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Research Article

Prospective study of histopathological patterns of ovarian tumours in a tertiary care centre

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ABSTRACT

Background: Ovarian tumours account for 3% of all cancers amongst women, being the second most common cancer of the female genital tract. The ovarian tumours are highly heterogenous with a wide range of histological patterns. Aim of current study was to study the histological patterns and the age incidence of the ovarian tumours in our institute.
Methods: The present study is a prospective study conducted in the department of pathology, Andhra Medical College, from August 2011 to July 2013.
Results: We received a total of 267 specimens of ovarian tumours during this period, out of which, 263 were primary and 4 were secondary tumours. Benign tumours were 209 (78.3%), borderline were 10 (3.7%) and malignant were 48 (18%) in numbers. Overall surface epithelial tumours constituted the majority of tumours accounting for 214 (80.2%) cases, followed by germ cell tumours 38 (14.2%) and sexcord stromal tumours 11 (4.1%). The single most common tumour diagnosed was serous cystadenoma. The most common malignant tumour was serous cystadenocarcinoma. The age groups affected ranged from 11-70 years. The peak age incidences for different histological types were as follows: surface epithelial tumours: 21-50 years, germ cell tumours: 21-30 years, sexcord stromal tumours: 51-60years. Benign tumours were more common in 21-40 years of age, borderline in 31-50 years and malignant tumours in 41-50 years age group.
Conclusion: The results from our study were comparable with those reported in literature; however malignant serous and mucinous tumours showed a lower peak age incidence in our study. Krukenberg tumours also occurred in younger age group in our study.

Keywords: Ovarian tumours, Histopathological patterns, Age groups

INTRODUCTION

Ovarian tumours account for 3% of all cancers in females, being the second most common cancer of the female genital tract, next only to uterine cancer.[1] They account for 30% of all cancers of the female genital tract.[2] Ovarian tumours often go undetected and present at a later stage. This is due to their location, lack of early screening modalities and, lack of specific symptoms and signs suggestive of malignant nature. The advanced stage at presentation of ovarian cancers results in a low mean 5 year survival rate and a poor prognosis.[2] The ovarian tumours are highly heterogenous with a wide range of histologic patterns enumerated in the WHO classification. The gross appearances are useful to a certain extent in distinguishing the individual tumours, more so for the

distinction of the benign from the malignant ones. However a sound knowledge of the microscopic features is essential for an accurate diagnosis. Age of the patient is one feature that helps and guides in diagnosis. Broadly the ovarian tumours are classified into primary and secondary tumours. Surface epithelial stromal tumours, Germ cell tumours and Sexcord stromal tumours are more common among the primary tumours of the ovary.

Aims

1. To study the histological patterns of ovarian tumours in our Institute.
2. To study the prevalence of ovarian tumours in various age groups.

METHODS

This is a prospective study conducted in the department of Pathology, Andhra Medical College from August 2011 to July 2013. We received a total of 267 specimens of ovarian tumours during this period. All the specimens were grossed according to standard grossing protocols. Formalin fixed paraffin embedded sections were stained with haematoxylin and eosin and examined microscopically. Immunohistochemistry studies were employed wherever necessary.

RESULTS

Out of the 267 ovarian tumours received, 263 were primary and 4 were secondary tumours. The age groups affected ranged from 11 years to 70 years. Majority ($4/5^{th}$) were surface epithelial stromal type (SEST) (80.2%) followed by germ cell tumours (GCT) (14.2%) and sexcord stromal tumours (SCST) (4.1%).The frequency distribution of the major subtypes is shown in Table 1.

Table 1: Major histologic subtypes of ovarian tumours in our institute.

Histologic type	Frequency
Total	267
Primary	263 (98.5%)
Surface epithelial stromal	214 (80.2%)
Germ cell	38 (14.2%)
Sexcord stromal	11 (4.1%)
Secondary	4 (1.5%)

Among the surface epithelial stromal tumours, benign tumours (Figure 1-5) were most frequent and malignant ones were more common than borderline tumours. Overall serous tumours were most common followed by mucinous, mixed epithelial and endometrioid tumours in decreasing order. In the malignant category, majority were serous tumours followed by mucinous and endometrioid tumours (Figure 6-11). In the borderline category mucinous tumours were more common. All the endomerioid tumours were malignant. The frequency distribution of the SEST and their sub-categorization into benign, borderline and malignant are shown in Table 2. Among the benign tumours, 7 were serous cystadenofibromas; there was one case of seromucinous cystadenofibroma in the borderline mixed epithelial group. We encountered 3 rare synchronous tumours of the ovary and uterus; one case of ovarian papillary serous cystadenocarcinoma with uterine endometrial carcinoma (Figure 24-26), one case of papillary serous cystadenocarcinoma with endocervical carcinoma and one case of ovarian endometrioid cancer with uterine endometrial cancer.

Table 2: Histologic subtypes of surface epithelial stromal tumours with sub-categorization into benign, borderline and malignant and their frequency distribution.

Histologic subtype	Total (Freq-uency)	Benign	Borde-rline	Malign-ant
Serous	109	90 (82.6%)	-	19 (17.4%)
Mucinous	84	69 (82.2%)	7 (8.3%)	8 (9.5%)
Mixed epithelial	13	10 (77%)	3 (13%)	
Endometri-oid	8	-	-	8 (100%)
Total	214	169 (79%)	10 (4.7%)	35 (16.3%)

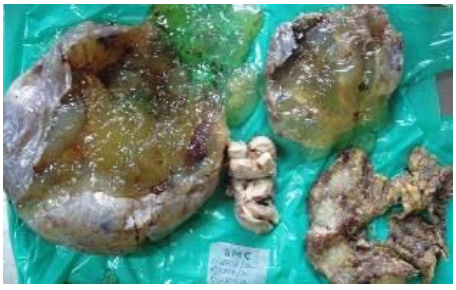

Figure 1: Mucinous cystadenoma: Gross photograph showing bilateral ovarian cysts filled with mucin, along with uterus and omentum.

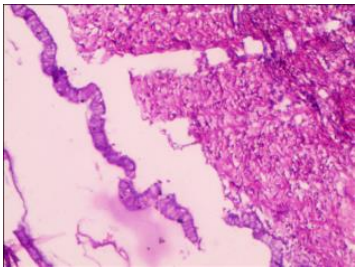

Figure 2: Mucinous cystadenoma: Photomicrograph showing cyst wall lined by columnar epithelium with mucin filled cytoplasm and basal nuclei (H&E: 100X).

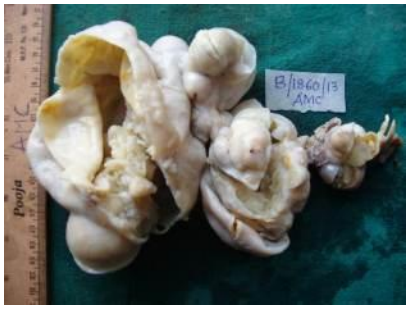

Figure 3: Mucinous cystadenofibroma: Gross photograph showing ovarian cyst with foci of solid areas.

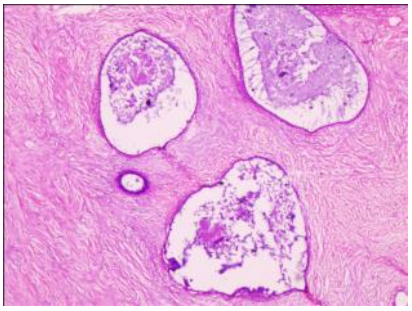

Figure 4: Mucinous cystadenofibroma: Photomicrograph showing mucin filled cysts embedded in fibrous stroma (H&E: 40X).

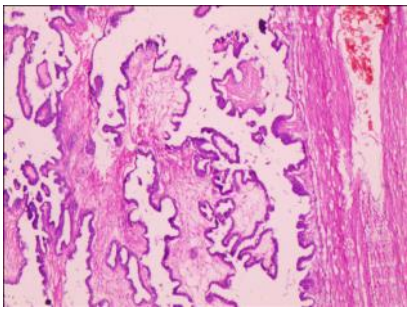

Figure 5: Papillary serous cystadenoma: Photomicrograph showing cyst wall with papillary excresences, lined by cuboidal epithelium (H&E: 40X).

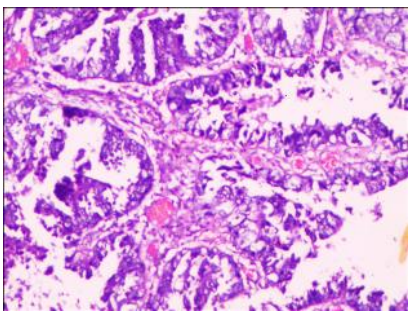

Figure 6: Papillary serous cystadenocarcinoma: Photomicrograph showing branching papillary structures with fibrovascular cores and lined by cells with atypical nuclei (H&E: 100X).

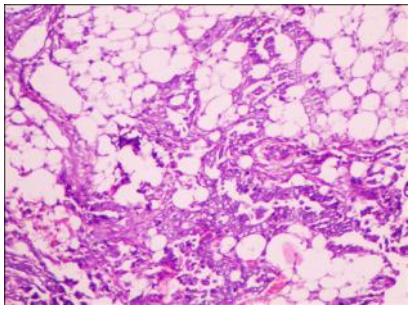

Figure 7: Papillary serous cystadenocarcinoma: Photomicrograph showing omental metastases. (H&E: 100X).

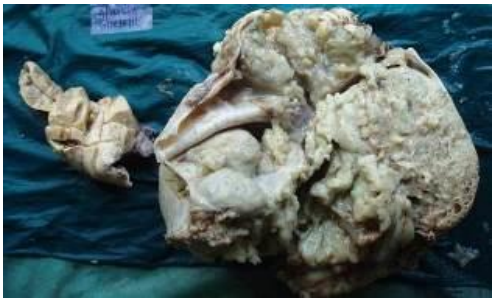

Figure 8: Mucinous adenocarcinoma: Gross photograph showing solid and cystic areas filled with mucinous material.

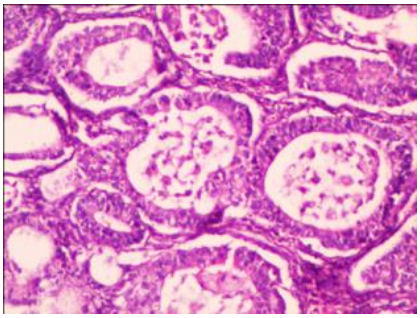

Figure 9: Mucinous adenocarcinoma: Photomicrograph showing irregular glandular structures lined by cells with atypical nuclei, lumen filled with mucin (H&E: 100X).

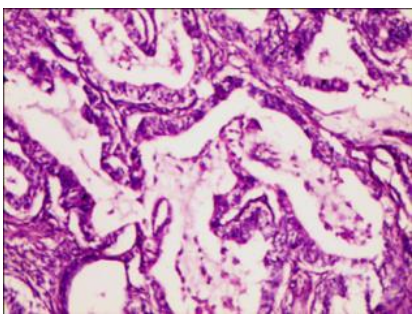

Figure 10: Mucinous adenocarcinoma: Photomicrograph showing irregular dilated glandular structures lined by cells with atypical nuclei, lumen filled with mucin (H&E: 100X).

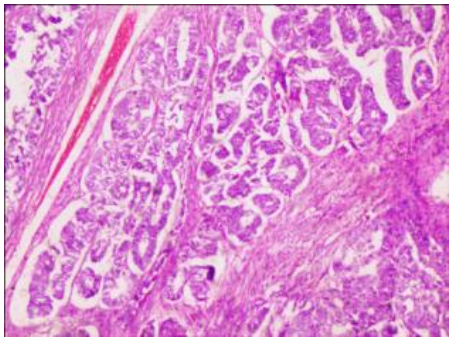

Figure 11: Endometrioid carcinoma: Photomicrograph showing closely packed malignant glands resembling endometrial glands (H&E: 100X).

In the germ cell category, mature cystic teratoma was the most common histologic subtype (86.8%) followed by dysgerminomas (Figure 12 and 13) and mixed germ cell tumours. The frequency distribution of the germ cell tumours is shown in Table 3. We encountered a rare case of mature cystic teratoma with foci of squamous cell carcinoma, which was confirmed by immunohistochemistry studies that showed positivity for CK 5/6 within the malignant foci (Figure 14-17). Among the mixed germ cell tumours one showed features of dysgerminoma with yolksac tumour, the other showed features of yolksac tumour with embryonal carcinoma.

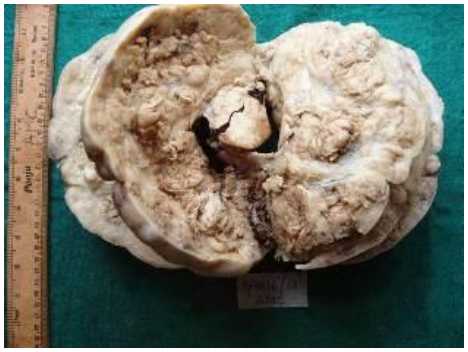

Figure 12: Dysgerminoma: Gross photograph showing solid tumour with lobulation on cutsection.

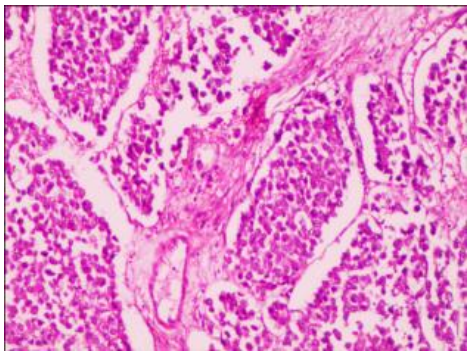

Figure 13: Dysgerminoma: Photomicrograph showing nests of tumour cells separated by fibrous septae, monotonous appearing cells with pale cytoplasm and uniform nuclei (H&E: 100X).

Table 3: Histologic subtypes of germ cell tumours and their frequency distribution.

Histologic subtype	Frequency
Total	38
Teratoma	34
Benign mature cystic	33
Mature cystic with SCC	1
Dysgerminoma	2
Mixed germ cell	2
Dysgerminoma with yolk sac tumour	1
Yolk sac tumour with embryonal carcinoma	1

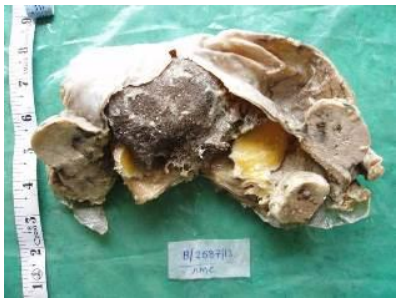

Figure 14: Mature cystic teratoma: Gross photograph showing cystic tumour with hair, adipose tissue along with a solid area (arrow).

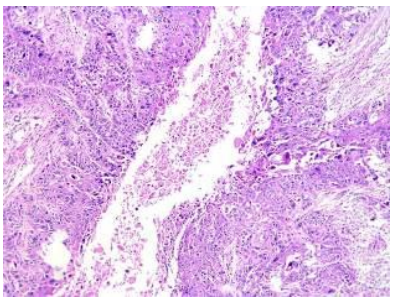

Figure 15: Photomicrograph of mature cystic teratoma showing foci with features of squamous cell carcinoma in sections taken from the solid area (H&E: 40X).

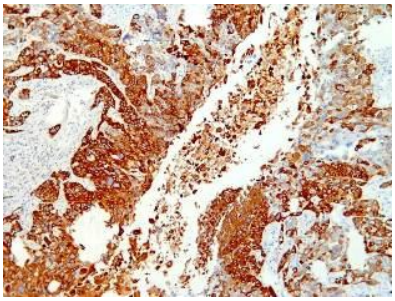

Figure 16: Mature cystic teratoma with foci of squamous cell carcinoma: Photomicrograph showing CK5/6 positivity in the malignant squamous cells (IHC: 40X).

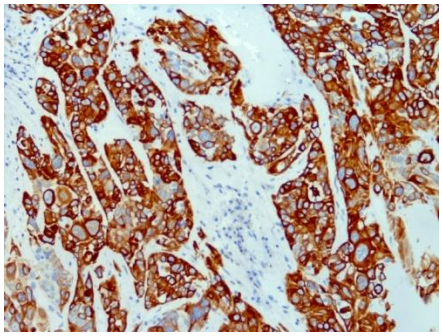

Figure 17: Mature cystic teratoma with foci of squamous cell carcinoma: Photomicrograph showing CK5/6 positivity in the malignant squamous cells (IHC: 100X).

In the sexcord stromal category, majority were fibrothecomas (45.5%) followed by granulosa cell tumours. (Figure 18 and 19). The frequency distribution of the SCST is shown in Table 4.

Figure 18: Adult granulosa cell tumour: Gross photograph showing solid and cystic areas.

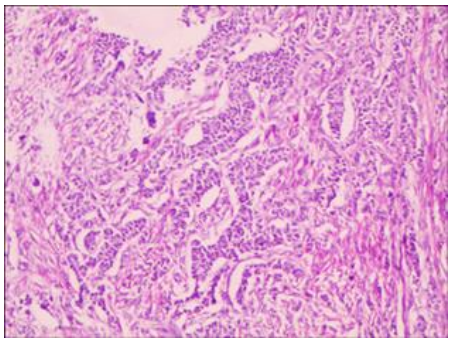

Figure 19: Adult granulosa cell tumour: Photomicrograph showing tumour cells arranged in trabeculae, cords with call-exner bodies (arrow) (H&E: 100X).

Among the secondary tumours, in one case with bilateral enlarged ovaries, one side ovary measured 17×13×6 cms and other side ovary measured 6×4×2 cms. (Figure 20-23).

Table 4: Histologic subtypes of sexcord stromal tumours and their frequency distribution.

Histologic subtype	Frequency
Total	11
Fibrothecoma	5 (45.5%)
Granulosa cell	4
Leydig cell	1
Steroid cell	1

Figure 20: Bilateral Krukenberg tumour: Gross photograph shows bilateral enlarged ovaries along with uterus and omentum.

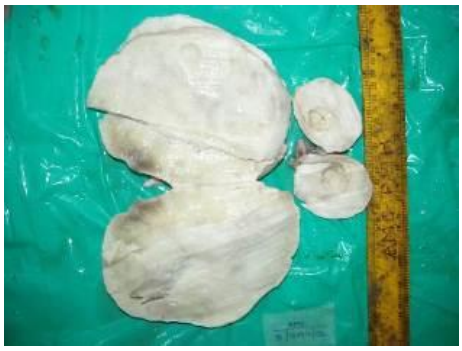

Figure 21: Bilateral Krukenberg tumour: Gross photograph shows bilateral enlarged ovaries; cutsection is uniform and solid.

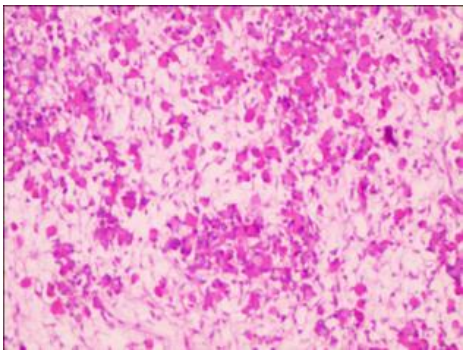

Figure 22: Bilateral Krukenberg tumour: Photomicrographs showing signet ring cells. (H&E: 100X).

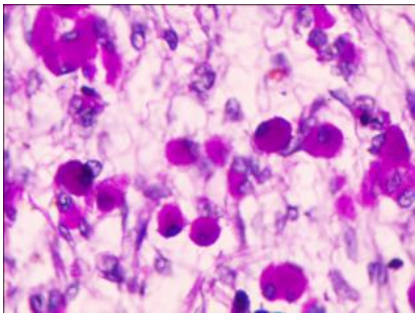

Figure 23: Bilateral Krukenberg tumour: Photomicrographs showing signet cells strongly positive with PAS stain (H&E: 400X).

Figure 24: Synchronous tumour: Gross photograph showing solid and cystic growth with papillary excrescences involving the ovary and a grey white polypoid growth involving uterine endometrium.

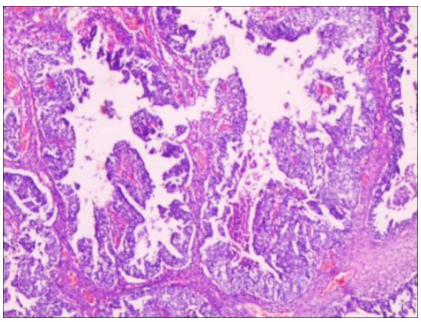

Figure 25: Synchronous tumour: Photomicrograph showing papillary serous adenocarcinoma in ovary (H&E: 40X).

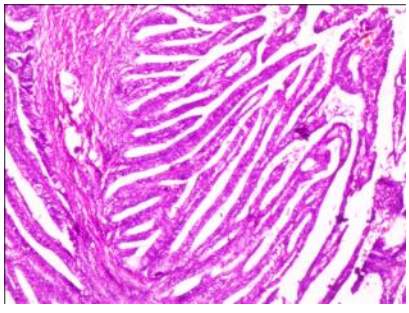

Figure 26: Synchronous tumour: Photomicrograph showing papillary adenocarcinoma involving the uterine endometrium (H&E:40X).

Laterality of the tumours

The primary ovarian tumours were mostly unilateral. All the secondary tumours were bilateral. Surface epithelial stromal tumours were bilateral in 7% of cases and they were mostly serous type. Among the serous tumours malignant ones were more often bilateral (5 out of 19 i.e. 26.3%) than benign ones (6 out of 90 i.e.6.7%).

Age distribution

In our study we found that ovarian tumours affected women between 11 years to 70 years of age. The peak age incidences are shown in table 5. Among surface epithelial stromal tumours, benign tumours were most common in 21-40 years, borderline tumours in 31-50 years and malignant tumours in 41-50 years age groups. The benign serous tumours were common in a wide age range of 21-50 years and malignant serous tumours showed a peak in the 41-50 years age group. There were no borderline serous tumours. The mucinous tumours were most common in 31-40 years age group in the benign, borderline and also malignant categories. The endometrioid tumours were more common in the 51-60 years age group. The peak age incidence was 21-30 years for germ cell tumours, 51-60 years for sexcord stromal tumours and secondary tumours occurred in subjects aged between 21-40 years.

Table 5: Peak age incidences for the major histologic subtypes of ovarian tumours.

Histologic subtype	Age group at incidence (years)
Surface epithelial	
Benign	21-40
Borderline	31-50
Malignant	41-50
Germ cell tumours	21-30
Sex cord stromal tumours	51-60
Secondary	21-40

DISCUSSION

In our study majority of the ovarian tumours belonged to the surface epithelial stromal category, accounting for four-fifths of total (80.2%) compared to two-thirds reported in literature[3]. GCT and SCST accounted for 14.2% and 4.1% respectively in our study compared to 30% and 6% reported in literature.[3] A similar but slightly lower rates of SEST (compared to our study) were observed in several other studies.[4-6] However in two other studies,[7,8] SEST constituted a much lesser percentage with a significant proportion being germ cell tumours. The majority were benign tumours in our study and also in other studies.[4,5,8-10] The single most common tumour in

our study was serous cystadenoma (33.7%) followed by mucinous cystadenoma (25.8%) and mature cystic teratoma (12.4%). Similar results were shown in several other studies.[4,5,10] In literature[3] the single most common ovarian tumour reported is mature cystic teratoma. Mature cystic teratoma was the most common followed by serous cystadenoma according to some other studies.[7,8] The most common malignant tumour was serous cystadenocarcinoma followed by mucinous and endometrioid carcinomas in the present study. Similar results were shown in studies by Santosh et al.[4] and Ameena Ashraf et al.[7] The relative frequencies of occurrence of the various tumours in our study are compared with results from other studies, shown in Tables 6, 7 and 8.

Table 6: Comparison studies - frequency distribution of the histologic subtypes of ovarian tumours.

	Present study	Santosh Kumar[4] et al.	Gupta[9] et al.	Kayastha[5] et al.	Pilli[6] et al.	Ameena Ashraf[7] et al.	R. Jha & S. Karki[8]
Total	267	957	96	95	282	127	161
Surface epithelial stromal	80.2% (214)	67.9%	48.8%	72.6%	70.9%	52.76%	52.2%
Germ cell	14.2% (38)	23.1%	23.9%	27.4%	21.2%	43.31%	42.2%
Sexcord stromal	4.1% (11)	5.6%	8.3%	-	6.75	3.15%	3.1%
Secondary	1.5% (4)	10.9%	2%	-	0.7%	0.78%	2.4%

Table 7: Comparison studies: relative frequencies of benign, borderline and malignant tumours.

	Present study	Santosh kumar[4] et al.	Gupta[9] et al.	Kayastha[5] et al.	Ameena Ashraf[7] et al.	R. Jha & S. Karki[8]	Sumaira Yasmin[10] et.al.
Total	267	957	96	95	127	161	68
Benign	78.3%	63.1%	72.9%	90.5%	64.57%	83.9%	89.71%
Borderline	3.7%	7.3%	4.1%	-	-	-	-
Malignant	18%	29.6%	22.9%	9.5%	35.43%	16.1%	10.29%

Table 8: Comparison studies: relative frequencies of various malignant histologic subtypes.

Histologic subtype	Present study	Santosh kumar et al.[4]
Surface epithelial stromal	72.4%	60.9%
Serous	7.1%	11.3%
Mucinous	3%	3.3%
Endometrioid	2.6%	1.25
Clear cell	-	1.5%
Germ cell	10.6%	24.2%
Sexcord stromal	8.5%	3.8%
Secondary	8.5%	8.83%

In the present study, benign serous tumours were found to affect women in a wide age range with a higher percentage in the 21-50 years age group. In literature[3] benign serous tumours are reported to occur at any age with a majority in 5th decade. Other studies[5,8] also showed that serous cystadenomas affect all age groups. The mucinous tumours (including benign, borderline and malignant) showed a peak incidence between 31-40 years in contrast to reports in literature[11] of increasing ages at incidence for benign, borderline and malignant tumours respectively. Endometrioid carcinomas were common in the 41-60 years age groups in our study. A mean age (at incidence) of 52 years was quoted in literature[12]. Most of the secondary tumours were known to occur between 40-50 years with good proportions occurring in women in 3rd decade. However in our study, all the 4 women with secondary ovarian tumours were aged between 21-40

years. The peak age at incidence in various tumours in our study are compared to results from other studies in Tables 9 and 10.

Table 9: Comparison studies: peak age at incidence for various histologic subtypes.

Histologic subtype	Present study	Santosh kumar et al.[4]	Kayastha et al.[5]
Surface epithelial stromal	>11 years (peak 31-50)	>16 years	31-50 years
Germ cell tumours	11-60 years (21-30)	0-30 years	21-30 years
Sexcord stromal tumours	21-70 years (51-60)	All Ages	-
Secondary	21-40	Variable	-

Table 10: Comparison studies: peak age at incidence for benign, borderline and malignant ovarian tumours.

	Present study	Santosh kumar et al.[4]	Kayastha et al.[5]
Benign	21-40 years	21-40 years	All ages
Borderline	31-50 years	21-40 years	
Malignant	41-50 years	41-50 years	>40 years
Benign	21-40 years	21-40 years	All ages

Majority of the ovarian tumours in our study were unilateral. Bilaterality was seen in 10.1% of serous tumours, 4.8% of mucinous tumours and in one case of benign teratoma. A significant proportion of malignant serous tumours were bilateral (26.3%) with even higher percentages quoted in two other studies.[4,8] In the study by Santosh kumar et.al.[4] malignant serous tumours were most common among the bilateral primary tumours. All secondary tumours were bilateral in our study similar to a study by R.Jhaetal[8]. In literature,[3] secondary tumours were reported as bilateral in 70% of the cases.

We encountered a rare case of mature cystic teratoma with foci of squamous cell carcinoma in a female aged 38 years. The incidence of malignancy arising in a mature cystic teratoma is 1-2% with 80% of the carcinomas being squamous cell type.[13] Ten such cases have been reported in one single study.[14]

We reported 3 cases of synchronous tumours. Synchronous tumours are rare and account for 0.7-1.8% of all cancers of the female genital tract,[15] the most common being associations of an ovarian cancer with endometrial cancer. When there is a similar microscopic pattern at both sites, it is most commonly endometrioid type.[16,17]

We also diagnosed one case of leydig cell tumour of the ovary with leydig cell hyperplasia of the other side ovary in a 54 year old postmenopausal woman who presented with hirsutism. Reports of concurrent leydig cell tumour with contralateral hilus cell hyperplasia in the same patient are known.[18]

CONCLUSION

The ovarian tumours in our institute represented a wide histological spectrum. The frequency distribution of the tumours was similar to reports in literature with surface epithelial tumours constituting greater proportions than reported in literature. The single most common tumour was serous cystadenoma in our study. The peak age at incidence for the malignant serous and mucinous tumours was at a younger age compared to those in literature. Metastatic tumours also occurred at younger ages. A significant proportion of the malignant serous tumours were bilateral in our study; bilaterality was more common in the malignant than benign serous tumours. Thus we concluded that malignant serous and mucinous tumours and metastatic tumours occurred at younger ages in our study population.

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Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethical Committee

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