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HISTOPATHOLOGICAL FEATURES OF ORAL CANCER DIAGNOSTIC AND PROGNOSTIC INDICATORS

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ABSTRACT

Background: Oral Cancer mainly oral squamous cell carcinoma (OSCC), was shown to be one of the principal causes leading to a great health burden worldwide with significant morbidity and mortality.
Objective: Our Study aimed to build an archetypal portrait of histopathological scenarios in oral cancer and the clinical importance that can be leveraged as efficacious diagnostic markers for conducting precision diagnostics.
Study Design: A Retrospective Study.
Duration and Place of the Study: This Study was conducted at Department Of Pathology Watim Medical And Dental College, Rawat Rawalpindi between 3rd February 2023 and 2nd January 2024.
Material and Methods: This Study included 200 patients with oral squamous cell carcinoma (OSCC) and other malignancies in the oral region. The inclusion criteria were a histologically confirmed oral cancer diagnosis, complete clinical records, and enough biopsy tissue samples. The exclusion criteria were recurrent tumours, previous chemotherapy or radiotherapy, and incomplete histopathological records.
Results: The study population was the 200 patients diagnosed with oral cancer. The mean age of our patients at the time of diagnosis was 58.4 ± 12.3. The age range was as follows: 16.0% of the patients were under 40, 53.5% were 40-60, and 30.5% were over 60. Well-differentiated tumours had a baseline HR of 1.00, whereas the HR in moderately differentiated cases was 1.45 (95% CI: 1.10-1.90, p=0.02) and in poorly differentiated 2.10 (95% CI: 1.50-2.90, p<0.01).
Conclusion: Our Study in oral cancer supplied a comprehensive assessment of its histopathological and IHC characteristics for revealing their diagnostic and prognostic functions.
Keywords: Histopathology, Oral Cancer, Diagnostic Indicators, Prognostic Markers.

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INTRODUCTION

Oral cancer mainly oral squamous cell carcinoma (OSCC), was shown to be one of the principal causes leading to a great health burden worldwide with significant morbidity and mortality [1, 2]. The prognosis of oral cancer is still poor because the disease continues to be diagnosed in its final stages, and due to this point, there are not always better curative strategies, even though current treatment regimens have improved during the last year [3]. Therefore, early, accurate diagnosis is key to improving patient outcome rates, necessitating potential new diagnostic and prognostic markers [4]. Histopathology is the mainstay of diagnosis for oral cancer [5]. It gives vital information regarding the cellular architecture, tissue organization and the presence of certain pathological features that separate malignant from benign lesions [6]. In addition, histopathological analysis can identify worse prognostic factors that predict disease evolution and patient survival and influence therapeutic decisions [7]. This Study strives to systematically elucidate the histopathological characteristics and their diagnostic or prognostic value in oral cancer. We will then analyze these through histopathological parameters such as cellular differentiation, keratinization rate, mitotic index and invasion of lymph vascular. We will also assess the expression of p53, Ki-67 and EGFR as factors involved in tumour behaviour and patient prognosis. The knowledge of these histopathological characteristics leads to improved precision of oral cancer diagnosis, which finally contributes to patient stratification and personalized therapy management [8, 9]. The objective of our Study was to build an archetypal portrait of histopathological scenarios in oral cancer and The clinical importance can be leveraged as efficacious diagnostic markers for precision diagnostics. All of these will add to better management clinical practice and thus improve outcomes and long-term patient survival.

MATERIAL AND METHODS

200 patients with oral squamous cell carcinoma (OSCC) and other malignancies in the oral region. Criteria for inclusion: patients with a histologically confirmed oral cancer diagnosis with complete clinical records and enough biopsy tissue samples. The exclusion criteria were recurrent tumours, previous chemotherapy or radiotherapy and incomplete histopathological records. Biopsy materials for histopathological examinations were collected and placed in 10% formalin at diagnosis. Four to five-micrometer sections were sliced and stained with hematoxylin-eosin (H&E) for histopathology. Immunohistochemical markers were also studied for quickly some sections forked engine pathologic concern.

HISTOPATHOLOGICAL EXAMINATION

Pathologists examined tissue differentiation for three levels of maturity using cellular arrangement evaluation to determine whether cancer cells appeared well, moderately or poorly organized.The examination included analysis of keratinization both in its presence and extent.The evaluation of tumor proliferative activity used a method which counted the number of active cell divisions per high-power field (HPF).A confirmed sign of lymphovascular Invasion existed due to the observations of cancer cells detected inside blood vessels and lymphatic structures.The analysis found tumor cells that infiltrated perineural spaces during thee valuation. Immunohistochemical Analysis The essential molecular markers were examined using immunohistochemistry evaluation techniques.The tumor suppressor protein p53 underwent assessment for both mutations together with overexpression analysis. Laboratory researchers consider Ki-67 as a nuclear marker for measuring tumor cell division rate through stained cell percentages.The analysis assesses Epidermal growth factor receptor (EGFR) because scientists evaluate its overexpression.Staining procedures for immunohistochemistry followed standardized methods where the expression levels received qualitative assessment by combining intensity grades and positive cell percentages.

APPROVAL FORM ETHICS COMMITTEE STATEMENT

This study was reviewed and approved by the Ethics Review Board (ERB-1178/07/2022) under the supervision of Principal Author Aiza Saadia at the Department Of Pathology Watim Medical And Dental College, Rawat Rawalpindi. Ethical clearance was obtained before the study's commencement, ensuring compliance with institutional guidelines for human research ethics.

DATA COLLECTION

Most of the tumours were located as follows: 40.5% in the tongue, 19.5% on the floor of the mouth, 24.0% in the buccal mucosa, and 16.0% in other locations. The cancer stage at

the time of diagnosis was as follows: 21.0% were stage I, 40.5% were stage II, 23.0% were stage III, and 15.5% were stage IV. The level of differentiation was as follows: 35.5% well differentiated moderately differentiated, and 18.0% poorly differentiated. Keratinization was present in 61.0% of the cases and absent in 39.0%. The mitotic index, a measure of cellular proliferation, was calculated: 26.5% of the Collection of clinical data Clinical information was tumours had less than five mitoses per high power field, obtained from medical records, which included patients 48.5% had between 5-10 mitoses, and 25.0% had more demographics: tumour stage; treatment details and than 10. The lymphovascular invasion was present in the final follow-up—the histopathological in 46.5% of the samples and absent in 53.5%. Perineural immunohistochemical features that detected the invasion were seen in 30.5% of the cases and not in the relationship between these factors compared to 69.5%. The IHC findings were as follows: p53 was clinical outcomes of overall survival (OS) and disease-positive in 67.0% and negative in 33.0%. The Ki-67Free survival (DFS).

STATISTICAL ANALYSIS

the index was less than 20% positive cells in 31.0%, 21.5% more than 50%, and 48.5% between 20-50% positive SPSS version 25.0 was used for statistical analysis of The cells. EGFR was positive in 51.5% of the cases, and descriptive statistics were summarized among the negative in 48.5%—the hazard ratios for various patient characteristics and histopathological features. Prognostic factors are given. Well-differentiated tumours DFS and OS were calculated using Kaplan-Meier and had a baseline HR of 1.00, whereas the HR in moderate survival analysis. The independent prognostic factors differentiated cases we r e 1.45 (95% CI: 1.10-1.90, were analyzed using Cox proportional hazards p=0.02) and in poorly differentiated 2.10 (95% CI: regression. Statistical analysis-significance was 1.50-2.90, p<0.01). Lymph vascular invasion was accepted at the <0.05 level of probability for p-values

ETHICAL CONSIDERATIONS

The Review Board (IRB) approved the study protocol. Tumour invasion HR 1.13 (95% CI: 1.37-1.30, p<0.02. The patients provided w r i t t e n i n f o r m e d c o n s e n t . Therefore, per neural invasion was a t r e n d a mo n g their guardians. Methods Declaration of Helsinki: significant adverse IHC was an adverse prognostic. All aspects of this project were by the factor with an HR of 2.20 (95% CI: 1.60-3.05, p<0.01) principles set down in the Declaration by Guiding in its presence, compared to cases without it, having Principles for Study Involving Animals and Human HR 1.02 (95% CI: 1.41-3.08, p=0.03). The Ki-67 score Beings.

RESULTS

The study population was the 200 patients diagnosed p=0.02), in cases with moderate scores – between 20- with oral cancer. The mean age of our patients at the 50% HR was 1.35 (95% CI: 1.00-1.80, p=0.04) in high time of diagnosis was 58.4 ± 12.3. The age range was – more than 50%, HR – 1.90 (95% CI: 1.40-2.55, as follows: 16.0% of the patients were under 40, 53.5% p<0.01). Therefore, our Study identified multiple patients who were 40-60, and 30.5% of patients who were over 60. The significant histopathological and IHC markers that were the majority of patients were males 73.5%, whereas Instrumental in the diagnosis and prognostication of oral cancer.

Table 1: Patient Demographics and Clinical Characteristics

Characteristics	Number of Patients (n=200)	Frequency (%)
Age, mean±(SD)	58.4 ± 12.3	
Age (years)		
<40 years	32	(16.0%)
40-60 years	107	(53.5%)
>60 years	61	(30.5%)
Gender		
Male	147	(73.5%)
Female	53	(26.5%)
Tumor Location		
Tongue	81	(40.5%)
Floor of mouth	39	(19.5%)
Buccal mucosa	48	(24.0%)
Other	32	(16.0%)
Tumor Stage		
Stage-I	42	(21.0%)
Stage-II	81	(40.5%)
Stage-III	46	(23.0%)
Stage-IV	31	(15.5%)

Table 1: Histopathological Features of Oral Cancer

Histopathological Feature	Category	Frequency (n)	Percentage (%)
Cellular Differentiation	Well Differentiated	82	41.0%
Moderately Differentiated	82	41.0%	
Poorly Differentiated	36	18.0%	
Keratinization	Present	122	61.0%
Absent	78	39.0%	
Mitotic Index (per HPF)	<5	53	26.5%
5-10	97	48.5%	
>10	50	25.0%	
Lymphovascular Invasion	Present	93	46.5%
Absent	107	53.5%	
Perineural Invasion	Present	61	30.5%
Absent	139	69.5%	

Table 02: Histopathological

Poorly differentiated	**36**	**(18.0%)**
Keratinization		
Present	122	(61.0%)
Absent	78	(39.0%)
Mitotic Index (per HPF)		
<5	53	(26.5%)
5-10	97	(48.5%)
>10	50	(25.0%)
Lymphovascular Invasion		
Present	93	(46.5%)
Absent	107	(53.5%)
Perineural Invasion		
Present	61	(30.5%)
Absent	139	(69.5%)

Table 3: Immunohistochemical Marker Expression

Marker Expression Level	Number of Patients (n=200)	Frequency (%)
p53		
Positive	134	(67.0%)
Negative	66	(33.0%)
Ki-67		
<20%	62	(31.0%)
20-50%	97	(48.5%)
>50%	43	(21.5%)
EGFR		
Positive	103	(51.5%)
Negative	97	(48.5%)

DISCUSSION

Accurate histopathological diagnosis and support the use of immunohistochemistry in oral cancer. Our cohort's mean age was 58.4 years old, which is coincident with other studies of oral cancer patients aged between 50 and 70 years. In our Study, the gender distribution showed a male predominance (73.5%), which was in concord with the global tendency of sex ratio among oral cancer cases as reported by Warnakulasuriya (2009) and Silverman (2001) [10, 11]. In our Study, the most commonly encountered site of tumours was on the tongue at 40.5%, followed by the floor of the mouth and buccal mucosa. These findings were supported by Llewellyn et al. (2001), who reported the tongue as the most common site for oral cancer [12].

Our data showed that the percentage distribution of tumours was well differential (35.5%), moderately differentiated (46.5%) and poorly differentiated carcinoma (18.0%). This is consistent with the results of Nagler et al. (2002), who reported similar differentiation percentages [13]. The positive presence of keratinization in 61.0% of well-differentiated SCC is also comparable to some previous studies and showed that it might be a prominent feature as the established sign for well-differentiated squamous cell carcinomas (Pindborg et al.,1997) [14]. These tumours are aggressive, as seen here by the mitotic index, with 48.5% of tumours demonstrating 5-10 per HPF, corroborating that previously published by Barnes et al.(2005), who demonstrated the relation between the

mitotic index and grading of oral cancers [15]. Lymphovascular invasion, detected in 46.5% of cases and perineural involvement, seen in 30.5%, are high-risk factors for increased local recurrence and poor prognosis leading to a significant proportion of distant metastasis. These invasion rates are compared with those found by Woolgar and Scott (1995), who reported 40-50% of cases and perineural invasion in about 25-30% [16]. Our immunohistochemical analysis identified 67.0% and 51.5% of the tumours as p53-positive, EGFR-expressing tumours; only 31.0% had Ki-67 indices >20%. However, the overexpression of p53 documented in our Study is similar to that observed by Smith et al. (1999), who found p53 positivity in 60-70% of oral cancers [17]. In another study, p53 positivity was detected in 60- 70% of cases of oral cancer. These findings are consistent with studies by Lo Muzio et al. (2005), where higher Ki-67 expression was associated with increased tumour aggressiveness [18]. It is similar to the findings of Park et al. (2022), but they found that higher Ki-67 expression was correlated with high tumour behaviour [19]. These results are also concordant with some studies, such as the one of Grandis and Tweardy (1993), which detected expression in 50-60% of oral cancers [20].In our survival analysis, differentiation status, lymphovascular invasion, perineural invasion, and Ki-67 index were significant risk factors. Poorly differentiated tumours showed the highest HR of 2.1,0, establishing poor differentiation as a bad prognostic indicator reported earlier by Bryne et al. (1992) [21]. Our findings of the outstanding prognostic relevance of lymphovascular and perineural invasion are confirmed by those from Schliephake et al. (1995), who have shown these factors to be closely correlated with reduced overall survival [22]. The Ki-67 index was also identified as a predictive marker in our series, highlighting the negative correlation between higher numbers of positive cells and survival probability, consistent with Alvarenga et al. (2000) [23]. P53 mutations and overexpression are associated with worse survival in the two cohorts studied, which agrees with a meta-analysis by Szymańska et al. (2011), that stressed p53 as a crucial tool for prognosis in head and neck cancers [24].

CONCLUSION

Our Study in oral cancer supplied a comprehensive assessment of its histopathological and IHC characteristics for revealing their diagnostic and prognostic functions. The data showed a predominance of moderately differentiated tumours with lymphovascular and perineural invasion, identifying the most common adverse prognostic features and varying levels of Ki-67, p53 and EGFR expression, which all correlate with tumour aggression and patient outcome.The practical application of such discoveries into clinical practice offers great potential to augment oral cancer detection and better match optimal treatment options for effective disease control, thus improving patient survival. Individually customized therapies targeting specific molecular pathways, based on the histopathological and pathological profiles of each tumour, aim to translate into better treatment efficacy and a favourable toxicity profile in individual patients, representing a new era of targeted therapy.

Authors Contribution

Concept & Design of Study: Momina khadija Abbasi

Drafting: Aiza saadia

Data Analysis: , Naila Abrar

Critical Review, Naila Abrar

Final Approval of version: All Mantion above .

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