SYSTEMATIC REVIEW

Salivary Micro RNA as a Biomarker to Predict the Malignant Transformation of Oral Potentially Malignant Disorders: A Systematic Review

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Abstract

Background: Oral potentially malignant disorders (OPMDs) are oral mucosal disorders which have a high potential to turn into malignancy. A recent report suggests that 16%-62% of epithelial dysplasia cases of OPMDs undergo malignant transformation, showing the need for early detection of malignancy in these disorders. Micro RNA (miRNA) plays an important role in cellular growth, differentiation, apoptosis, and immune response, and hence, deregulation of miRNA is considered a signature of oral carcinogenesis.

Materials and Methods: A search was done using MeSH terms in the PubMed/Medline, Scopus, EBSCO and Springerlink and finally, twelve studies were included in this systematic review. A quality assessment based on the Quality Assessment of Diagnostic Accuracy Studies 2 tool was used to obtain a graph of risk of bias using Revman 5.4.1 software.

Results: The results of the study revealed that miR-21, miR-31, and miR-184 were overexpressed in OPMDs, whereas miR-145 was under-expressed in OPMDs. It was demonstrated that study by Maheshwari et al. had the lowest risk of bias.

Conclusion: This systematic review explored the potential of expression of salivary miRNA in OPMDs. This could pave the way to utilize saliva as a surrogate marker in diagnosing early malignant changes in OPMDs.

Keywords: Biomarkers, Malignant, MicroRNA, miRNAs, Oral Squamous Cell Carcinoma

Introduction

Oral Potentially Malignant Disorders (OPMDs) are diseases of the oral mucosa that have a high potential to transform into malignant diseases. The common premalignant disorders prevalent among Indian population are leukoplakia, erythroplakia, lichen planus and oral submucous fibrosis (OSMF). OPMDs develop after prolonged exposure to carcinogens, which are habit-related lifestyles like paan or betel nut chewing, tobacco smoking, having spicy foods, or drinking alcohol. Early diagnosis and effective treatment of OPMDs are critical for reducing mortality and morbidity and improving overall prognosis[1]. The data suggest that all individuals diagnosed with OPMDs should be monitored periodically. It was found that the hazard ratio of the malignant transformation rate was 8.19 times higher in the OPMD group than in the comparison cohort[2,3].

MicroRNAs or miRNAs have emerged as one such diagnostic tool for the early detection of carcinomas. These are small non-coding RNAs involved in the post-transcriptional regulation of protein expression and implicated in the control of numerous cellular processes. Due to the stability of their structures, miRNAs can exist in harsh biological environments, for example, in saliva, plasma, or other body fluids. This property makes salivary miRNAs an effective diagnostic tool in determining and predicting the prognosis of oral diseases, but also systemic diseases, and overall health[2].

Oral carcinogenesis is a complex, multistep process, and there is a need for the discovery of new biomarkers such as salivary microRNA for early diagnosis, as 16-62% of Oral

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TABLE 1- Study characteristics and key features of included studies

S. No	Authors	Study Design	Sample Size	MiRNA Investigated	Results	Outcome/ recommendations
1.	Cervigne et al 2009[22]	Cross-sectional study	miRNA expression changes in 43 sequential progressive samples from 12 patients and four non-progressive leukoplakias from four different patients, using TaqMan Low-Density Arrays.	MiRNA signature	miR-21, miR-181b and miR-345 expressions were consistently increased and associated with an increase in lesion severity during progression.	miR signature- potentially useful for identifying leukoplakias at risk of malignant transformation
2.	Momen-Heravi et al 2014[21]	Cross-sectional study	34 subjects: 9 OSCC patients before treatment, 8 patients with OSCC-R, 8 patients with OLP, and 9 HCs.	More than 700 miRNAs tested	11 miRNAs were underexpressed (miRNA-136, miRNA-147, miRNA-1250, miRNA-148a, miRNA-632, miRNA-646, miRNA668, miRNA-877, miRNA-503, miRNA-220a, miRNA-323-5p), and 2 miRNAs were overexpressed (miRNA-24, miRNA-27b).	Overexpression of miRNA-27b appeared to be a promising OSCC salivary biomarker.
3.	Ghallab et al [2017]	Cross-sectional study	Sixty oral biopsy specimens were harvested from 30 healthy subjects and 30 OLP patients; subdivided into reticular, atrophic, and erosive groups (n=10 each).	miRNA 138 and CCND1 relative gene expression and immunohistochemical analysis to determine CCND1 protein expression.	Downregulation of miRNA-138 increases the gene and protein expression of its potential target CCND1 in OLP	miRNA-138 might be considered a potential novel therapeutic target for atrophic and erosive OLP patients
4.	Uma Maheswari et al 2018[15]	Systematic review	167 – oral cancer 78-OPMD 147- Healthy controls 20 – Disease controls	miRNAs	Upregulation of miRNA 184, mi RNA21 Downregulation of miRNA 145	Increased levels of miRNA 184 and 21 noted Suggests further studies to assess miRNAs
5.	Uma Maheswari et al 2020[9]	Cross-sectional study	36 Patients newly diagnosed With OPMD, 12 With OSMF, 8 With Leukoplakia, 9 With Oral Lichen Planus, 7 With OSMF And Leukoplakia.	miRNA 21 and 31	Upregulation of miRNA21 was significant	Increased levels of miRNA 184 and 21 noted Suggests miRNA21 as a better tool than miRNA 31
6.	Hsi-Feng Tu et al 2022[11]	Cross-sectional study	OPMD - 45. Healthy Controls -24	miRNA-375	Downregulation of miRNA -375	The author quotes down-regulation of miRNA 200a and miRNA-125a from other studies

Squamous Cell carcinoma (OSCC) develop from OPMDs. miRNA plays an important role in cell growth, differentiation, apoptosis, invasion, metastasis, and immune response, and thus miRNA deregulation is considered a hallmark of oral carcinogenesis[3,4]. Elevated levels of certain miRNAs cause malignancy progression, while some suppress malignancy. Therefore, they are considered human gene regulators as they are involved in gene transcription[5]. In vitro studies on cell lines have demonstrated the importance of miRNA as cancer signatures. In 2007, Tran et al. suggested that non-coding RNAs

7.	Hung et al, 2014[12]	Cohort study	20 Saliva Samples 46Tissue Sample Of OPMD	miRNA31	Significant upregulation of miRNA 31	The author suggests Assessment of p53 and VEGF levels as supplementary diagnostic tools
8.	Prasad etal, 2020[16]	Cross-sectional study	185 Samples- 61 Patients Had Chewing Habits But Did Not Have Osmf (Group 2), And 63 Were Normal Healthy Patients (Control Group) Without Any Chewing Habits (Group 3).	MiRNA 21	Upregulation of miRNA 21	The author suggests further studies with large sample sizes and with other OPMDs
9.	Khan et al 2021[14]	Case control study	50 Individuals Participated in the Study With 25 Subjects In Group I (Healthy Individuals) And 25 Subjects In Group II 25 Diagnosed Cases Of (Oral Submucous Fibrosis).	miRNA 31	Upregulation of miRNA 31 in OSMF cases	Other OPMDs not studied
10.	Hung et al., 2016[13]	Cohort study	20 Saliva Samples Of OPMD	Mir-21 Mir-31		Significantly Increased Salivary Mir-21 And Mir-31 Expression ($P = 0.003$ And $P < 0.001$, Respectively) Was Observed In Patients With OPMD Compared To Control Individuals
11.	Stasio, et Al 2019[10]	Case-control study	Five Patients Of Oral Lichen Planus And Control Group By Five Healthy Subjects	MiRNA-27b, Recorded 98 differentially expressed miRNAs in the Saliva Of Patients With Oral Lichen Planus Compared to the Control Group		Levels Of Mir-21, Mir- 125b, Mir-203 And Mir15b Were Increased ($P<0.001$) In Study Group While Levels Of Mir-27b Were About 3.0-Fold Decreased Compared To Controls ($P<0.001$) Of Mir-27b Expression In Olp Saliva
12.	Li Y et al 2022[23]	Review article	100 subjects, consisting of 20 clinically healthy controls, 40 patients with oral potentially malignant disorders (OPMDs) [20 with dysplastic lesions and 20 without dysplasia], 20 with biopsy-confirmed oral squamous cell carcinoma (OSCC), and 20 with Recurrent aphthous stomatitis (RAS) as disease controls.	miRNA-21, miRNA-184, and miRNA-145	There was a highly significant increase in salivary miRNA-21 and miRNA-184 in OSCC and OPMD (with and without dysplasia) when compared to healthy and disease controls ($P < 0.001$). Conversely, miRNA-145 levels showed a highly significant decrease in OSCC and OPMD overall ($P < 0.001$).	Salivary determination of the miRNAs might furnish a noninvasive, rapid adjunctive aid for revealing malignant transformation in oral mucosal lesions, particularly miRNA-184.

such as miRNA play an important role in carcinogenesis based on cell line studies of head and neck carcinomas[6]. Scully et al. demonstrated that clinical and histopathological assessment of OPMD is not sufficient to predict malignant transformation; therefore, assessment of miRNA in these lesions would be helpful[7].

The aim of this systematic review is to find the diagnostic efficacy of salivary miRNA in predicting the malignant transformation of OPMDs. The review was conducted to address the following research question. Which microRNA is commonly expressed in OPMD Patients?

This systematic review was conducted according to the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analysis) guidelines and the Joanna Briggs Institute guidelines for reviews. A PICO statement was drafted to search the relevant articles. The population included in the study were patients with Oral Potentially Malignant Disorders. As this article finds evidence for diagnostic tools the intervention in this article is the biomarker. Comparison is made between different biomarkers and the outcome is the predictability of malignant transformation. A systematic search was done in PubMed/MEDLINE, SCOPUS, EBSCO, and Springer Link using the MeSH terms. The selection was supplemented by a manual search and screening of the entire reference lists of included studies.

Analytical studies, clinical studies, comparative studies, and randomized control trials whose content was associated with miRNAs as diagnostic markers of OPMDs using saliva as a diagnostic tool, in vitro studies that evaluated the role of miRNA in OPMDs, articles on miRNA published between June 2015 and June 2022, articles with OPMD cases confirmed by histopathological analysis are included in the study.

Articles describing miRNA extracted exclusively from tissue, blood, plasma, or serum for both OPMD and oral cancer, review articles and book chapters, conference proceedings, articles published before or after the specified dates, studies based only on bioinformatics prediction approaches without experimental analysis, animal studies and internet searches identified approximately 250 studies, of which 134 were screened and excluded from this study. Articles that did not have control group or pre and post operative assessments were excluded. After applying the inclusion and exclusion criteria, a total of 12 studies were included, which had been performed on saliva samples from OPMDs.

A total of 12 articles met the inclusion criteria and the data were tabulated. The data collected includes the patient's sample

TABLE 2: Quality Assessment Tool for Diagnostic Accuracy Studies (QUADAS)-2

AUTHOR	Risk of Bias				Applicability Concerns		
	Patient selection	Index test	Reference standard	Flow and timing	Patient selection	Index test	Reference standard
HIS- FENG TU, 2022	-	-	+	+	-	+	+
HUNG, 2016	?	-	+	-	-	+	?
HUNG92),2016	+	-	+	-	+	?	-
KHAN, 2021	+	-	+	-	+	-	+
MAHESWARI 2017	+	-	+	-	+	-	?
MAHESWARI,2022	+	+	+	-	+	+	-
PRASAD,2020	-	-	-	-	+	?	-
STASIO, 2019	+	?	+	-	+	?	-
CERVIGNE, 2009	+	-	+	-	+	-	-
MOMEN-HERAVI, 2014	?	-	+	-	+	-	+
GHALLAB, 2017	+	?	+	-	+	?	-
LI Y 2022	+	?	+	-	+	?	+

size, existing premalignant condition, and increase or decrease in expression of miRNAs. All extracted data were entered into a custom spreadsheet program to eliminate possible errors. (Table 1).

Quality assessment of studies: The quality of these twelve studies was assessed using the Quality Assessment of Diagnostic Accuracy Studies (QUADAS)-2 instrument (recommended by the Cochrane Collaboration, the Agency for Health Care Research and Quality, and the UK National Institute of Health and Clinical Excellence for assessing the quality of diagnostic studies). This instrument includes 14 items that assess the risk of bias and sources of variation in diagnostic studies[8].

Risk of bias and applicability concerns: A quality assessment based on the Quality Assessment of Diagnostic Accuracy Studies 2 tool was used to obtain a graph of risk of bias using Revman 5.4.1 software, and it was demonstrated that the 2022 study by Maheshwari et al. had the lowest risk of bias. Risk of bias and applicability QUADAS-2 includes four domains. These data were entered into the Review Manager software (Revman 5.4.1) to provide a color-coded representation of the risk of bias and applicability concerns. The study by Maheshwari et al (2020)[9] had the lowest risk of bias among the eight studies, followed by the study by Stasio et al. (2019)[10]. On the other hand, the five studies by His-Feng Tu et al[11], Hung et al[12], Hung et al[13], Khan et al[14], and Maheshwari et al[15] had a moderate risk of bias. The study of Prasad et al[16] had a high risk of bias. The lesser the bias in the study, the higher the clinical applicability. (Table 2)

Discussion

Late diagnosis is often the cause of poor prognosis in carcinoma patients. Studies on miRNAs have shown that early screening prevents the incidence of cancer or progression to malignancy. Clinicians have reported that late diagnosis leads to lymphatic spread and recurrence. There are thousands of genes that transcribe messenger RNA, microRNA(miRNA), etc[17]. miRNAs have been shown to be signatures of oral carcinogenesis in recent studies. As oral tissues are immersed in saliva, recent studies have demonstrated that saliva is not only a surrogate pool of biomarkers but has been shown to be more significant in biomarker expression. It is well known that deregulation of salivary miRNAs is associated with many diseases. Salivary miRNAs are stable and can potentially be used in the detection of oral cancer[18]. Studies on miRNA expression in oral cancer began in 2009[11].

Out of the 12 studies included in this review, OSMF is commonly studied with the control group. Two studies included all the OPMDs, however, the sample size appears to be less. Of all the miRNAs reported Uma et al suggested miRNA 21 expression was significantly higher than miRNA31. Other authors claimed significant expression of miRNA 31 in OPMDs. Uma et al reported that miR-21, miR-31, and miR-184 were overexpressed in OPMD, whereas miR-145 was under-expressed in OPMD[19].

Few down regulations of miRNA have been reported. miRNA 145, miRNA 375, miRNA 200a, and miRNA 125a have been identified to be expressed in low levels in patients progressing to malignancy. The same levels have been found to be higher in patients with non-progression to malignancy. miRNA 375 has been reported to show significantly decreased levels. These studies reveal that there can be upregulations as well as downregulations ofcertain miRNA. Aberrant expression of miR-375 in saliva was detected in OPMD patients and distinguished them from matched control subjects and dysplasia patients from subjects without dysplasia, indicating a potential clinical application for oral lesion-specific miRNA signatures in saliva. This is a convenient and less invasive method that highlights miR-375 as a biomarker for OPMD.[11,12]

The mean value for miR-21 was reported to be 3.7 only in the study by Zahran et al, who concluded that miRNA-21 is increased 4-fold in OPMD compared with controls, with an area under the ROC curve of 0.73 at 65% sensitivity and specificity[20]. In two studies, Momen et al and Zahran et al statistically demonstrated sensitivity and specificity for four salivary miRNAs, namely miRNA 27b, miRNA 145, miRNA 181, and miRNA21[20,21]. Several miRNAs have been studied in the context of oral PMDs, including miRNAs 21, 27b, 145, 181, 181b, and 345. Cervigne et al reported that overexpression of miRNA 21, miRNA 181b, and miRNA 345 may play an important role in the malignant transformation of leukoplakia. Several studies have demonstrated that miRNA 27b, miRNA 145, miRNA 181, and miRNA 21 have statistically significant sensitivity and specificity for detecting early malignancy[22]. Previous studies have shown that miRNAs play a role in the pathogenesis of oral lichen planus (OLP) by enhancing inflammation in OLP lesions. Since miRNAs are involved in the pathogenesis of OLP, some of the studies also investigated the potential of miRNAs in the saliva of these patients as diagnostic and prognostic biomarkers[23]. Ghallab et al showed that miR-138 was downregulated in the lesions of OLP, whereas another study by Danielsson and colleagues reported lower expression of miR-125b and higher expression of miR-21 and miR-203 in OLP lesions[24].

Of the eight studies, the study by Maheshwari et al[9] had the lowest risk of bias, followed by the study by Stasio et al[10], Maheshwari et al[9] found that miRNA-21 and miRNA-31 were significant in oral leukoplakia and oral lichen planus and minimal in OSMF and OSMF with leukoplakia groups. Stasio et al[10] reported that the 89 miRNAs were upregulated in OLP. In contrast, the five studies by His-Feng Tu et al[11], Hung et al[12], Hung (2) et al[13], Khan et al[15], and Maheshwari et al[14] showed a moderate risk of bias. The study by Prasad et al[16] had a high risk of bias.

Hsi-Feng Tu et al (2022)[11] detected deregulated miR-375 levels in saliva, which may serve as biomarkers for early detection and prognostic indicators in OPMD patients. Regardless of the pathological condition, the expression of miR-375 in the saliva of patients with OPMD was significantly lower than in healthy individuals, as shown by a mean -ΔCt value of 8.97 in OPMD patients compared with a value of 10.17 in controls. Differences in miR-375 levels were found between clinical subgroups of patients, e.g., with or without dysplasia; this difference was statistically significant. Khan S et al added that high expression levels of miRNA31 in oral submucosal

fibrosis suggest an ideal screening marker for the progression prediction of OSMF cases. Prasad et al[16] observed a marked increase in miRNA-21 expression in OSMF cases compared to normal cases without areca nut chewing habits. This study showed a high risk of bias. Hung et al. 2016[12] showed significantly increased expression of miR-21 and miR-31 in saliva ($P = 0.003$ and $P < 0.001$, respectively) in patients with OPMD compared with control subjects. In subjects diagnosed with recurrent OPMD and/or malignant transformation, the expression of miR-31, but not miR-21, was further increased in the epithelium. Moreover, increased miR-31 expression was an independent risk factor for the progression of OPMD. This indicates that the detection of miR-31 expression is a useful method for screening high-risk OPMDs, as its expression synergistically with dysplastic epithelium predicts the malignant and recurrent potential of OPMDs. miRNA-31 was upregulated nearly 20-fold in cancer tissues compared with adjacent healthy tissues and mediates oncogenesis by targeting a molecule that inhibits hypoxia-inducing factors in oral cancer [25]. Liu et al examined miRNA-31 in the saliva of 10 verrucous leukoplakia, 45 OSCC, and 24 healthy controls and concluded that the mean value for miRNA-31 was 8.3, with an area under the ROC curve of 0.71 and a specificity of 100%.

The present systematic review finds evidence for miRNAs as a diagnostic tool in the early detection of carcinomas. However, this includes only a case-control study and one systematic review. Studies with OSMF and control groups have been reported by many authors. There appears to be a lack of sufficient evidence for other OPMDS.

Conclusion

This systematic review claims the diagnostic efficacy of salivary miRNAs as a diagnostic tool and a less invasive method in the early detection of carcinoma in OPMDS. It also recommends that both the upregulated and downregulated miRNAs be used as diagnostic tools as it would be more confirmatory. Study also suggests future scope for studies to identify lesion-specific biomarkers and more clinical trials with increased sample size would strengthen the evidence for the results of this review.

References

1. Lorini L, BescósAtín C, Thavaraj S, Müller-Richter U, Alberola Ferranti M, Pamias Romero J et al. Overview of Oral Potentially Malignant Disorders: From Risk Factors to Specific Therapies. Cancers (Basel). 2021 Jul 23;13(15):3696.doi: 10.3390/cancers13153696.
2. Kaunein N, Ramani RS, Koo K, Moore C, Celentano A, McCullough M et al Systematic Review of MicroRNA Signatures Associated with the Progression of Leukoplakia with and without Epithelial Dysplasia. Biomolecules. 2021 Dec 14;11(12):1879
3. Osan C, Chira S, Nutu AM, Braicu C, Baciut M, Korban SS, et al. The Connection between MicroRNAs and Oral Cancer Pathogenesis: Emerging Biomarkers in Oral Cancer Management. Genes (Basel). 2021;12:1989.
4. Macfarlane LA, Murphy PR. MicroRNA: Biogenesis, Function and Role in Cancer. Curr Genomics. 2010;11:537-561.
5. Kerr, A. R., & Lodi, G. Management of oral potentially malignant disorders. Oral Diseases, 2021;27:2008– 2025.
6. He B, Zhao Z, Cai Q, Zhang Y, Zhang P, Shi S, et al. miRNA-based biomarkers, therapies, and resistance in Cancer. Int J Biol Sci. 2020;16(14):2628-2647
7. Scully C. Challenges in predicting which oral mucosal potentially malignant disease will progress to neoplasia. Oral Dis. 2014;20:1–5.
8. Whiting PF, Rutjes AW, Westwood ME, Mallett S, Deeks JJ, Reitsma JB et al; QUADAS-2 Group. QUADAS-2: a revised tool for the quality assessment of diagnostic accuracy studies. Ann Intern Med. 2011;155(8):529-36.
9. Uma Maheswari TN, Nivedhitha MS, Ramani P. Expression profile of salivary micro RNA-21 and 31 in oral potentially malignant disorders. Braz Oral Res. 2020 Feb 10;34: e002
10. Stasio DD, Mosca L, Lucchese A, Cave DD, Kawasaki H, Lombardi A et al . Salivary mir-27b Expression in Oral Lichen Planus Patients: A Series of Cases and a Narrative Review of Literature. Curr Top Med Chem. 2019;19(31):2816-2823
11. Tu HF, Lin LH, Chang KW, Cheng HW, Liu CJ. Exploiting salivary miR-375 as a clinical biomarker of oral potentially malignant disorder. J Dent Sci. 2022 Apr;17(2):659-665.
12. Hung KF, Liu CJ, Chiu PC, Lin JS, Chang KW, Shih WY et al. MicroRNA-31 upregulation predicts increased risk of progression of oral potentially malignant disorder. Oral Oncol. 2016 Feb;53:42-7
13. Hung PS, Tu HF, Kao SY, Yang CC, Liu CJ, Huang TY, et al. miR-31 is upregulated in oral premalignant epithelium and contributes to the immortalization of normal oral keratinocytes. Carcinogenesis. 2014 May;35(5):1162-71
14. KhanS,ButtSA,Hassan S,Khan R.Expression of salivary miRNA -31 in oral submucous fibrosis.Journal of Advances in Medicine and Medical Research,2021;33:137-144
15. Maheswari T N, Venugopal A, Sureshbabu NM, Ramani P. Salivary microRNA as a potential biomarker in oral potentially malignant disorders: A systematic review. Tzu Chi Med J 2018;30:55-60
16. Prasad SR, Pai A, Shyamala K, Yaji A. Expression of Salivary miRNA 21 in Oral Submucous Fibrosis (OSMF): An Observational Study. Microrna. 2020;9:295-302.
17. Montero PH, Patel SG. Cancer of the oral cavity. Surg Oncol Clin N Am. 2015;24:491-508.
18. Mariam A, Miller-Atkins G, Moro A, Rodarte AI, Siddiqi S, Acevedo-Moreno LA, et al. Salivary miRNAs as non-invasive biomarkers of hepatocellular carcinoma: a pilot study. PeerJ. 2022 Jan 5;10: e12715.
19. Rapado-González Ó, Majem B, Muinelo-Romay L, Álvarez-Castro A, Santamaría A, Gil-Moreno A, et al. Human salivary microRNAs in Cancer. J Cancer. 2018;9:638-649.
20. Zahran F, Ghalwash D, Shaker O, Al-Johani K, Scully C. Salivary microRNAs in oral cancer. Oral Dis. 2015; 21:739-47.
21. Momen-Heravi F, Trachtenberg AJ, Kuo WP, Cheng YS. Genomewide study of salivary microRNAs for detection of oral cancer. J Dent Res. 2014;93:86S-93S.
22. Cervigne NK, Reis PP, Machado J, Sadikovic B, Bradley G, Galloni NN, et al. Identification of a microRNA signature associated with progression of leukoplakia to oral carcinoma. Hum Mol Genet. 2009;18:4818-29.
23. Li Y, He Y, Xiang J, Feng L, Wang Y, Chen R. The Functional Mechanism of MicroRNA in Oral Lichen Planus. J Inflamm Res. 2022;15: 4261-4274.
24. Ghallab NA,Kasem RF, Safa Fathy Abd El-Ghani, Shaker OG. Gene expression of mirna-138 and cyclin d1 in oral lichen planus. Egyptian dental journal. 2017;63: 625:638.
25. Kumari P, Syed SA, Wahid M, Qureshi MA, Kumar R. Expression of miR-31 in saliva-liquid biopsy in patients with oral squamous cell carcinoma. J Taibah Univ Med Sci. 2021;16(5):733-739.
26. Liu CJ, Lin SC, Yang CC, Cheng HW, Chang KW. Exploiting salivary miR-31 as a clinical biomarker of oral squamous cell carcinoma. Head Neck. 2012;34(2):219-24.