +91 8789474713
Tannu Kumari - E-mail: tankashra@gmail.com; Phone: +91 8126783502
Ansul Kumar - E-mail: docansul@gmail.com; Phone: +91 9650965875

Abstract:
Oral submucous fibrosis (OSMF) is a chronic, progressive and potentially malignant disorder with limited evidence on the long-term sustainability of treatment outcomes. This prospective longitudinal study evaluated 12-month outcomes of Unani formulations versus conventional allopathic antioxidant therapy following completion of a randomized controlled trial. Participants received treatment for 12 weeks and were followed for 12 months without additional intervention, with disease status and oral health-related quality of life (OHRQoL) assessed using predefined criteria and the OPMDQoL questionnaire. Among 88 participants (45 Unani and 43 allopathy), stable disease predominated (66.7% vs. 56.5%), with no significant between-group differences (all P>0.05), while OHRQoL improved significantly within the Unani group (P=0.001). Thus, unani formulations and allopathic antioxidant therapy showed comparable 12-month outcomes, maintaining disease stability and improving OHRQoL.

Keywords: Antioxidants, long-term follow-up, oral health-related quality of life, oral submucous fibrosis (OSMF), randomized controlled trial, unani medicine

Background:
Oral submucous fibrosis (OSMF) is a chronic, progressive and potentially malignant disorder predominantly associated with areca nut consumption. The disease is characterized by progressive fibrosis of the oral mucosa, resulting in restricted mouth opening, burning sensation, impaired tongue mobility and difficulties in mastication, swallowing and speech **[1, 2].** Despite the availability of several treatment modalities, including antioxidants, corticosteroids, physiotherapy, surgical interventions and herbal therapies, the management of OSMF remains challenging because of its chronic nature and potential for disease progression. Previous studies have primarily focused on short-term clinical outcomes such as improvement in mouth opening, reduction in burning sensation and enhancement of oral function following treatment **[3].** However, the long-term sustainability of treatment benefits remains an important clinical concern **[4, 5].** Although numerous interventions have demonstrated favorable short-term results, evidence regarding long-term post-treatment outcomes is limited. In particular, there is a paucity of data evaluating disease resolution, disease progression and maintenance of clinical improvement following completion of therapy. Furthermore, comparative evidence assessing long-term outcomes after Unani and allopathic interventions in OSMF is scarce. Most published studies have evaluated treatment efficacy over periods ranging from 8 to 12 weeks, with little information available regarding the durability of treatment effects after therapy has ended. Consequently, clinicians have limited evidence to guide expectations regarding long-term disease behaviour and treatment sustainability **[6, 7].** Furthermore, because oral submucous fibrosis is a chronic and potentially malignant disorder, long-term follow-up is essential to evaluate whether treatment benefits are sustained after completion of therapy. Longitudinal assessment also provides valuable information regarding disease stability, progression and long-term patient outcomes, which are critical for guiding clinical management and follow-up strategies. In a previously conducted randomized controlled trial, we compared the efficacy of the Unani formulations Zuroor-e-Qula and Jawarish Amla Sada with allopathic antioxidant therapy in patients with early-intermediate stage OSMF. The study showed significant improvements in mouth opening, mandibular excursions, burning sensation, quality of life and biochemical parameters in both groups, with superior outcomes observed in the Unani treatment arm. However, the long-term maintenance of these treatment benefits has not been reported. To our knowledge, evidence regarding the long-term comparative outcomes of Unani formulations and allopathic antioxidant therapy in patients with oral submucous fibrosis remains limited. Therefore, it is of interest to evaluate the long-term clinical outcomes of Unani and allopathic therapy in patients with early-intermediate OSMF, with particular emphasis on disease resolution, disease stability, disease progression and oral health-related quality of life during a 12-month post-treatment follow-up period.

Materials and Methods:
Study design:
This study was a prospective longitudinal cohort follow-up of participants who had completed a previously conducted randomized controlled trial comparing Unani formulations (Zuroor-e-Qula and Jawarish Amla Sada) with allopathic antioxidant therapy in patients with early-intermediate stage oral submucous fibrosis (OSMF). In the randomized controlled trial, participants received the allocated intervention for 12 weeks. Following completion of treatment, no additional therapeutic intervention was administered. Participants were subsequently followed for 12 months to evaluate the long-term sustainability of treatment outcomes. During the follow-up

period, clinical assessments were performed at predetermined intervals to monitor disease status and persistence of treatment benefits. The primary outcomes of the follow-up study included disease resolution, stable disease, disease progression and patient retention.

Study site:
The study was conducted at the Department of Oral Medicine and Radiology, Dental Institute, Rajendra Institute of Medical Sciences (RIMS), Ranchi, Jharkhand, India. Participants included in the present follow-up study were those who had completed the treatment phase of a previously conducted randomized controlled trial at the same institution. All post-treatment follow-up assessments were carried out at the Department of Oral Medicine and Radiology by trained investigators using standardized clinical examination protocols.

Study duration:
Participants received the allocated intervention for 12 weeks as part of the randomized controlled trial. Following completion of treatment, they were prospectively followed for 12 months to evaluate the long-term treatment outcomes. Follow-up assessments were conducted at predetermined intervals to monitor disease resolution, stable disease, disease progression, quality of life and participant retention throughout the follow-up period.

Ethical approval:
The study was conducted in accordance with the ethical principles of the Declaration of Helsinki and the Indian Council of Medical Research (ICMR) National Ethical Guidelines for Biomedical and Health Research Involving Human Participants. Ethical approval was obtained from the Institutional Ethics Committee, Rajendra Institute of Medical Sciences (RIMS), Ranchi (Approval No. ECR/769/INST/JH/2015/RR-18). The randomized controlled trial was prospectively registered with the Clinical Trials Registry–India (CTRI/2019/06/019734). Written informed consent was obtained from all participants before enrolment, including consent for long-term follow-up and the use of anonymized data for research and publication.

Study participants:
Participants included in the present follow-up study were patients with early intermediate stage oral submucous fibrosis (OSMF) who had completed the 12-week randomized controlled trial comparing Unani formulations (Zuroor-e-Qula and Jawarish Amla Sada) with allopathic antioxidant therapy. A total of 120 participants were initially enrolled in the randomized controlled trial and allocated equally to the Unani and allopathic treatment groups. Following completion of the treatment phase, all participants were invited to participate in the long-term follow-up study. At the 3-month follow-up assessment, 88 participants (45 in the Unani group and 43 in the allopathy group) were available for assessment. Participants who attended the scheduled follow-up visits were included in the analysis. No new participants were recruited for the follow-up study. Those who withdrew consent, were lost to follow-up, or developed medical conditions that precluded further evaluation were excluded from subsequent follow-up assessments.

Intervention:
During the randomized controlled trial, participants were allocated in a 1:1 ratio to receive either Unani therapy or allopathic antioxidant therapy for 12 weeks. The Unani treatment group received Jawarish Amla Sada (6 g orally twice daily) and topical Zuroor-e-Qula (2.5 g twice daily), while the allopathic treatment group received an antioxidant formulation (Capsule SM Fibro, Warren Pharma Ltd.) at a dose of one capsule twice daily. In addition, all participants received standardized physiotherapy exercises and tobacco cessation counselling as part of routine care. Following completion of the 12-week treatment phase, no further study intervention was administered. Participants entered the follow-up phase and underwent periodic clinical evaluations over 12 months to assess the long-term sustainability of treatment outcomes.

Outcome measures:
The primary outcome of the study was the long-term clinical status of patients with oral submucous fibrosis during the 12-month post-treatment follow-up period. Disease status was assessed at each follow-up visit and categorized as disease resolution, stable disease, or disease progression based on changes in clinical parameters compared with the end-of-treatment assessment. Disease resolution was defined as sustained improvement in clinical parameters, including increased inter-incisal mouth opening, reduction in burning sensation, improved tongue protrusion and enhanced mandibular excursion. Disease status was assessed by trained investigators using standardized clinical examination procedures at each follow-up visit. Stable disease was defined as the absence of clinically significant improvement or deterioration during follow-up. Disease progression was defined as worsening of one or more clinical parameters, including decreased mouth opening, increased burning sensation, reduced tongue protrusion, or reduced mandibular excursion. The secondary outcomes included assessment of oral health-related quality of life using the Oral Potentially Malignant Disorders Quality of Life (OPMDQoL) questionnaire and participant retention during the follow-up period.

Data collection:
Data were collected prospectively during the 12-month follow-up period using a standardized case record form. Participants attended scheduled follow-up visits, during which clinical examinations were performed by trained investigators using standardized assessment procedures. At each visit, disease status was evaluated based on inter-incisal mouth opening, burning sensation, tongue protrusion and mandibular excursion. Oral health-related quality of life was assessed using the Oral Potentially Malignant Disorders Quality of Life (OPMDQoL) questionnaire. Information on tobacco cessation status, participant retention and the occurrence of any disease-related

complications or malignant transformation was also recorded. All clinical findings were documented in the study database for subsequent statistical analysis.

Sample size:

No separate sample size calculation was performed for the present follow-up study. The study population comprised participants who had been enrolled in the previously conducted randomized controlled trial comparing Unani formulations with allopathic antioxidant therapy in patients with early-intermediate stage oral submucous fibrosis. A total of 120 participants (60 in each treatment group) completed the treatment phase and were eligible for long-term follow-up. It analyses were performed on participants who attended the scheduled follow-up visits, while loss to follow-up at each assessment was documented.

Statistical analysis:

Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS) version 25.0 (IBM Corp., Armonk, NY, USA). Continuous variables were expressed as mean ± standard deviation (SD), while categorical variables were presented as frequencies and percentages. All statistical tests were two-tailed and a p-value < 0.05 was considered statistically significant. Baseline demographic and clinical characteristics of the two treatment groups were compared using the independent samples t-test for continuous variables and the Chi-square test or Fisher's exact test for categorical variables, as appropriate. During the 12-month follow-up, disease status (disease resolution, stable disease and disease progression) was summarized as frequencies and percentages at each follow-up visit. Between-group comparisons of categorical outcomes were performed using the Chi-square test or Fisher's exact test, where appropriate. Changes in oral health-related quality of life (OPMDQoL scores) during follow-up were analyzed using repeated-measures analysis or the Friedman test according to the distribution of the data. Participant retention and loss to follow-up were analyzed descriptively throughout the following period.

Results:

The baseline demographic and clinical characteristics of the parent randomized controlled trial have been reported previously. Of the participants who completed the treatment phase, 88 participants (45 in the Unani group and 43 in the allopathy group) attended the 3-month follow-up visit and were included in the long-term follow-up analysis **(Table 1).** The mean age of participants was 34.07 ± 9.84 years in the Unani group and 35.70 ± 9.60 years in the allopathy group, with no statistically significant difference between the groups (p = 0.434). The study population was predominantly male, comprising 42 (93.3%) participants in the Unani group and 41 (95.3%) participants in the allopathy group, while females accounted for 3 (6.7%) and 2 (4.7%) participants, respectively. The sex distribution was comparable between the treatment groups (p = 0.683). At the initiation of the follow-up period, Grade I OSMF was the predominant clinical stage, observed in 32 (71.1%) participants in the Unani group and 33 (76.7%) participants in the allopathy group, while Grade II OSMF was present in 13 (28.9%) and 10 (23.3%) participants, respectively. There was no statistically significant difference in the distribution of OSMF grades between the two groups (p = 0.548), indicating that the demographic and clinical characteristics of the participants were comparable at the commencement of the long-term follow-up. The distribution of long-term disease status at each follow-up visit is presented in **Table 2**. At 3 months, disease progression was the most frequently observed outcome in both groups, affecting 28 (65.1%) participants in the Unani group and 29 (67.4%) participants in the allopathy group, while disease resolution was observed in 2 (4.7%) and 1 (2.3%) participants, respectively. Stable disease was noted in 15 (33.3%) participants in the Unani group and 13 (30.2%) participants in the allopathy group. The distribution of disease status did not differ significantly between the treatment groups (p = 0.839). At 6 months, the proportion of participants with stable disease increased to 37.5% in the Unani group and 45.7% in the allopathy group, whereas disease progression decreased to 55.0% and 51.4%, respectively. Disease resolution remained infrequent in both groups (7.5% vs 2.9%), with no significant between-group difference (p = 0.576). By 9 months, the frequency of disease resolution increased in both groups to 18.4% in the Unani group and 20.0% in the allopathy group, while disease progression further declined to 34.2% and 36.7%, respectively. Stable disease became the predominant outcome, occurring in 47.4% of participants receiving Unani treatment and 43.3% receiving allopathic treatment. No statistically significant difference was observed between the treatment groups (p = 0.946). At the 12-month follow-up, stable disease remained the most common outcome, affecting 20 (66.7%) participants in the Unani group and 13 (56.5%) participants in the allopathy group. Disease resolution was observed in 5 (16.7%) participants in the Unani group and 6 (26.1%) participants in the allopathy group, while disease progression was recorded in 5 (16.7%) and 4 (17.4%) participants, respectively. The distribution of disease status remained comparable between the treatment groups, with no statistically significant difference at the final follow-up assessment (p = 0.678).Overall, both treatment groups demonstrated a similar pattern of long-term disease status throughout the 12-month follow-up period, with no statistically significant differences in the distribution of disease resolution, stable disease, or disease progression at any follow-up visit. The oral health-related quality of life (OPMDQoL) scores at each follow-up assessment are presented in **Table 3**. At the 3-month follow-up, the mean OPMDQoL score was 13.94 ± 7.60 in the Unani group and 12.78 ± 5.19 in the allopathy group, with no statistically significant difference between the groups (p = 0.531). At 6 months, the mean scores were 13.53 ± 7.44 in the Unani group and 12.17 ± 4.35 in the allopathy group (p = 0.437). At 9 months, the corresponding mean OPMDQoL scores were 12.16 ± 6.32 and 11.70 ± 3.61, respectively (p = 0.755). By the 12-month follow-up, the mean OPMDQoL scores had decreased to 10.19 ± 3.76 in the Unani group and 11.65 ± 3.58 in the allopathy group,

with no statistically significant difference between the treatment groups (p = 0.152).Overall, the mean OPMDQoL scores demonstrated a gradual reduction over the follow-up period in both treatment groups, suggesting sustained improvement in oral health-related quality of life, while maintaining comparable outcomes between the Unani and allopathy groups throughout the study period. Bonferroni-adjusted pairwise comparisons of OPMDQoL scores during the follow-up period are presented in **Table 4**. In the Unani group, there was no significant difference in OPMDQoL scores between 3 and 6 months (mean difference = 0.406, 95% CI: −0.505 to 1.318; p = 1.000). However, significant reductions in OPMDQoL scores were observed between 3 and 9 months (mean difference = 1.781, 95% CI: 0.426 to 3.137; p = 0.005), 3 and 12 months (mean difference = 3.750, 95% CI: 0.671 to 6.829; p = 0.010), 6 and 9 months (mean difference = 1.375, 95% CI: 0.357 to 2.393; p = 0.004) and 6 and 12 months (mean difference = 3.344, 95% CI: 0.437 to 6.250; p = 0.017). Although the mean difference between 9 and 12 months was 1.969 (95% CI: −0.139 to 4.077), this change did not reach statistical significance (p = 0.079). In the Allopathy group, no statistically significant changes in OPMDQoL scores were observed between any follow-up assessments. The mean difference between 3 and 6 months was 0.609 (95% CI: −0.664 to 1.881; p = 1.000), between 3 and 9 months was 1.087 (95% CI: −0.437 to 2.611; p = 0.304), between 3 and 12 months was 1.130 (95% CI: −0.451 to 2.712; p = 0.301), between 6 and 9 months was 0.478 (95% CI: −0.484 to 1.440; p = 0.982), between 6 and 12 months was 0.522 (95% CI: −0.539 to 1.582; p = 1.000) and between 9 and 12 months was 0.043 (95% CI: −0.083 to 0.170; p = 1.000). These findings indicate that OPMDQoL scores remained relatively stable throughout the follow-up period in the allopathy group. Within-group repeated-measures ANOVA demonstrated a significant change in OPMDQoL scores over time in the Unani group (Greenhouse–Geisser corrected: F = 10.462, df = 1.230, 38.120, p = 0.001, partial η^2 = 0.252), indicating a significant improvement in oral health-related quality of life during the 12-month follow-up. In contrast, although the Allopathy group showed a reduction in OPMDQoL scores over time, the overall within-group change did not reach statistical significance (Greenhouse–Geisser corrected: F = 3.291, df = 1.582, 34.803, p = 0.060, partial η^2 = 0.130) presented in **Table 5.**

Table 1: Demographic and clinical characteristics of participants at the commencement of the long-term follow-up

Variable		Unani (n = 45)	Allopathy (n = 43)	p-value
Age (years),	Mean ± SD	34.07 ± 9.84	35.70 ± 9.60	0.434
Sex, n (%)	Male	42 (93.3)	41 (95.3)	0.683
	Female	3 (6.7)	2 (4.7)	
OSMF Grade, n (%)	Grade I	32 (71.1)	33 (76.7)	0.548
	Grade II	13 (28.9)	10 (23.3)	

Values are presented as mean ± standard deviation (SD) or number (%). Continuous variables were compared using the independent samples t-test and categorical variables were compared using the Chi-square testor Fisher's exact test, as appropriate. Percentages are calculated within each treatment group.

Table 2: Comparison of disease resolution, stable disease and disease progression between the unani and allopathic groups during the 12-month follow-up period

Follow-up	Disease Status	Unani n (%)	Allopathy n (%)	p-value
3 Months	Resolution	2 (4.7)	1 (2.3)	**0.839**
	Stable	15(33.3)	13 (30.2)	
	Progression	28 (65.1)	29 (67.4)	
6 Months	Resolution	3 (7.5)	1 (2.9)	**0.576**
	Stable	15 (37.5)	16 (45.7)	
	Progression	22 (55.0)	18 (51.4)	
9 Months	Resolution	7 (18.4)	6 (20.0)	**0.946**
	Stable	18 (47.4)	13 (43.3)	
	Progression	13 (34.2)	11 (36.7)	
12 Months	Resolution	5 (16.7)	6 (26.1)	**0.678**
	Stable	20 (66.7)	13 (56.5)	
	Progression	5 (16.7)	4 (17.4)	

Values are presented as number (%). Percentages were calculated within each treatment group at each follow-up visit. Between-group comparisons at each follow-up were performed using the Pearson Chi-square test. A two-sided p value < 0.05 was considered statistically significant.

Table 3: Comparison of oral health-related quality of life (OPMDQoL) scores between the Unani and allopathy groups during the 12-month follow-up

Follow-up	Unani Mean ± SD	Allopathy Mean ± SD	p-value
3 Months	13.94 ± 7.60	12.78 ± 5.19	0.531
6 Months	13.53 ± 7.44	12.17 ± 4.35	0.437
9 Months	12.16 ± 6.32	11.70 ± 3.61	0.755
12 Months	10.19 ± 3.76	11.65 ± 3.58	0.152

Values are presented as mean ± standard deviation (SD). Between-group comparisons at each follow-up time point were performed using the estimated marginal means from the repeated-measures analysis of variance (ANOVA). A two-sided p value < 0.05 was considered statistically significant.

Table 4: Bonferroni-adjusted pairwise comparisons of oral health-related quality of life (OPMDQoL) scores during the 12-month follow-up

Time comparison	Unani Mean Difference (95% CI)	p-value	Allopathy Mean Difference (95% CI)	p-value
3 vs 6 Months	0.406 (−0.505 to 1.318)	1.000	0.609 (−0.664 to 1.881)	1.000
3 vs 9 Months	1.781 (0.426 to 3.137)	0.005	1.087 (−0.437 to 2.611)	0.304
3 vs 12 Months	3.750 (0.671 to 6.829)	0.010	1.130 (−0.451 to 2.712)	0.301
6 vs 9 Months	1.375 (0.357 to 2.393)	0.004	0.478 (−0.484 to 1.440)	0.982
6 vs 12 Months	3.344 (0.437 to 6.250)	0.017	0.522(−0.539 to 1.582)	1.000

9 vs 12 Months	1.969 (−0.139 to 4.077)	0.079	0.043 (−0.083 to 0.170)	1.000

Pairwise comparisons were performed using the Bonferroni adjustment following repeated-measures ANOVA. Mean differences represent changes in OPMDQoL scores between follow-up assessments. A p value < 0.05 was considered statistically significant.

Table 5: Within-group repeated-measures analysis of variance (ANOVA) for oral health-related quality of life (OPMDQoL) scores during the 12-month follow-up

Effect	Unani	Allopathy
F-value	10.462	3.291
Degrees of freedom (Greenhouse–Geisser)	1.230, 38.120	1.582, 34.803
p-value	0.001	0.060
Partial η²	0.252	0.130

Repeated-measures ANOVA were performed to evaluate changes in OPMDQoL scores over the follow-up period within each treatment group. Greenhouse–Geisser corrected degrees of freedom and p-values are reported because Mauchly's test indicated violation of the sphericity assumption in both groups.

Discussion:

The present study evaluated the long-term clinical outcomes of patients with oral submucous fibrosis following completion of treatment with either Unani formulations or conventional allopathic therapy over a 12-month follow-up period. The principal findings demonstrated that both treatment groups maintained comparable long-term clinical outcomes throughout follow-up. Although disease progression predominated during the early follow-up period, the proportion of patients with stable disease increased progressively over time, while disease progression declined substantially by 12 months. At the end of follow-up, stable disease represented the most common clinical outcome in both treatment groups (66.7% in the Unani group and 56.5% in the allopathic group), whereas disease progression was observed in only 16.7% and 17.4% of participants, respectively. No statistically significant differences in disease status were observed between the treatment groups at any follow-up. These findings are broadly consistent with the 12-month follow-up reported by Pethani and Borate **[7]**, who observed sustained improvements in burning sensation, mouth opening and tongue protrusion following medical treatment of OSMF. However, their retrospective cohort evaluated a single novel drug combination, whereas the present study prospectively compared long-term outcomes between Unani and conventional allopathic antioxidant therapy after completion of active treatment. The progressive decline in disease progression and the corresponding increase in stable disease observed during follow-up are biologically plausible and likely reflect the combined effects of successful habit cessation, completion of active therapy and continued supportive care. Oral submucous fibrosis is primarily driven by persistent exposure to areca nut and other tobacco-related products, which stimulate fibroblast proliferation, excessive collagen deposition and reduced collagen degradation. Elimination or substantial reduction of these etiological factors following treatment may interrupt the fibrotic stimulus, allow stabilization of the disease process and prevent further deterioration. The standardized tobacco cessation counselling provided to all participants during the parent randomized controlled trial may have contributed to the successful cessation of areca nut and tobacco habits. Although

Long-term abstinence was not objectively verified during follow-up, continued avoidance of these habits by a proportion of participants may have contributed substantially to the increasing proportion of patients demonstrating stable disease and the declining frequency of disease progression observed over the 12-month period. Physiotherapy exercises prescribed during the treatment phase may have produced benefits extending beyond the active intervention period. Regular mouth-opening exercises improve tissue flexibility, reduce functional restriction and help maintain mandibular mobility. Participants who continued these exercises after treatment completion may have been better able to preserve the gains achieved during therapy, thereby limiting functional deterioration during follow-up. While adherence to physiotherapy was not formally assessed in the present study, its continued practice may partly explain the sustained clinical improvements observed in both treatment groups. From a biological perspective, the sustained clinical benefits observed after completion of therapy are also plausible. The Unani formulations and antioxidant therapy evaluated in the parent trial have previously demonstrated improvements in mouth opening, burning sensation and functional outcomes during active treatment. The Unani perspective on OSMF has also been discussed by Adil *et al.* **[8]**, who described the traditional Unani understanding of OSMF and its therapeutic approaches alongside contemporary concepts of disease pathogenesis and management. Their review highlights the relevance of Unani principles and therapeutic approaches in the context of OSMF, although it does not provide direct comparative clinical evidence for the specific Unani formulations evaluated in the present study. Similarly, Gayakwad *et al.* **[9]** reported improvements in burning sensation, mouth opening and buccal mucosal flexibility following a 12-week therapeutic intervention in patients with Grade II and III OSMF. Their study evaluated a combination of oral colchicine and intralesional Placentrex and reported significant improvement in several clinical parameters after treatment. However, direct comparison with the present study is limited because of differences in treatment regimen, disease severity, study design and follow-up duration. While their assessment focused on short-term post-treatment clinical improvement, the present study evaluated disease status and oral health-related quality of life over a 12-month period following completion of active treatment. Once inflammation is reduced, oxidative stress decreases and functional rehabilitation is achieved, these therapeutic gains may persist provided that patients avoid repeated exposure to fibrogenic agents. Consequently, the present findings suggest that the long-term maintenance of treatment benefit is influenced not only by the pharmacological effects of the initial intervention but also by continued behavioural modification and supportive management during follow-up. Oral health-related quality of life

scores improved over time in both groups, with repeated-measures analysis demonstrating a significant improvement across time in the Unani group and a comparable overall trend in the allopathic group, while no significant between-group differences were identified. Although the present study demonstrated a gradual improvement in OPMDQoL over the 12-month follow-up, direct comparison with previous evidence is limited because most clinical trials and systematic reviews in oral submucous fibrosis have primarily evaluated clinical outcomes such as maximum mouth opening, burning sensation, tongue protrusion and cheek flexibility rather than patient-reported quality of life. The recent systematic review by Chen *et al.* (2023) **[10]** summarized 34 clinical studies involving 2,136 participants and concluded that current evidence predominantly focuses on clinical improvement, with limited assessment of patient-centred outcomes such as oral health-related quality of life. Previous evidence syntheses, including the Cochrane review by Jones *et al.* (2024) **[11]** and the umbrella review by Gopinath *et al.* (2026) **[12]**, have also examined the efficacy of therapeutic interventions for OSMF. The findings of the present study are consistent with those of Patil *et al.* (2022) **[13]**, who demonstrated that treatment of oral submucous fibrosis significantly improved patients' quality of life, with marked reductions in pain, swallowing difficulty, speech impairment, social eating problems and social interaction limitations. The authors emphasized that assessment of quality of life should be incorporated as an integral outcome measure in the management of OSMF. Similarly, Memon *et al.* (2022) **[14]** evaluated oral health-related quality of life using the OHIP-14 questionnaire and reported significant improvements in overall OHRQoL following treatment, with notable gains in functional limitation, physical pain, physical disability, psychological discomfort, social disability and handicap domains. The findings of Shriram *et al.* (2025) **[15]** further highlight the importance of assessing oral health-related quality of life in patients with OSMF alongside clinical outcomes.

Conclusion:

Both Unani and conventional allopathic antioxidant therapy showed comparable clinical outcomes in patients with oral submucous fibrosis during the 12-month follow-up, with no statistically significant between-group differences in disease status or oral health-related quality of life. Oral health-related quality of life improved in both groups, with significant within-group improvement observed in the Unani group, while stable disease was the predominant outcome at 12 months. Further multicentre studies with larger sample sizes and longer follow-up are warranted to evaluate the durability of treatment outcomes, recurrence patterns and risk of malignant transformation.

Clinical implications:

Long-term follow-up remains an essential component of OSMF management because the disease is characterized by chronic progression and an inherent risk of malignant transformation. The present findings indicate that both Unani and allopathic treatment strategies were able to maintain favourable clinical outcomes during the 12-month follow-up period. The increasing proportion of patients with stable disease and the reduction in disease progression highlight the importance of continued monitoring after completion of active treatment. These findings also emphasize the need for regular clinical review, reinforcement of habit cessation, nutritional counselling, physiotherapy exercises and patient education as part of comprehensive long-term management. Monitoring patients beyond the treatment phase enables early identification of clinical deterioration and facilitates timely intervention, thereby improving long-term prognosis.

Strengths and limitations:

The present study has several strengths. It prospectively evaluated long-term outcomes over a 12-month follow-up period using standardized clinical criteria and a validated disease-specific quality-of-life instrument. The study simultaneously assessed objective clinical outcomes and patient-reported outcomes, thereby providing a comprehensive evaluation of treatment sustainability. However, several limitations should be acknowledged. Participant attrition during the 12-month follow-up should be considered when interpreting the study findings. Of the 120 participants who completed the treatment phase of the parent randomized controlled trial, 88 attended the first scheduled follow-up assessment and were included in the long-term analysis. Attrition occurred primarily because participants did not attend scheduled follow-up visits, withdrew consent, or were unavailable for subsequent evaluations. Importantly, the loss to follow-up was comparable between the Unani and allopathic treatment groups, thereby reducing the likelihood of differential attrition bias. Nevertheless, the reduced sample size during follow-up may have decreased the statistical power to detect small between-group differences and may limit the precision and generalizability of the findings. Despite this limitation, the prospective follow-up design, standardized outcome assessment and balanced retention across treatment groups support the validity of the observed long-term clinical outcomes. Secondly, this study was conducted at a single centre, which may limit the generalizability of the findings to other populations.

Future directions:

Future multicenter studies with larger sample sizes and extended follow-up periods are required to determine whether the favourable clinical outcomes observed in the present study can be sustained beyond one year. Incorporating objective biomarkers of fibrosis, imaging techniques and repeated patient-reported outcome measures may further improve the understanding of long-term disease behaviour. Future research should also investigate the influence of habit cessation, nutritional status and treatment adherence on long-term clinical outcomes and quality of life in patients with OSMF.

Advancement to knowledge:
This study provides prospective 12-month follow-up data on the long-term clinical outcomes of Unani and allopathic antioxidant therapy in patients with oral submucous fibrosis. It describes the patterns of disease resolution, stability, progression and oral health-related quality of life after completion of treatment. The findings contribute to the limited evidence on the sustainability of treatment outcomes in oral submucous fibrosis.

Acknowledgments:
The authors sincerely acknowledge the Ministry of AYUSH, Government of India, for providing the financial support for this study. We are also grateful to the management team of the Dental Institute, RIMS and the Multidisciplinary Research Unit (MRU), RIMS, for their invaluable assistance and support throughout the research. The authors extend heartfelt thanks to all the participants of this clinical trial for their cooperation and contribution.

Conflict of interest:
No potential conflicts of interest were found concerning the research study, authorship and article publication

Registration:
The registration of the study in the Clinical Trial Registry of India (CTRI) was done before the recruitment of the patient (Registration No. CTRI/2019/06/019734)

Funding:
This work was funded by the Ministry of AYUSH, Government of India

References:
[1] Mokal CN *et al. Front Cell Dev Biol*. 2026 **13**:1754209. [PMID: 41660015]
[2] Tang J*et al. Int J Oral Sci*. 2025 **17**:8. [PMID: 39890798]
[3] More CB *et al. J Oral Biol Craniofac Res*. 2020 **10**:552. [PMID: 32939334]
[4] Gondivkar SM *et al. Oral Dis*. 2018 **24**:1442. [PMID: 29928774]
[5] Ramani P *et al. J Oral Maxillofac Pathol*. 2026 **30**:2. [PMID: 42064137]
[6] Tadakamadla J *et al. Oral Surg Oral Med Oral Pathol Oral Radiol*. 2017 **123**:338. [PMID: 28094217]
[7] Pethani KH & Borate SJ. *J Maxillofac Oral Surg*. 2024 **23**:1267. [PMID: 39376750]
[8] Adil A *et al. Int J Unani Integ Med*. 2026 **10**:01. [DOI: 10.33545/2616454X.2026.v10.i2a.429]
[9] Gayakwad N *et al. J Oral Med and Dent Res*. 2024 **5**:1. [DOI: 10.52793/JOMDR.2024.5(2)-57]
[10] Chen X *et al. BMC Oral Health*. 2023 **23**:748. [PMID: 37828490]
[11] Jones A *et al. Cochrane Database Syst Rev*. 2024 **2**:CD007156. [PMID: 38415846]
[12] Gopinath D *et al. Oral Dis*. 2026. [PMID: 42216734]
[13] Patil N *et al. J Oral Med Oral Surg*. 2022 **28**:7. [DOI: 10.1051/mbcb/2022007]
[14] Memon AB *et al. Int J Environ Res Public Health*. 2022 **19**:1821. [PMID: 35162842]
[15] Shriram PC *et al. Bioinformation*. 2025 **21**:1467. [PMID: 40978593]

Caveat Emptor is applicable among the literate community where required and possible. The publisher, its journal, editors and the internal/external reviewers take adequate steps to check, evaluate, correct, edit, revise and improve content where possible and required.