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ISSN Online 2704-4890 | ISSN Print 2720-7609

Online first publication

Systematic Review

HSI Journal (2025) Volume 7 (Issue 2):1339-1347. https://doi.org/10.46829/hsijournal.2025.12.7.2.1339-1347

Open Access

Prognostic value of immuno-expression of Epidermal Growth Factor Receptor (EGFR) & B-Cell Lymphoma (BCL-2) as apoptotic biomarkers in oral squamous cell carcinoma: A systematic review and meta-analysis

Priyanka DEBTA [1*], Chandrachur CHATTERJEE [1], Neeta MOHANTY [1], Saurav PANDA [2]

[1] Department of Oral Pathology and Microbiology, Institute of Dental Sciences, Siksha O Anusandhan, Bhubaneswar, Odisha, India; [2] Department of Periodontia and Implantology, Institute of Dental Sciences, Siksha O Anusandhan, Bhubaneswar, Odisha, India

Received July, 2025; Revised October, 2025; Accepted November, 2025

Abstract

Background: Apoptosis, or programmed cell death, plays a crucial role in cancer development and progression. Biomarkers like EGFR and BCL-2 are known to regulate apoptosis and have been studied in various cancers, including oral squamous cell carcinoma (OSCC). The expression patterns and prognostic implications of these biomarkers could help in predicting patient outcomes. To address this research question, we conducted a systematic review and meta-analysis of studies examining the prognostic significance of two apoptotic biomarkers, EGFR (Epidermal Growth Factor Receptor) and BCL-2 (B-cell lymphoma 2), in OSCC.

Objective: By elucidating the prognostic value of EGFR and BCL-2 immunoexpression in OSCC, this systematic review aimed to contribute to predicting the immunoexpression value of EGFR and BCL-2.

Methods: This systematic review and meta-analysis investigated the prognostic significance of immunostaining of EGFR and BCL-2 in patients with OSCC. The PICO criteria were applied to OSCC patients, defining the population, intervention (immunoexpression of EGFR and BCL-2), and outcome (prognostic significance). This systematic review was registered with PROSPERO to ensure transparency and avoid duplication. A comprehensive search strategy was developed using relevant keywords and Medical Subject Headings (MeSH) terms related to OSCC, EGFR, BCL-2, immunohistochemistry, and prognosis. Electronic databases such as PubMed and SCOPUS were searched, along with reference lists from relevant articles. Data extraction included author, publication year, patient characteristics (sample size, age, gender), and outcomes related to overall survival.

Results: EGFR is frequently overexpressed in OSCC, and its expression has been associated with aggressive tumour behaviour and poor prognosis. High EGFR expression is often correlated with reduced survival rates in OSCC patients. High BCL-2 expression has been associated with tumour progression and poor prognosis in OSCC patients.

Conclusion: Overall, the immunohistochemical expression of EGFR in Oral Squamous Cell Carcinoma (OSCC) appears to hold significant prognostic value. However, further research is needed to validate these findings and to optimise the clinical utility of EGFR as a prognostic biomarker in OSCC management. Likewise, evidence suggests a prognostic role for BCL-2 immunohistochemical expression in OSCC. Additional studies are required to fully elucidate its significance and potential implications for patient management and treatment decision-making.

Keywords: Oral squamous cell carcinoma, apoptosis, immunohistochemistry, EGFR, BCL-2, biomarkers, prognosis,

Cite the publication as Debta P, Chatterjee C, Mohanty N, Panda S (2025) Prognostic value of immuno-expression of Epidermal Growth Factor Receptor (EGFR) & B-Cell Lymphoma (BCL-2) as apoptotic biomarkers in oral squamous cell carcinoma: A systematic review and meta-analysis. HSI Journal 7 (2):1339-1347. https://doi.org/10.46829/hsijournal.2025.12.7.2.1339-1347

INTRODUCTION

Squamous Cell Carcinoma (OSCC) is a malignant tumour of the oral cavity. OSCC is commonly associated with tobacco use, low socioeconomic status, and a lack of awareness about risk factors and early detection. Despite being classified at similar stages, OSCC tumours exhibit diverse clinical behaviours due to their inherent heterogeneity in invasion and metastatic potential. Tumour morphology, keratinisation, and immunohistochemistry (IHC) analysis help assess tumour behaviour [1]. Immunohistochemistry (IHC) uses antibodies to detect

* *Corresponding author*
Email: priyankadebta@soa.ac.in

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tissue antigens, aiding in cancer diagnosis and prognosis. OSCC develops through genetic alterations affecting apoptosis [2]. EGFR and BCL-2 are key IHC apoptotic biomarkers. EGFR, a transmembrane receptor, promotes malignant transformation and is often overexpressed in head and neck squamous cell carcinomas. Its strong expression correlates with advanced stages and shorter relapse-free periods by influencing invasion, angiogenesis, and lymphangiogenesis [3].

EGFR, a tyrosine kinase receptor in the ErbB family, is crucial for the growth and progression of solid tumours. Its structure includes ligand-binding, transmembrane, and cytoplasmic domains, making it a key therapeutic target in carcinomas. EGFR gene amplification is observed in 15.4% – 31.2% of OSCC cases [4]. BCL-2 is a 25-kDa apoptosis regulatory protein in the membranes of mitochondria, endoplasmic reticulum, and nuclear envelope. It promotes cell survival, proliferation, and tissue development by inhibiting apoptosis. Overexpression of BCL-2, observed in precancerous lesions, can be counteracted by pro-apoptotic proteins like Bax. EGFR overexpression is also commonly documented in epithelial tumours, including OSCC [5]. Apoptosis, a regulated process that controls tissue size and eliminates damaged cells, is influenced by genes such as the BCL-2 family, which can either promote or inhibit apoptosis. BCL-2, an anti-apoptotic protein, plays a key role in regulating this process. Biomarkers such as EGFR and BCL-2 are studied to predict OSCC prognosis, with existing publications analysing their impact on overall survival [6,7,8,9,10].

MATERIALS AND METHODS

This systematic review has been conducted with respect to the Preferred Reporting for Systematic Review and Meta-Analysis checklist [PRISMA]. This systematic review was registered in the PROSPERO database and received the registration number CRD42023396316.

Study design

This systematic review focused on observational and cohort studies involving human subjects to examine the prognostic implications of EGFR and BCL-2 immunohistochemical expression in OSCC. The selected studies specifically examined the relationship between these biomarkers and overall survival outcomes in patients diagnosed with OSCC.

Inclusion criteria
1. Sample - Human cohort studies that have observed prognostic significance of the immunoexpression of EGFR and BCL-2 in Oral squamous cell carcinoma in terms of overall survival.
2. Clinical data - The basic clinical data, such as age, gender, sample size and sample population, were provided.
3. Immunohistochemistry- Original Immunohistochemistry studies.
4. Prognostication - Overall Survival In terms of Hazard's ratio (multivariate COX proportional Hazard regression analysis)

Exclusion criteria
1. Studies in which clinical details of included cases were missing.
2. Articles published in a language other than English.
3. Studies where no prognostic outcome was mentioned related to EGFR and BCL-2 immunoexpression.
4. Studies on cancers other than OSCC.
5. Studies whose full texts were not available.
6. Review articles of EGFR and BCL-2 biomarkers.

Data extraction
For each article included in this review, we systematically collected detailed information to facilitate comprehensive analysis and comparison. The data extracted comprised the following elements: the name of the first author, year of publication, the population studied, and the sample size. Additionally, we recorded the male-to-female ratio and the age of participants. Information regarding apoptotic biomarkers and their immunoexpression was also documented. Where available, we extracted statistical data relevant to overall survival, specifically the hazard ratio and its corresponding 95% confidence interval, as reported in each study.

Data analysis
We considered only EGFR and BCL-2 immunoexpression in OSCC cases where overall survival statistical data were mentioned. The guidelines from the Strengthening the Reporting of Observational Studies in Epidemiology [STROBE] were used to evaluate the quality of included studies. The meta-analysis was conducted in RevMan (version 5.4.1). Forest plots were constructed for each reported outcome, showing risk ratios and 95% confidence intervals, which were extracted from the original values reported in selected articles.

Study selection
In the first step, 4,997 articles were selected from PubMed and SCOPUS databases. There were 501 articles after removing the duplicate studies and other reasons. A further comprehensive evaluation of titles and abstracts was conducted, which excluded 436 articles, leaving 65 for screening in this review. Of these articles, 16 were excluded because they were not published in English. Forty-nine articles were assessed for eligibility, and 33 articles were excluded for various reasons. A total of 16 articles were retrieved for this systematic review (Figure 1).

RESULTS

Of the 16 articles included in this systematic review, 12 investigated the immunoexpression of EGFR in oral squamous cell carcinoma (OSCC) (Table 1), while the remaining 4 examined the immunoexpression of BCL-2 in OSCC in relation to overall survival (Table 2). In our

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systematic review, we found a hazard ratio (HR) greater than 1 in all selected original research articles for the EGFR biomarker and the BCL-2 biomarker. Only one research article for the BCL-2 marker showed a value of less than 1, specifically 0.970. Altogether, these findings suggest that both biomarkers play a significant role in the expression of oral squamous cell carcinoma cases compared to the control group. The risk of bias and quality assessment of the selected studies were performed using the Newcastle-Ottawa scale, with higher scores indicating lower risk of bias (Table 3). Our meta-analysis favours this systematic review result with improved precision, 95% CI for EGFR (Figure 1 & Graph 1) and BCL-2 (Figure 2 & Graph 2) were respectively 1.31 and 1.75. These provide a powerful tool for synthesising research evidence, leading to more reliable conclusions than individual studies alone can offer. Thus, we suggest that the prognostic value of immunostaining for the biomarkers EGFR and BCL-2 is important in oral squamous cell carcinoma.

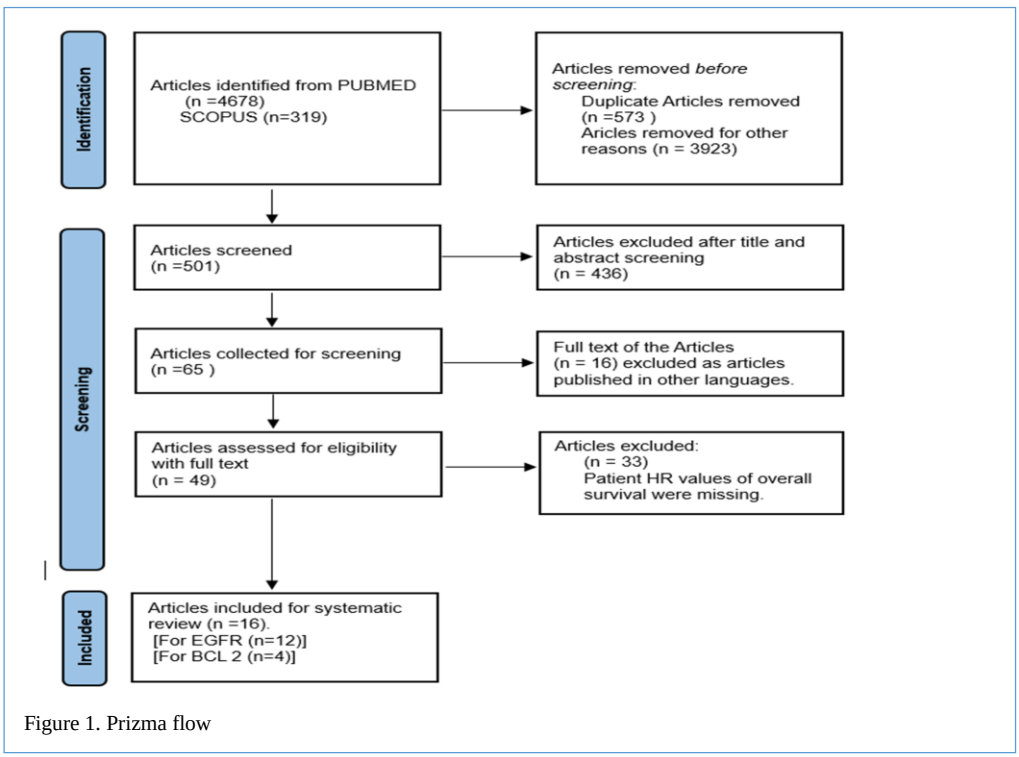


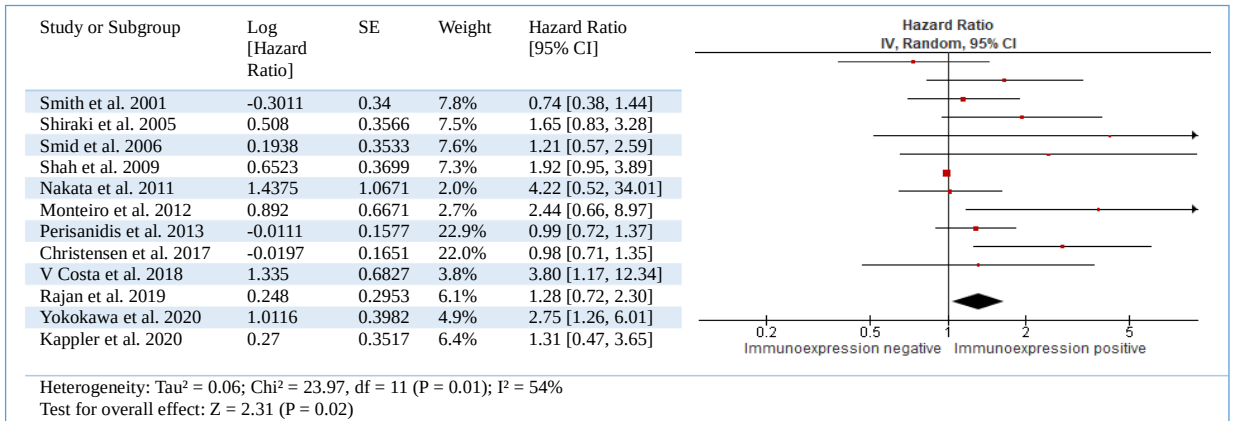
Figure 1. Prizma flow

Table 1. Articles and demographic data for studies on EGFR biomarker in OSCC

Sl NO.	Author Name	Year	Population	Sample size	Male: Female	Average Age	Hazards Ratio (95% CI)
1.	Kappler et al.	2020	Germany	45	31:14	57	1.31 (0.47, 3.60)
2.	Yokokawa et al.	2020	Japan	208	129:79	59.1	2.75 (1.26, 6.01)
3.	Rajan et al.	2019	United State	141	82:59	58(M) 66(F)	1.28(0.90,1.90)
4.	V. Costa et al.	2018	Brazil	Target Group- 21 Control group- 39	TG 2:1 CG 30:9	TG≤ 40 CG≥ 50	3.8 (1.17,12.48)
5.	Christensen et al.	2017	Denmark	191	126:65	59	1.02 (0.65,1.60)
6.	Perisanidis et al.	2013	Austria	97	NA	NA	0.99 (0.96,1.00)
7.	Monteiro et al.	2012	Portugal	74	55:19	62.3	2.44(0.66,8.96)
8.	Nakata et al.	2011	Japan	89	62:27	60	4.21(0.52,34.34
9.	Shah et al.	2009	India	135	101:34	45	1.92 (0.95, 3.86)
10.	Smid et al.	2006	Netherlands	165	108:57	58	1.15(0.70, 1.90)
11.	Shiraki et al.	2005	Japan	140	98:42	59	1.65 (0.83, 3,29)
12.	Smith et al.	2001	United State	32	NA	NA	0.74(0.38,1.43)

Table 2. Articles and demographic data for studies on BCL-2 biomarker in OSCC

Sl NO.	Author Name	Year	Population	Sample size	Male: Female	Average Age	Hazards Ratio (95% CI)
1.	Trivedi et al.	2010	India	135	101:34	45	1.98(0.77,5.09)
2.	Shah et al.	2009	India	135	101:34	45	1.81 (0.93,3.52)
3.	Lo Muzito et al.	2005	Italy	66	44:22	66	2.31(1.00,5.34)
4.	Ito et al.	1999	Japan	57	NA	NA	0.970 (0.36,2.62)



Heterogeneity: $Tau^2 = 0.06$; $Chi^2 = 23.97$, df = 11 (P = 0.01); $I^2 = 54\%$
Test for overall effect: Z = 2.31 (P = 0.02)

Figure 2. Meta-analysis of EGFR Expression in OSCC studies

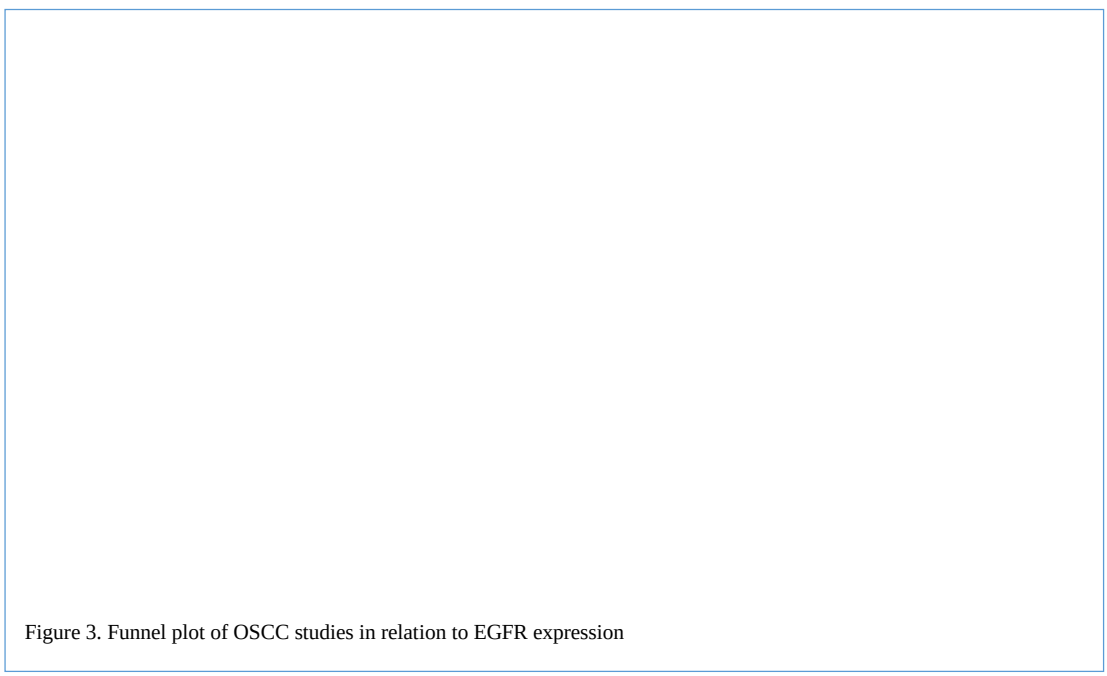


Figure 3. Funnel plot of OSCC studies in relation to EGFR expression

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Table 3. Studies of quality assessment by the Newcastle Ottawa scale, with a higher score indicating a lower risk of bias

Study	Selection	Comparability	Outcome	NOS Score
Kappler et al.	●●●●	●●	●○●	8
Yokokawa et al.	●●●●	●●	●○○	7
Rajan et al.	●●●●	●●	●○○	7
V. Costa et al.	●●●●	●●	●○○	7
Christensen et al.	●●●●	●●	●○○	7
Perisanidis et al.	●●●●	●●	●○●	8
Monteiro et al.	●●●●	●●	●○○	7
Nakata et al.	●●●●	●●	●○○	7
Shah et al.	●●●●	●●	●○●	8
Smid et al.	●●●●	●●	●○○	7
Shiraki et al.	●●●●	●●	●○○	7
Smith et al.	●●●●	●●	●○●	8
Trivedi et al.	●●●●	●●	●○○	7
Lo Muzito et al	●●●●	●●	●○○	7
Smith et al.	●●●●	●●	●○●	8

Study or Subgroup	Log [Hazard Ratio]	SE	Weight (%)	Hazard Ratio [IV, Random, 95% CI]	Year
Ito et al. 1999	-0.0305	0.5057	17.5	0.97 [0.36, 2.61]	1999
Lo Muzito et al. 2005	0.8372	0.4272	24.5	2.31 [1.00, 5.34]	2005
Shah et al. 2009	0.5933	0.3397	38.1	1.81 [0.93, 3.52]	2009
Trivedi et al. 2010	0.6831	0.4189	19.8	1.98 [0.77, 5.09]	2010
Total (95% CI)			100	1.75 [1.16, 2.65]	

Heterogeneity: Tau² = 0.00; Chi² = 1.86, df = 3 (P = 0.60); I² = 0%
Test for overall effect: Z = 2.65 (P = 0.008)

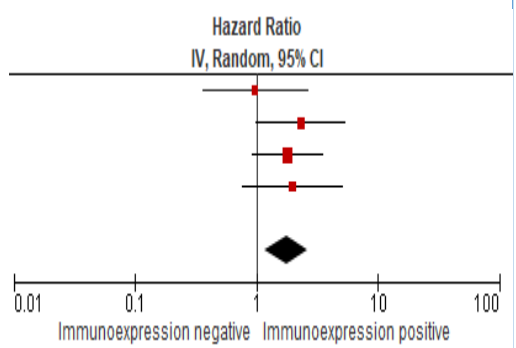

Figure 4. Overall survival meta-analysis of OSCC studies in relation to BCL-2 expression

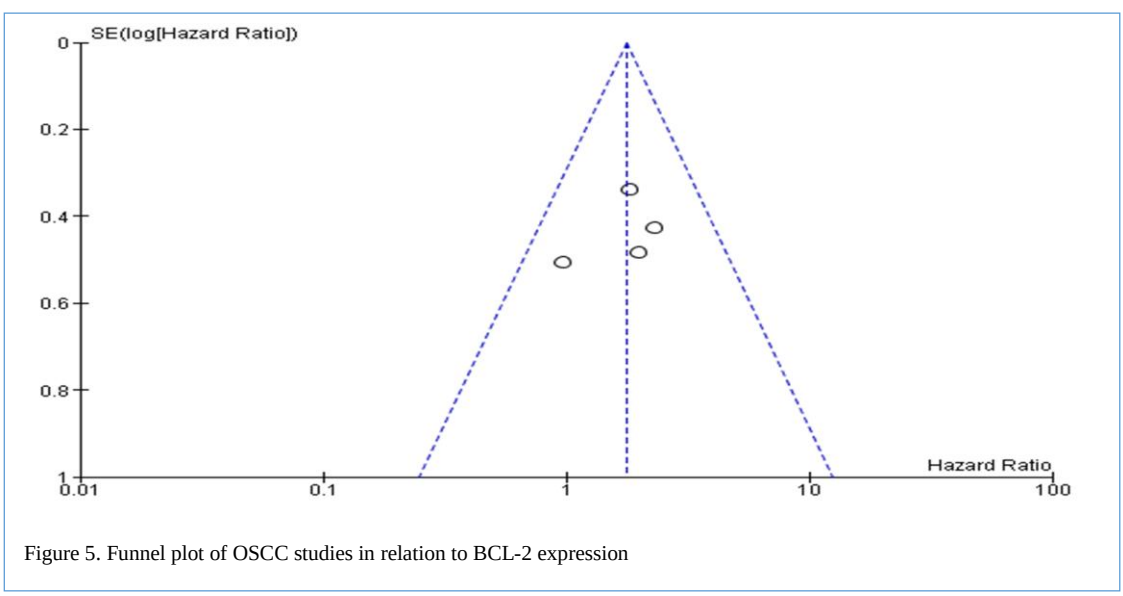

Figure 5. Funnel plot of OSCC studies in relation to BCL-2 expression

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DISCUSSIONS

This systematic review and meta-analysis aimed to investigate the prognostic importance of immunostaining of EGFR and BCL-2 in patients with OSCC. We found that a poor clinical outcome is associated with the overexpression of both biomarkers, as indicated by hazard ratios greater than 1. This is strong evidence suggesting the significant prognostic value of EGFR and BCL-2 immunostaining in OSSC.

EGFR and BCL-2 immunoexpression have been studied in many cases of OSCC. In the meta-analysis, all of our selected studies showed HR values greater than 1 for EGFR with a pooled estimate of 1.31, suggesting that overexpression of EGFR correlates with reduced survival. This finding is consistent with previous research demonstrating that EGFR contributes to tumour invasion, proliferation, and metastasis [11,12,13,14]. Its overexpression has also been reported with increased recurrence and poor outcome in patients with OSCC [15,16,17]. It has also been observed in previous studies that the overexpression of EGFR may be associated with resistance to chemoradiotherapy and radiotherapy; thus, this evidence further supports its association with poor prognosis [18,19,20,21]. Many previous studies also reinforce the finding that EGFR overexpression is a reliable prognostic indicator [22,23]. These findings support the results of our meta-analysis and suggest that EGFR is a potential biomarker for risk stratification in OSCC cases.

BCL-2 causes tumour cell survival by affecting the process of programmed cell death. In the present meta-analysis, we found a pooled hazard ratio (HR) value of 1.75 for BCL-2 overexpression, indicating its association with poor survival in OSCC. This finding is consistent with previous studies, which have suggested that higher BCL-2 expression promotes tumour progression and is associated with lymph node involvement and reduced survival [11,19, 24]. Previous studies have also demonstrated that the aggressive behaviour of the tumour and resistance to therapy are associated with increased BCL-2 expression and dysregulation of apoptotic pathways [25,26]. Overexpression of EGFR also affects survival and response to treatment [27-33]. Regarding clinical implications, the findings of this meta-analysis suggest that the overexpression of EGFR and BCL-2, as determined by immunohistochemistry, can serve as important prognostic biomarkers in OSCC. Thus, these biomarkers help to identify patients with high risk who require more aggressive treatment or a targeted therapeutic approach. EGFR inhibitors have already been explored as a therapeutic option, suggesting the benefit of personalised treatment strategies [26-33]. Similarly, targeting the BCL-2 pathway could also help overcome resistance to conventional therapies [34]. Many studies have also reported that the transformation from premalignant to malignant lesions is associated with increased BCL-2 expression, supporting the role of BCL-2 in carcinogenesis and tumour progression [35-40]. Additionally, BCL-2 family protein expression has been shown to affect prognosis in OSCC, which further reinforces our meta-analytic findings [40].

One of the challenges in the prognosis of OSCC is marked heterogeneity, which is observed among tumours diagnosed at the same stage. This heterogeneity can be differentiated by the molecular expression of EGFR and BCL-2, which affect invasion, metastatic potential, and treatment response [25-32]. By integrating molecular profiling and identifying variations in biomarker expression, we can perform prognostic assessments. We used the Newcastle-Ottawa scale to assess the quality of the studies included in this meta-analysis, which indicates a low risk of bias and thus strengthens the reliability of our pooled estimates. The meta-analysis enables a more definitive conclusion regarding the prognostic roles of EGFR and BCL-2 in comparison to any single study. This systematic review and meta-analysis demonstrated the strong prognostic relevance of the overexpression of EGFR and BCL-2 in OSCC. Given their role in tumours, this marker may serve as a valuable tool to identify high-risk OSCC cases, thereby further guiding personalised and targeted therapeutic strategies.

Conclusion

The immunohistochemical expression of EGFR and BCL in OSCC holds notable prognostic significance, with evidence suggesting that higher expression of both biomarkers is associated with poorer outcomes. This highlights their potential as indicators for guiding personalised treatment strategies. However, further research is needed to understand their roles better and refine their implications for patient management and therapeutic decisions.

DECLARATIONS

Ethical consideration

Ethical approval for the study was obtained from IDS, Siksha' O' Anusandhan, BBSR, Odisha.

Consent to publish

All authors agreed on the content of the final paper.

Funding

None

Competing Interest

The authors declare no conflict of interest

Author contribution

PD and CC conceptualised and designed the study. NM and SP performed the statistical analysis.

Acknowledgement

We would like to acknowledge the Honourable President of Siksha' O' Anusandhan, Prof. (Dr.) Manojranjan Nayak for providing research facilities.

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Availability of data

Data is available on request from the corresponding author.

REFERENCES

1. Guruprasad Y, Thippeswamy SH, Naik D, Naik VR, Prabhu V, Sushma M, et al. (2023) Evaluation of immunohistochemical markers in oral squamous cell carcinoma. J Oral Maxillofac Pathol 27(4):624–632
2. Munjal MK, Ramalingam K, Sihmar SS, Gill K, Khan MI (2022) BCL2 expression in OPMD and OSCC—An immunohistochemical study on 70 samples. J Pharm Negat Results 13:1177–1191
3. O-charoenrat P, Rhys-Evans PH, Modjtahedi H, Eccles SA (2002) The role of c-erbB receptors and ligands in head and neck squamous cell carcinoma. Oral Oncol 38:627–640
4. Costa V, Kowalski LP, Coutinho-Camillo CM, Begnami MD, Calsavara VF, Neves JI, et al. (2018) EGFR amplification and expression in oral squamous cell carcinoma in young adults. Int J Oral Maxillofac Surg 47:817–823
5. Cuneo KC, Nyati MK, Ray D, Lawrence TS (2015) EGFR targeted therapies and radiation: optimising efficacy by appropriate drug scheduling and patient selection. Pharmacol Ther 154:67–77
6. Pansini PF, do Valle IB, Damasceno TCD, de Abreu PM, Có ACG, López RVM, et al. (2021) Differential expression of potential biomarkers of oral squamous cell carcinoma development. Head Neck Pathol 15:1127–1136
7. Solomon MC, Vidyasagar MS, Fernandes D, Guddattu V, Mathew M, Shergill AK, et al. (2016) The prognostic implication of the expression of EGFR, p53, cyclin D1, BCL and p16 in primary locally advanced oral squamous cell carcinoma cases: a tissue microarray study. Med Oncol 33:138
8. Arya V, Singh S, Daniel MJ (2016) Clinicopathological correlation of Bcl-2 oncoprotein expression in oral precancer and cancer. J Oral Biol Craniofac Res 6:18–23
9. McDonnell TJ, Troncoso P, Brisbay SM, Logothetis C, Chung LW, Hsieh JT, et al. (1992) Expression of the protooncogene BCL in the prostate and its association with emergence of androgen-independent prostate cancer. Cancer Res 52:6940–6944
10. Sarkis SA, Abdullah BH, Abdul Majeed BA, Talabani NG (2010) Immunohistochemical expression of epidermal growth factor receptor in oral squamous cell carcinoma. Head Neck Oncol 2:13
11. Popović B, Jekić B, Novaković I, Luković LJ, Tepavcević Z, Jurisić V, et al. (2007) BCL expression in oral squamous cell carcinoma. Ann N Y Acad Sci 1095:19–25
12. Bernardes VF, Almeida OP, Pinto CA, Silva CB, Carvalho AL, Kowalski LP, et al. (2013) EGFR status in oral squamous cell carcinoma. J Oral Pathol Med 42(3):220–225
13. Kappler M, Dauter K, Reich W, Bethmann D, Schwabe M, Rot S, et al. (2020) Prognostic impact of cytoplasmatic EGFR upregulation in patients with oral squamous cell carcinoma: a pilot study. Mol Clin Oncol 13:88
14. Monteiro LS, Diniz-Freitas M, Warnakulasuriya S, Garcia-Caballero T, Forteza J, Fraga M (2018) An immunohistochemical score to predict the outcome for oral squamous cell carcinoma. J Oral Pathol Med 47:375–381
15. Nakata Y, Uzawa N, Takahashi KI, Sumino J, Michikawa C, Sato H, et al. (2011) EGFR gene copy number alteration is a better prognostic indicator than protein overexpression in oral tongue squamous cell carcinomas. Eur J Cancer 47:2364–2372
16. Perisanidis C, Wrba F, Brandstetter A, Kornek G, Mitchell D, Seemann R, et al. (2013) Impact of EGFR, MET and IGF1R expression on survival in oral and oropharyngeal cancer. Br J Oral Maxillofac Surg 51:234–240
17. Shiraki M, Odajima T, Ikeda T, Sasaki A, Satoh M, Yamaguchi A, et al. (2005) Combined expression of p53, cyclin D1 and EGFR improves prognosis estimation in resected oral cancer. Mod Pathol 18:1482–1489
18. Smid EJ, Stoter TR, Bloemena E, Lafleur MVM, Leemans CR, van der Waal I, et al. (2006) Immunohistochemical expression of EGFR in oral cavity SCC treated with surgery and radiotherapy. Int J Radiat Oncol Biol Phys 65:1323–1329
19. Smith BD, Smith GL, Carter D, DiGiovanna MP, Kasowitz KM, Sasaki CT, et al. (2001) Molecular marker expression in oral and oropharyngeal squamous cell carcinoma. Arch Otolaryngol Head Neck Surg 127:780–785
20. Yokokawa M, Morita KI, Oikawa Y, Kayamori K, Sakamoto K, Ikeda T, et al. (2020) Co-expression of EGFR and MET in oral squamous cell carcinoma. J Oral Pathol Med 49:235–242
21. Rajan A, Gibson-Corley KN, Choi AB, Ofori-Amanfo GK, Ten Eyck P, Espinosa-Cotton M, et al. (2019) Nuclear IL-1α and EGFR expression in oral SCC: impact on recurrence and survival. J Oncol 2019:5859680
22. Shah NG, Trivedi TI, Tankshali RA, Goswami JV, Jetly DH, Shukla SN, et al. (2009) Prognostic significance of molecular markers in oral squamous cell carcinoma. Head Neck 31:1544–1556
23. Christensen A, Kiss K, Lelkaitis G, Juhl K, Persson M, Charabi BW, et al. (2017) uPAR, TF and EGFR expression patterns and prognostic value in oral cancer. BMC Cancer 17:572
24. Ito T, Fujieda S, Tsuzuki H, Sunaga H, Fan G, Sugimoto C, et al. (1999) Decreased Bax expression correlates with poor prognosis in oral and oropharyngeal carcinoma. Cancer Lett 140:81–81
25. Trivedi TI, Tankshali RA, Goswami JV, Shukla SN, Shah PM, Shah NG (2011) Site-specific prognostic biomarkers in oral SCC. Neoplasma 58:217–226
26. Lo Muzio L, Falaschini S, Farina A, Rubini C, Pezzetti F, Campisi G, et al. (2005) BCL as prognostic factor in head and neck squamous cell carcinoma. Oncol Res 15:249–255
27. Altuna Mariezkurrena X, Algaba Guimerá J, Wang Rodríguez J, Weisman R, Ongkeko W (2005) Immunohistochemistry study of EGFR in head and neck SCC. Acta Otorrinolaringol Esp 56:143–146
28. Li JC, Zhao YH, Wang XY, Yang Y, Pan DL, Qiu ZD, et al. (2014) Clinical significance of EGFR-pathway protein expression in esophageal SCC. Tumour Biol 35:651–657

29. Shahsavari F, Miri R, Ghorbanpour M (2020) EGFR expression in oral and esophageal SCC. Dent Res J (Isfahan) 17:85–91

30. El-Zayat AAE, Pingree TF, Mock PM, Clark GM, Otto RA, Von Hoff DD (1991) EGFR amplification in head and neck cancer. Cancer J 4:375–381

31. Dassonville O, Formento JL, Francoual M, Ramaioli A, Santini J, Schneider M, et al. (1993) EGFR expression and survival in upper aerodigestive tract cancer. J Clin Oncol 11:1873–1878

32. Ang KK, Andratschke NH, Milas L (2004) EGFR and therapy response in head-and-neck carcinoma. Int J Radiat Oncol Biol Phys 58:959–965

33. Rubin Grandis J, Melhem MF, Gooding WE, Day R, Holst VA, Wagener MM, et al. (1998) TGF-α and EGFR levels in head and neck SCC and survival. J Natl Cancer Inst 90:824–832

34. Thomas S, Quinn BA, Das SK, Dash R, Emdad L, Dasgupta S, Wang XY, Dent P, Reed JC, Pellecchia M, Sarkar D, Fisher PB (2013) Targeting the Bcl-2 family for cancer therapy. Expert Opin Ther Targets 17:61–75

35. Juneja S, Chaitanya NB, Agarwal M (2015) Immunohistochemical expression of BCL in oral dysplasia and carcinoma. Indian J Cancer 52:505–510

36. Jordan RC, Catzavelos GC, Barrett AW, Speight PM (1996) Differential expression of BCL and Bax in oral cavity SCC. Eur J Cancer B Oral Oncol 32B:394–400

37. Kato K, Shimasaki M, Kato T, Segami N, Ueda Y (2018) Sphingosine kinase-1 expression correlates with invasiveness and poor prognosis in oral SCC. Anticancer Res 38:1361–1368

38. Singh BB, Chandler FW, Whitaker SB, Forbes-Nelson AE (1998) Immunohistochemical evaluation of BCL in oral dysplasia and carcinoma. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 85:692–698

39. Piattelli A, Rubini C, Fioroni M, Iezzi G, Santinelli A (2002) p53, BCL and Ki-67 expression and apoptosis in normal, premalignant and malignant oral epithelium. J Oral Maxillofac Surg 60:532–540

40. Camisasca DR, Honorato J, Bernardo V, da Silva LE, da Fonseca EC, de Faria PAS, et al. (2009) BCL family protein expression and survival in oral SCC. Oral Oncol 45:202–208