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Original Article

Pathology Section

Histopathological and Immunohistochemical Expression of Ovarian Tumours: A Cross-sectional Study from a Tertiary Care Centre Indore, India

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ABSTRACT

Introduction: Ovarian tumours constitute 3% of all malignancies in women and 30% of all cancers affecting the Female Genital Tract (FGT). Cervical and endometrial cancers have a higher incidence than ovarian cancer. According to GLOBOCAN 2022 (Global Cancer Observatory's estimates for the year 2022), there were 722,138 ovarian cancer cases worldwide, including 45,333 new cases reported in India. India has the second highest incidence of ovarian cancer globally (6.6%), with the highest rates noted in Pune and Delhi. Immunohistochemical (IHC) markers play a crucial role in subtyping, grading, and assisting in the diagnosis and prognosis of ovarian tumours.

Aim: The present study aimed to analyse the histopathological and immunohistochemical expression of ovarian tumours and evaluate the role of IHC in differentiating primary ovarian neoplasms from metastatic tumours.

Materials and Methods: The present ambispective two-year cross-sectional study was conducted from January 2023 to December 2024 on 188 cases at Sri Aurobindo Institute of Medical Sciences, Indore, Madhya Pradesh, India. Haematoxylin and Eosin (H&E)-stained sections along with IHC-stained slides of ovarian neoplasms were prepared and examined. IHC was performed in 58 cases using common primary markers such as Cytokeratin 7 (CK7), Cytokeratin 20 (CK20), Paired Box Gene 8 (PAX8), and Wilms' Tumour Gene 1 (WT1) to identify primary ovarian tumours. Secondary markers such as Caudal-Type Homeobox 2 (CDX2), Special Adenine-Thymine-rich Sequence-Binding Protein 2 (SATB2), Oestrogen/Progesterone Receptors (ER/PR), and Calretinin were used to differentiate tumours of FGT, Gastrointestinal Tract (GIT), breast, and metastatic origin. Additional markers like Inhibin and Octamer-Binding Transcription Factors (OCT) were used for morphological subtyping of sex cord-stromal and germ cell tumours.

Results: Out of the 188 cases, surface epithelial tumours were the most common (149 cases), including 82 benign serous cystadenomas, 24 malignant Serous Carcinomas (SCs), and 22 mucinous cystadenomas. Most metastatic tumours (21 cases) presented with omental nodules and abdominal pain and were predominantly of SC type. IHC was performed on 58 cases using CK7/CK20 followed by WT1 and Napsin A, which helped differentiate ovarian tumours from other genitourinary tract tumours. Of these, 37 cases were confirmed as primary ovarian tumours. These included 24 cases of SC, 4 adult granulosa cell tumours, and one case each of Mucinous Carcinoma (MC), neuroendocrine carcinoma (small cell carcinoma), Sertoli-Leydig cell tumour, seromucinous cystadenoma, borderline serous tumour, and mature cystic teratoma.

Conclusion: The most common neoplasms observed were surface epithelial tumours, with benign serous cystadenoma being the predominant type, most frequently affecting women of reproductive age. IHC played a significant role in tumour differentiation, grading, and prognostication.

Keywords: Immunohistochemical inhibin, Ovarian malignancy, Serous adenocarcinoma

INTRODUCTION

Ovarian tumours account for 3% of all malignancies in women and 30% of all cancers affecting the female genital system. Cervical and endometrial cancers have a higher incidence compared to ovarian cancer. Immunohistochemistry (IHC) in ovarian pathology has advanced significantly in recent years [1].

In India, 722,138 cases of ovarian cancer were reported globally, including 45,333 new cases, according to GLOBOCAN 2022. A total of 32,978 deaths were attributed to ovarian cancer [2]. Among Indian females, the prevalence rate is 15.65 per 100,000. According to the 2018 World Ovarian Cancer Coalition Atlas, India has the second-highest incidence of ovarian cancer globally. The cancer registries of Pune and Delhi reported the highest frequency of ovarian tumours. Ovarian cancer accounts for approximately 6.6% of all cancers in Indian women [3].

Epithelial ovarian carcinoma commonly begins as Serous Tubal Intraepithelial Carcinoma (STIC) in the Fallopian Tube Epithelium (FTE), caused by Tumor Protein p53 (TP53) mutations, which eventually progress to invasive carcinoma. Malignant cells may detach from the tumour and disseminate throughout the peritoneal cavity, forming multicellular clusters known as spheroids. Various mutations, including activating missense mutations in PIK3CA (Phosphatidylinositol-4,5-bisphosphate 3-Kinase Catalytic subunit Alpha), loss-of-function deletions in PTEN (Phosphatase and TENsin homolog deleted on chromosome 10), and amplifications in AKT serine/threonine kinase 1 (AKT1), AKT serine/threonine kinase 2 (AKT2), and AKT serine/threonine kinase 3 (AKT3), are documented across the histotypes of human Epithelial Ovarian Cancer (EOC) [4]. Ovarian tumours can be classified into three major categories-benign, malignant, and metastatic-each with unique IHC profiles that aid diagnosis. IHC is especially valuable in distinguishing primary ovarian carcinomas from metastatic adenocarcinomas [1].

Cytokeratins are water-insoluble intracellular fibrous proteins present in nearly all epithelial cells. They serve as effective markers of epithelial differentiation regardless of whether the tumours originate

from endodermal, neuroectodermal, mesenchymal, or germ cell lineages. Cytokeratin expression is a helpful tool in identifying both primary and metastatic ovarian tumours. The present study evaluates the efficacy of cytokeratin expression in malignant ovarian tumours [5,6]. Differentiating primary mucinous ovarian tumours from metastatic mucinous tumours can be challenging, especially when metastases originate from the gastrointestinal tract, pancreas, or biliary tree. Although several immunohistochemical antibodies are available, some tumours cannot be accurately classified without strong clinicopathological correlation [7].

Elderly patients with serous adenocarcinoma tend to have higher tumour grades, poorer performance status, and often receive undertreatment compared to younger patients. Elevated levels of 8-hydroxy-2′-deoxyguanosine (8-OHdG) in leukocyte Deoxyribonucleic Acid (DNA) have been associated with increasing age and poorer prognosis in serous adenocarcinoma patients [8].

Patients commonly present with abdominal or pelvic pain, increasing abdominal size or bloating. Less common symptoms include altered bowel habits, loss of appetite, weight loss, palpable abdominal mass, respiratory symptoms, vaginal bleeding, urinary frequency, and other gastrointestinal complaints [9].

The diagnosis of ovarian tumours depends on distinguishing primary from metastatic lesions, particularly among epithelial tumours. Common IHC markers include CK7, CK20, WT1, p53, PAX8, CDX2, and ER. Low-Grade Serous Carcinoma (LGSC) typically shows positivity for WT1, p53, and CK20, with p16 being negative or only patchy. Mucinous ovarian carcinoma displays positivity for CEA, CK7, CK20, and weak CA-125 expression. Endometrioid ovarian carcinoma is positive for CK7, ER, PR, PAX8, and keratin, and negative for WT1, CDX2, and Napsin A. Brenner tumours are positive for p63 and GATA, and negative for ER, PR, and WT1 [10,11].

Borderline epithelial tumours, such as serous borderline tumours, show positivity for PAX8, ER, PR, and WT1, and are negative for p53, p16, and CK20. In contrast, High-Grade Serous Carcinoma (HGSC) demonstrates strong positivity for WT1, p53, CK20, ER, p16, and Calretinin [12,13].

Among sex cord-stromal tumours, adult granulosa cell tumours show positivity for Forkhead box protein L2 (FOXL2), Steroidogenic Factor 1 / NR5A1 (SF1), and Inhibin A and are negative for Epithelial Membrane Antigen (EMA) and CK7. Sertoli-Leydig cell tumours are positive for Inhibin, Calretinin, SF1, Vimentin, Melan-A, CK20, and CDX2, and negative for CK7 and EMA [12,13].

Mesenchymal tumours such as endometrial stromal sarcoma show positivity for vimentin and CD10. Leiomyosarcoma demonstrates positivity for caldesmon, desmin, and SMA [10,11].

Thus, IHC markers today play a significant role in the subtyping and grading of ovarian tumours and are essential in their diagnosis and prognosis.

The 2020 edition of the World Health Organisation (WHO) Classification of Female Genital Tumours categorises ovarian epithelial neoplasms into six primary histotypes (also known as histological types). Seven histotypes were initially described in the first edition released in 1973, indicating that phenotype-based histotype classification has remained relatively stable over time. The table shows the WHO changes in ovarian tumour classification [14].

Nakamura K et al., discovered that serous carcinomas develop via a dualistic pathway, with low-grade tumours harboring Mitogen-Activated Protein Kinase (MAPK) pathway mutations {Kirsten rat sarcoma viral oncogene homolog (KRAS), v-Raf murine sarcoma viral oncogene homolog B (BRAF), and Neuroblastoma RAS viral oncogene homolog (NRAS), and others}, while High-grade Serous Carcinoma (HGSCs) are now universally characterised by TP53 mutations. As a result, serous carcinomas are recognised as two distinct histotypes-Low-grade Serous Carcinoma (LGSC) and HGSC-rather than a single continuum of grades [15].

The 4th (2014) and 5th (2020) editions also introduced changes to uncommon histotypes. Seromucinous carcinoma, previously defined as a tumour composed of serous and endocervical-type mucinous epithelium with clear cells, is now considered a subtype of endometrioid adenocarcinoma with mucinous differentiation. Carcinosarcoma-a biphasic neoplasm containing high-grade carcinomatous and sarcomatous elements-is now classified as a variant of carcinoma rather than a true mixed epithelial-mesenchymal tumour [16]. A comparison of WHO classification updates for ovarian tumours is shown in [Table/Fig-1].

WHO 1973, 1st edition	WHO 2003, 2nd edition	WHO 2014, 3rd edition	WHO 2020, 5th edition
Serous	Serous	High-grade serous	High-grade serous
		Low-grade serous	Low-grade serous
Mucinous	Mucinous	Mucinous	Mucinous
		Seromucinous	
Endometrioid	Endometrioid	Endometrioid	Endometrioid
Clear cell	Clear cell	Clear cell	Clear cell
Brenner	Transitional cell squamous	Brenner	Brenner
Undifferentiated	Undifferentiated	Undifferentiated	Mesonephric like
			Undifferentiated
			Carcinosarcoma
Mixed	Mixed	Mixed	Mixed

[Table/Fig-1]: Comparison of various WHO updates in ovarian tumours classifications [16].

Study objectives:

- To study the histomorphological features, age-related occurrence, and types of ovarian tumours.
- To evaluate ovarian tumour expression using IHC markers.
- To differentiate between primary ovarian tumours and metastatic tumours based on IHC.

MATERIALS AND METHODS

The present ambispective cross-sectional study was conducted on 188 cases at Sri Aurobindo Institute of Medical Sciences, Indore, Madhya Pradesh, India, after obtaining approval from the Institutional Research Board and Ethics Committee (Reference No. SAIMS/IEC/50/24). The study included two years of data: 13 months of retrospective cases from January 2023 to January 2024, and 11 months of prospective cases from February to December 2024.

Inclusion criteria: All core needle biopsies of ovarian masses, oophorectomy specimens, and omental biopsy specimens received in 10% formalin in the Department of Pathology during the study period.

Exclusion criteria: All biopsies/specimens reported as non-neoplastic lesions.

Study Procedure

Histopathology and IHC slides of all newly diagnosed ovarian neoplasms were retrieved from the Surgical Pathology section. Details including investigations, clinical history, physical examination findings, and provisional diagnoses were collected from the Medical Records Department for admitted patients. Tissue samples were processed as per standard operating procedures, and sections were stained with routine H&E stain and examined microscopically. IHC was performed in 58 cases-37 adnexal mass cases and 21 metastatic cases with adnexal involvement. Common primary markers used were CK7, CK20, PAX8, and WT1 to identify primary ovarian tumours. Secondary markers such as CDX2, SATB2, ER, PR, GATA Binding Protein 3 (GATA3), and Calretinin were utilised to differentiate tumours of FGT, GIT, breast, and metastatic origin. Additional markers like Inhibin and Octamer-binding transcription

factor 3/4 (OCT3/4) were used for morphological subtyping of sex cord-stromal and germ cell tumours.

Appropriate positive and negative controls were included in each batch of IHC staining [10,11]. An Immunohistochemical Composite Score (ICS) was calculated by multiplying the distribution and intensity scores (range: 0-5). Intensity, distribution, and ICS were assessed by calculating the percentage of positive nuclei in a count of 100 nuclei in the best-stained area (400×).

Scoring was as follows:

0 = negative or occasional positive cells

1+ = <10% cells positive

2+ = 10-25% cells positive

3+ = 26-50% cells positive

4+ = 51-75% cells positive

5+ = >75% cells positive

Key IHC markers and their expression patterns are summarised below.

* p53: A significant marker for HGSC.

HGSC: Shows strong, diffuse nuclear staining (indicative of a missense mutation).

- **p53:** A significant marker for HGSC.
  - **HGSC:** Shows strong, diffuse nuclear staining (indicative of a missense mutation).
  - **LGSC:** Shows weak or focal staining.
- **WT1:** Another marker that is diffusely positive in HGSCs.
  - **HGSC:** High staining scores.
  - **LGSC:** Lower staining scores.
- **p16:** High p16 staining is also more frequent in high-grade serous tumours than in low-grade tumours [17].

All tumours with a 3+ score were taken as positive and included in the study.

STATISTICAL ANALYSIS

Data analysis was performed using Microsoft Excel spreadsheets, and Microsoft (MS) Word was used to generate tables and graphs. Proportions were expressed as percentages. Data were reported as mean±standard deviation. The frequency of lesions was described using numbers and percentages.

RESULTS

Age: A total of 188 cases were studied. The median age of the patients was 51 years, with 115 patients above 50 years of age and 73 patients below 50 years. The oldest patient was 75 years old with serous carcinoma, and the youngest was a 14-year-old diagnosed with a Leydig cell tumour.

Symptoms: The most common presenting symptom was an abdominopelvic mass, seen in 78 cases (41.48%), followed by 40 cases (21.27%) of ascites. Pain over the flanks was noted in 28 cases (14.89%), and weight loss in 13 cases (6.91%). Less common symptoms included omental nodules and pain in five cases (2.65%). Four cases (2.12%) each reported nausea, change in bowel habits, loss of appetite, feeling of fullness, urinary frequency, and breathing difficulty.

Laterality: Based on radiological imaging, among the 188 cases, 153 were unilateral ovarian masses, of which 131 (85.62%) were benign, 16 (10.45%) were borderline, and 6 (3.92%) were malignant.

A total of 35 cases had bilateral ovarian masses, of which 33 (94.28%) were malignant and 2 (5.71%) were benign. The distribution according to laterality is shown in [Table/Fig-2]. In the current study, surface epithelial tumours comprised 149 cases (79.25%) and were the most common tumour group. These included 82 benign serous cystadenomas (43.61%), 24 malignant serous adenocarcinoma (12.76%), and 22 mucinous cystadenomas (11.70%). Most metastatic tumours (21 cases), presenting with omental nodules and pain, were of serous carcinoma type [Table/Fig-3].

Laterality	Benign (n=133)	Borderline (n=16)	Malignant (n=39)
Unilateral	131(85.62%)	16 (10.45%)	6 (3.92%)
Bilateral	2 (3.71%)	-	33 (94.28%)
	133	**16**	**39**
Total	**188 (100%)**		

[Table/Fig-2]: Distribution of ovarian masses as per laterality (n=188).

Type of tumours		No. of cases	Percentage
Total suface epithelial tumours		**149 (79.25%)**	
Surface epithelial tumours	Benign	104 cases (55.31%)	
	Serous cystadenoma	82	43.61%
	Mucinous cystadenoma	22	11.70%
	Borderline epithelial cell tumour	16 cases (18.5%)	
	Serous Borderline Tumours (SBT)	11	5.85%
	Mucinous Borderline Tumours (MBT)	5	2.65%
	Malignant	29 cases (15.42%)	
	Primary serous adenocarcinoma	24	12.76%
	Poorly differentiated carcinoma	3	1.59%
	Neuroendocrine carcinoma (small cell carcinoma)	1	0.53%
	Mucinous carcinoma	1	0.53%
Total sex cord stromal tumours		**8 (4%)**	
Sex cord stromal tumours	Fibroma	3	1.59%
	Adult granulosa cell tumour	4	2.12%
	Sertoli-Leydig cell tumour	1	0.53%
Germ cell tumours		**2 (2%)**	
	Mature cystic teratoma	2	1.06%
Total tumour like lesion		**8 (4%)**	
Tumour like lesion	Simple follicle cyst	2	1.06%
	Corpus luteal cyst	6	3.19%
Total cases of metastases		**21 (11%)**	
Distant metastases	Metastatic serous carcinoma	20	10.63%
	Metastatic papillary carcinoma	1	0.60%
Total cases		**188 (100%)**	

[Table/Fig-3]: Distribution of cases as per histological types of ovarian neoplasms (n=188).

Of the 188 total cases, 58 cases were selected for IHC evaluation, including 37 cases of primary ovarian tumours. The distribution was as follows: 27 serous carcinomas, 4 adult granulosa cell tumours, and one case (1%) each of mucinous carcinoma, neuroendocrine carcinoma (small cell carcinoma), Sertoli-Leydig cell tumour, seromucinous cystadenoma, borderline serous tumour, and mature cystic teratoma [Table/Fig-4]. A total of 21 cases were metastatic carcinomas, with the final IHC diagnosis being metastatic serous adenocarcinoma of ovarian origin [Table/Fig-5].

Immunohistochemical evaluation of primary ovarian tumours: IHC evaluation was performed using common markers for the FGT, including CK7, CK20, WT1, ER, and PAX8. Serous adenocarcinoma, the most common ovarian tumour marker profile, showed positivity for WT1 and PAX8.

Specific differentiating markers included:

- CK20- / inhibin+ for granulosa cell tumour
- Inhibin and Melan-A for Sertoli-Leydig cell tumour

To differentiate metastatic ovarian tumours from gastrointestinal and other origins, markers such as CK7, CK20, CDX2, SATB2, Cancer

Final IHC diagnosis	IHC markers									Other specific markers
	No	CK7	CK20	CDX2	SATB2	PAX8	WT1	ER	Inhibin	
Serous carcinoma	27	27+	27-	27-	27-	26+1-	27+	24+3-	-	
Adult granulosa cell tumour	4	4+	4-	4-	4-	2+2-	4-	3+1-	3+	
Mucinous carcinoma	1	+	-	-	-	+	-	-	-	MUC1+, CA125+,P53+
Neuroendocrine (Small cell carcinoma)	1	-	-	+	-	-	-	-	-	PANCK+, Synaptophysin, chromogranin+, KI67-40%
Sertoli Leydig cell tumour	1	+	-	-	-	-	+	-	+	Melanin+,CD99+WT1+,MUC1-
Seromucinous cystadenoma	1	+	-	-	-	+	+	-	-	MUC1+
Borderline serous tumour	1	+	-	-	-	-	+	+	-	P16-, P53-
Mature teratoma	1	+	-	-	-	-	-	-	-	Panck+,OCT3/4 focal+, AFP focal+, GATA +, CD117-, SALL4-
Total ovarian tumours	37									

[Table/Fig-4]: Distribution of ovarian tumour cases as per IHC results (n=37).

Final IHC diagnosis of metastatic carcinoma of ovarian origin	IHC markers									Other specific markers
	Serial No	CK7	CK20	CDX2	SATB2	PAX8	WT1	ER	Inhibin	
Serous carcinoma	21	21+	21-	21-	21-	21+	21+	21+	21-	AE1/AE3, CA125+, TTF1-, Desmin-, GATA3-

[Table/Fig-5]: IHC evaluation of metastatic tumour cases (n=21).

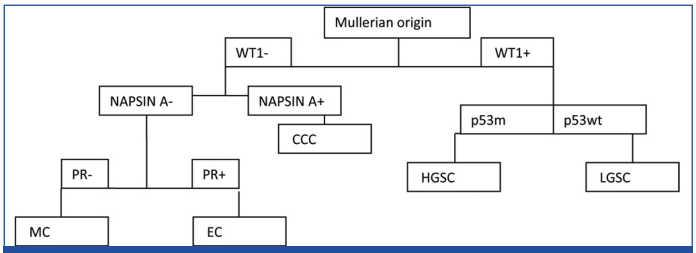
Antigen 125 (CA125), Thyroid Transcription Factor 1 (TTF-1), desmin, and GATA3 were used.

DISCUSSION

The IHC evaluation approach for ovarian tumour: IHC evaluation for primary ovarian tumours used common FGT markers (CK7, CK20, WT1, ER, PAX8). Serous adenocarcinoma commonly showed WT1 and PAX8 positivity. Granulosa cell tumours were identified using CK20- / inhibin+ markers, and Sertoli-Leydig cell tumours with inhibin and Melan-A. For distinguishing metastatic tumours from gastrointestinal origins, markers such as CK7, CK20, CDX2, and SATB2 were utilised.

After several revisions, a four-marker IHC panel capable of distinguishing the five major histotypes of ovarian carcinomas with ~90% accuracy was developed and validated. Integrating morphology with ancillary IHC increases diagnostic precision to >95%, given that morphological diagnosis alone has ~90% accuracy [10]. [Table/Fig-6,7] present the IHC panel used for differentiating the major histotypes of ovarian carcinomas [18].

Age: In the present study, out of a total of 188 cases, the median age of the patients was 51 years. Among them, 115 patients were above 50 years of age and 73 were below 50 years. The oldest patient was 75 years old and diagnosed with serous carcinoma, while the youngest patient was 14 years old and diagnosed with a Leydig cell tumour. The age-wise comparison of cases with various studies is shown in [Table/Fig-8] [3,19,20].



[Table/Fig-6]: A primary panel of four marker IHC panel can differentiate the five major histotypes of ovarian carcinomas: high-grade serous, low-grade serous, endometrioid, clear cell, and MCs. PAX8 can be used as a general Mullerian marker however it has weak sensitivity for endometrioid and MCs, as well as limited specificity for renal and thyroid primary. NAPSA is an abbreviation for napsin A, which is used to treat endometrioid and MCs with a focus on the kidney and thyroid [18].
MC: Mucinous carcinoma; EC: Endometrioid carcinoma

Symptoms: In the present study, the most common presenting symptom was a lump or mass in the abdomen or pelvic region (n=78, 41.48%), which is similar to the findings of Dilley J et al., [9] (n=225, 39.19%) and Chandanwale SS et al., (n=19, 38.00%) [3].

Histotype 1	Histotype 2	First line panel	Second line panel
HGSC	EC	WT1/p53: WT1+/p53abn combination is 99% specific for HGSC	MMR and ARID1A have limited sensitivity (12% and 25%, respectively) for EC but are specific. PR, ELAPOR1 have limited discriminatory values as they are present in 85% of ECs versus 40% of HGSCs. Nuclear CTNNB1 expression is specific for ECs and present in -50%, mostly low grade ECs with squamous differentiation. Consider testing for somatic BRCA1/2 or HRD.
HGSC	LGSC	P53: p53abn excluded LGSC (100% specific); however, 2-4% of HGSCs can show p53 wild type staining despite harbouring a TP53 mutation due to a non-functional but expressed protein.	p16: in the context of p53 wild type staining, if p16shows normal patchy/ heterogenous expression, the probability of LGSC is 84%, if p16 is block diffuse, the probability of HGSC is 88%. Rare cases of p53wild, p16 block diffuse LGSC do exist, but they seem to carry an adverse outcome. Consider sequencing for MAPK pathyway mutations.

[Table/Fig-7]: First and second-line immunohistochemical panels for differential diagnoses of two specific histotypes of ovarian carcinoma. (i.e., any staining) + is present; - means absent expression. Certain markers have specific cut-off [14].
MMR: Mismatch repair; p53abn: p53 abnormal; HRD: Homologous repair deficiency; ELAPOR1: Endosome/Lysosome-Associated Apoptosis and Autophagy Regulator 1; CTNNb1: Catenin beta-1; BRCA1: BReast CAncer gene 1; HRD: Homologous recombination deficiency

Age group	Present study 2024 n=188	Prakash A et al., [19] 2017 n=229	Chandanwalle SS et al., [3] 2017 n=50	Bankhead Cr et al., [20] 2008 n=46
>50 years age group	n=115, 61.17%	n=135, 59.1%	n=28, 56.00%	n=17, 38.63%
>50 years age group	n=73, 38.82%	n=94, 40.9%	n=22, 44.00%	n=29, 65.90%

[Table/Fig-8]: Age group wise comparison of cases with previous studies [3,19,20].

In contrast, the study by Kanthikar SN et al., reported this symptom in 20.00% of cases, whereas Goff BA et al., reported it in 63.63% of cases. The second most common symptom in our study was abdominal or pelvic pain (n=40, 21.27%). This finding is comparable to the study by Dilley J et al., (n=227, 39.54%), Goff BA et al., (n=8, 18.18%), and Chandanwale SS et al., (n=8, 16.00%). In the study by Kanthikar SN et al., abdominal pain was reported in 22 cases (29.33%) [Table/Fig-9] [3,9,21,22].

Laterality: Based on radiological imaging and patient history, out of 188 cases in the present study, 153 were unilateral, of which

Clinical presentation	Comparison of clinical presentation with other studies				
	Present study, 2024 (n=188)	Diley J et al., [9], 2020 (n=574)	Chandanwalle SS et al., [3], 2017 (n=50)	Kanthikar SN et al., [21], 2014 (n=75)	Goff BA et al., [22], 2004 (n=44)
Lump/mass/ increased abdominal size felt over abdomen/ pelvic region	78 (41.48%)	225 (39.19%)	19 (38.00%)	15 (20.00%)	28 (63.63%)
Abdomen or pelvic pain	40 (21.27%)	227 (39.54%)	8 (16.00%)	22 (29.33%)	8 (18.18%)
Ascites with bloating	28 (14.89%)	-	-	-	-

[Table/Fig-9]: Comparison of clinical presentation of cases with previous studies [3,9,21,22].

131 (85.62%) were benign, 16 (10.45%) were borderline, and 6 (3.92%) were malignant. A total of 35 cases were bilateral fused masses, including 2 (5.71%) benign and 33 (94.28%) malignant tumours.

These findings are comparable to earlier studies: Jindal M et al., [23]: Among 358 cases, 143 were unilateral (134 benign, 1 borderline, 8 malignant). Among 215 bilateral cases, 150 (69.76%) were malignant, 3 (1.39%) borderline, and 62 (28.83%) benign. The findings of the present study are in concordance with these studies, indicating that benign tumours predominantly present unilaterally, while malignant tumours are more commonly bilateral.

Ovarian histological types: In the current study, the histomorphological classification of ovarian tumours was performed according to the WHO 2020 guidelines. A total of 188 cases were analysed, of which:

149 cases (79.25%) were surface epithelial tumours:

- Benign tumours (n = 104; 55.31%): Serous cystadenoma and mucinous cystadenoma
- Borderline tumours (n = 16; 10.73%): Serous and mucinous borderline tumours
- Malignant tumours (n = 29; 19.46%): Primary serous carcinoma, poorly differentiated carcinoma, neuroendocrine carcinoma, and mucinous carcinoma
- 21 cases (11.17%) were metastatic serous carcinoma of ovarian origin
- 8 cases (4.25%) were sex cord-stromal tumours (fibromas)
- 2 cases (1.06%) were germ cell tumours (mature cystic teratoma)
- 8 cases (4.25%) were tumour-like lesions (2 simple follicular cysts and 6 corpus luteal cysts) [Table/Fig-10] [23-27]

The findings of the present study are consistent with the observations of Jindal M et al., Sudha V et al., Gaikwad S et al., Gupta N et al., Shanthi V et al., who also reported surface epithelial tumours as the most common histological type [23-27].

IHC profile in primary surface epithelial tumours of ovary: In the present study, based on morphological types, 58 out of 188 cases underwent IHC evaluation. Among these 58 cases, 50 were malignant ovarian tumours, including 27 (46.55%) cases of primary serous carcinoma, and 21 (36.20%) cases of metastatic carcinoma (20 metastatic serous carcinomas and 1 metastatic papillary carcinoma of the ovary). Additionally, there was 1 (1.72%) case of mucinous carcinoma and 1 (1.72%) case of neuroendocrine carcinoma (small cell carcinoma). A few benign ovarian tumours were also evaluated using IHC markers. Out of the 58 cases assessed, 8 were benign: 4 (50%) cases of adult granulosa cell tumour, 1 (12.50%) borderline serous cystadenoma, 1 (12.50%) Sertoli-Leydig cell tumour, 1 (12.50%) seromucinous cystadenoma, and 1 (12.50%) mature teratoma.

The findings of the present study are in concordance with the studies by Kriplani D et al., Ji R et al., and Baloglu D et al., in which CK7 and WT1 showed 100% positivity, while CK20 was negative in all cases. In contrast, Kanwal M et al. studied 63 cases of serous adenocarcinoma and reported CK7 positivity in 38 (60%) cases and WT1 positivity in 50 (79%) cases [Table/Fig-11] [1,28-30]. [Table/Fig-12] shows IHC images of primary ovarian serous carcinoma demonstrating CK7 and WT1 positivity with CK20 negativity. [Table/Fig-13] shows IHC images of metastatic serous carcinoma with CK7 and ER positivity, along with Ki-67 nuclear proliferation index positivity.

IHC profile in metastatic ovarian adenocarcinoma: In the present study, 21 cases of metastatic ovarian carcinoma were identified, presenting as omental deposits, peritoneal deposits, or malignant ascites. IHC evaluation was performed using an algorithmic approach starting with CK7+/CK20-, followed by markers to exclude other primary origins: SATB2 and CDX2 for gastrointestinal tumours; GATA3 for breast carcinoma; and WT1, ER, PAX8, and p53 to differentiate Endometrioid Carcinoma (EC) of endometrial origin from that of ovarian origin.

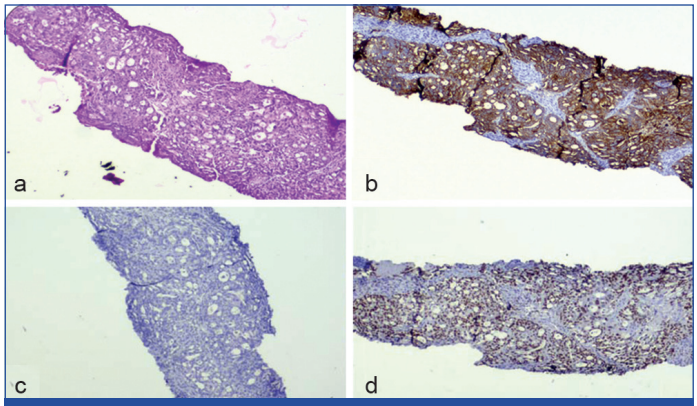
Studies	Total cases (N)	Surface epithelial cells tumour	Sex cord stromal cell tumour	Germ cell tumour	Tumour like lesion	Metastatic tumour of ovarian origin
Sudha V et al., [23], 2023	92	59(64.13%)	8(8.69%)	24(26.08%)	-	1(1.08%)
Gaikwad SL et al., [24], 2020	84	63(75.00%)	4(4.76%)	17(20.23%)	-	-
Jindal M et al., [25], 2019	358	288(80.44%)	40(11.17%)	26(7.26%)	2(0.55%)	2(0.55%)
Gupta N et al., [26], 2019	214	152(71.02%)	8(3.73%)	47(21.96%)	5(2.33%)	2(0.93%)
Shanti V et al., [27], 2015	156	132(84.61%)	6(3.84%)	17(10.89%)	-	1(0.64%)
Present study (2024)	188	149(79.25%)	8(4.25%)	2(1.06%)	8(4.25%)	21(11.17%)

[Table/Fig-10]: Comparison of histological types of ovarian tumours with other studies [23-27].

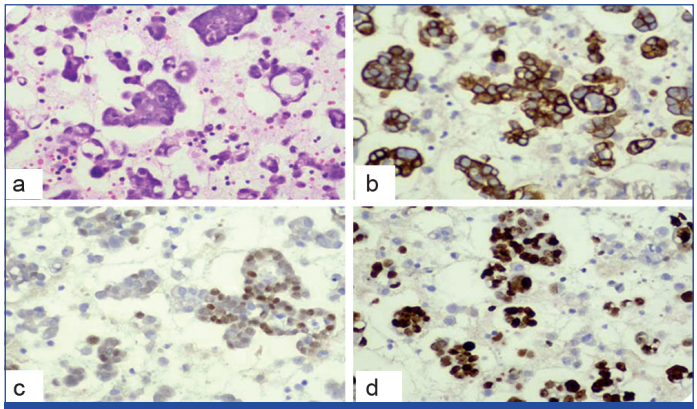
Comparison of studies	IHC markers for comparison									Other specific markers
	(N)	CK7	CK 20	CDX2	SATB2	PAX8	WT1	ER	Inhibin	
Serous carcinoma										
Kanwal M et al., [28] 2024	63	38+ (60%) 23-	-63 (100%)	-	-	-	50+ 13- (79%)	40+ 23- (63%)	-	P53 53+, CA125 48+,
Baloglu D et al., [29] 2020	16	16+ (100%)	15- 1+ (90%)	-	-	8+ 8- (50%)	-	16+ (100%)	-	
Ji R et al., [30], 2020	49	46+ (+93%)	3+ 46- (6%)	-	-	-	-	49+ (100%)	-	Her246-,

Kriplani D et al., [1] 2013	22	22+ (100%)	22- (100%)	-	-	18+ (81%)	18+ (81%)	8+ (36%)	-	CA125,
Present study, 2024	27	27+ (100%)	27- (100%)	27-	27-	26+ 1- (98%)	27+ (100%)	24+ 3- (88%)	-	
Mucinous carcinoma										
Kanwal M et al., [28] 2024	4	4+ (100%)	1+ 3-	-	-	-	-	3+ 1-	-	CA125 3+
Kriplani D et al., [1] 2013	5	1+ (10%)	4- (100%)	-	-	-	5-	5-	-	CEA 3+, CA125 1+
Present study 2024	1	1+ (100%)	-	-	-	1+	-	-	-	MUC1+, CA125+,P53+

[Table/Fig-11]: Comparison of IHC evaluation of ovarian tumours with previous studies [1,28-30].



[Table/Fig-12]: a) Histopathological examination of HGSC on core biopsy of lobules, nest and sheets; b) CK7 IHC showing diffuse positive; c) CK20 negative for core biopsy; d) WT1 nuclear positivity in the tumour cells.



[Table/Fig-13]: a) Clusters of metastatic serous carcinoma of ovary in pleural fluid; b) CK7 positive tumour cells; c) ER positive tumour cells in nucleus of clusters of cells; d) Ki67 shows nuclear positivity for tumour cells.

Limitation(s)

The present study included IHC evaluation for only 58 cases, which limits the overall dataset. Correlation with serological tumour markers was not performed, which could have strengthened the diagnostic associations.

CONCLUSION(S)

Ovarian neoplasms exhibit a wide range of clinico-morphological and histological features. Surface epithelial tumours, particularly benign serous cystadenomas, were the most common neoplasms observed and typically affected women in the reproductive age group. IHC has played a significant role in recent years as an essential diagnostic tool in ovarian pathology. A judiciously selected panel of IHC markers, combined with clinical correlation, gross examination, and extensive microscopic sampling, enhances diagnostic accuracy.

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