# Clinicopathological analysis of ovarian Sertoli-Leydig cell tumors with emphasis on heterologous differentiation: A series of ten cases from a tertiary cancer centre in South India

Silky Rai1*, Preethi T R1, Neelima Radhakrishnan1, Lakshmi Haridas K2, Priyakumari T3, Jagathnath Krishna K.M4

1 Department of Pathology, Regional Cancer Centre, Trivandrum, Kerala, India

2 Department of Medical Oncology, Regional Cancer Centre, Trivandrum, Kerala, India

3 Department of Paediatric Oncology, Regional Cancer Centre, Trivandrum, Kerala, India

4 Department of Cancer Epidemiology & Biostatistics, Regional Cancer Centre, Trivandrum, Kerala, India

**Introduction:**

Ovarian Sertoli–Leydig cell tumors (SLCTs) are rare sex cord-stromal neoplasms (<0.5%) occurring predominantly in young women [1,2]. They exhibit diverse clinical presentations, including abdominal mass and androgenic manifestations [3,4]. Histologically, SLCTs range from well to poorly differentiated tumors, with retiform and heterologous variants adding diagnostic complexity; heterologous elements are seen in ~20% of cases [2,4]. Immunohistochemistry aids diagnosis, with expression of inhibin, calretinin, and SF1 [2,5]. Molecularly, DICER1 and FOXL2 mutations define distinct subtypes [6–8]. Also, dedicated study focusing exclusively on SLCTs, remain limited in Indian literature [9]. Hence, this case series integrates the WHO/IARC classification with our institutional experience to describe the clinicopathologic spectrum, immunoprofile, and disease progression of SLCTs, identify prognostic factors, and emphasize the significance of heterologous differentiation in our population.

**Aim:** To evaluate the clinicopathological spectrum of ovarian SLCTs.
**Objectives:**

1. To describe clinicopathological features.
2. To correlate histology with stage and outcomes.
3. To identify prognostic factors, especially heterologous differentiation.

**Materials & Methods :**

A retrospective observational study was conducted at a tertiary cancer center (2016–2025). Histologically confirmed SLCT cases were included. Clinical, radiological, operative, and pathological data were analyzed. Tumors were assessed for morphology, grade, heterologous elements, and stage. Immunohistochemistry (inhibin, calretinin) supported diagnosis.

**Results:**

A total of **10 cases** of ovarian Sertoli–Leydig cell tumors (SLCTs) were analyzed.

❖ **Demographics:**

The mean age at presentation was **26.7 years** (range: **11–54 years**), highlighting a predominance in younger females.

❖ **Histopathology:**

Moderately differentiated (MD): **5/10 (50%)**

Moderate to poorly differentiated (MD–PD): 4/10 (40%)

Poorly differentiated (PD): 1/10 (10%)

❖ **Heterologous differentiation:**

Present in **4/10 cases (40%)** (2 rhabdomyosarcomatous and 2 mucinous)

❖ **Laterality & treatment:** Tumors were typically unilateral and often managed with fertility-sparing surgery in younger patients.

❖ **Tumor size:** The tumors demonstrated substantial size variation, with a mean largest dimension of ~ 19 cm.

❖ **Architectural pattern:**

**Retiform pattern:** 2/10 cases (20%)

❖ **Stage distribution:**

**Stage IA:** 7/10 (70%)

**Stage IC1:** 1/10 (10%)

**Stage IV:** 2/10 (20%) showed nodal and peritoneal metastasis.

❖ **Immunohistochemistry (IHC):** Inhibin & calretinin supported sex-cord stromal differentiation.

❖ **Clinical outcomes:**

Patient expired : 01 (10%)

Patient alive with disease free survival on regular follow ups : 05 (50%)

Patients lost to follow up : 04 (40%)

**Recurrence observed:** 2/10 cases (20%)

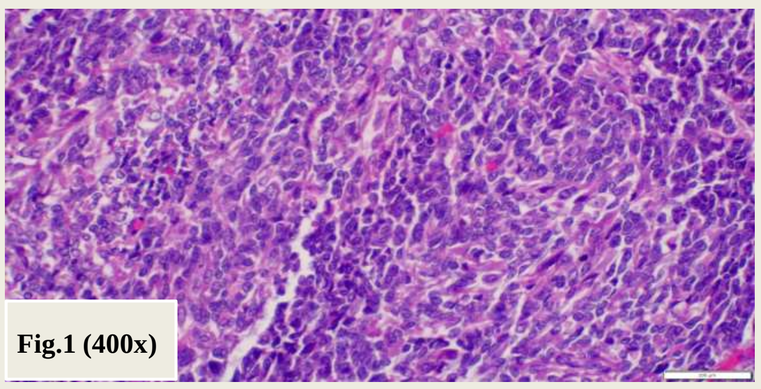

**Fig.1 (400x)**

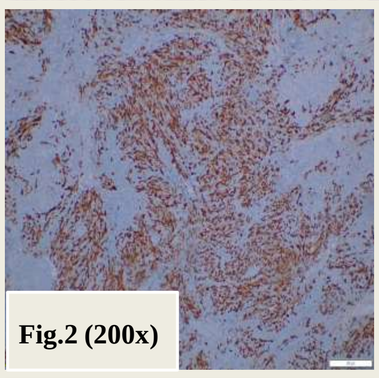

**Fig.2 (200x)**

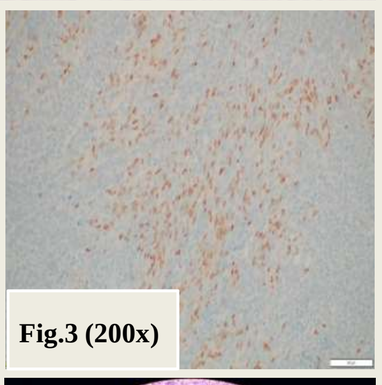

**Fig.3 (200x)**

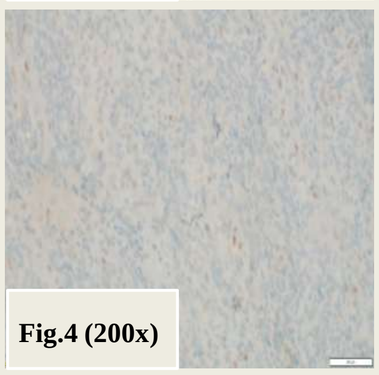

**Fig.4 (200x)**

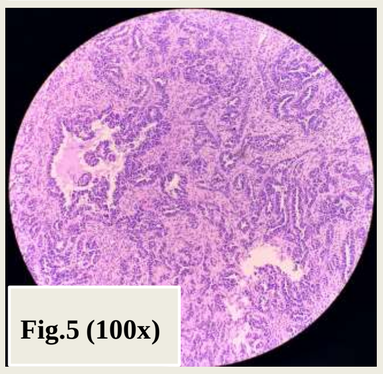

**Fig.5 (100x)**

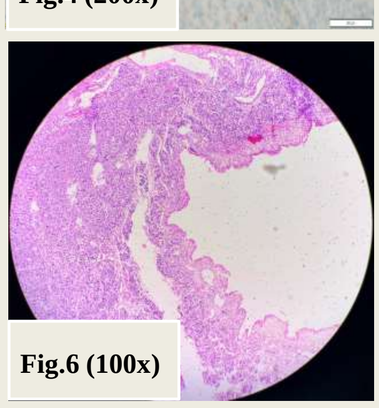

**Fig.6 (100x)**

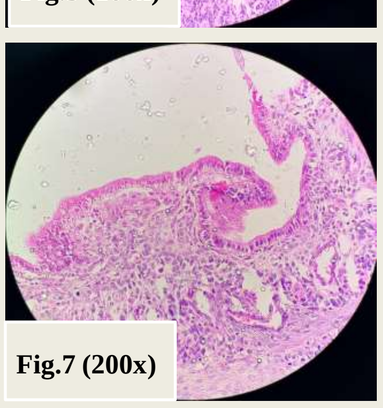

**Fig.7 (200x)**

**(Fig. 1) H&E stained section of heterologous element in the form of rhabdomyosarcomatous component in 2/10 cases.**

**(Fig. 2) – IHC for desmin is strongly positive in the rhabdomyosarcomatous component along with myogenin (Fig. 3) and myoD1 - (Fig. 4).**

**(Fig. 5) – H&E stained section shows prominent retiform pattern in 2/10 cases.**

**(Fig. 6 & Fig. 7) – H&E stained sections show Sertoli Leydig cell tumor with heterologous mucinous component of intestinal type epithelium.**

**Discussion:**

- Ovarian Sertoli–Leydig cell tumors (SLCTs) are rare neoplasms with significant morphological diversity and variable biological behavior. In the present series, the **mean age of 26.7 years** is consistent with the known predilection for younger females [1].
- A key finding in our study is the **high proportion of moderately to poorly differentiated tumors (50%)**, which is clinically relevant as tumor grade is a well-established prognostic factor. Poorly differentiated tumors are known to exhibit more aggressive behavior and higher metastatic potential [2].
- Notably, **heterologous differentiation was identified in 40% of cases**, which is considerably higher than the ~20% reported in literature [2]. This observation underscores the importance of **extensive sampling and meticulous histopathological evaluation**, as heterologous elements - especially rhabdomyosarcomatous differentiation - are associated with adverse prognosis. This higher incidence may reflect referral bias in a tertiary cancer center or true regional variation.
- The **retiform pattern (20%)** observed aligns with previous studies [3] and is typically associated with younger patients. Most tumors presented at **early stage (≥60%)**, which is encouraging and supports favorable outcomes with appropriate management. However, the presence of **advanced-stage disease (20%) and recurrence in 20% cases** highlights the heterogeneity in tumor behavior.
- The findings reinforce that **histological grade, stage, and heterologous elements** remain the most critical determinants of prognosis. Integration of morphology with immunohistochemistry is essential to avoid misdiagnosis, especially in cases with unusual differentiation. Emerging molecular insights, such as *DICER1* mutations, may further refine risk stratification in future studies.

**Conclusion:**

- This study highlights the **clinicopathological heterogeneity of ovarian SLCTs**, with a notably **high frequency of heterologous differentiation (40%)** and a significant proportion of **higher-grade tumors (50%)**.
- While most tumors present at an early stage, the observed **recurrence rate (20%)** emphasizes the need for careful prognostic assessment. **Histopathological grading and identification of heterologous elements** are crucial for guiding management and predicting outcomes.
- As the differentiation of heterologous component determines the prognosis, **an extensive sampling of the specimen** should be done to identify the components. Poorly differentiated tumors with heterologous component are **advised for platinum-based adjuvant chemotherapy along with surgical resection.**
- **Hence, Thorough sampling, appropriate immunohistochemical workup, and close clinical follow-up** are essential to optimize patient care. Larger studies incorporating molecular profiling are warranted to better understand tumor biology and improve prognostication.

**References:**

1. Young RH, Scully RE. Ovarian Sertoli–Leydig cell tumors: a clinicopathologic analysis of 207 cases. Am J Surg Pathol. 1985;9(8):543–69.
2. Kommoss F, Karnezis AN, Buza N, et al. Sertoli-Leydig cell tumour. In: WHO Classification of Tumours Editorial Board. Female genital tumours [Internet]. 5th ed. Lyon (France): International Agency for Research on Cancer; 2020 [cited 2026 Apr 10]. (WHO Classification of Tumours Series, vol. 4). Available from: https://tumourclassification.iarc.who.int/chaptercontent/34/82
3. Schneider DT, Jänig U, Calaminus G, Göbel U, Harms D. Ovarian sex cord-stromal tumors--a clinicopathological study of 72 cases from the Kiel Pediatric Tumor Registry. Virchows Arch. 2003 Oct;443(4):549-60. doi: 10.1007/s00428-003-0869-0. Epub 2003 Aug 9. PMID: 12910419.
4. Varghese A, Lele S. Rare Ovarian Tumors. In: Lele S, editor. Ovarian Cancer [Internet]. Brisbane (AU): Exon Publications; 2022 Sep 8. Chapter 1. Available from: https://www.ncbi.nlm.nih.gov/books/NBK585991/doi: 10.36255/exon-publications-ovarian-cancer-rare-ovarian-tumors
5. College of American Pathologists. Protocol for the examination of specimens from patients with primary tumors of the ovary, fallopian tube, or peritoneum. Version 1.5.0.0. Posted June 2024; required use March 2025. Northfield (IL): CAP; 2024.
6. Heravi-Moussavi H, Anglesio MS, Cheng SWG, Senz J, Yang W, Prentice L, et al. Recurrent somatic DICER1 mutations in ovarian Sertoli–Leydig cell tumours. N Engl J Med. 2012;366(3):234–42.
7. Schultz KAP, Harris AK, Finch M, Dehner LP, Brown JB, Gershenson DM, Young RH, Field A, Yu W, Turner J, Cost NG, Schneider DT, Stewart DR, Frazier AL, Messinger Y, Hill DA. DICER1-related Sertoli-Leydig cell tumor and gynandroblastoma: Clinical and genetic findings from the International Ovarian and Testicular Stromal Tumor Registry. Gynecol Oncol. 2017 Dec;147(3):521-527. doi: 10.1016/j.ygyno.2017.09.034. Epub 2017 Oct 14. PMID: 29037807; PMCID: PMC5716477.
8. Buza N, Wong S, Hui P. FOXL2 Mutation Analysis of Ovarian Sex Cord-Stromal Tumors: Genotype-Phenotype Correlation With Diagnostic Considerations. Int J Gynecol Pathol. 2018 Jul;37(4):305-315. doi: 10.1097/PGP.0000000000000426. PMID: 28700438.
9. Chowdhury Z, Agrawal S, Gupta S, Rai S, Jethani R, Saha S, et al. The many faces of ovarian sex cord stromal tumors: a clinicopathological analysis at a tertiary cancer center in North India. Surg Exp Pathol. 2025;8:13.

**Declaration**: All authors confirm that this work is not affiliated with any commercial sponsor or external organisation that could affect independence or objectivity