## A STUDY ON CLINICOPATHOLOGICAL SPECTRUM OF OVARIAN TUMOURS IN A TERTIARY CARE CENTRE

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#### ABSTRACT

#### BACKGROUND

Ovarian cancer is the 6<sup>th</sup> most common cancer in worldwide among female population, whereas in India, it is the third most common cancer among women, 1 in 70 women have their lifetime risk to develop this tumour. Survival rate depends on the stage of diagnosis. Although, geographic and racial differences in the incidence of ovarian tumours are well-recognised information regarding any dissimilarity in clinicopathological behaviour is scarce. In the present study, the clinicopathological features of patients with ovarian tumours are evaluated.

## MATERIALS AND METHODS

In a series of 96 clinically and diagnostically-proved ovarian tumours, case history was taken and clinical examination was done. Surgical staging done according to laparotomy, gross morphology and histopathological study was done.

Study Type- Observational study, done in between December 2015-March 2017 in Konaseema Institute of Medical Sciences and RF (Research Foundation).

## RESULTS

Out of 96 cases are studied in Konaseema Institute of Medical Sciences and RF, 59 cases are benign and 32 cases are malignant tumour and 5 cases are borderline malignant potential tumours. Most of the tumour presented within 2 months of onset of symptoms, abdominal distension is commonest presentation in (51% of cases). Almost, 71% of the malignant tumour diagnosed at stage III/IV of the disease.

## CONCLUSION

On histopathological study of these tumours, 73% are surface epithelial tumours. Among surface epithelial tumours, serous tumour is the commonest one. So, early diagnosis and prompt treatment (surgery and chemotherapy) definitely reduce the mortality from ovarian tumour.

#### **KEYWORDS**

Ovarian Tumour, Staging Laparotomy, Abdominal Distension, Surface Epithelial Tumour.

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## BACKGROUND

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Ovarian cancer accounts for about 3% of all cancers in women.<sup>1</sup> It accounts for 15-25% of all gynaecological malignancies, yet it is responsible for approximately 50% of the deaths.<sup>2,3</sup> Among cancers of the female genital tract, the incidence of ovarian cancer ranks only below carcinoma of the cervix and the endometrium.<sup>4</sup> Hormone Replacement Therapy (HRT),<sup>5</sup> tobacco consumption,<sup>6</sup> family history of ovarian cancer and breast cancer<sup>7</sup> and mutation of BRCA1 and/or BRCA2<sup>7</sup> are the principal risk factors of ovarian cancer particularly of Surface Epithelial Tumours (SETs). They arise from different cell lineages and hence constitute

Financial or Other, Competing Interest: None. Submission 08-04-2017, Peer Review 15-04-2017, Acceptance 26-04-2017, Published 06-05-2017. Corresponding Author: Dr. Meenakshi Mohapatro, Room 211, Godavari Block, KIMS Hospital, Amalapuram, East Godavari District, Andhra Pradesh-533201. E-mail: drmeenakshi1988@gmail.com DOI: 10.18410/jebmh/2017/436 a wide variety of neoplastic entities with diverse morphological and clinical manifestations. According to World Health Organization, histological classification, ovarian tumours are subdivided into 5 main categories on the basis of cell of origin according to the tissue of originsurface epithelial stromal tumours, sex cord stromal tumours and germ cell tumours, malignant and not otherwise specified and metastatic non-ovarian tumours from nonovarian primary. Germ cell tumour (mature cystic teratoma) is the commonest benign tumour and epithelial cell tumour (serous cystadenocarcinoma) is the commonest malignant tumour.<sup>8</sup>

Clinicians, especially the gynaecological oncologists face great difficulties in its detection. In early stage, it is mostly either asymptomatic or have nonspecific symptoms and at an advanced stage they can be easily diagnosed, but associated with poor prognosis despite the new chemotherapeutic treatment modalities. This is attributed to the fact that at the time of diagnosis about 70.0% of ovarian cancers have already been widespread intraperitoneal

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metastases.<sup>9</sup> It also represents great challenge to the pathologists because of the wide variety of morphological features. Further, certain nonneoplastic lesions of ovary frequently produce mass lesion in the pelvic or maybe functional with abnormal hormonal manifestations, thus potentially mimicking ovarian neoplasm.

The clinical and gross characteristics provide important diagnostic tool in formulating the differential diagnosis. Age of the patient<sup>10</sup> and the laterality are two important clinical characteristic features. Benign ovarian tumours are more common in young females and malignant tumours are more common in elderly females.<sup>10</sup> Gross features also help to a certain degree in the differential diagnosis like most benign tumours of epithelial origin are cystic. On the other hand, the finding of solid element and papillary projections make malignancy more likely. Nevertheless, accurate diagnosis primarily depends on the histology.<sup>11</sup>

Due to the fatal outcome of this disease, early and accurate diagnosis of ovarian tumour is needed. The recognition of the various histological patterns is important for correct diagnosis, which has important implications for treatment and prognosis.

#### **Aims and Objectives**

This study was carried out with an aim to view the clinicopathological spectrum and sociodemographic variables of ovarian cancer patients and to find out the frequency of different histological types of ovarian tumours, which are prevalent in this part of the country (southern part in the Konaseema area).

#### MATERIALS AND METHODS

This is a prospective cum retrospective study of all patients diagnosed with ovarian tumours during 15-month period from December 2015 to March 2017. Nonneoplastic lesions of ovary were excluded from the study. Clinical data (age), clinical features and gross findings were obtained from the histopathology record section of the institute and haematoxylin and eosin-stained slides were retrieved and reviewed. The available PAS (Periodic Acid-Schiff) stained and mucicarmine-stained slides were also studied and where necessary blocks were recut, stained and reviewed. All the cases of ovarian tumours were classified according to the World Health Organization Classification of Tumours 2003.<sup>12</sup> Data collected were statistically analysed using window-based computer software.

#### **Inclusion Criteria**

In a 96 clinically and diagnostically-proved ovarian tumours, case history and clinical examination done, surgical staging done according to laparotomy, gross morphology and histopathological study was done.

#### **Exclusion Criteria**

Tumour-like lesion and secondary deposits in ovary are excluded from the study.

#### RESULTS

Out of 96 cases studied, majority are benign tumour constituting about 59 (61%) cases, 5 cases are low malignant potential tumour or borderline malignant potential and 32 (33.3%) cases are malignant tumour.

Among the benign tumour, 84% of the cases are seen in 20-40 years of the age group, whereas 81% of cases of malignant tumour are seen after 40 years of age. Median age at which diagnosis can be made is 33 years for benign tumour, 39 years for low malignant potential tumour and around 48 years for malignant tumour. 93% of benign tumour are found in reproductive age group, whereas only 7% of benign tumour are found in menopausal age group. Almost, LMP tumours all are found in reproductive age group and 69% are found in menopausal age group.

Though ovarian tumour mostly associated with nulliparity in our study, 68% of ovarian tumours are associated with parity.

Most of the tumours presented within 2 months from the onset of symptoms accounting for about 54% of cases, 35% of cases are presented within 2-6 months from the onset of symptoms, remaining 11% of cases are presented after 6 months from the onset of symptoms.

Among the presenting symptoms, 52% presented with abdominal distension, 32% presented with pain abdomen, 14% presented with mass abdomen, rest few cases are presented with constitutional symptoms, GI symptoms. 5% of the benign tumour remain asymptomatic.

Coming to histopathological study, among most of the tumours diagnosed, 73% belong to epithelial group, 20% are germ cell tumour, 4% are sex cord stromal tumours and 2% tumours are metastatic. Among epithelial groups, 67% are serous tumours, 30% are mucinous tumours and 3% are Brenner tumour.

With reference to gross appearance, 88% of benign tumour are cystic in consistency, whereas 65% malignant tumours are of variegated consistency. Coming to size of the tumours, for most of low malignant potential mucinous tumours the size ranges approximately 30-40 cm in diameter.



Graph 1. Laparotomy findings in Ovarian Tumours

On laparotomy findings, ascites is associated with 3.38% of benign tumours, 40% of low-malignant potential tumours and 46.8% of malignant tumour. Out of all malignant tumours, 28.1% are diagnosed in stage I/II and 71.8% are diagnosed in stage III/IV.

Age Groups	Benign N=59	Malignant N=32	Borderline Tumour N=5	Total N=96				
1. Premenarchal	-	1 (3.1%)						
2. Reproductive	55 (93.3%)	9 (28.1%)	5 (100%)	96				
3. Postmenopausal	4 (6.7%)	22 (68.8%)						
Parity								
Nulliparity	19 (32.2%)	10 (31.2%)	3 (60%)	96				
Multiparty	40 (67.8%)	22 (68.7%)	2 (40%)					
Total	59	32	5					
Table 1. Demographic Study of Ovarian Tumour								

able 1.	Demographic	Study of	Ovarian	Tumour

Presenting Symptoms	Benign N=59	Malignant N=32	Borderline Malignant N=55	Total N=96				
Abdominal distension	23 (38.9%)	23 (71.8%)	3 (60%)	49 (51.4%)				
Abdominal pain	14 (23.7%)	16 (50%)	-	30 (31.2%)				
Abdominal mass	10 (16.9%)	5 (15.6%)	1 (20%)	16 (16.6%)				
Gastrointestinal and other gynaecological symptoms	11 (18.6%)	4 (12.5%)	1 (20%)	17 (17.7%)				
Asymptomatic	5 (9.6%)	-	-	5 (5.2%)				
Table 2. Clinical Spectrum of Ovarian Tumours (Some of the Tumours are Having More Than One Presenting Symptoms)								

Duration of Symptoms	Benign N=59	Malignant N=32	Borderline N=5	Total N=96			
<2 months	32 (54.2%)	17 (53.1%)	2 (40%)	51 (53.1%)			
2-6 months	18 (34.6%)	14 (43.7%)	2 (40%)	34 (35.4%)			
>6 months	9 (15.2%)	1 (3.1%)	1 (20%)	11 (11.4%)			
Total	59	32	5	96			
Table 3 Clinical Study with Reference to Duration of Symptoms Among Ovarian Tumours							

	Number	mbor Moon Moon		Consistoney			Locularity		Bilatorality	
Benign Tumour	Number	59 Age	n Mean		Consist	ency	Uni	Multi	Dilaterality	
	N=59		5120	Solid	Cystic	Variegated				
Dermoid cyst	15	27.5	7.6 cm		11	4	15	-	3	
Serous cystadenoma and serous cystadenofibroma	29	36.6	11.8 cm		29		23	6	5	
Mucinous cystadenoma	12	31.2	19.4 cm		12		4	8	1	
Fibroma, fibrothecoma	2	42.5	6.2 cm	2			2	-	-	
Sclerosing stromal tumour	1	21	10.5 cm			1	1	-	-	
	Table 4. Histopathological Study of Benign Ovarian Tumours									

	Number	Mean	Mean	Consistency			Locu	Ilarity	Bilaterality
LMP rumours	N=5	Age	Size	Solid	Cystic	Variegated	Uni	Multi	
Serous tumours	3	41	11.8 cm		3		2	1	1
Mucinous tumours	2	36.5	35 cm		2			2	-

Table 5. Histopathological Study of Borderline Ovarian Tumours

Malignant Tumour	Number	Mean	Mean		Consist	ency	Multilocularity		Bilaterality	
Mangnant Tumour	N=32	Age	Size	Solid	Cystic	Variegated	Uni	Multi		
Serous cystadenocarcinoma	15	50.1	9.7 cm		2	13	4	11	3	
Mucinous cystadenocarcinoma	7	43.1	18.6 cm		1	6		7	1	
Brenner's tumour	2	53	11 cm		1	1		2	1	
Granulosa cell tumour	1	52	10 cm	1						
Dysgerminoma	2	21	12.5 cm	2				I		
Metastatic tumour	3	46	8.5 cm	3					3	
Dermoid with malignant transformation	2	30	9.3 cm		1	1		2	2	
Tab	Table 6. Histonathological Study of Malignant Ovarian Tumours									

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Graph 2. Major Histological Catagories of Ovarian Tumours



Figure 1. HE 200X - Fibrothecoma



Figure 2. HE 200X - Dermoid Cyst



Figure 3. HE 200X - Serous Cystadenoma

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Figure 4. HE 200X - Sclerosing Stromal Tumour



Figure 5. HE 200X - Serous Cystadenofibroma



Figure 6. HE 200X - Papillary Serous Cystadenocarcinoma



Figure 7. HE 200X - Squamous Cell Carcinoma Arising in Teratoma (Malignant Transformation in a Teratoma)

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Figure 8. HE 200X - Mucinous Cystadenoma



Figure 9. HE 200X - Ca Colon Metastatic to Ovary



Figure 10. HE 200X - Granulosa Cell Tumour



Figure 11. HE 200X - Fibroma



Figure 12. Sclerosing Stromal Tumour



Figure 13. Carcinoma Colon Metastatic to Ovary



Figure 14. Mucinous Cystadenoma Ovary



Figure 15. Atypical Proliferative Serous Tumour (Borderline Papillary Serous Cystadenoma)



Figure 16. Granulosa Cell Tumour

#### DISCUSSION

Above study was carried out with an aim to evaluate the clinicopathological findings and sociodemographic variables in ovarian cancer. In our study, benign tumour constitutes about 61% of cases, which is almost similar to other studies conducted in different parts of India by Rathore R et al,<sup>13</sup> Dr. M. Yogambal et al.<sup>14</sup> Again, benign tumour constitutes about 84% among the women belonging to 20-40 years, whereas the malignant tumour constitutes about 81% of cases in women above 40 years of age group. This study is quite similar to study conducted by R Jha et al.<sup>15</sup> In our case, median age at which diagnosis is made is 48 (range 14 to 59) year for malignant tumour, which in contrast to Surveillance, Epidemiology, and End Results Calculations (SEER) cancer statistics data base where it is 63 for western population. But, in India, for ovarian malignancies median age is 45 years.<sup>16</sup> For borderline and benign ovarian tumour, median age at diagnosis is mostly reproductive age group similar to study conducted in different parts of the world.<sup>17</sup> Menopausal status is not responsible for development of ovarian cancer as in our study almost 69% of malignant tumour and only 7% of benign tumour could be diagnosed in postmenopausal women as found by Patrica G. Moorman et al.<sup>18</sup> It is well known that parity is a well-established protective factor for development of ovarian cancer (Hankinson and Dan Forth, 2006), however, in our study,

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almost 67% and 68% of ovarian tumour are associated with multiparity among benign and malignant tumours, respectively. Recently, it has been found, high BMI is significantly associated with increased risk of ovarian cancer that maybe present in the nulliparous women and most of the parous women in the present study. Similarly, use of OCPs use is not protective in such women as proposed by the famous theory of incessant ovulation (M.F. Fathalla, 1971). Increasing use of ovarian stimulating drugs, origin of ovarian cancer from fimbrial end of fallopian tube and its association with high-grade serous carcinomas (Scientific Impact Paper No. 44, 2014, RCOG) are some of the explanations in this changing trend with regards to multiparity. Study by C Bodelon et al<sup>19</sup> shows that 84% of parous lady have ovarian cancer at the time of diagnosis. In our study from being symptomatic to the diagnosis, interval is 2 months in 54% cases, 2-6 months in 35% cases, >6 months in 11% cases, similar to study done by Christina M Nagle et al;<sup>20</sup> where 70% of the tumours are diagnosed within 2 months of onset of symptoms, 22% cases are diagnosed in 2-6 months, remaining 8% cases diagnosed after more than 6 months. However, early diagnosis have no impact on the prognosis of disease, whatever maybe the duration from being symptomatic to disease onset.

In our study, abdominal distension is the commonest symptom followed by pain abdomen similar to study conducted by CR Bankhead et al<sup>21</sup> in four leading hospitals of U.K. As per his observation, persistent abdominal distension is the commonest presentation of an ovarian mass. So, clinicians should be able to distinguish persistent abdominal distension from fluctuating abdominal distension.

Coming to the histopathological pattern in our study, 73% belong to surface epithelial group followed by germ cell tumour (19.7%), which is quite similar to study by Deepti Vijay Mankar et al<sup>22</sup> where surface epithelial tumour constitutes about 68.48%. Among the surface epithelial tumours, almost 59% tumour (serous and mucinous cyst adenoma) are benign, 7% are LMP tumours and 34% are malignant. Serous tumour accounts for almost 67% cases followed by mucinous tumours constituting 30% of cases, 3% are the Brenner tumours. The study conducted by Nalini Modepalli et al<sup>23</sup> shows similar results, which is comparable to our study. The surface epithelial tumours are mostly embryonic in origin. They are derived from coelomic epithelium (modified mesothelium), which lines underlying ovary. As the women approaches menopause, the surface epithelium usually invades the underlying stroma forming inclusion glands. These glands sometimes undergoes enormous proliferation leading to formation of cystic nature of tumour. Simultaneously, the amount of stroma it usually contains leading to solid nature of tumours. If these glands contain tubal epithelium, it leads to formation of serous tumours. If it contains endocervical gland, it leads to formation of mucinous tumours. Following epithelial tumours, germ cell tumours present the second most common group, among them, dermoid cyst constitutes about 68% of cases.

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In present study, bilaterality is associated with 20% of cases, out of which majority are associated with metastatic tumour (almost 100%), followed by serous tumour. Most of the bilateral cases are associated with malignant ovarian tumours as compared to benign ones, whereas the study by Dr. Vaddatti Tejeswini et al<sup>24</sup> shows that only 66.6% of metastatic tumours are bilateral, serous carcinoma are bilateral in 25% of cases. In our study, gross tumour size ranges from 6 cm to 35 cm, the largest one belong to

borderline mucinous tumour category similar to study done by Agrawal et al<sup>25</sup> where mucinous tumours are the largest among all. In our study, majority, i.e. 88% of benign ovarian tumours are cystic in consistency, whereas 65% of malignant tumours are variegated in consistency similar to study conducted by Rashmi K S and SB Patil<sup>26</sup> where almost 88% benign tumours are cystic and 56% malignant tumours are variegated in consistency.

Ovarian Tumour	Bhattacharya et al <sup>10</sup>	Dhakal R et al <sup>27</sup>	Jha et al <sup>15</sup>	Kant RH et al <sup>28</sup>	Sumanlatha G.R. et al <sup>29</sup>	Present Study			
Benign	64.07%	89.18%	83.9%	71.87%	64%	69%			
Malignant	28.52%	5.4%	16.1%	28.18%	34.5%	33.3%			
Epithelial tumours	61.6%	45.9%	52.2%	65%	74.84%	73%			
Sex cord stromal tumours	6.8%	Nil	3.1%	2.5%	4.66%	4.1%			
Germ cell tumours	24.8%	54.1%	42.2%	7.5%	16.46%	19.7%			
Commonest symptom/sign	Lump in abdomen or distension of abdomen	Abdominal pain	-	Lower abdomen pain	-	Distension of abdomen			
Peak age groups of benign cases	Reproductive age (20-40 yrs.)	31-40 yrs.	21-40 yrs.	30-39 yrs.	31-40 yrs.	21-40 yrs.			
Peak age groups of malignant cases	>40 yrs.	10-30 yrs.	>40 yrs.	30-39 yrs.	41-50 yrs.	>40 yrs.			
Bilaterality	-	16.8%	12%	13.1%	7.7%	20%			
Table 7. Comparison of Our Study With Other Studies									

## CONCLUSION

Ovarian tumours show a wide spectrum of clinical and histological features. Though ovarian cyst and tumour can be predicted clinically to some extent, histopathological examination of the ovarian tumour is essential for knowing accurately the nature of the tumour and so also planning for the treatment. Benign tumours can be safely removed by surgery and malignant tumours are managed according to the histological type, grading and stage of the tumour. In the modern era of immunohistochemistry and molecular pathology where the diagnosis depends on these to a greater extent. But in the institutes with limited resources, clinicoradiological correlation and histopathological examination are important in the diagnosis and management of the ovarian tumours. Hence, the combined efforts of gynaecologist, radiologist and pathologist is essential in reaching the correct diagnosis and guide the patient in getting correct and timely treatment.

Ovarian cancer is associated with overall mortality of 75%, but can be cured in 90% of cases if the disease is still limited to ovary. Risk factor recognition is very important to scrutinise the women who are in the very high-risk group to develop ovarian cancer.

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