Original Research Paper

Volume - 15 | Issue - 06 | June - 2025 | PRINT ISSN No. 2249 - 555X | DOI : 10.36106/ijar

Clinical Biochemistry

COMPARATIVE STUDY OF SERUM UREA, URIC ACID, AND CREATINE KINASE IN ORAL CANCER AND OPMDS

Shreya Mahapatra Scholar, Department of Biotechnology, Techno India University, EM-4, EM-4/1, EM Block, Sector V, Bidhannagar, Kolkata, West Bengal 700091

Nabarun Sasmal Faculty, Raja Narendralal Khan Women's College [Autonomous], Dept. of B.M.L.T, West Bengal, Medinipur, Paschim Medinipur

Surajit Bose* Associate Professor, Department of Oral and Maxillofacial Pathology and Microbiology Kusum Devi Sunderlal Dugar Jain Dental College and Hospital, Kolkata, West Bengal, India *Corresponding Author

ABSTRACT Oral cancer (OC) and oral potentially malignant disorders (OPMDs) are significant public health challenges with increasing incidence globally. Early detection through biochemical markers may improve patient outcomes. To compare serum levels of urea, uric acid, and creatine kinase (CK) in individuals with OC, OPMDs, and Healthy controls (HC), and estimate their potential as analytical biomarkers. Serum samples were collected since histologically confirmed OC (n=30), OPMDs (n=30), and Healthy Controls (n=30). Biochemical analysis for urea, uric acid, and CK was performed. Statistical significance was determined using ANOVA and t-test analysis. Elevated serum levels of urea and CK in OC and OPMDs, and distinct patterns of uric acid, suggest metabolic alterations during malignant progression. These parameters could serve as non-invasive biomarkers for the early detection and examination of oral pathology. The observed variations in serum urea, uric acid, and CK levels reflect underlying metabolic dysregulation associated with the pathogenesis of oral malignancies.

KEYWORDS : Biomarkers, Serum Urea, Uric Acid, Creatine Kinase.

INTRODUCTION

Oral cancer, particularly oral squamous cell carcinoma (OSCC), ranks among the top ten most common cancers globally, with a notably high prevalence in South and Southeast Asia. It often arises subsequently the mucosal lining of the oral cavity and has a high mortality rate due to late diagnosis. The major etiological factors contributing to its development include tobacco usage (smoking and smokeless forms), excessive alcohol use, infection with speculative strains of human papillomavirus (HPV), chronic irritation, poor oral hygiene, and genetic predisposition[1,2].

OPMDs refer to a heterogeneous group of disorders—such as leukoplakia, erythroplakia, oral submucous fibrosis, and erosive lichen planus—that exhibit a higher risk of progressing to malignancy. Studies have estimated that approximately 5–10% of OPMDs may transform into oral cancer over time. Early identification and monitoring of these conditions are critical for effective prevention and intervention strategies[3].

In recent years, research has increasingly focused on discovering non-invasive biomarkers that can aid in the early detection and prognosis of oral diseases. Biochemical alterations in the serum can serve as early indicators of systemic changes that accompany malignant transformation. Among these, serum urea, uric acid, and CK are gaining attention due to their association with oxidative stress, metabolic dysfunction, and tissue injury—hallmarks of cancer progression[4].

Urea, a byproduct of protein metabolism, may be elevated in systemic stress conditions and cancer-induced cachexia. Uric acid is a major antioxidant in plasma, and its fluctuating levels reflect the balance between oxidative stress and antioxidant defence. Elevated uric acid in premalignant states may represent a protective antioxidant surge, whereas a decline in advanced malignancy could indicate oxidative depletion. CK, an enzyme involved in cellular energy metabolism, is known to rise in conditions involving muscle or tissue damage, and its elevated levels in cancer may reflect rapid cell turnover or invasive behaviour [5].

Despite the growing understanding of these biochemical markers in systemic diseases, limited data exist on their comparative evaluation in OPMDs and oral cancer. Exploring the differences in their serum concentrations could provide valuable insights into the metabolic alterations accompanying oral carcinogenesis and help establish diagnostic and prognostic markers for clinical use.

Therefore, this study aims to comparatively evaluate the serum levels of urea, uric acid, and creatine kinase in patients diagnosed with oral cancer, those with OPMDs, and healthy controls, to assess their potential role as biochemical indicators of disease progression[6].

MATERIALS AND METHODS

This observational study with a cross-sectional design was hospital-based and carried out jointly by the Department of Oral and Maxillofacial Pathology and Microbiology at Kusum Devi Sunderlal Dugar Jain Dental College and Hospital, along with the Department of Biotechnology at Techno India University, Kolkata. Before starting, ethical clearance was granted by the Institutional Ethics. All participants provided scripted informed consent.

Analysis of Population and Grouping

Patients reporting to the Oral Pathology Department with clinically suspicious lesions were subjected to incisional biopsy for histopathological confirmation. Only after the histological diagnosis, subjects were grouped into: Group I – Healthy Controls (HC): Individuals with no history or clinical signs of oral mucosal lesions and no systemic illness. Group II – OPMDs: Patients with histologically confirmed OPMDs (e.g., leukoplakia, oral lichen planus, Erythroplakia). Group III (OC) Patients with histologically confirmed OSCC.

Subjects comprised in the study were individuals aged 18 years and above who had a histologically confirmed diagnosis of either OPMDs or OSCC. Only those who voluntarily agreed to participate and provided written informed consent were enrolled. Individuals with systemic conditions known to affect serum urea, uric acid, or CK levels, such as renal disease, muscular disorders, or gout and HIV, HBV—were excluded from the study. Additional exclusion criteria included patients undergoing chemotherapy or radiotherapy at the time of sample collection, as well as individuals with a recent history of trauma or surgical intervention.

Sample Collection and Processing

After histopathological diagnosis, venous blood samples were collected from each subject under aseptic conditions. Around 5 mL of blood was drawn, left to clot, then spun in a centrifuge to obtain serum. The serum was stored between 2 and 8°C and assessed within a day.

Biochemical Estimation

The following serum parameters were measured using standardized kits on a semi-automated clinical chemistry analyzer: Urea (mg/dL) – measured via enzymatic urease method and for Uric Acid (mg/dL) – measured using uricase-peroxidase method [1]. CK (U/L) – estimated using the CK-NAC (N-acetylcysteine) method.

Statistical Analysis

Descriptive statistics were presented as mean ± standard deviation (SD). To assess differences among the three groups, a one-way analysis of variance (ANOVA) was performed. A p-value less than 0.05 was regarded as statistically significant. All statistical computations were carried out using Microsoft Excel (version 16.89.1, 2024).

RESULT

Histopathological Evaluation

Histological examination revealed distinct differences in epithelial architecture and cellular features across the study groups. In Group I (Healthy Controls), the epithelium exhibited uniform thickness with no signs of dysplasia or abnormal mitotic figures. The inflammatory response was minimal, with a completely intact basement membrane and a normal vascular pattern, indicating no malignant potential (Figure 5).

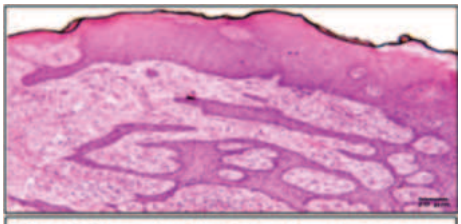


Figure 5: Biopsy of the Healthy Control normal epithelial cell. Histological image showing in Hematoxylin-Eosin; 40x.

In contrast, Group II (OPMDs) biopsies showed histological alterations including hyperkeratosis or epithelial thinning with mild dysplasia and increased nuclear atypia. A condensed, band-like lymphocytic infiltration was observed at the epithelial-connective tissue interface (Figure 6), though the basement membrane remained intact. Vascularity was normal to slightly increased, and the overall malignant potential ranged from low to moderate.

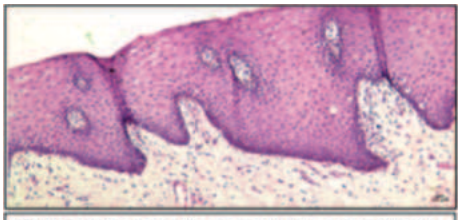


Figure 6: Histological section of oral potentially malignant disorder (OPMD) showing a dense, band-like lymphocytic infiltration at the epithelial-connective tissue junction, along with localized areas of hyperkeratinized epithelium (H&E stain).

Group III (OC) samples presented the most severe histopathological deviations. The epithelium was abnormally thickened and disorganised, with prominent cellular atypia, including pleomorphism and increased mitoses. A moderate to intense inflammatory stromal infiltration was observed. Crucially, the basement membrane was breached, confirming invasive behaviour. Vascularity was markedly elevated, indicative of tumour-induced angiogenesis, and the overall malignant potential was high, consistent with keratinising oral squamous cell carcinoma (Figure 7). These histological observations clearly demonstrate a progressive spectrum of epithelial and stromal changes from benign to malignant stages, reinforcing the diagnostic value of microscopic examination in conjunction with biochemical and clinical findings.

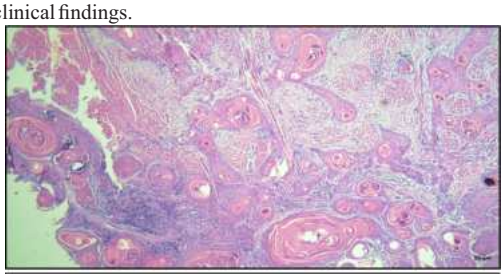
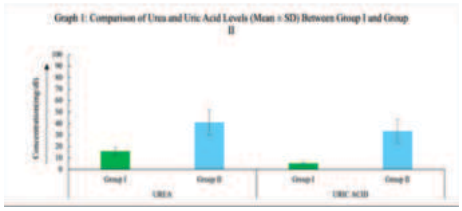


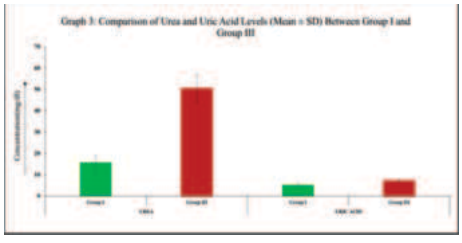
Figure 7: Biopsy of OC shows Multiple irregular epithelial nests, pearls, and islands are seen infiltrating the underlying connective tissue stroma. These are characteristic of invasive squamous cell carcinoma.

Statistical Analysis

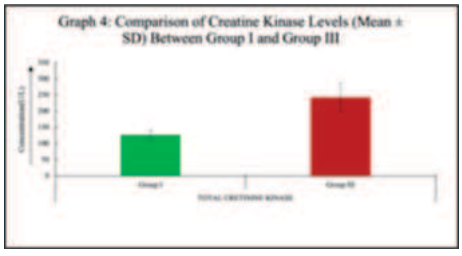
The present study evaluated serum levels of urea, uric acid, and CK across three groups: healthy controls, patients with OPMDs, and OC patients. One-way ANOVA revealed statistically significant differences in all three biomarkers among the groups ($p < 0.0001$ for all). These results were further validated through pairwise comparisons using independent two-tailed Student's t-tests.



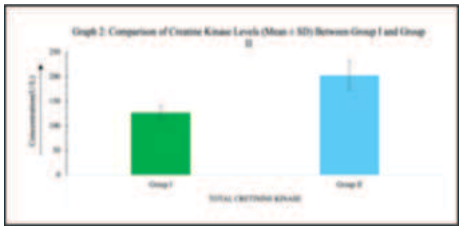
Urea levels demonstrated a marked elevation in disease conditions (Graph 1, Graph 3). The mean serum urea in healthy controls was 15.92 mg/dL, significantly increasing to 41.02 mg/dL in the OPMD group ($t = 3.99$, $p = 0.0451$) and further to 50.67 mg/dL in the OC group ($t = 7.26$, $p = 0.0125$). However, the difference between the OC and OPMD groups was not statistically significant ($t = 2.46$, $p = 0.0695$), indicating a possible plateau in urea elevation during malignant transformation.



Uric acid levels exhibited a distinct trend (Graph 1, Graph 3). The OPMD group showed the highest mean value of 33.45 mg/dL, significantly exceeding both the control group (6.12 mg/dL, $t = 11.02$, $p = 0.0074$) and the OC group (7.42 mg/dL, $t = –10.24$, $p = 0.0082$). Additionally, the OC group also had significantly elevated levels compared to controls ($t = 4.05$, $p = 0.0165$). This biphasic pattern suggests an initial compensatory increase in antioxidant defense during premalignancy, followed by depletion as malignant progression ensues.



Creatine kinase (CK) levels rose progressively across the study groups (Graph 2, Graph 4), with mean values of 126.92 U/L in controls, 202.83 U/L in OPMDs, and 242.43 U/L in OC patients. The OC group showed a statistically significant increase compared to controls ($t = 4.44$, $p = 0.0437$), whereas the OPMD vs. control comparison was not statistically significant ($t = 3.00$, $p = 0.0918$). Similarly, the dissimilarity between the OC and OPMD groups was not significant ($t = 0.71$, $p = 0.5185$), indicating that CK levels tend to rise with disease progression, although the transition from premalignancy to malignancy may not be sharply delineated.



DISCUSSION

Alterations in serum metabolites reflect the underlying biochemical changes associated with the progression from healthy tissue to premalignant and malignant states. Elevated urea levels may indicate increased protein catabolism or subclinical renal stress in response to neoplastic changes. The paradoxical pattern observed in uric acid levels—with elevation in OPMDs followed by a decline in

OC—suggests an initial upregulation of antioxidant mechanisms that are eventually exhausted during malignant transformation. Elevated CK levels, particularly in OC, are indicative of increased cellular turnover, tissue breakdown, and muscle or epithelial invasion—hallmarks of tumor progression.

These findings are consistent with existing literature that identifies metabolic dysregulation and oxidative stress as critical factors in oral carcinogenesis. The significant biomarker variations observed support the potential role of urea, uric acid, and CK as adjunctive diagnostic indicators in the early detection and monitoring of OPMDs and oral cancer (Patel et al., 2018; Singh & Bansal, 2020)[7-9].

CONCLUSION

The present study highlights significant alterations in serum levels of urea, uric acid, and CK among patients with OPMDs and oral cancer OC compared to healthy individuals. The progressive elevation of urea and CK suggests their potential role in reflecting underlying metabolic stress and cellular turnover associated with disease progression. Conversely, the biphasic trend in uric acid levels underscores the dynamic nature of oxidative stress and antioxidant response during oral carcinogenesis.

Collectively, these findings suggest that routine evaluation of these serum biomarkers may serve as valuable adjunctive tools for early detection, risk assessment, and monitoring of disease progression in patients with OPMDs and oral cancer. Further longitudinal studies with larger cohorts are suggested to certify these markers and explore their prognostic utility in clinical practice.

Acknowledgments

The authors express their sincere gratitude to Dr. Surajit Bose and the faculty members of Techno India University and Kusum Devi Sunderlal Dugar Jain Dental College for their continuous support and encouragement throughout the study. Special thanks are also extended to Mr. Nabarun Sasmal, Faculty, Department of BMLT, Raja Narendra Lal Khan Women's College (Autonomous), for his valuable guidance and assistance during the research work.

REFERENCES

1. Sasmal, N., Mukherjee, R., Nandi, D. K., & Bose, S. (2025). Biochemical Metabolite Profiling In Oral Potentially Malignant Disorders: A Diagnostic And Prognostic Approach. International Journal of Advanced Research, 13, 127–134. https://doi.org/10.21474/ijar01/20360
2. Fatima, J., Fatima, E., Mehmood, F., Ishtiaq, I., Khan, M. A., S Khurshid, H. M., & Kashif, M. (2024). Comprehensive Analysis of Oral Squamous Cell Carcinomas: Clinical, Epidemiological, and Histopathological Insights With a Focus on Prognostic Factors and Survival Time. Cureus, 16(2), e54394. https://doi.org/10.7759/cureus.54394
3. Kumari, P., Debta, P., & Dixit, A. (2022). Oral Potentially Malignant Disorders: Etiology, Pathogenesis, and Transformation Into Oral Cancer. Frontiers in Pharmacology, 13, 825266. https://doi.org/10.3389/fphar.2022.825266
4. Hu, C., Wang, G., Gao, Z., Qing, F., Pan, S., Liu, Y., & Li, F. (2025). Emerging salivary biomarkers for early detection of oral squamous cell carcinoma. World Journal of Clinical Oncology, 16(4), 103803. https://doi.org/10.5306/wjco.v16.i4.103803
5. Gherghina, E., Peride, I., Tiglis, M., Neagu, T. P., Niculae, A., & Checherita, I. A. (2022). Uric Acid and Oxidative Stress—Relationship with Cardiovascular, Metabolic, and Renal Impairment. International Journal of Molecular Sciences, 23(6), 3188. https://doi.org/10.3390/ijms23063188
6. Hu, C., Wang, G., Gao, Z., Qing, F., Pan, S., Liu, Y., & Li, F. (2025). Emerging salivary biomarkers for early detection of oral squamous cell carcinoma. World Journal of Clinical Oncology, 16(4), 103803. https://doi.org/10.5306/wjco.v16.i4.103803
7. Caruntu, A., Moraru, L., Ciubotaru, D. A., Tanase, C., Scheau, C., & Caruntu, C. (2021). Assessment of Serum Urea, Creatinine and Uric Acid in Oral Cancer. Journal of Clinical Medicine, 11(12), 3459. https://doi.org/10.3390/jcm11123459
8. Patel et al., 2018 Patel, P. S., Shah, M. H., Jha, F. P., Raval, G. N., Rawal, R. M., Patel, M. M., & Patel, J. B. (2018). Role of oxidative stress and antioxidant balance in oral cancer and potentially malignant disorders: A biochemical study. Journal of Oral Pathology & Medicine, 47(8), 728–736. https://doi.org/10.1111/jop.12721
9. Singh & Bansal, 2020 Singh, N., & Bansal, A. (2020). Serum biomarkers in oral precancer and cancer: A comparative study. Journal of Clinical and Diagnostic Research, 14(6), ZC10–ZC13. https://doi.org/10.7860/JCDR/2020/43612.13772