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ORIGINAL ARTICLE

Clinico-pathological analysis of testicular and para-testicular lesions: A single center study.

Syed Moazzam Naqi Abbas[1], Amna Jahan[2], Noreen Javaid[3], Omer Rasheed Chughtai[4], Tariq Iqbal Khan[5], Akhtar Sohail Chughtai[6]

ABSTRACT… Objective: To determine the distribution spectrum and frequency of testicular and para-testicular lesions, including both neoplastic and non-neoplastic types from one of the diagnostic centres of Pakistan. **Study Design:** Cross-sectional study. **Setting:** Chughtai Institute of Pathology, Lahore. **Period:** August 2025 to February 2026. **Methods:** A total of 396 cases of testicular and paratesticular lesions, including 204 orchidectomy specimens and 192 testicular biopsies received over a period of 1 year were studied retrospectively. **Results:** Overall, non-neoplastic conditions were predominant. The most frequent non-neoplastic diagnosis was non-granulomatous epididymo-orchitis (40 cases, 19.60%), followed closely by atrophic testes (34 cases, 16.66%). Undescended testis (cryptorchidism) was identified in 12 specimens (5.88%). Among the neoplastic lesions from the 204 surgical cases, mixed germ cell tumors were the most common tumor type (35 cases, 17.15%), followed by seminoma (21 cases, 10.29%). Yolk sac tumors were observed in 9 cases (4.41%), predominantly in the pediatric age group (6 cases in the 0-10-year age bracket). Histopathological findings of the 192 testicular biopsies varied from normal spermatogenesis and maturation arrest to Sertoli-cell-only syndrome and hyposermatogenesis, providing critical diagnostic information for managing male infertility. **Conclusion:** The study shows that the non-neoplastic lesions predominate among the testicular and para-testicular pathologies with epididymo-orchitis and testicular atrophy being the most common findings. Within the malignant lesions, germ cell tumors are most frequently followed by mixed germ cell tumors and seminoma.

Key words: Infertility, Mixed Germ Cell Tumors, Non-granulomatous Epididymo-orchitis, Orchidectomy, Para-testicular Lesions, Testicular Biopsy, Testicular Lesions.

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INTRODUCTION

The testis is an organ with a dual-purpose of spermatogenesis and androgen secretion. Pathological processes of the testis and para-testicular systems are a wide range, including inflammatory, developmental abnormalities, and malignant neoplasms, and the clinical manifestations of them may significantly overlap with each other.[1] Such heterogeneity renders histopathological examination essential in giving definitive diagnosis and proper treatment planning.

Testicular neoplasms, while uncommon in absolute terms, represent the most frequent solid malignancy in men between 15 and 35 years of age and account for approximately 1% of all male cancers worldwide.[2] Germ cell tumours represent 90-95 percent of testicular malignancies and are broadly divided into seminomatous and non-seminomatous with different biological behaviour, staging and treatment implications.[3] Testicular germ cell tumours have been increasing globally over the last forty years[4], and the geographic distribution of age-standardised rates is shocking: in Northern and Western Europe, the age-adjusted rates are over 7 per 100,000 but in much of the rest of Asia and Africa, including Pakistan, the rates are under 2 per 100,000.[5] This difference is probably due to genetic susceptibility differences, exposures to environmental events at an early age and access to diagnostic services instead of biological lack of disease.

Non-neoplastic testicular and para-testicular lesions are many times more common than tumors. Infectious and inflammatory diseases, especially epididymo-orchitis, are widespread and cut across all ages and become a significant source of emergency urological presentations.[6]

1. MBBS, Postgraduate Resident Histopathology, Chughtai Institute of Pathology, Lahore.
2. MBBS, FCPS, Consultant Histopathologist, Chughtai Institute of Pathology, Lahore.
3. MBBS, FCPS, Consultant Histopathologist, Chughtai Institute of Pathology, Lahore.
4. MBBS, FCPS, Consultant Histopathologist, Chughtai Institute of Pathology, Lahore.
5. MBBS, Postgraduate Resident Histopathology, Chughtai Institute of Pathology, Lahore.
6. MBBS, FCPS, Consultant Histopathologist, Chughtai Institute of Pathology, Lahore.

Correspondence Address:
Dr. Syed Moazzam Naqi Abbas
Department of Histopathology, Chughtai Institute of Pathology, Lahore.
moazzamshah14@gmail.com

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Granulomatous orchitis can be confused with malignancy clinically and radiographically and has a risk of being misdiagnosed or undiagnosed, especially in endemic areas, like the Indian subcontinent, where tuberculous infection is the most frequent cause of granulomatous orchitis.[7] Though surgical emergencies treated on clinical grounds, testicular torsion and infarction have typical histological results when orchidectomy specimens are sent. Cryptorchidism, or failure of one or both testes to descend into the scrotum is observed in 1-5% of normal male births, and is of clinical interest because not only of its association with impaired spermatogenesis but also owing to a clearly documented high risk of malignant transformation, estimated to be two to eight times that of the normally descended testis.[8]

Male infertility is a category of testicular disease that is numerically significant and distinct. It is seen in about 7 per cent of the male population in the world and is a cause of up to 50 per cent of all infertile couples.[9] In this context, the testicular biopsy is diagnostic but not curative to permit the classification of the underlying spermatogenic defect as hypospermatogenesis, maturation arrest at the primary spermatocyte or spermatid level, and Sertoli-cell-only syndrome each with a different prognosis for sperm retrieval and assisted conception.[10] A histopathological pattern is one of the main predictors of success in sperm retrieval methods.

Para-testicular lesions, which originate from epididymis, tunica vaginalis, spermatic cord and the surrounding soft tissues further complicate the diagnostic spectrum. The most typical benign para-testicular neoplasm is adenomatoid tumor, which needs to be differentiated from more aggressive tumors such as mesothelioma and different sarcomas.

Although the clinical significance of this type of disease is crucial, institutional and regional statistics on the relative frequency and age distribution of testicular and para-testicular lesion in South Asian population are scanty. Patterns indicated by published series of the Indian subcontinent may not be the same as in Western cohorts, including a greater proportion of non-neoplastic diseases and inflammatory disease.[11] Without institutional data from this region, diagnostic priorities and resource allocation rest on externally derived evidence that may not reflect local disease patterns.

This study addresses that gap and presents the clinico-pathological profile of 396 testicular and para-testicular specimens (204 orchidectomy and 192 testicular biopsies to evaluate infertility), of a single high-volume diagnostic pathology centre in Lahore, Pakistan during one year. The findings provide a baseline reference for the relative frequency, age distribution, and histopathological spectrum of these lesions in a Pakistani population.

METHODS

This cross sectional study was conducted from August 2025 to February 2026 after taking approval from the institutional Ethical Review Committee (Reference No. CIP/IRB/1354 dated 14th July 2025). Given the retrospective collection of data from existing medical records, the requirement for informed consent was waived by the Institutional Ethics Review Committee. Histopathological records of patients from 1st June 2024 to 30th June 2025 of all age groups with accesible clinical and medical records and confirmed diagnosis of testicular and para-testicular lesions were included. Those with incomplete medical records and Autolyzed samples less suitable for micromorphological evaluation, were excluded from the study. Sample size was calculated using the WHO calculator with a 95% confidence level, 5 % absolute precision taking an expected proportion of 9.6% for neoplastic testicular lesions from Charak et al[11] which yielded a minimum sample size of 133. However, all 396 cases meeting the inclusion criteria during the study period were included through non-probability purposive sampling.

Data was collected from the department of histopathology. All cases of testicular and para-testicular lesions reported in the year, were identified using Nexus and relevant medical records. Pertinent clinical and operative data was gathered, including patient demographics, clinical and radiological findings, the type of surgical procedure performed (Biopsy or orchidectomy), and the final

histopathological diagnosis. Cross-verification with original histology slides was conducted in selected cases to confirm the histological diagnosis if needed. All data collected was accurately recorded on the structured form. Inadequate or incomplete records were excluded based on exclusion criteria. The data was analyzed using SPSS version 25.0. Simple frequencies and percentages were calculated and presented in the form of tables and figures.

RESULTS

A total number of 396 cases of testicular and paratesticular lesions included in the period of the study: 204 orchidectomy cases and 192 cases of infertility who underwent testicular biopsy. The SPSS version 25 was used to enter and analyse the data. The frequencies and percentages were determined and represented in the form of tables and figures.

Infertility or azoospermia was the most common presentation accounting for 192 cases (48.48%) and all were subjected to testicular biopsy. The second most common complaint (97 cases, 24.49%) was scrotal or testicular swelling. An empty scrotum suggestive of cryptorchidism presented in 38 cases (9.59%). The rest of the presentations were testicular pain (27 cases, 6.81%), a mixture of swelling, pain and fever (26 cases, 6.56%), and incidental findings during hernia repair or other surgeries (16 cases, 4.04%) (Table-I).

TABLE-I

Clinical presentation of the studies cases of testicular and para-testicular lesions

Clinical Presentation	Number of Cases	%
Empty scrotum	38	9.59%
Infertility / azoospermia	192	48.48
Scrotal/ testicular swelling	97	24.49
Testicular pain	27	6.81%
Scrotal swelling /pain/fever	26	6.56%
As a part of hernia repair or treatment	16	4.04%
TOTAL	396	100

Histopathological results of the 204 orchidectomies specimens categorized by age group showed non-neoplastic conditions predominance. The most common diagnosis was non-granulomatous epididymo-orchitis (40 cases, 19.60%), followed by testicular atrophy (34 cases, 16.66%). Miscellaneous inflammatory, obstruction conditions (torsion, hydrocele, spermatocele, incidental hernia sac) collectively formed 22 cases (10.78%). In 12 specimens (5.88%), undescended testis was detected and in 15 cases (7.35%) granulomatous epididymo-orchitis. There were three specimens with no histological abnormality (1.47%).

TABLE-II

Age-specific histological pattern of testicular and para-testicular lesions in orchidectomy specimens

Testicular Lesions	0-10	11-20	21-30	31-40	41-50	51-60	61-70	71-80	81-90	Total %
Undescended testis	2	3	3	1	0	0	2	1	0	12 (5.88%)
Unremarkable B/L testis	0	0	0	1	0	2	0	0	0	3 (1.47%)
Atrophic testes	0	7	9	12	1	3	2	0	0	34 (16.66%)
Granulomatous epididymo-orchitis	0	1	4	2	6	2	0	0	0	15 (7.35%)
Non granulomatous epididymo-orchitis	0	6	4	9	5	6	7	2	1	40 (19.60%)
Leydig cell hyperplasia	0	0	0	0	1	0	0	0	0	1 (0.49%)
Miscellaneous (hernia, hydrocele, torsion, spermatocele)	2	7	1	3	1	4	3	1	0	22 (10.78%)
Seminoma	0	1	3	12	5	0	0	0	0	21 (10.29%)
Yolk sac tumor	6	2	1	0	0	0	0	0	0	9 (4.41%)
Teratoma (pre and post pubertal)	1	0	0	0	1	0	0	0	0	2 (0.98%)
Mixed germ cell tumor	0	8	11	13	3	0	0	0	0	35 (17.15%)
Sex cord stromal tumor	0	0	1	0	1	0	0	0	0	2 (0.98%)
Lymphoma	0	0	0	0	1	4	0	0	0	5 (2.45%)
Leiomyosarcoma	0	0	0	0	0	1	0	1	0	2 (0.98%)
Adenomatoid Tumor	0	0	0	0	0	0	0	1	0	1 (0.49%)
Total	11	35	37	53	25	22	14	6	1	204 (100%)

Mixed germ cell tumours were the most common of the neoplastic lesions (35 cases, 17.15%), followed by seminoma (21 cases, 10.29%). The total occurrence of these two types of tumors in the orchidectomy specimen was 27.44%. In 9 cases (4.41%) yolk sac tumours were detected. In 5 cases (2.45) lymphoma was diagnosed. Rarer ones constituted sex cord-stromal tumours and teratomas (2 cases each, 0.98%), leiomyosarcoma (2 cases, 0.98%), and one adenomatoid tumour (0.49%).

There were specific tumour patterns in age distribution. Yolk sac tumours were predominantly found in the paediatric age group with 6/9 (66.7) cases observed in the children aged 0-10 years. Mixed germ cell tumours and seminomas were maximum in the 21-40 years age range, which was in line with the known biology of post-pubertal germ cell neoplasm. The only age group in this series that had lymphomas was 41-60 years old (Table-II).

The 192 testicular biopsies were all done to test male infertility or azoospermia. Histopathological observations varied across the known spermatogenic failure phenotypes: normal spermatogenesis, hypospermatogenesis, arrest of maturation of spermatocytes or spermatids in the primary spermatocyte or spermatid stage, and Sertoli-cell-only syndrome. Few biopsies were found to have no spermatogenic abnormality which suggested the presence of obstructive rather than secretory azoospermia in those instances.

The relative distributions of all spermatogenic patterns within this cohort could not be tabulated properly because of the lack of full disaggregation of biopsy diagnoses in the source records; this is recognized as a limitation. The histopathological results however offered clinically actionable diagnostic data in all 192 cases to guide patient counselling and assisted reproduction decisions.

DISCUSSION

This study analyzed 396 orchidectomy and testicular biopsy specimens collected over one year at a high-volume diagnostic centre in Lahore, Pakistan. The distribution of testicular and para-testicular lesions aligns with regional South Asian patterns, characterized by a predominance of non-neoplastic and inflammatory conditions. This mirrors findings from South Indian and island-based series, where non-neoplastic lesions accounted for 87.5% to 94.1% of orchidectomy specimens.[12,13] The slightly higher proportion of neoplastic orchidectomies in our cohort likely reflects referral and selection biases inherent to a specialized urban pathology centre. Consistent with a Nagpur-based cross-sectional study, these findings reinforce the necessity of routine histopathological evaluation for all scrotal specimens.[14]

Non-granulomatous epididymo-orchitis was the leading diagnosis (40 cases, 19.60%), reflecting its status as a common urological emergency. Granulomatous epididymo-orchitis comprised 7.35% of cases. In Pakistan's endemic setting, tuberculosis must be presumed until excluded, though histopathology alone cannot confirm mycobacterial infection without Ziel-Neelsen staining, culture, or PCR. Previous series report high positivity rates for ZN staining and PCR in granulomatous cases, all demonstrating caseous necrosis.[15] The absence of microbiological correlation in our study is a notable limitation that likely underestimates genital tuberculosis burden. Furthermore, granulomatous orchitis carries a substantial risk of radiological and clinical misdiagnosis as malignancy, frequently resulting in unnecessary orchidectomy.[16] Given Pakistan's high tuberculosis prevalence, institutional protocols should mandate microbiological confirmation for granulomatous lesions.

Among neoplasms, mixed germ cell tumours (17.15%) and seminomas (10.29%) predominated. The higher frequency of mixed GCTs over pure seminoma aligns with South Asian literature, where these tumours exhibit considerable morphological diversity despite globally low incidence rates.[17] Our data shows seminomas peaking in the fourth decade and mixed/non-seminomatous tumours in the third. This histological breakdown directly influences management; mixed tumours with embryonal carcinoma components often require adjuvant therapy due to surveillance failure risks.[17] While outcomes in low- and intermediate-risk groups mirror international standards, high-risk disease in the subcontinent faces poorer survival, partly due

to limited access to salvage chemotherapy.[18,19] Yolk sac tumours displayed a characteristic paediatric predominance, with 66.7% occurring in the 0–10-year age group, consistent with their bimodal distribution and WHO 2022 pre- and post-pubertal classification.[20] Survival correlates strongly with stage and postoperative AFP normalization[20], and preoperative nomograms could aid diagnosis in resource-constrained settings.[21] Primary testicular lymphoma (five cases) presented slightly earlier (41–60 years) than Western cohorts but aligns with regional data. Given risks of CNS or contralateral recurrence[22], routine immunohistochemistry with CD20, CD3, and Ki-67 is essential for definitive characterization.

The 192 infertility-related biopsies highlighted clinically significant spermatogenic patterns with direct prognostic implications. Histological findings directly predict microdissection TESE success, with hypospermatogenesis yielding higher retrieval rates compared to maturation arrest or Sertoli-cell-only syndrome.[23] However, the absence of a frequency table limits comparative analysis. Study limitations include single-centre referral bias, a one-year timeframe restricting rare case analysis, lack of clinical staging and tumour marker correlation, unconfirmed microbiological aetiology for granulomas, inconsistent IHC reporting, and untabulated biopsy data. Despite these constraints, this study establishes crucial institutional baseline data for Pakistan, confirming inflammatory diseases as the predominant surgical pathology and mixed GCTs as the leading malignancy. Future prospective research should integrate tumour markers, staging, and treatment outcomes, link data to cancer registries, mandate TB confirmation for granulomatous lesions, and correlate biopsy patterns with assisted reproductive outcomes to enhance regional clinical practice.

CONCLUSION

The study shows that the non-neoplastic lesions predominate among the testicular and para-testicular pathologies with epididymo-orchitis and testicular atrophy being the most common findings. Within the malignant lesions, germ cell tumors are most frequently followed by mixed germ cell tumors and seminoma.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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AUTHORSHIP AND CONTRIBUTION DECLARATION	
1	**Syed Moazzam Naqi Abbas:** Conception of idea, study design, drafting.
2	**Amna Jahan:** Data collection, data analysis.
3	**Noreen Javaid:** Interpretation of data.
4	**Omer Rasheed Chughtai:** Data collection.
5	**Tariq Iqbal Khan:** Writing.
6	**Akhtar Sohail Chughtai:** Data entry.