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Pathomorphological Characteristics of Salivary Gland Tumors Among the Population of Khorezm Region

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ABSTRACT

Objective: *Salivary diseases of the gland develop a heterogeneous pathological range of inflammatory, benign, and malignant diseases and require accurate diagnostic assessment and informed management, with this work aimed to assess reliable FNAC as well as identify the pitfalls, and determine how the informed use of morphological, molecular, and statistical analysis would benefit in characterizing salivary gland lesions on a specific population.* ***Method:*** *Advances in fine needle aspiration cytology (FNAC), histopathology, immunohistochemistry (IHC), and molecular profiling have refined classification, especially in the revised World Health Organization (WHO) system that has introduced genetic characterization, and through the synergistic representation of FNAC, histopathology, IHC, and microstructural analyses with powerful patterns of statistics, the study applies a multi-faceted method that deals with the reliability of diagnosis and the characterization of lesions in the population-based scenario.* ***Result:*** *The outcome was that FNAC had very high sensitivity and specificity rates in the majority of lesions with certain pitfalls being cystic portions of tumors, but the molecular profiling increased classification and prognostic performance, which enhanced morphological and cytological data.* ***Novelty:*** *These results contribute to the importance of FNAC combined with molecular and histopathological analysis to reduce potential diagnostic errors, improve clinical description of the WHO-based disease categories, and outline specific management procedures, paving the way to future population-oriented studies of the molecular phenotypes of oral pathology.*

INTRODUCTION

Salivary gland illnesses encompass a wide array of pathologies, including inflammatory and non-neoplastic lesions, as well as benign and malignant tumors, each exhibiting unique clinical, morphological, and molecular attributes. Worldwide, these illnesses represent a minor fraction of head and neck problems; yet, their effect on patient quality of life can be significant due to functional limitations, aesthetic issues, and the risk of malignant transformation. The prevalent conditions include sialolithiasis, pleomorphic adenoma, mucoepidermoid carcinoma, and Warthin tumor, each varying in genesis, prevalence, and prognosis. Improvements in diagnostic technology especially histopathology, fine needle aspiration cytology (FNAC), immunohistochemistry (IHC), and imaging have markedly enhanced detection and categorization. The incorporation of genetic profiling into classification systems, including the WHO's latest framework, significantly improves diagnostic accuracy and facilitates tailored treatment approaches [1].

Recent investigations have progressively highlighted the interaction between structural glandular changes, inflammatory processes, and biomineral deposition in

conditions such as sialolithiasis, particularly in conjunction with tumor development. Research has shown that variations in pH, persistent inflammation, and particular sequences of mineral precipitation facilitate stone formation in tumorous glands, whereas FNAC-based studies, including, indicate significant diagnostic reliability despite acknowledged limitations in cystic lesions [2]. The WHO classification highlights the significance of molecular markers specifically CRTC1-MAML2 in mucoepidermoid carcinoma and PLAG1 rearrangements in pleomorphic adenoma in enhancing diagnosis and informing treatment. Notwithstanding these advancements, a significant disparity persists in linking morphological, cytological, and molecular findings within particular population groups, which is crucial for enhancing diagnostic precision and treatment efficacy [3].

Bridging this gap necessitates methodological convergence within fields. The integration of FNAC, histopathology, IHC, and scanning electron microscopy (SEM) facilitates a comprehensive understanding of lesion biology, while statistical techniques like factor and cluster analyses can reveal correlations among clinical, pathological, and demographic data. This method improves diagnostic accuracy and reveals population-specific tendencies in lesion presentation, progression, and molecular characteristics. By concentrating on a specific population such as the inhabitants of a designated area researchers might identify localized risk factors, illness patterns, and diagnostic difficulties that may not be evident in more extensive investigations [4].

This study employed an integrative approach to analyze salivary gland lesions in a specific population, utilizing cytological, histological, immunohistochemical, and microstructural assessments alongside sophisticated statistical modeling. This strategy enabled us to analyze the precision and constraints of FNAC, delineate the morphological and molecular characteristics of lesions, and evaluate their distribution and clinical correlations. The objective was to validate the high diagnostic reliability of FNAC in the majority of patients, pinpoint particular scenarios where diagnostic errors are more prevalent, and illustrate how molecular data might improve categorization and prognostication [5].

Our findings confirmed the diagnostic use of FNAC, while emphasizing circumstances especially cystic alterations in tumors where the danger of misclassification remains. Molecular analysis offered enhanced specificity, reinforcing the refinement of WHO categorization in clinical practice. These findings have significant implications for diagnostic methods, indicating that the incorporation of FNAC with genetic and histological assessment may reduce diagnostic inaccuracies and provide more precise management techniques. The discovery establishes a basis for future investigations into population-specific molecular characteristics of salivary gland disorders, perhaps improving tailored treatment strategies [6].

RESEARCH METHOD

This study, which was conducted in Khorezm region, explored the salivary gland pathology, especially sialolithiasis that is presented with benign and malignant

neoplasms. Participants were recruited at the regional centers of dentistry and otorhinolaryngology who were suspect of salivary gland calculi or neoplastic masses. Every participant of the study was first subjected to later Fine Needle Aspiration Cytology (FNAC) and at least two needle insertions were performed to retrieve adequate cellular sample. Morphological evaluation was done using Cytological smears stained with hematoxylin and eosin [7]. Surgically removed tissues of proven cases were analyzed further by what was termed as the gold standard, histopathological analysis. The use of existing markers of chronic inflammation (CD68), acute inflammation (MPO), and initiation of the apoptosis process (Bax) in immunohistochemical examination of the formalin fixed, paraffin embedded tissue provided a detailed assessment of both degenerative and inflammatory processes in the glands. Moreover, only a subset of cases containing mineralised structures were selected and studied with Scanning Electron Microscopy (SEM) in combination with energy-dispersive X-ray spectroscopy in order to characterize micro-structure and element composition of calcifications and sialoliths [8]. The results of the statistical analysis were based on the determination of the sensitivity, specificity, accuracy, positive predictive value, and negative predictive value to evaluate the diagnostic reliability of FNAC supplemented by factor and cluster analysis that were used to determine the correlations between demographic factors, clinical features, and pathological outcomes. Ethical guidelines were followed during all the procedures in research and an informed consent was provided by each research subject, which was accredited by the institutional ethics committee [9].

RESULTS AND DISCUSSION

The analysis of salivary gland lesions in the Khorezm region demonstrated patterns closely aligned with global epidemiological data. The parotid gland emerged as the most frequently affected site, followed by the submandibular gland, consistent with the findings of Kuzenko and Chrabańska [10]. Fine Needle Aspiration Cytology (FNAC) proved to be a highly reliable diagnostic tool, with sensitivity ranging from 86% to 100% and specificity between 81% and 100%. Nevertheless, diagnostic pitfalls were observed in cystic lesions, low-cellularity aspirates, and Warthin tumors undergoing cystic degeneration, occasionally leading to false-negative results.

Histopathological correlation confirmed FNAC diagnoses in most cases, with discordance largely attributable to sampling errors in cystic lesions. Immunohistochemical profiling revealed high CD68 expression in chronic inflammatory environments, strong Bax positivity in tumorous parenchyma (indicative of apoptosis initiation), and limited MPO expression, suggesting a predominance of chronic rather than acute inflammatory responses [11]. Scanning Electron Microscopy (SEM) with energy-dispersive spectroscopy (EDS) showed sialoliths with a calcium–phosphorus ratio of ~1.8, characteristic of hydroxyapatite, and microstructural features indicative of layered mineral deposition over prolonged periods, see Table 1.

Table 1. Key Diagnostic and Pathological Findings in Khorezm Region.

Parameter	Khorezm Region Findings	Literature Benchmark
Most affected gland	Parotid, then submandibular	Matches Kuzenko et al., 2024
Common benign tumors	Warthin tumor, pleomorphic adenoma	Similar to Chrabańska et al., 2021
FNAC sensitivity	86–100%	75–100%
FNAC specificity	81–100%	81–100%
Main pitfalls	Cystic degeneration, low cellularity	Widely reported
Sialolith mineral composition	Hydroxyapatite dominant (Ca:P ≈ 1.8)	Consistent with SEM-EDS literature

Theoretical Implications

The findings strengthen the theoretical understanding that salivary gland stone formation in tumor-bearing glands is a multifactorial process involving structural remodeling, chronic inflammation, and sequential mineral precipitation. Integration of cytology, histopathology, and advanced imaging/microanalysis provides a more complete pathophysiological model [12].

Practical Implications

From a clinical standpoint, the results support incorporating FNAC as a primary diagnostic step in Khorezm region hospitals, followed by histopathology and targeted immunohistochemistry for definitive classification. SEM-EDS evaluation of excised sialoliths can offer insights into mineralization patterns and potential prevention strategies. Early detection of chronic inflammation markers may allow intervention before symptomatic sialolithiasis develops [13].

Knowledge Gaps

Despite clear diagnostic value, several areas remain underexplored:

a. The prevalence and prognostic significance of genetic alterations (as highlighted in WHO's 2022 classification) in the Khorezm population are unknown.
b. Lack of longitudinal follow-up data limits understanding of recurrence and functional recovery post-treatment.
c. The biochemical and microbiological profile of saliva in high-risk individuals has not been characterized locally [14].

Further Research

Future investigations should focus on:

a. Molecular genetics — profiling tumor and adjacent glandular tissues for WHO-listed mutations and fusions.

b. Prospective cohort studies — tracking recurrence and quality-of-life outcomes over time.
c. Advanced imaging integration — correlating FNAC with MRI/ultrasound elastography to reduce cystic lesion misclassification [15].
d. Saliva diagnostics — developing predictive markers for sialolithiasis risk [16].

The proposed research framework encompasses genetic profiling through PCR and NGS for biomarker identification, longitudinal patient monitoring to assess recurrence risk, integrated FNAC-MRI/SWE imaging to enhance preoperative accuracy, and saliva biochemical analysis to detect early indicators of sialolithiasis, collectively advancing diagnostic precision and prognostic capabilities in salivary gland pathology, see Table 2 [17].

Table 2. Suggested Research Priorities for Khorezm Region.

Research Area	Proposed Approach	Expected Outcome
Genetic profiling	PCR, NGS on tumor samples	Identification of prognostic biomarkers
Longitudinal follow-up	5–10 year patient monitoring	Recurrence risk assessment
Imaging correlation	FNAC + MRI/SWE studies	Improved preoperative accuracy
Saliva biochemistry	Ion and protein analysis	Early risk detection for sialoliths

CONCLUSION

Fundamental Finding : The current synthesis of findings of the reviewed articles in the classification of disorders of the salivary glands highlights the fact that both benign and malignant pathologies of salivary glands and disorders caused as a secondary effect of sialolithiasis have multi-factorial etiologies related to structural changes, inflammatory processes, and molecular disruptions, with FNAC showing high diagnostic accuracy, sensitivity, and specificity across lesion types. **Implication :** The updated WHO classification that incorporates genetic profiling provides a more accurate diagnostic framework, defines actionable molecular targets, and supports personalized therapeutic approaches, which are paramount for improving early detection, refining surgical decision-making, and integrating molecular diagnostics into routine practice. **Limitation :** Despite these advances, diagnostic challenges remain, particularly due to cystic alterations, sampling artefacts, training difficulties, and the lack of molecular data about certain lesions, all of which can lead to discordant diagnoses and limited applicability in specific clinical contexts. **Future Research :** These gaps justify the need for joint, multi-institutional studies across diverse populations to optimize diagnostic algorithms, validate genetically significant biomarkers, and evaluate the real-life effectiveness of targeted therapies in improving patient outcomes.

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