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# Ovarian Granulosa Cell Tumor :FIGO Staging, Prognostic Factors And Follow Up

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***Abstract***
***Background*** *Granulosa Cell Tumours of Ovary (GCT )are slow growing, of low malignant potential with a well-known predilection to spread beyond the ovary.*
***Aims:*** *To stage all GCTs which is the most significant prognostic factor and to correlate with the clinical and pathological prognostic factors along with the follow up of patients .*
***Materials and Methods:***
*A prospective descriptive study was done on 30 GCT Ovary cases with FIGO Staging from January 2003 to June 2006 analyzing the case records .13 patients were followed up with the data .*
***Results:***
*The median age at diagnosis was 48 years ( 25-65 years). Bleeding was the most common symptom( 40% ) . The median diameter of tumor was 10 cm ( 4–28 cm) with no evidence of tumour rupture .56.6% of the patients presented with Stage I a.8 patients with stage I had better survival (mean duration 11-25 months) and five patients with Stage III had a mean survival period as 8.2 months.*
***Conclusion:***
*Majority of the patients of GCT present in early stage. Advanced stage and presence of residual disease were associated with poor survival and needs future cohort study predicting survival.*
***Keywords****: Granulosa cell tumour Ovary, FIGO Staging, Follow up, Prognosis*

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## I. Introduction

GCTs of the ovary are rare neoplasms accounting for 3 to 5% of all ovarianmalignances.The majority of patients arediagnosed at an early stage with a relativelyfavourableprognosis.Surgery is the most preferred treatment modality. Radiotherapy and Chemotherapy could play some role in advanced or recurrent disease after operative debulking.There are many factors of prognostic significance including the Stage at the time of presentation,age, tumor size and histologic parameters. Recurrences are often delayed extendingupto three decades.

## II. Aims And Objectives

To stage all GCTs usingtheFIGO Stagingwhich is the most significant prognostic factor and to correlate with the clinical and pathological prognostic factors along with the follow up of patients.

## III. Materials And Methods

A prospective descriptive study was done on 30 GCT Ovary cases from 475 patients with ovarian tumors. The hospital case files of the Departments of Pathology, Institute of Obstetrics and Gynaecology and Kasthurba Gandhi Hospital from January 2003 to June 2006 were analyzed . Samples included total abdominal hysterectomy with bilateral salpingo oophorectomy, debulking, vaginal hysterectomy with bilateral oophorectomy.Surgical specimens of these tumors were subjected to meticulous gross and microscopic examinations. The specimens were fixed in 10% neutral buffered formaldehyde. Extensive sampling was done , processing and paraffin blocks (number of blocks depending on the size of the tumor) were made. Uterus with cervix, other ovary, lymphnodes and omental tissues were also studied. Histologic Sections (5 to 6 µm) were stained with Hematoxylin and Eosin , special stains like PAS (periodic acid - Schiff), Reticulin by Gomori's method were done. (Figure 23) Additional sections were made for Immunohistochemistry Panel in a poorly differentiated GCT
Ethical clearance for conducting this study was obtained from the Institutional ethics committee.

## IV. Results

In the present study spanning three and half years, there were 475 ovarian Neoplasms and 165 were malignant. 30 of them were GCTs (18.8 %). Among them,the mean(sd) age was 46.16(9.72) and the median age at diagnosis was 48 years (range 25-65 years).

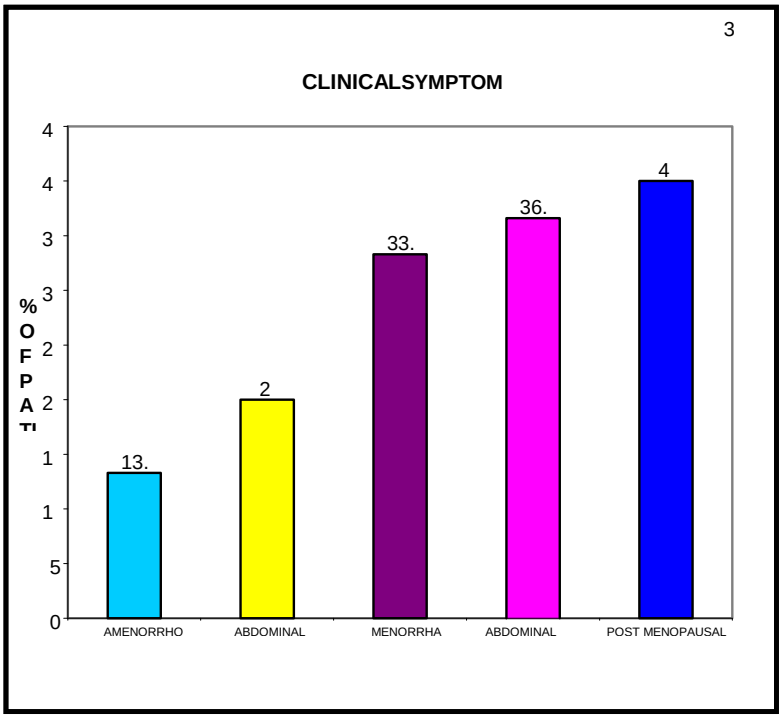
**Table 1– Frequency among the type of treatment**

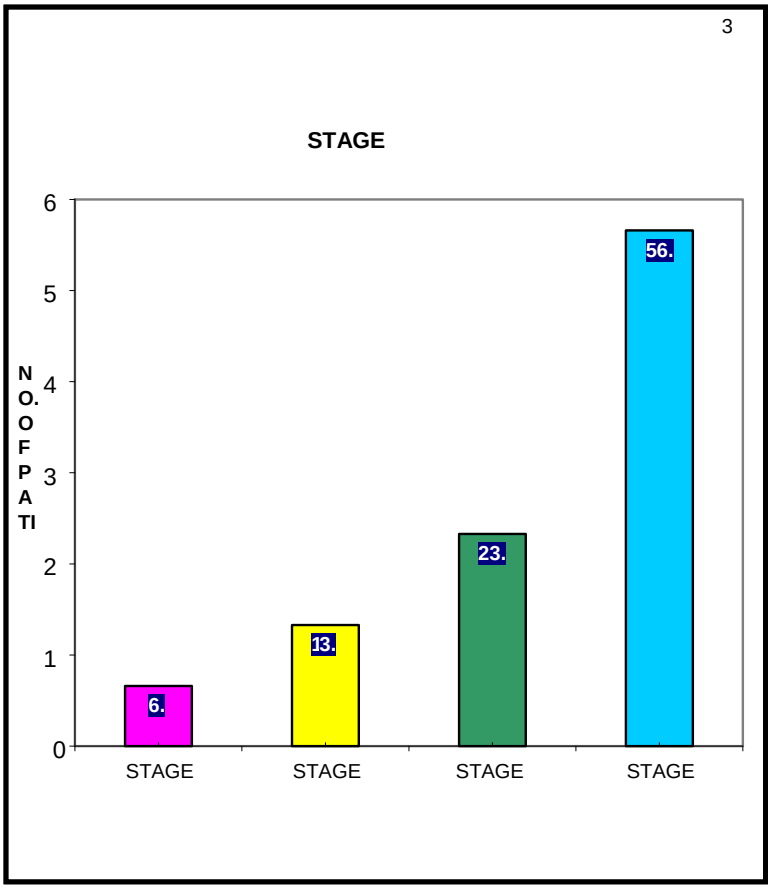
| | Frequency | Percent |
|---|---|---|
| Debulking | 4 | 13.3 |
| TAH with (R) Ovariotomy | 1 | 3.3 |
| TAH with BSO | 24 | 80.0 |
| VH with B/L Oopherectomy | 1 | 3.3 |
| Total | 30 | 100.0 |

Majority (80%) had under gone TAH with BSO . Out of 30 Patients, follow up records were available for 13 cases. The duration of follow up ranged from 2 months to 24 months. 8 cases were above 40 years , one patient with 40 years and 4 cases were below 40 yrs at the time of diagnosis. Bilaterality was observed in 2 cases. The tumor size varied from 5 cm to 28 cm. The median diameter of tumor was 10 cm (range, 4–28 cm) with no evidence of tumourrupture.The mean duration of symptoms is 8 months.

### 4.1 Profile of the study participants

| Clinical Parameters | Number of patients (%) |
|---|---|
| Age in years | |
| ≤ 40 Years | 10 (33%) |
| > 40 Years | 20 (66.7%) |
| Menopause | |
| Pre | 14 (46.7%) |
| Post | 16 (53.3%) |
| Stage | |
| I - II | 23 (76.7%) |
| III - IV | 7 (23.3%) |
| Residual Disease | |
| Present | 4 (13.3%) |
| Absent | 26 (86.7%) |
| Size | |
| ≤ 15 cm | 25 (83.3%) |
| > 15 cm | 4 (16.7%) |




**Clinical Parameters of GCT Compared With Other Studies**

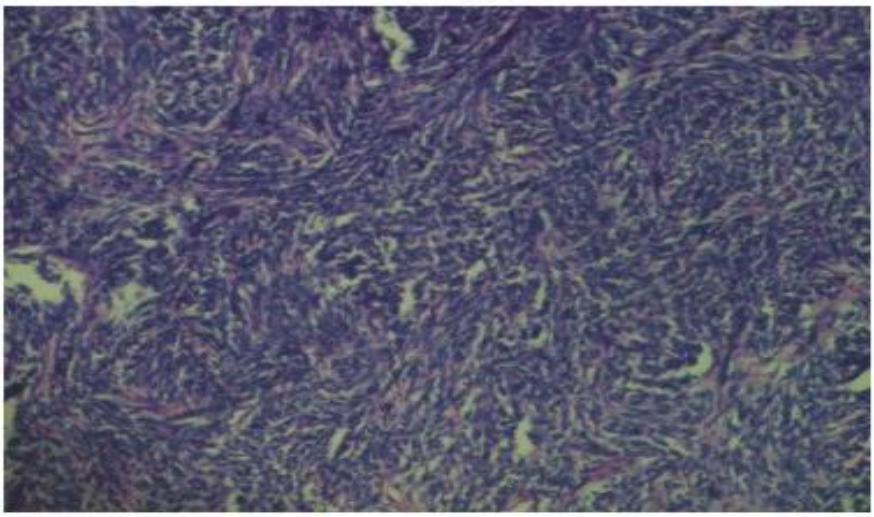
| Clinical Parameters | No. of cases | | |
|---|---|---|---|
| | Kazim et al | Himanshu et | Our |

| | | al | s t u d y |
|---|---|---|---|
| A G E ( y ) | | | |
| ≤ 40 | 18 | 14 | 10 |
| > 40 | 2 7 | 1 3 | 2 0 |
| MENOPAUSE | | | |
| Pre | 25 | 18 | 14 |
| Post | 2 0 | 1 9 | 1 6 |
| STAGE | | | |
| I - II | 23 | 25 | 23 |
| III-IV | 2 2 | 1 2 | 7 |
| RESIDUAL DISEASE | | | |
| Present | 30 | 3 | 4 |
| Absent | 1 5 | 3 4 | 2 6 |
| SIZE | | | |
| ≤15 cm | - | 25 | 25 |
| >15 cm | - | 1 2 | 4 |

**GCT- Predominantly Solid**

| Table 2 Disribution of Histopathological Patterns in follow up cases | | |
|---|---|---|
| **Histopathological type** | Frequency | Percent |
| Diffuse -Sarcomatoid | 5 | 3 8 . 5 |
| M a c r o - f o l l i c u l a r | 1 | 7 . 7 |
| M i c r o - f o l l i c u l a r | 5 | 3 8 . 5 |
| Micro & Macro-follicular | 1 | 7 . 7 |
| T r a b e c u l a r | 1 | 7 . 7 |
| T o t a l | 1 3 | 1 0 0 . 0 |

Also Table 2 depicts that out of 13 cases ,diffuse-Sarcomatoid and Micro-follicular patterns were equally distributed. Call Exner bodies were seen in 4 cases of micro follicular, 1 case of micro and macro follicular types and occasionally seen in 1 case of diffuse type.



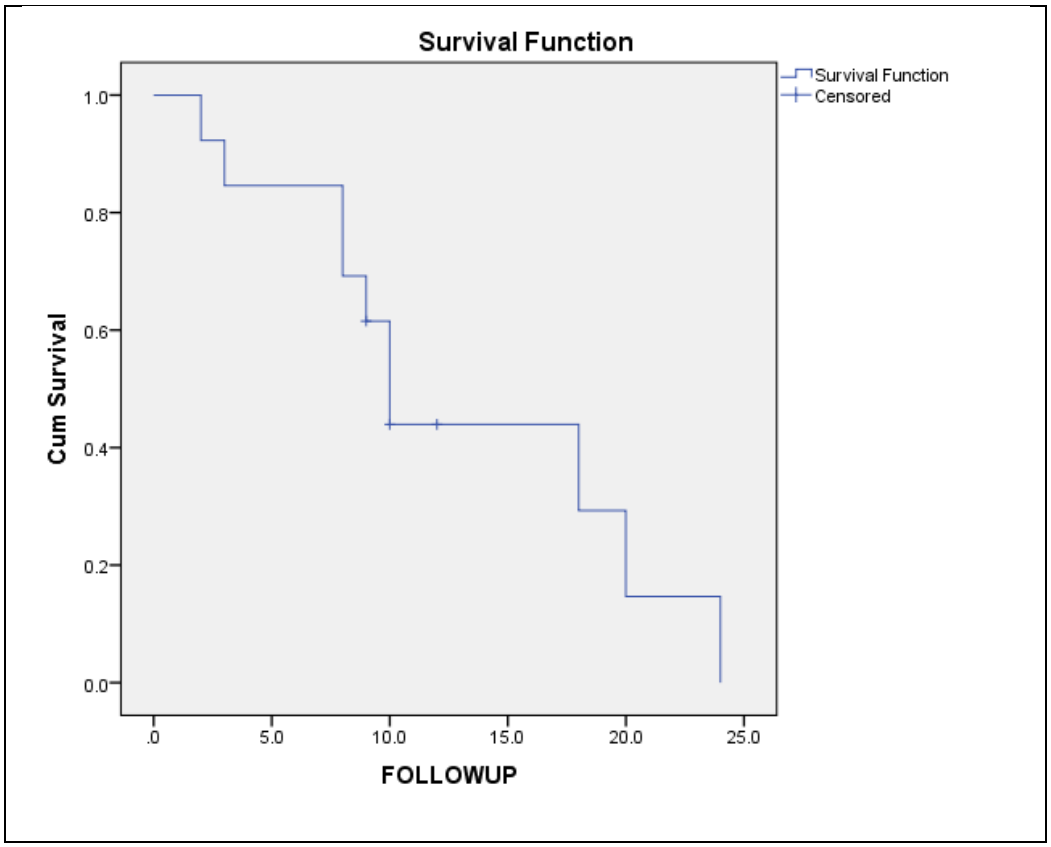
GCT- DiffuseSarcomatoid 10x10 Hpe

**Clinical And Pathological Findings Of Thirteen Patients On Follow Up**

| Case No | HPE.No | Age in years | Tumor size | Tumor pattern | FIGO stage | Call-Exner | L.V invasion | Mitotic Count | Luteinization | Nuclear Aypia | Omental Deposit | Capsular Invasion | Follow up |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1. | 10/03 | 36 | 5 cm | Micro follicular | Ia | + | - | 1+ | Nil | 1+ | - | - | 24 months |
| 2. | 872/03 | 45 | 11 cm | Micro follicular | Ia | + | - | 1+ | Nil | 1+ | - | - | 3 months Ascites, Icterus |
| 3. | 2803/03 | 50 | R-12cm L-10cm | Diffuse | IIIc | - | + | 2+ | Nil | 2+ | + | + | 2 months |
| 4. | 3625/03 | 30 | 14cm | Diffuse | IIIc | - | + | 2+ | Nil | 2+ | + | + | 9 months CT given with paclitaxel and carboplatin |
| 5. | 3916/03 | 58 | 7cm | Trabecular | IIIc | - | - | 2+ | Nil | 2+ | + | + | 12 months patient expired |
| 6. | 10/04 | 48 | 7 cm | Microfollicular | Ia | + | - | 1+ | + | 1+ | - | - | 18 months |
| 7. | 1016/04 | 38 | 20cm | Micro &macrofollicular | Ia | + | - | + | focal | 1+ | - | - | 20 months |
| 8. | 649/05 | 55 | R-25cm L-28cm | Microfollicular | Ia | + | - | 1+ | + | 1+ | - | - | 6 months |
| 9. | 1466/05 | 25 | 16 cm | Macrofollicular | IIIc | - | - | 1+ | + | 2+ | + | + | 8 months |
| 10. | 3656/05 | 41 | 14 cm | Diffuse | Ic | occasional | - | 1+ | - | 1+ | + | + | 10 months |
| 11. | 3799/505 | 63 | 8 | Diffuse | IIIc | - | + | 2+ | - | 3+ | + | + | 10 months CT given with paclitaxel and carboplatin |
| 12. | 45/06 | 40 | 11 | Diffuse | Ia | - | + | 2+ | - | 2+ | - | - | 9 months |
| 13. | 3876/06 | 43 | 8cm | microfollicular | Ia | - | - | 1+ | - | 1+ | - | - | 10 months |

The Figure 1 survival curve shows the relapse occurring after the treatment during the follow up of 24 months, the curve interprets there is an 40% of relapse occurred at the time period between 6 months to 10 months. Hence 60% of the patients had survived without relapse at the 24 months follow up.

Figure 1: Survival Curve for Relapse after the treatment




The estimation of mean time for relapse after the surgery is 13.15months( 2.202) with the 95% of CI (8.835 – 17.466)

. Of 13 patients , 6 patients were in clinical stage Ia, 6 patients in Stage IIIc and 1 patient was in Stage Ic as per FIGO (International Federation of Gynaecologists and Obstetricians criteria

| STAGE | Frequency | Percent |
|---|---|---|
| Ia | 6 | 46.2 |
| Ic | 1 | 7.7 |
| IIIc | 6 | 46.2 |
| Total | 13 | 100.0 |

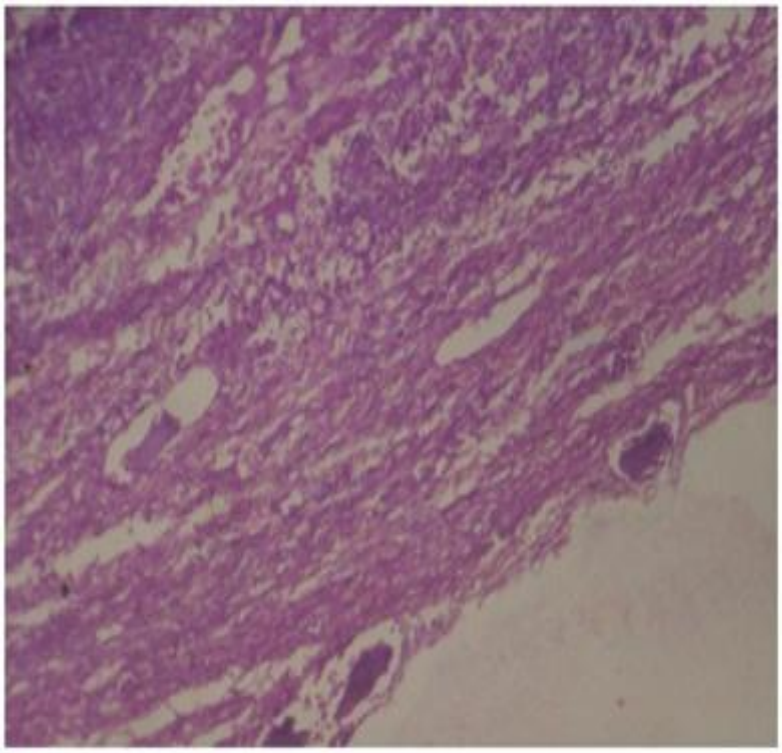
Table 3 shows that the Stage Ia (14.00 ±3.235) mean value is more than the Stage IIIc (9.22±1.455).

**Table 3 Descriptive among the stage**

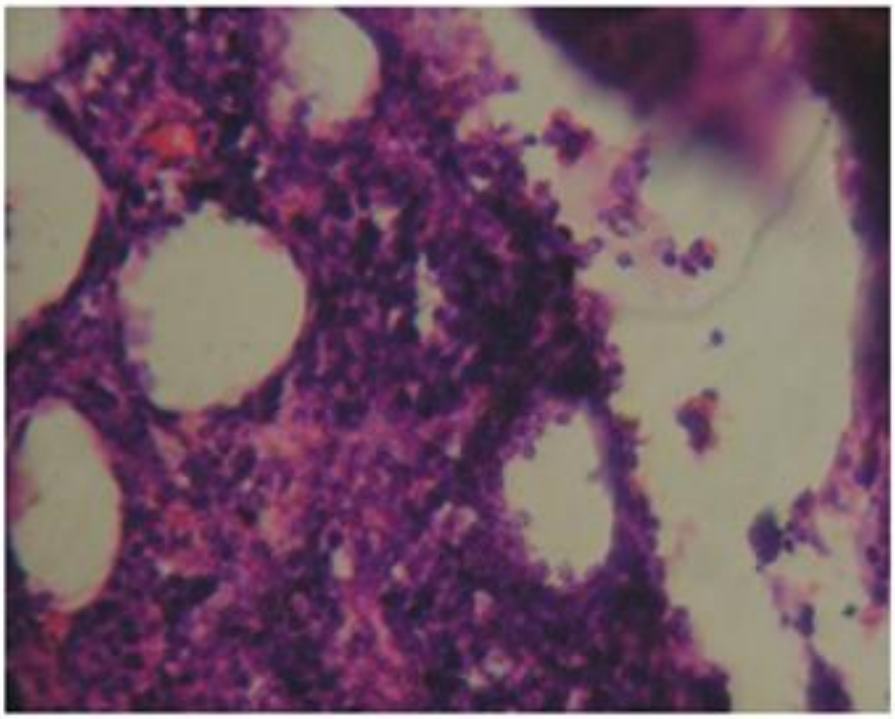
| Stage | Mean | Std. Error | 95% Confidence Interval | |
|---|---|---|---|---|
| | | | Lower Bound | Upper Bound |
| Ia | 14.000 | 3.235 | 7.659 | 20.341 |
| IIIc | 9.222 | 1.455 | 6.370 | 12.074 |
| Overall | 13.579 | 2.353 | 8.968 | 18.191 |

The duration of follow up ranged from 2 to 24 months. The tumor size varied from 5 cm to 28 cm. The tumor size was > 10 cm in 3 cases of Diffuse and 1 macro follicular variants presented with Stage IIIc. Only one patient with Stage III c had the tumor size < 10 cm with trabecular variant. 8 patients with stage I had better survival (mean duration 11-25 months), of which six cases presented with micro follicular pattern and two with diffuse pattern. Five patients (three diffuse, one trabecular and one macrofollicular pattern) presented with Stage III with the mean survival period as 8.2 months . Two patients had post-operative chemotherapy and one patient expired of intestinal obstruction after 12 months of follow up.Of the 13 patients who had a follow up, omental deposits and capsular invasion were present in six cases including 5 cases of Stage III c and 1 case of Stage Ic (46%). Omental deposits were present in 1 Bilateral, diffuse type, 2 diffuse types with unilateral presentation, 1 trabecular, 1 macro follicular variants and all cases presenting with Stage III c and 1 diffuse

type with Stage I c presentation.Capsular invasion was present in 3 cases presenting as Stage IIIc with diffuse type.



GCT- Diffuse- Lympho Vascular Invasion.Hpe 10x10



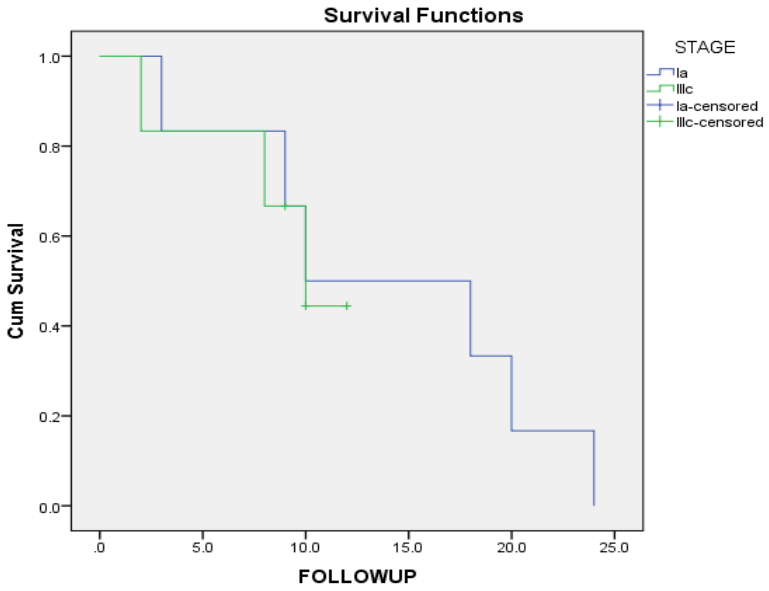
O

**OMENTAL DEPOSITS IN POORLY DIFFERENTIATED GCT.HPE 10X10**

On follow up, 1 patient had Chemo therapy for 9 months and the other case had for 10 monthswhereas one patient had lost follow up after 2 months . Capsular invasion was also reported in one

trabecular type ,one Macro follicular type with Stage IIIc, and one diffuse type in Stage IIIc.StageIIIc patients had predominantly 4 diffuse types , one trabecular and one macro follicular types. Mitoses were 2+ in 4 cases of diffuse and one case of trabecular types. Nuclear atypia was 2 + in 4 cases of diffuse types, one trabecular and one macro follicular types. Nuclear atypia was 3+ in one diffuse type with Stage IIIcpresentation.Lympho vascular invasion was present in four cases of diffuse types including 1 bilateral tumour (31%).

**Figure 2** shows the survival curves. Stage of GCT and the relapse period.




The figure 2 compares the relapse of the Stage Ia and Stage IIIc at the time period of 24 months. The curve shows that the relapse occured at the time period between 9 to 12 months in the stage IIIcwhereas in the stage Ia , no relapse had occured after the treatment. Mean Survival was worse in patients with residual disease as compared to patients without residual disease but it was not statistically significant using Log rank test ( Chisquare = 0.042; P value = 0.837)

## V. Discussion

GCTs are rare neoplasms with indolent behavior. The present study highlights our institutional experience with these rare tumours. Though GCTs have bimodal age distribution, the peak incidence is in postmenopausal periodwith median age of diagnosis at 48 years ( 25-65 years) in this study. Mostly patients present with abdominal pain, distension, mass and menstrual disturbances. In this study, most of the patients presented withpostmenopausal bleeding (40%) . The median diameter of tumor was 10 cm ( 4–28 cm) with no evidence of tumour rupture.Tumors greater than 10-15 cm in diameterhave been associated with high recurrence rates independent of Stage. Also, patientswithresidual disease after surgery might have a poor prognosis.Over 90% of GCTs are stage I when diagnosed and ten year survival is 85- 90%. Busby and Anderson observed that the operative stage is a more valuable prognostic indicator than the histological grade. Malmstrom et al found 94% survival rates after 5 years in stageI as compared to 44% in Stages II and III. Patients with high risk stage I disease associated with large tumor size (≥10-15 cm), stage IC,poorly differentiated tumor, high mitotic index, or tumor rupture should be considered for adjuvant chemotherapy so as to avoid relapses Prognosis is less favourable for bilateral tumors. Diffuse sarcomatoid cell types are associated with increased mortality. Fox et al observed that the prognosis was worse for women with large and solidtumors. In the present study,56.6% of the patientswere presented with Stage I a.8 patients with stage I had better survival (mean duration 11-25 months). 5 patients presented withStage III hada mean survival period as 8.2 months.

## VI. Conclusion

Majority of the patients with GCT ovary present in early stage with afavorable prognosis. Advanced stage and presence of residual disease were associated with poor prognosis. The limitations of our study are smallnumber of patients and prospective multicentric trial is needed to address therole of adjuvant therapies along with future cohort study predicting survival.

**Acknowledgements**:
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