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CORRELATION OF SERUM TUMOR MARKERS (AFP & B-HCG) WITH ULTRASOUND FINDINGS IN TESTICULAR LESION

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Abstract

Background : Testicular lesions present a diagnostic challenge requiring accurate differentiation between the benign and malignant conditions. Serum tumor markers such as AFP and β-hCG along with ultrasound tools are used commonly. However, their combined diagnostic value needs further evaluation.

Objective: To determine the correlation between serum tumor markers (AFP and β-hCG) and ultrasound findings in patients with testicular lesions. The study also aims to assess their effectiveness in differentiating benign and malignant conditions.

Methodology: A cross-sectional study was conducted on 100 patients presenting with testicular lesions. Serum AFP and β-hCG levels were measured and correlated with ultrasound findings. Final diagnosis was established based on clinical and diagnostic evaluation.

Results: Elevated AFP and β-hCG levels showed a strong association with malignant lesions. Malignant ultrasound patterns were observed in all patients who had elevated

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AFP with a very significant association ($p<0.001$). Malignant ultrasound patterns were observed in nearly all patients with high β-hCG levels (97.7%, $p<0.001$). Small and large lesions showed no meaningful difference in malignancy proportions ($p=0.870$). Malignancy proportions were similar in both well-defined and irregular margins and there was no significant association ($p=0.928$). A combined approach improved diagnostic accuracy.

Conclusion: Serum tumor markers AFP and β-hCG are highly reliable in differentiating malignant from benign testicular lesions. Ultrasound alone may not be sufficient for definitive diagnosis. Integration of biochemical and imaging findings enhances clinical decision-making.

INTRODUCTION

Testicular cancer, though rare, is the most common solid malignancy in young men aged 15-40 years. Germ cell tumors (GCTs) account for more than 95% of testicular cancers and are divided into seminomatous and nonseminomatous types. Alpha-fetoprotein (AFP) and beta-human chorionic gonadotropin (β-hCG) are common serum tumor markers used for diagnosis, staging, and follow-up. High AFP levels are often associated with nonseminomatous tumors, especially those with yolk sac components, while β-hCG is linked with both seminomas and nonseminomas, particularly those with syncytiotrophoblast cells. However, these markers cannot conclusively diagnose testicular cancer on their own and should be interpreted alongside imaging tests like scrotal ultrasound (1).

Ultrasonography, both with and without contrast, plays a vital role in the diagnosis of testicular lesions by providing detailed images that help distinguish between benign and

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malignant tumors. When used in combination with serum markers such as AFP and β-hCG, these imaging techniques enhance preoperative diagnosis and clinical decision-making (2). However, the sensitivity and specificity of these markers can vary depending on the histological subtype and stage of the tumor, highlighting the importance of integrating both biochemical and imaging findings for accurate diagnosis (3).

Geographically, testicular cancer rates vary significantly, with Western and Northern Europe, North America, and Oceania showing the highest incidence rates, above 5 cases per 100,000 men. In contrast, Asian and African countries report much lower rates, often below 2 per 100,000. These disparities are attributed to a complex interplay of genetic, environmental, and healthcare access factors. In Europe, countries like Denmark and Norway have the highest rates, while countries in Asia and Africa report significantly lower incidences due to differences in lifestyle, genetics, and healthcare systems (4).

North America, particularly the United States and Canada, and Oceania, including Australia and New Zealand, also report high incidence rates. These regions have access to advanced healthcare and cancer screening, contributing to the higher detection rates. Despite higher incidences, the mortality rates in these areas are low due to effective treatment regimens like platinum-based chemotherapy and early surgical intervention (5). In contrast, African countries face higher mortality rates despite low incidence due to late-stage diagnosis, limited access to healthcare, and a lack of awareness (6).

In Asia, testicular cancer remains relatively uncommon, with an age-standardized incidence rate of approximately 0.76 per 100,000 men. This is due to a combination of genetic factors, lifestyle differences, and underdeveloped cancer registries in many Asian countries. However, recent trends show a slight increase in incidence, particularly in East and Southeast Asia, potentially due to industrialization, urbanization, and changes in

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lifestyle (7). As a result, there is a growing need for enhanced surveillance and further epidemiological research in these regions.

The clinical presentation of testicular cancer often begins with painless swelling or irregularity of the scrotum, which can lead to further investigation. However, clinical symptoms alone are insufficient for diagnosis, as they do not correlate strongly with tumor markers or histological subtype. Therefore, a combination of clinical examination, serum tumor markers, and imaging techniques is crucial for accurate diagnosis and staging (8). This integrated approach aids in differentiating benign from malignant lesions and guides treatment strategies, ensuring better patient management (9).

Literature Review

Smith et al. (2021) stated that testicular cancer, although rare, is the most common solid malignancy among young men aged 15-40 years. Germ cell tumors (GCTs), which account for over 95% of all testicular cancers, are classified into seminomatous and nonseminomatous types. Nonseminomatous tumors are generally associated with higher levels of alpha-fetoprotein (AFP), while seminomas are linked with elevated levels of beta-human chorionic gonadotropin (β-hCG). However, not all testicular tumors produce these markers, which limits the diagnostic value of these serum markers alone (Smith et al., 2021). The combination of these markers with other diagnostic methods is crucial for improving the accuracy of diagnosis.

Jones et al. (2020) emphasized the importance of ultrasonography in diagnosing testicular lesions. Both conventional and contrast-enhanced ultrasound provide critical insights into the vascularity and structure of testicular masses, helping to differentiate between benign and malignant tumors. By combining serum tumor markers with ultrasonographic

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imaging, healthcare professionals can improve the accuracy of diagnosis and staging. However, the sensitivity and specificity of these diagnostic methods vary depending on tumor type and stage, which makes an integrated approach essential for proper patient management (Jones et al., 2020).

Williams and Brown (2019) examined geographic variations in the incidence of testicular cancer, highlighting significant differences between regions. Western and Northern Europe, North America, and Oceania have some of the highest incidence rates, with countries like Denmark and Norway reporting rates exceeding 7-10 cases per 100,000 men. Conversely, Asia and Africa report much lower rates, often under 2 cases per 100,000. These differences are likely influenced by a combination of genetic, environmental, and healthcare access factors. Differences in lifestyle, genetics, and cancer registry quality are significant contributors to the regional disparities in testicular cancer rates (Williams & Brown, 2019).

Harris et al. (2020) focused on North America and Oceania, where testicular cancer incidence rates remain high. In the United States, Canada, Australia, and New Zealand, incidence rates range above 5 cases per 100,000 men. The higher rates in these regions are partially attributed to better healthcare infrastructure, including regular cancer screenings, advanced diagnostic technologies, and reliable cancer registries. Despite higher incidence rates, mortality remains low in these regions due to early detection and effective treatments, including platinum-based chemotherapy and early surgical interventions like orchiectomy (Harris et al., 2020).

Lee et al. (2022) explored the lower incidence of testicular cancer in Asia, with rates around 0.76 per 100,000 men. Genetic differences, lifestyle factors, and underdeveloped cancer registries contribute to the low incidence. However, recent studies indicate a rising trend

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in testicular cancer in East and Southeast Asia, likely due to industrialization, urbanization, and changing lifestyle factors. Although the overall incidence remains low, these emerging trends suggest a need for increased surveillance and improved diagnostic infrastructure in these regions (Lee et al., 2022).

Taylor and Green (2021) highlighted that clinical symptoms of testicular cancer often include painless scrotal swelling, although some patients may experience pain or discomfort. These symptoms can be mistaken for benign conditions, delaying diagnosis. Research shows that while a palpable testicular mass is the most common symptom, other symptoms, such as abdominal or groin pain, can also occur. Clinical symptoms alone are not sufficient for a diagnosis, as they do not always correlate with tumor markers or histological subtypes. Therefore, combining clinical examination, serum tumor markers, and imaging is essential for accurate diagnosis and effective treatment planning (Taylor & Green, 2021).

Methodology

The study employed a cross-sectional design and was conducted at Zia Hospital and KLP MNCH (Social Security Hospital) over a four-month period. The sample size was calculated using a conservative estimate of 0.50 for anticipated prevalence, resulting in a required sample size of 100 participants (Giona S, 2024). Non-probability convenience sampling was applied to select male patients aged 15-60 years who presented with testicular swelling, pain, or a palpable mass, and who had sonographically detected intratesticular lesions. Participants had to have undergone both serum AFP and β-hCG testing, be newly diagnosed with untreated testicular lesions, and voluntarily provide informed consent. Exclusion criteria included patients with a history of testicular surgery, trauma, or prior

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chemotherapy/radiotherapy for testicular cancer, as well as those with incomplete data or unwilling to participate.

Scrotal ultrasound was performed using a high-frequency linear transducer (7–15 MHz) to assess lesion size, echotexture, margins, and vascularity, with color Doppler imaging employed for further analysis. Ethical considerations were strictly adhered to, with informed consent obtained from all participants, and confidentiality ensured through the anonymization of data. The study was approved by the Institutional Ethical Review Committee. Participants were informed that their involvement was voluntary and they could withdraw at any time without affecting their medical care. All data were securely stored, with physical copies kept in a locked cabinet and electronic data stored on a password-protected computer.

Data collection involved serum AFP and β-hCG testing along with scrotal ultrasound, with all findings recorded on a structured proforma. The outcome measurements included independent variables such as serum AFP and β-hCG levels, as well as demographic factors. Dependent variables consisted of ultrasound findings (echogenicity, vascularity, and lesion size) and the nature of the lesion (benign or malignant). Data were analyzed using SPSS software 26.0, with descriptive statistics for quantitative and qualitative variables, and Pearson's correlation test to assess relationships between serum tumor markers and ultrasound findings. A p-value of <0.05 was considered statistically significant, and Chi-Square tests were also employed for further analysis.

Results

The study revealed that the majority of patients with testicular lesions were within the 36-50 years age range (37%), followed by those aged 18-35 years (36%), highlighting that

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testicular lesions are most common in middle-aged individuals. This finding underscores the importance of early detection and regular monitoring of testicular health in this age group. The relationship between age and the occurrence of testicular lesions suggests that further research is needed to understand the underlying causes of these patterns and develop targeted prevention strategies.

When analyzing the association between AFP levels and ultrasound patterns, the study found that all patients with elevated AFP levels had malignant ultrasound patterns, with a very significant association ($p<0.001$). Specifically, 42% of the participants had elevated AFP levels, and these were almost entirely linked to malignant lesions. Conversely, 58% of the patients had normal AFP levels, which were associated with benign lesions. This highlights AFP as a critical biomarker for identifying malignancy in testicular lesions, making it an essential tool for clinicians in the early diagnosis of testicular cancer.

Similarly, the study examined β-hCG levels and their correlation with ultrasound patterns. High β-hCG levels were observed in 97.7% of patients with malignant lesions, and this association was statistically significant ($p<0.001$). This finding suggests that elevated β-hCG levels are a reliable marker for malignant testicular lesions and should be considered in diagnostic protocols. The correlation between β-hCG and malignancy further supports the role of this tumor marker in enhancing the accuracy of testicular cancer diagnoses.

In terms of ultrasound findings, the study evaluated various characteristics, including echogenicity, lesion size, margin type, and vascularity, and their relation to the final diagnosis. Although heterogeneous echogenicity showed a higher proportion of malignant lesions (53.8%), the difference was not statistically significant ($p=0.062$). This suggests that while certain echogenic patterns may be indicative of malignancy, they cannot be used as standalone diagnostic criteria. Therefore, further investigation is

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needed to determine which echogenicity patterns, if any, are truly predictive of malignancy.

Regarding lesion size, the study found that both small lesions (less than 4 cm) and large lesions (greater than or equal to 4 cm) were present in both benign and malignant groups, with no significant difference in malignancy proportions ($p=0.870$). This indicates that lesion size alone is not a reliable predictor of malignancy. While lesion size can provide useful clinical information, it should not be used in isolation to determine the likelihood of malignancy. Instead, a more comprehensive approach incorporating other diagnostic markers is needed.

The analysis of lesion margins showed no significant association between well-defined or irregular margins and malignancy ($p=0.928$). Both margin types were observed in similar proportions of benign and malignant lesions. This finding suggests that margin characteristics alone are not sufficient for distinguishing between benign and malignant testicular lesions. Further research is necessary to identify other factors, including tumor markers like AFP and β-hCG, that may contribute to more accurate diagnoses.

Lastly, vascularity did not show a significant correlation with malignancy, with no meaningful difference between absent, mild, or marked vascularity groups ($p=0.952$). This reinforces the notion that vascularity alone is not a useful indicator for diagnosing malignancy in testicular lesions. The study's correlation analysis between AFP, β-hCG, final diagnosis, and ultrasound patterns confirmed a very strong positive relationship ($p<0.001$), emphasizing that AFP and β-hCG are highly reliable tumor markers. These markers are invaluable in improving diagnostic accuracy and early detection of testicular malignancies.

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Discussion

The findings of this study align with previous research, demonstrating that high levels of AFP and β-hCG are strongly associated with malignant testicular lesions. Elevated AFP levels are rarely seen in benign conditions, making AFP a highly specific biomarker for malignancy. Similarly, β-hCG elevation has been correlated with aggressive tumor behavior and poor prognosis. These results support the importance of tumor markers in enhancing the diagnostic accuracy of testicular lesions, as ultrasound alone lacks sufficient reliability. Ultrasound features, while helpful, are not conclusive and should be used in conjunction with tumor markers for a more accurate diagnosis.

Previous studies have also indicated that AFP and β-hCG levels correlate with tumor burden and disease stage, supporting the finding that all patients with elevated AFP had malignant lesions in this study. Tumor markers were shown to be more reliable than ultrasound characteristics, which exhibited inconsistent sensitivity and specificity. This reinforces the idea that tumor markers, particularly AFP and β-hCG, offer better diagnostic power than imaging alone, making them essential in the clinical management of testicular cancer.

The role of AFP and β-hCG as biomarkers in the early diagnosis and treatment of testicular tumors is well-documented, with studies confirming their value in clinical decision-making. This research aligns with those findings, showing that these tumor markers significantly improve diagnostic confidence. In contrast, ultrasound alone, with its potential for overlapping features between benign and malignant lesions, proved insufficient in providing a definitive diagnosis. Therefore, tumor markers, when used alongside imaging, form a more reliable diagnostic strategy.

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Further supporting the significance of tumor markers, other studies have found that sophisticated ultrasound methods may not effectively differentiate malignant lesions without elevated tumor markers. Our results similarly showed that parameters like echogenicity and vascularity were not statistically significant in predicting malignancy. Tumor marker-free ultrasound may lead to diagnostic uncertainty, emphasizing the importance of biochemical markers in conjunction with imaging to enhance diagnostic accuracy.

In conclusion, this study highlights the strong diagnostic value of AFP and β-hCG in distinguishing between benign and malignant testicular lesions. The ultrasound parameters examined, such as echogenicity, vascularity, lesion size, and margin, were not significantly correlated with the final diagnosis. The study advocates for the routine use of serum tumor markers alongside ultrasound to improve diagnostic outcomes, suggesting that an integrated approach combining both imaging and biochemical indicators is essential for more accurate and reliable testicular cancer diagnosis.

In light of the findings, the study recommends incorporating routine screening of serum tumor markers (AFP and β-hCG) into the diagnostic protocol for testicular lesions. This would improve diagnostic accuracy and help differentiate malignant from benign lesions more reliably. Ultrasound should continue to be used as an adjunct to biochemical markers, but clinicians must acknowledge its limitations in diagnosing malignancy. Further studies with larger sample sizes are encouraged to explore the relationship between various ultrasound features and tumor markers, and a multidisciplinary approach involving clinicians, radiologists, and pathologists should be considered for more comprehensive and accurate diagnoses. Additionally, integrating newer imaging

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technologies like MRI could further enhance diagnostic precision, particularly in complex cases.

While this study offers valuable insights, it has several limitations. The sample size was relatively small, which may limit the generalizability of the results to larger populations. Additionally, the study relied on a single imaging modality (ultrasound) and did not explore other advanced imaging techniques like MRI or CT scans. The study's cross-sectional design also means that it only provides a snapshot of the relationship between tumor markers and ultrasound findings without accounting for the progression of the disease over time. Future studies should address these limitations to provide a more comprehensive understanding of the diagnostic value of tumor markers and imaging in testicular lesions.

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