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# Clinicopathological Study on Borderline and Invasive Mucinous Carcinoma of Ovary at Young Age Less than 30 Years

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## ABSTRACT

**Purpose:** To evaluate the clinicopathological entities of Mucinous Borderline and Mucinous carcinoma of ovary at age less than 30 years.

**Method:** Retrospective analysis of twelve cases of borderline and mucinous carcinoma of ovary at age less than or equal to 30 years managed at VPS Lakeshore hospital, Kochi, India from 2013 to 2018. Results: 434 ovarian cancers were managed in 6 years duration. 54 cases (12.4%) were in age group  $\leq 30$  years. Malignant germ cell tumor was the most common ovarian cancer in this age group (28 cases, 51.9%) followed by epithelial cell tumor (21 cases, 38.9%) and sex cord stromal tumor (4 cases, 7.4%). Borderline tumor and mucinous carcinoma accounted for 5.5% and 16.7% respectively of all epithelial ovarian carcinoma in this age group respectively. Mean age of diagnosis was 22.5 years. Pain abdomen was the most common presenting symptoms. Clinically palpable abdominal mass was present in 8 (66.7%) cases. CEA was raised in 16.7% of cases. Multiloculated large cyst was consistent finding in the ultrasound study with mean diameter of 13.75 cm. All cases were of FIGO stage I. Total 6 cases received adjuvant chemotherapy. There were 2 cases (1 in each group) of contralateral ovarian involvement in mean duration of 13 months. Overall disease free period was 36.27 months. One case (8.3%) expired due to the disease process and three cases (25%) conceived after treatment.

**Conclusion:** Mucinous carcinoma is more common than borderline tumor at young age, mostly unilateral and detected at early stage. Laparoscopic management is difficult due to its large size. Systematic lymphadenectomy can be omitted and unilateral salpingoophorectomy at early stage is an optimal management for fertility preservation.

**Keywords:** Borderline, mucinous, ovarian carcinoma, germ cell tumour, mucinous carcinoma, ovary, recurrence, survival, young age.

## Introduction

Among the gynecological malignancy, ovarian malignancy is the most lethal due to its late diagnosis and aggressive tumor biology.<sup>1</sup> Incidence increases after 35 years of age and peaks at 55-64 years.<sup>2</sup> In general, epithelial ovarian cancer (EOC) is the most common form of ovarian tumor. Serous pathology is a common variant. Mucinous variant is rare with reported incidence varying from 3% to 12%.<sup>3,4,5</sup> It has separate tumor biology and molecular signature, often diagnosed at early age, early stage and confined to ovary at the time of diagnosis in comparison to its serous counterpart. But once advanced, mucinous histology

has poor outcome compared to other histological subtype, may be due to aggressive tumor biology and relative chemotherapy resistance.

In young age group, germ cell tumor is a common ovarian malignancy. EOC is a rare occurrence before the age of 30 years.<sup>5</sup> Hence there is not much more literature on malignant mucinous tumor of ovary in young age.

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Pattern of metastasis and clinical behaviors is not well understood for mucinous ovarian malignancy due to its rarity at all ages. This is even more uncertain for early age group (before 30 years). Here we present a clinical profile of 12 cases of mucinous carcinoma of ovary in young age.

## MATERIAL AND METHODS

This is hospital based, retrospective descriptive study of patient attending Gynecologic Oncology and Medical Oncology department of VPS Lakeshore Hospital Research Centre–Cochin, Kerala. Cases of ovarian malignancy managed at this hospital from year 2013 to 2018 were enlisted from the hospital records. Age of less than or equal to 30 years were identified and those cases with malignant mucinous tumor (either borderline or invasive) were selected for study. Clinical details were obtained from hospital record section. Telephonic interview was made to get information where necessary. Cases were labeled as lost to follow-up when information could not be obtained for the last 6 months. Data was collected in a performa and entered in microsoft excelsheet. Statistical analysis was done with SPSS program version 16.

## RESULT

Total 434 cases of ovarian cancer were identified from year 2013 to 2018. Out of them, 54 (12.4% cases were of age group < 30 years and among them 21 cases (38.8%) were of EOC as shown in Table 1. There were 12 cases of mucinous variant of which

3 cases (5.5% of EOC) were of borderline mucinous tumor and 9 cases (16.7% of EOC) were of mucinous carcinoma in this age group. Clinical characteristics and primary management has been shown in Table 2 and 3 respectively. Stage, adjuvant therapy and recurrence, mortality and pregnancy outcomes has been shown in Table 4, 5 and 6 respectively.

## DISCUSSION

Ovarian cancer is rare before 40 years of age.<sup>6</sup> Almost half of the cases of ovarian cancer do occur at mean age of 63 years and above.<sup>6</sup> In young age (less than 30 years), germ cell tumor is the most common ovarian malignancy<sup>5</sup> which is same in this study also (Table 1). EOC is rare in young age group. Less than 1% of EOCs are found in age group less than 30 years.<sup>5</sup> Mucinous tumours are more commonly seen in younger women as compared to serous tumor.<sup>1</sup> Borderline tumors are of malignant potential and share common risk factors with mucinous carcinoma. They are believed to be more common than invasive carcinoma and comprises up to 67% of mucinous tumor.<sup>7,8</sup> But this study shows that invasive mucinous carcinoma is more common in young age than borderline mucinous tumor with ratio of 1:2.6. This may also represent the referral pattern of a tertiary care center.

There is not much literature on borderline and malignant mucinous tumor of ovary in this age group. Serous adenocarcinoma has been reported as most common EOC (56.3%) in age group <35 years followed by mucinous carcinoma (30.9%).<sup>9</sup> But this study reveals borderline and invasive mucinous carcinoma as most common EOC, together contributing 54.5% (12 out of 22) of EOC in this age group. In this study mean age of diagnosis was 22.5 years and abdominal pain was most common mode of presentation. Self palpable abdominal mass is the most common mode of presentation of EOC in young age.<sup>9</sup> But in this study, only one case presented with mass abdomen.

Abdominal ultrasound is primary mode of investigation. Usual findings of mucinous tumors are large multilocular cyst. Loculi within the cyst have been reported to give indirect evidence for malignant potential of lesion. Benign cyst usually have 2-10 loculi, borderline tumor has more than 10 loculi. Invasive lesion usually contains solid component and are multilocular.<sup>10</sup> In this study, most of the cases

**Table 1**

Histological type of ovarian malignancy below 30 years of age

Histological type of tumor	f (n = 54)	%
Malignant Germ Cell Tumor	28	51.9
Epithelia Ovarian Cancer	21 (Mucinous-12, Non-mucinous 9)	38.9
Sex Cord Stromal Tumor	4	7.4
Others (Primary Neuroectodermal Tumor)	1	1.9

**Table 2**

Clinical characteristics of patient

	Frequency (f), (n = 12)	%
<b>Mucinous ovarian tumor</b>		
Mucinous carcinoma	9	75
Borderline tumor	3	25
<b>Age (in years)</b>		
<15	1	8.3
15-20	2	16.7
21-25	7	58.3
26-30	2	16.7
Mean - 22.5 years		
Range = 13 - 30 years		
<b>Clinical presentation</b>		
Pain abdomen	7	58.3
Menstrual disorders	4	33.3
Mass per abdomen	1	8.3
<b>Marital status</b>		
Unmarried	9	75
Married	3	25
<b>Parity</b>		
0	9	75
1	3	25
<b>Clinically palpable mass</b>		
Yes	8	66.7
No	4	33.3
<b>Ultrasound feature of mass</b>		
Multiloculated cyst only	8	66.7
Multiloculated cyst, ascites	3	25
Multiloculated cyst with solid component, ascites	1	8.3
<b>Tumor markers</b>		
Ca125 (U/ml)	10	83.3
<35	2	16.7
>35		
<b>CEA (ng/ml)</b>		
<3	10	83.3
>3	2	16.7
<b>Site</b>		
All unilateral tumors (12)	3	25
Right	9	75
Left		
<b>Usg diameter</b>		
>10cm	9	75
<10 cm	3	25
Average tumor size	13.75 cm ± 4.5 (Range 8-20 cm)	

**Table 3**

Primary management of adnexal mass of the cases

Primary surgery	f (n = 12)	%
Laparotomy, salpingoophorectomy and staging	4	36.4
Laparoscopic Adenectomy	3	27.3
Laparotomy and salpingoophorectomy only	4	27.3
Total abdominal hysterectomy bilateral salpingo ophorectomy, infracolic omentectomy, pelvic lymph nodes dissection, para aortic node dissection.	1	9.1
Revision surgery for complete staging done in 3 cases – 2 from open salpingoophorectomy group and 1 from laparoscopic adenectomy group.		

were reported as multiloculated cyst only and solid component was reported in one case only.

Most of mucinous carcinoma are unilateral and large with average size of 16-20 cm or even larger.<sup>7</sup> However in case of metastatic ovarian mucinous tumor, it can be bilateral and sonological size is usually less than 11-12 cm. In 32-48% of the cases, metastatic carcinoma will have size >10 cm.<sup>7</sup> This study shows similar result in young age, all being primary mucinous cancer, unilateral and early stage with large tumor size.

CEA is useful tumor marker for diagnosis and follow up for mucinous carcinoma. CA 125 is generally not raised in this variant and is more useful for serous counterpart. CEA may be raised in about 3% of borderline mucinous tumor.<sup>11</sup> In mucinous carcinoma, it has been found to be very high 41-88% of cases.<sup>12-14</sup> This study reveals that CEA and CA125 may not be elevated in borderline or mucinous carcinoma in this age group. One case of borderline mucinous tumor had concomitant increase in CA125 and CEA, one case of mucinous carcinoma had raised CA125 only and one case of mucinous carcinoma had raised CEA only. Majority of the cases had normal tumor markers in this age group.

Management of mucinous ovarian carcinoma should be individualized depending upon age and stage of the disease. Intact removal of suspected ovarian mass is the aim of surgical procedure. Since they are large tumors, laparoscopic management is difficult without spillage. In this study also, all the 3 cases which were managed laparoscopically, had surgical spillage and subjected for adjuvant chemotherapy. There has been reports of

**Table 4**

Stage, adjuvant therapy and recurrence

Stage	f (n = 12)	Chemotherapy		Recurrence (duration for recurrence)
		Yes	No	
1A	3 carcinoma 2 borderline	0	5	1 recurrence, case of borderline mucinous tumor (7 months )
1C1	4 carcinoma 1 borderline	5	0	1 recurrence, case of mucinous carcinoma (10 months)
1C2	2 carcinoma	2	0	No recurrence
Total	12	7	5	Total 2 recurrence

**Table 5**

Recurrence and mortality

Recurrence	1 case in stage 1A (case of borderline tumor) 1 case in stage 1C1 (case of mucinous carcinoma) 1 case lost follow up (recurrence status unknown) Involvement of Contralateral ovary in both cases.	Mean duration of recurrence - 8.5 months	Overall disease free period = 36.27 months
Mortality	1 case of mortality – case of Mucinous Carcinoma with recurrence.		

**Table 6**

Pregnancy outcome

Stage	Number of case	Fertility
1A	3 ( none received chemotherapy)	3 cases of pregnancy i.e in 25% of cases (2 cases of mucinous carcinoma and 1 case of borderline mucinous tumor)

laparoscopic management of large ovarian cyst >10 cm.<sup>15</sup> The chance of unexpected malignancy in the management of overall adnexal mass with laparoscopy has been reported as low as 0.04% to 1.5% and it did not change patient prognosis.<sup>16,17</sup> Though borderline tumor are of low malignant potential, port site metastasis has been reported.<sup>18</sup> When laparoscopic management is chosen for any adnexal mass, it should be done by skilled surgeon with all precaution to prevent spillage and with low threshold to convert to laparotomy when spillage is anticipated.<sup>7</sup>

Mucinous neoplasm is peculiar from its serous counterpart due to its unilaterality, early presentation, and early stage, mostly confined to ovary at the time of diagnosis and less chance of pelvic or paraaortic nodal metastasis in stage I and II.<sup>19-23</sup>

In general, 83% of mucinous tumours are diagnosed at stage I. So extensive lymph node dissection may be omitted for this group of cancer. In this study also,

lymph node dissection or sampling were done in 5 cases only and no node involvement was detected in those cases. Rest had not undergone nodal analysis. However, in advanced stage, they are more aggressive compared to serous tumor due to relative chemo resistant and tumor biology.<sup>24</sup>

Fertility preservation is a special concern in this age group. Salpingo oophorectomy is the optimal treatment in most of the cases of borderline and mucinous carcinoma when grossly confined to ovary without affecting the prognosis.<sup>25,26</sup> Currently National Comprehensive Cancer Network (NCCN) recommends fertility sparing surgery only in early stage disease. There are reports of fertility preservation even in stage II disease.<sup>26</sup> In our study, 3 cases conceived after completing treatment. All were of stage 1A and did not receive chemotherapy.

For borderline mucinous ovarian tumor, there is no standard guideline to suggest adjuvant chemotherapy

even in case advance stage disease with invasive implants.<sup>27</sup> But in case of mucinous carcinoma, chemotherapy is indicated when there are signs of residual tumor. Borderline tumor is thought to have better prognosis than invasive tumor. Recurrence rate of 3-10% has been reported for borderline mucinous tumor while for invasive cancer it is 6.8% irrespective of age group.<sup>27,28</sup> But in young age, there has been not such reports. In this study recurrence was seen in 2 cases, one in borderline variety and one in mucinous carcinoma and in both cases contralateral ovaries were involved. The recurrence for borderline tumor was 33% (1 out of 3 cases) and for mucinous tumor it was 11.1% (1 out of 9 cases) for age group less than 30 years in this study. Since the date of surgery, there was only one mortality due to disease condition. Young age itself has been considered as an independent factor with survival benefit in EOC.<sup>29</sup>

### Limitation of Study

This study was a retrospective study and had small sample size that included both borderline and invasive mucinous carcinoma for evaluation. Further studies with larger sample size with individual variant of mucinous tumor should be done to know the nature of behaviour in this young age group of <30 years.

### CONCLUSION

Mucinous ovarian carcinoma is more common than borderline tumor at young age. It has good prognosis at early stage and nodal metastasis is rare compared to its serous counterpart. Laparoscopic management is challenging due to its large size and chances of spillage. Pelvic and para aortic lymphadenectomy can be omitted. Fertility preserving surgery is possible in most of the cases. Unilateral salpingoophorectomy and adjuvant chemotherapy is an optimal treatment in early stage disease in young age.

### Source of Support

Nil

### Conflict of Interest

There are no conflicts of interest.

### Financial Disclosure

Nil

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