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EVALUATION OF COAGULATION PROFILE IN PATIENTS WITH ORAL SQUAMOUS CELL CARCINOMA

Hemato-Pathology

Dr. Puneet Saini	Junior Resident , Department of Pathology
Dr. Kavita Kumari*	Associate Professor, Department of transfusion medicine and immunohematology *Corresponding Author
Dr. Jaspreet Singh	Professor, Department of Pathology
Dr. Permeet Kaur Bagga	Professor and Head, Department of Pathology
Ishrat Kaur Kauldhar	MBBS Student, Cmc Ludhiana
Dr. Pooja	Senior Resident, Department of Pathology
Dr. Sunidhi Sharma	Senior Resident, Department of Pathology
Dr. Saurabh Kumar Wadhwa	Senior Resident, Department of Pathology

ABSTRACT

Background: Oral cancer represents an enormous global health challenge, with an exceptionally high disease burden in the Indian subcontinent due to widespread tobacco and areca nut consumption. Beyond localized tissue destruction, oral squamous cell carcinoma (OSCC) causes systemic hemostatic abnormalities. This study aims to evaluate the baseline coagulation profile that are Prothrombin time (PT), International normalized ratio (INR) and activated partial thromboplastin time (aPTT) in OSCC patients and correlate these parameters with clinicopathological features, establishing accessible surrogate markers of tumor aggressiveness. **Methodology:** This prospective observational study enrolled 75 histopathologically confirmed female and male patients with OSCC at Government Medical College, Amritsar, Citrated plasma was isolated via centrifugation to determine PT, INR, and aPTT utilizing a semiautomated photo-optical coagulometer. Statistical analysis was conducted using SPSS version 20.0 via Chi-square tests, independent t-tests, and one-way ANOVA. **Results:** The cohort demonstrated a strong male predominance (86.7%) with a peak incidence in the fifth and sixth decades of life. Well-differentiated squamous cell carcinoma (WDSCC) was discovered in (64%) of cases, followed by moderately differentiated (MDSCC, 33.3%) and poorly differentiated tumors (PDSCC, 2.7%). Worsening histological differentiation was significantly linked with a progressive prolongation of coagulation values: PT: WDSCC ("15.15±3.73 s)" , MDSCC "(21.11±4.58 s"), PDSCC ;"(28.73±11.07 s)" p = 0.000. INR: WDSCC "(1.12±0.30"), MDSCC "(1.65±0.42)" , PDSCC "(2.40±1.04)" ; p = 0.000. aPTT: WDSCC "(38.66±9.77 s)" , MDSCC "(44.73±11.10 s)" , PDSCC "(46.85±6.01 s"); p = 0.044. Posterior/deep oral cavity sites (such as the oropharynx and tonsillar fossa) presented with significantly advanced tumor grades (p = 0.0001) and more pronounced systemic coagulation derangements compared to anterior anatomical landmarks (p < 0.05). Platelet counts remained stable across all groups (p = 0.079). **Conclusion:** A clear, statistically significant correlation exists between advanced histopathological tumor grade and deranged coagulation pathways in OSCC. Routine preoperative baseline coagulation evaluation serves as a crucial, cost-effective non-invasive biomarker for perioperative risk stratification and tracking tumor biology within resource-limited clinical environments.

KEYWORDS

Oral Squamous Cell Carcinoma, Coagulation Profile, Prothrombin Time, Semiautomated Coagulometer, Tumor Differentiation, Disseminated Intravascular Coagulation.

INTRODUCTION

Oral cavity cancer ranks among the top three malignancies in India, where it accounts for over 30% of all localized cancer cases and presents an age-adjusted occurrence of 20 cases per 100,000 individuals[2-3]. This high local disease burden is primarily triggered by widespread exposure to known carcinogens, including smoking, betel quid chewing with areca nut, and smokeless tobacco alternatives, which are directly associated with approximately 80% of regional cases. Despite advancements in multi-modal therapeutic approaches, the overall five-year survival rate for oral squamous cell carcinoma (OSCC) has remained stationary between 50% and 60% due to late clinical stage at presentation, locoregional disease recurrence, and early occult distant metastasis [1].

A bidirectional clinical axis connects malignant progression with host hemostasis[4-5]. Patients diagnosed with solid tumors suffer a four- to seven-fold elevated risk of venous thromboembolism (VTE) relative to healthy populations, making cancer-associated thrombosis the second leading cause of mortality in oncology fields following the primary disease itself [5]. This systemic "cancer-associated coagulopathy" spans from mild, subclinical laboratory irregularities to overt, life-threatening consumptive syndromes or disseminated intravascular coagulation (DIC)[5].

Evaluating these hemostatic networks in oral oncology holds vast clinical utility, particularly within resource-constrained environments. Unlike high-cost molecular tests, routine coagulation screening assets—such as PT, INR, and aPTT—represent universally accessible, low-cost baseline tests[6]. If validated as functional indicators of aggressive tumor profiles, these inexpensive markers can augment tumor staging networks, guide targeted prophylactic anticoagulation choices, and identify high-risk surgical or chemotherapeutic candidates without imposing excessive financial loads on public healthcare setups[6].

Methodology

This prospective observational study was conducted within the Department of Pathology at Government Medical College, Amritsar, from June 2024 to December 2025. A sample size of 75 patients was accrued using a prospective sampling matrix. All treatment-naive patients with a firm, histopathologically confirmed diagnosis of oral squamous cell carcinoma who were willing to provide written consent were included in the study. Patients presenting with a documented history of congenital or acquired blood coagulation disorders[5]; a recent history of acute cardiovascular events (e.g., myocardial infarction, deep vein thrombosis)[5]; clinical presentation of active DIC or vaso-occlusive crises[5]; concurrent diagnosis of Chronic Lymphocytic Leukemia (CLL)[5]; presence of a mechanical cardiac valve[5]; or current

use of systemic anticoagulant therapies[5] were excluded from the study. Specimen Processing and Laboratory Assays Peripheral blood samples (2 ml) were drawn via clean venipuncture into vacuum collection tubes containing 3.2% trisodium citrate anticoagulant (maintaining a precise 9:1 blood-to-anticoagulant volumetric ratio). Any specimens failing to reach 90% of the standard fill capacity were immediately rejected. Automated centrifugation was performed at 1500 X g for 15 minutes to isolate cell-free plasma. Analytical testing was completed within 2 hours of collection using a semiautomated photo-optical coagulometer (Transasia)[7].

PT/INR Testing: Semiautomated analysis utilized a human recombinant tissue factor reagent. Patient plasma "(50 µl") was incubated inside a standard reaction chamber cuvette at 37°C for 120 seconds, followed by the automated addition of "(100 µl)" pre-warmed PT reagent to record clot detection times.

aPTT Testing: Semiautomated testing applied a phospholipid reagent with a integrated particulate activator. Reagent"(50 µl)" was combined with ("50 µl) " of patient plasma, incubated for 3 minutes at 37°C, and recalcified via the addition of ("50 µl) of " calcium chloride to trigger and log final clot formation metrics.

HistoPathological Grading

Surgical specimens or tissue biopsies were processed through routine formal fixation, paraffin embedding, and standard H&E staining protocols. Tumors were stratified according to cell differentiation boundaries into: Well-Differentiated (WDSCC), Moderately Differentiated (MDSCC), and Poorly Differentiated Squamous Cell Carcinoma (PDSCC).

Ethical Approval

Was obtained from the Institutional Ethics Committee. Written informed consent was secured from all participants. Patient confidentiality was maintained through the study.

Data Analysis: Data were compiled in Microsoft Excel and analyzed using SPSS Version 20.0. Continuous variables are expressed as Mean "± " Standard Deviation (SD). Proportional distributions across categorical variables were assessed using the Chi-square test. Variations in continuous hematological and coagulation indices across multiple differentiation classes were analyzed using one-way Analysis of Variance (ANOVA), while two-group metric variations were calculated using independent-samples t-tests. Statistical significance was defined by a p-value < 0.05.

Observations and results

Among the 75 enrolled OSCC patients, the 41–50 and 51–60 age categories accounting for major portion of 29.3% each (n=22). The overall mean age was calculated at ("55.28±11.26) years" . A distinct male predominance was recorded, with males making up 86.7% (n=65) and females representing 13.3% (n=10) of the study group. A significant history of active tobacco use or smoking was reported by 76% of the cohort (n=57), all of whom were male; no female tobacco users were enrolled. Geographic analysis revealed that 68% of patients (n=51) originated from rural areas, whereas urban environments accounted for 32% (n=24).

Histopathologically results

WDSCC was discovered to be the most common histological variant at 64% (n=48), followed by Moderately Differentiated MDSCC at 33.3% (n=25), and Poorly Differentiated tumors PDSCC at 2.7% (n=2). Anatomical subsite analysis tracked a significant link between tumor site and histopathological differentiation (p = 0.001). Cancers originating at the lip line were exclusively well-differentiated (100% WDSCC, 8/8). Tongue lesions (n=19) and buccal mucosa presentations (n=20) were also predominantly well-differentiated (78.9% and 70.0% WDSCC, respectively). In contrast, posterior sites demonstrated an aggressive differentiation profile: tonsillar fossa tumors presented with 80% MDSCC (4/5), while oropharyngeal malignancies showed 50% PDSCC (2/4), accounting for all poorly differentiated cases documented in the study.

Furthermore, urban dwellers presented exclusively with WDSCC (100%), whereas rural groups displayed an aggressive, heterogeneous pathology mix (47.05% WDSCC, 49.01% MDSCC, and 3.92% PDSCC), establishing a statistically significant relationship between geographic residency and grade at diagnosis (p = 0.000). No meaningful statistical links were detected on crossing baseline age (p = 0.517) or gender (p = 0.500) against tumor differentiation scores.

Coagulation Parameter Profile results by Tumor Differentiation Grade

Semiautomated coagulation analysis indicated a progressive, statistically significant prolongation of all plasma timing vectors as histopathological differentiation shifted from well to poorly differentiated states.

Table 1: Coagulation Parameters Stratified by Histopathological Grade (n=75)

Parameter Evaluated	Well-Differentiated (WDSCC) (n=48)	Moderately Differentiated (MDSCC) (n=25)	Poorly Differentiated (PDSCC) (n=2)	Combined Study Total (n=75)	p-value (ANOVA)
PT (seconds, Mean ± SD)	15.15±3	21.11±4	28.73±1	17.61±3	0.001
INR (Mean ± SD)	1.12±0.3	1.65±0	2.40±1.0	1.33±0.	0.001
aPTT (seconds, Mean ± SD)	38.66±9	44.73±1	46.85±6	40.91±1	0.044
Platelets (cells/microL, Mean ± SD)	271,312	251,040	367,000	267,106	0.079

While PT, INR, and aPTT parameters verified a strong correlation with advanced cellular dedifferentiation ($p < 0.05$), circulating platelet counts remained within normal reference parameters, reflecting a statistically non-significant distribution across the clinical tiers (p = 0.079).10

Coagulation Parameter Profiles by Anatomical Subsite

Hemostatic metrics altered significantly on mapping parameters against primary tumor locations.

Table 2: Coagulation Parameters Stratified by Anterior vs. Posterior Oral Subsite Location [Anatomical subsite] (n=75)

Coagulation Marker	Anterior Oral Cavity Lesions (n=57)	Posterior Oral Cavity Lesions (n=18)	p-value (t-test)
PT (seconds, Mean ±SD)	16.00 ± 3.95	21.39 ± 5.64	0.0003
INR (Mean ± SD)	1.22 ± 0.34	1.68 ± 0.53	0.0009
Aptt(seconds,Mean ±SD)	38.84 ± 9.38	45.46 ± 11.74	0.032

Anatomically, anterior lesions (including the lips, tongue, and buccal mucosa) maintained relatively stable coagulation values. Conversely, tumors situated within posterior regions (such as the oropharynx, tonsillar fossa, and deep posterior borders) demonstrated a marked extension of baseline PT, INR, and aPTT values. This subsite divergence aligned directly with tumor differentiation maps: 100% of PDSCC and 52.2% of MDSCC cases originated within posterior subdivisions, confirming that site-specific coagulation prolongation is driven primarily by tumor differentiation biology rather than purely local anatomical factors.[10]

DISCUSSION

The systemic hypercoagulable state observed in solid malignancies is an established pathological axis, yet its precise patterns across unique regional cohorts remain an open area of clinical investigation[5]. This study confirms a clear, statistically significant correlation between worsening histopathological differentiation and progressive prolongation of routine coagulation times (PT, INR, and aPTT) in

patients diagnosed with oral squamous cell carcinoma. The demographic profile of this cohort mirrors trends reported across other specialized Indian centers. The median age clustering in the fifth and sixth decades of life corresponds with data from Shenoi et al.[12] and Krishna et al.[13], reflecting the long latency period required for carcinogen exposure to culminate in overt oral cancer. The strong male predominance (86.7%) and high history of active tobacco use (76.0%) emphasize persistent gender habits in northern India, where a strong social stigma often restrains comparable tobacco use among women.

A compelling finding from this prospective study is the stark contrast in tumor differentiation seen between urban and rural patients ($p = 0.001$). Urban patients %presented exclusively with well-differentiated tumors, whereas nearly half of the rural patients presented with advanced intermediate or poorly differentiated variants. This structural imbalance matches the findings of Debnath et al.[14] and Khanna et al.[14], who attributed advanced stage at presentation to systemic disparities in rural areas, including limited local oncology facilities, poor regional awareness, lack of transport, and a lack of routine diagnostic screening resources.

Our primary laboratory findings closely parallel the cross-sectional data published by Shaikh et al.[10], who identified progressive derangement of baseline hemostatic indexes with advancing histological differentiation across 126 patients with squamous cell carcinoma. Similarly, Khichariya et al[9]. analyzed 252 cancer profiles, noting that advanced oral sub-types frequently show an extended INR alongside a prolonged aPTT due to ongoing factor consumption. Patel et al[8]. also demonstrated a significant association between aggressive disease stages and higher PT/aPTT scores, pointing to subclinical compensated intravascular coagulation as the underlying driving mechanism.

This study also highlights a clear association between the primary anatomical site and systemic hemostatic profiles. Anterior oral cavity cancers (e.g., lip and anterior tongue) maintained stable, near-normal coagulation values, while posterior lesions (e.g., oropharynx and tonsillar fossa) exhibited prolonged baseline intervals. Rather than being driven by site-specific anatomy, this pattern tracks closely with tumor biology: posterior sites hosted significantly more aggressive, poorly differentiated variants[10]. Well-differentiated tumors are typical of accessible anterior borders where mechanical irritation or solar actinic changes occur, while less-differentiated tumors are more common in deep posterior regions.

Preoperative coagulation profiling holds significant clinical value for guiding surgical planning in OSCC11. Liang et al.10 demonstrated that critically ill oncology cohorts experience sharp increases in mortality when baseline PT values exceed 22 seconds. The poorly differentiated cohort in this study reached a mean PT of" (28.73±11.07) seconds" , a critical threshold that signals an elevated risk of clinical consumptive failure during long operations. Furthermore, Khromov et al.15 utilized predictive modeling to identify preoperative INR and aPTT lengths as key indicators of major complications following extensive tissue reconstructive procedures. Consequently, baseline coagulation assays should be considered standard components of the preoperative workup, offering a reliable, cost-effective window into tumor biology and patient risk.

CONCLUSION

This study demonstrates a clear and statistically significant correlation between advanced histopathological tumor grade and deranged coagulation parameters (PT, INR, and aPTT) in oral squamous cell carcinoma[10]. As cellular differentiation worsens from well to poorly differentiated variants, systemic hemostatic markers show a progressive prolongation, reflecting subclinical factor consumption driven by tumor biology[10]. This systemic derangement is more pronounced in posterior subsite locations, which tend to harbor more aggressive tumor grades compared to anterior regions.

Given that this simple laboratory tests are widely available and inexpensive, routine preoperative coagulation profiling offers dual clinical utility as both an indicator of surgical risk and a accessible surrogate marker of tumor aggressiveness[6]. Integrating these baseline parameters into the standard preoperative workup can improve risk stratification and clinical management within resource-limited oncology settings.

Conflict of Interest: NIL

Fundings: NIL

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