Clinicopathological Pattern and Surgical Outcomes in Ovarian Neoplasms Diagnosed in Women Age Less than 40 Years in a Tertiary Care Centre

Dr. Vismaya J¹ Dr. Amrutha Ramachandran²; Dr. Jayasree S² (Co Authors) Government Medical College, Kozhikode

ABSTRACT

> Introduction:

Ovarian cancer is an important cause of morbidity and mortality among women. About 15–20% of all gynecological cancers are ovarian cancer. According to the Age Specific Incidence Rate (ASIR) for ovarian cancer, the incidence of disease increases starting at age of 35 and peaks between ages 55 and 64. Ovarian tumors frequently go undetected until they are large or in an advanced stage because their symptoms are vague and subtle. Mortality and recurrence depend on the stage of disease, tumor histology, initial treatment and any residual disease after surgery. Women with epithelial malignancies, advanced-stage disease and those who had residual tumors after cytoreductive surgery are more likely to experience recurrence and die. Health care professionals must be aware of the clinicopathology, epidemiology and histological type of ovarian cancer in order to do screening, early identification and management. There is a relative paucity of studies on ovarian tumors in younger age as compared to those in older age group. There is a need for further studies to define the clinicopathological criteria underlying ovarian tumors in the younger age.

> Objectives:

- To analyze the clinicopathological pattern of ovarian neoplasms, diagnosed and operated in women 15 years to 40 years of age at government medical college Kozhikode from 1st April 2021 to 1st April 2022.
- To analyze the surgical and treatment outcomes of these patients over a period of 6 months.

> Materials and Methods:

A Prospective cohort study conducted among 60 consecutive patients, aged 15 years to 40 years diagnosed with ovarian neoplasms who underwent surgery, either laparoscopy or laparotomy at government medical college Kozhikode. The study period was from 1st APRIL 2021 to 1st APRIL 2022 and they were followed up for 6 months after treatment. Statistical tests of association using SPSS (version 25.0) wereemployed at the level of significance of 5%.

A proforma designed with history, examination, investigations, ultrasonography, serum tumor markers, CECT and details of surgery were recorded for these patients. Patients were followed up to 6 months after the surgery. Histopathological findings collected. Details of further treatment and recurrence was obtained. Tumor markers and USG were done 6 months after surgery. Data collected were analyzed.

> Results

Out of 60 cases, 22% were between 15-20 years, 38% were between 20-30 years and 40% were >30 years. 31.7% patients underwent staging laparotomy and hysterectomy. 5% patients underwent interval cytoreduction surgery and hysterectomy. Ovariancystectomy done for 18.3% and ovariotomy done for 38.4% patients. Para ovarian cystectomy and laparoscopic cystectomy done for 5% and 1.7% patients respectively. 43 cases (71.67%) were benign,5 cases (8.3%) were borderline and 12 cases (20%) were malignant. Among them 39 were surface epithelial tumors (65%), germ cell tumors 17(28%), sex cord stromal tumors 3(5%) and metastasis 1(2%). Among benign ovarian tumors 37.2% were serous cystadenoma,35% were mature cystic teratoma, 23.2% mucinous cystadenoma and fibroma 4.6% respectively. Among the malignant tumors 72% were epithelial,14% germ cell tumors and sex cord stromal tumors and metastasis 7%. Among the epithelial cancers 51% were serous tumors, 37% endometroid cancers and 12% mucinous tumors. 10 patients required chemotherapy and 2 patients had recurrence-1 mucinous carcinoma & 1 case of high-grade serous carcinoma.

> Conclusion

In this study on ovarian neoplasms among women 15 to 40 years of age, most common presenting symptoms was abdominal pain/abdominal distension. IOTA simplerule has sensitivity of 91.67% and specificity of 93.9% in predicting malignant tumorsfrom benign tumors. Tumor markers has no predictive ability in diagnosing malignantovarian neoplasm in this study. Staging laparotomy with hysterectomy and interval cytoreduction with hysterectomy done in 36.7% cases. Fertility preserving surgeries were done in 63.33% cases and they were benign. Surface epithelial tumors is the most common type of tumor, followed by germ cell tumors. Benign tumors (71.67%) are more common than malignant tumors (20%). Most common tumor was serous cystadenoma. Most common malignant tumor was serous epithelial tumors. On followup 2 patients had recurrence within 6 months and they were having stage 3 disease.

Keywords:- Ovarian Tumors, Clinicopathological Patterns, Surgical Outcomes.

CONTENTS

| SL No. | Title | Page No. |
|-----------------------|--|----------|
| | ABSTRACT | 637 |
| | LIST OF ABBREVATIONS USED | 641 |
| CHAPTER ONE | INTRODUCTION | 642 |
| \blacktriangleright | AIMS AND OBJECTIVES | 643 |
| CHAPTER TWO | REVIEW OF LITERATURE AND BACKGROUND | 644 |
| CHAPTER THREE | MATERIALS AND METHODS | 650 |
| CHAPTER FOUR | RESULTS AND ANALYSIS | 651 |
| CHAPTER FIVE | DISCUSSION | 664 |
| CHAPTER SIX | SUMMARY | 668 |
| CHAPTER SEVEN | CONCLUSION | 670 |
| | LIMITATIONS | 671 |
| | REFERENCES | 672 |
| | ANNEXURE | 674 |
| \checkmark | Consent form | 674 |

LIST OF TABLES

| SL.NO | TABLES | PAGES |
|-------|--|-------|
| 1 | FIGO Staging for Primary Carcinoma of the Ovary, Fallopian Tube, or Primary Peritoneal Cancer (13) | 645 |
| 2 | Age Wise Distribution | 651 |
| 3 | History of Treatment for Ovarian Factor Infertility | 651 |
| 4 | Parity and Incidence of Ovarian Tumors | 652 |
| 5 | Previous Gynecological Procedures done for Diagnostic Purpose | 652 |
| 6 | Previous Gynecological Procedures done for Therapeutic Purpose | 652 |
| 7 | Symptoms | 652 |
| 8 | Family History of other Cancers | 653 |
| 9 | BMI and Incidence of Ovarian Tumors | 653 |
| 10 | CA 125 Frequency | 654 |
| 11 | CEA Frequency | 654 |
| 12 | LDH Frequency | 654 |
| 13 | AFP Frequency | 654 |
| 14 | BHCG Frequency | 654 |
| 15 | IOTA Simple Rules | 654 |
| 16 | Echogenicity | 655 |
| 17 | Locularity | 655 |
| 18 | Septations | 655 |
| 19 | Vascularization | 655 |
| 20 | Types of Surgery | 655 |
| 21 | Ascitic Fluid | 655 |
| 22 | Capsule of Tumors | 656 |
| 23 | Size of Tumors | 656 |
| 24 | Laterality of Tumors | 656 |
| 25 | Consistency of Tumors | 656 |
| 26 | Types of Tumors | 657 |
| 27 | Benign Ovarian Tumors | 657 |
| 28 | Borderline Ovarian Tumors | 658 |
| 29 | Malignant Ovarian Tumors | 658 |
| 30 | Epithelial Ovarian Cancers | 659 |
| 31 | Types of Ovarian Tumors | 659 |
| 32 | Types of Tumors and Age Wise Distribution | 660 |
| 33 | Parity and Type of Ovarian Tumors | 660 |
| 34 | CA 125 and Type of Tumors | 660 |
| 35 | CA 125 Levels and Malignant Tumors | 661 |
| 36 | CEA and Types of Tumors | 661 |
| 37 | LDH Levels and Types of Tumors | 661 |
| 38 | IOTA Simple Rules and Types of Tumors | 662 |
| 39 | IOTA and Malignancy | 662 |
| 40 | Size of Tumors and Types of Tumors | 662 |
| 41 | Types of Tumors and Laterality | 663 |
| 42 | Types of Tumors and Consistency | 663 |
| 43 | Stage of Ovarian Malignancy | 663 |
| 44 | Treatment after Surgery | 663 |

LISTS OF FIGURES

| SL.NO | FIGURES | PAGES |
|-------|---|-------|
| 1 | Age Wise Distribution | 651 |
| 2 | History of Treatment for Ovarian Factor Infertility | 651 |
| 3 | Parity and Incidence of Ovarian Tumors | 652 |
| 4 | Symptoms | 653 |
| 5 | BMI and Incidence of Ovarian Tumors | 653 |
| 6 | Size of Tumors | 656 |
| 7 | Types of Tumors | 657 |
| 8 | Benign Ovarian Tumors | 657 |
| 9 | Borderline Ovarian Tumors | 658 |
| 10 | Malignant Ovarian Tumors | 658 |
| 11 | Epithelial Ovarian Cancers | 659 |
| 12 | Types of Ovarian Tumors | 659 |
| 13 | Roc Curve of CA 125 Levels | 661 |

LIST OF ABBREVATIONS USED

| RMI | - | Risk of Malignancy IndexCA 125 - Cancer Antigen 125 |
|-----------|---|--|
| AFP | - | Alpha-fetoprotein |
| Beta-HCG | - | Beta Human Chorionic GonadotropinCEA - Carcinoembryonic antigen |
| LDH | - | Lactate dehydrogenaseBRCA - Breast Cancer gene |
| HNPCC | - | hereditary conditions such as hereditary nonpolyposiscolorectal cancer |
| BMI | - | Body mass index |
| USG | - | Ultrasonography |
| PARP | - | poly (ADP-ribose) polymerase |
| TAH + BSO | - | Transabdominal hysterectomy with bilateral salphingo-oophorectomy |
| EOC | - | Epithelial ovarian cancer |
| AUC | - | Area under the curve |
| CECT | - | Contrast enhanced computed tomographyOCP - Oral contraceptive pill |
| BEP | - | Bleomycin, etoposide and cisplatinCP - Carboplatin, paclitaxel |
| | | |

CHAPTER ONE INTRODUCTION

Ovarian cancer is an important cause of morbidity and mortality in women. Ovarian malignancy represents about 15-20% of all gynecological cancers (1). Age- standardized incidence rates of ovarian cancer in several area registries in India range from 0.26 to 2.44% each year, according to trend analysis. An upwards trend may be caused by increased awareness of risk factors, increased exposure to them, or an increase in the proportion of older women (2). Even though they offer crucial diagnostic hints in creating a differential diagnosis, the clinical or physical characteristics of the majority of ovarian cancers cannot be reliably used to distinguish one from another.

Age of patient is one of the most significant clinical indicators. Post-menopausal women account for more than 80% of epithelial ovarian cancer cases. Invasive epithelial ovarian cancer incidence peaks at 56 to 60 years of age. Nearly 70% of ovarian cancers in the first two decades of life have germ cell origin, with one third being malignant. Juvenile granulosa cell tumors are less common (5%), with adult granulosa cell tumors accounting for the majority (95%) of cases. Juvenile granulosa cell tumors are diagnosed in women under 30 years of age, but adult granulosa cell tumors almost invariably occur in postmenopausal women (3). According to the Age Specific Incidence Rate (ASIR) for ovarian cancer, the disease worsens with age and reaches a peak between the ages 55- 64. (4)

Laterality of tumors can also reveal information about their nature; for instance, sex cord stromal tumors are often restricted to a single ovary, but most metastatic tumors are bilateral. Gross characteristics can aid in differential diagnosis and depict the overall behavior of a tumor, for example, most benign epithelial tumors are cystic, whereas the discovery of solid elements and papillary projections increases the likelihood of malignancy. However, a precise diagnosis is mostly based on the variety of microscopic characteristics they display. (5)

Epithelial and germ cell tumors were the predominant type of ovarian tumors followed by stromal cell tumors. The majority are benign epithelial tumors, with benign serous cystadenoma being the most prevalent type. Mature cystic teratoma was the most common variety of germ cell tumor. The most frequent tumor in children and adolescents are germ cell tumor (6). Studies show that malignant tumors can manifest at a younger age. Ovarian tumors frequently go undetected until they are large or in an advanced stage because their symptoms are vague and subtle. Early detection ishindered by late presentation and inadequate screening techniques.

Tumor markers: **CA-125** - Positive in epithelial carcinoma: used to assist in diagnosis, estimate treatment response, and monitor for recurrence, particularly in serous carcinomas. **Alpha-fetoprotein** (AFP) used in malignancies of ovarian germ cells. used to evaluate the stage, prognosis, and therapy response. **Beta-HCG** (Beta Human Chorionic Gonadotropin) used in malignancies of ovarian germ cells. used to evaluate the stage, prognosis, and therapy response. **CEA** (Carcinoembryonic antigen) elevated in epithelial ovarian tumors, raised in mucinous carcinoma, pseudo myxomatous peritonei, and krukenberg tumor and may be used to assess treatment response. **LDH** positive in epithelial carcinoma and dysgerminoma and other solid germ cell tumors.

Surgery is often the initial treatment of choice for ovarian cancer. Neoadjuvant chemotherapy, followed by interval debulking surgery, and further chemotherapy, should be considered for patients who are not candidates for optimal debulking. Surgery aims to resect any visible tumors, establish the extent of the disease, and confirm the diagnosis. In addition to chemotherapy with a taxane and a platinum complex (e.g., paclitaxel plus carboplatin), surgery should be done. Following surgery and/or chemotherapy, maintenance therapy with Olaparib may considerably increase survival in patients with BRCA mutations (7). Even after a thorough search, primary tumors are usually undetected in women who have peritoneal carcinomatosis and no pelvic mass detected at the time of presentation. These individuals can be treated with cytoreductive surgery and platinum-based chemotherapy if it is assumed that they haveprimary peritoneal carcinoma or ovarian carcinoma.

Appropriate surgical approach depends, whether illness is visible outside the ovaries. Adequate surgical staging is crucial, because microscopic metastases occur often in patients with no cancer visible outside the ovaries. Individualized surgery is necessary for patients with stage IV disease, especially when the disease is in the liver and above the diaphragm. If medically fit, patients who are at stage IV disease due to small-volume illness in the thorax, abdominal wall, or liver may be candidates for cytoreductive surgery. Perform a total abdominal hysterectomy and remove the contralateral ovary if the patient does not want to become fertile in the future. If mucinous tumors are diagnosed appendectomy can be performed. All visible tumors should be removed if there is macroscopic disease present outside of the ovary. This might necessitate major surgery, such as splenectomy, colon resection, removal of peritoneal implants, liver resection, and omentectomy. The degree of intestinal resection should be determined by its contribution for achieving the greatest amount of cytoreduction. The standard care for ovarian cancer includes surgical exploration for primary staging and for cytoreduction or debulking. Comprehensive surgical staging is recommended if it seems that the disease is limited to the pelvis. Regardless of the approach, staging needs a number of key elements. All peritoneal surfaces, the liver, the large and small bowels, the mesentery, the stomach, the appendix, the kidneys, the spleen, the retroperitoneal spaces, and all pelvic structures should be carefully examined and/or palpated. Peritoneal cytology, multiple

peritoneal biopsies, omentectomy, pelvic and para-aortic lymph node biopsy, and peritoneal cytology should all be included in the staging procedure. (8)

Five-year survival rates range from 30-50% for all stages of ovarianmalignancies. (9) The seventh leading cause of mortality and morbidity for women is ovarian cancer. The worst gynecological cancer for women worldwide is ovarian cancer. According to statistics, ovarian cancer is the 18th deadliest disease in the world. In general, ovarian cancer has a relative survival rate of 45%. (10) Ovarian cancer has become a public health concern as a result of rising incidence rates and longer life expectancies. The diagnosis and prognosis of ovarian cancers depend on their histological type. Hence it is crucial for patient treatment to identify the distinct histological patterns of ovarian tumors (5). Time to death and recurrence depended on the stage of disease, tumor histology, first treatment, and any remaining disease at surgery. Women with epithelial malignancies, advanced-stage disease, and those who had residual tumor after cytoreductive surgery have higher mortality and recurrence rates. (11) Therefore, an understanding of clinicopathological epidemiological factors and histological type of ovarian cancer is important for health care providers for screening, early detection and management.

➤ Aims and Objectives of Study

- To analyze the clinicopathological pattern of ovarian neoplasm, diagnosed and operated in women 15yrs to 40 years of age at government medical college Kozhikode from 1st April 2021 to 1st April 2022.
- To analyze the surgical and treatment outcomes of these patients over a period of 6 months.

CHAPTER TWO

REVIEW OF LITERATURE AND BACKGROUND

➢ Epidemiology

Ovarian cancer is the fifth most common cause of death from malignancy in women. The most frequent ovarian/fallopian malignancy is epithelial carcinoma, and more than two-thirds of patients had advanced illness at initial diagnosis. Ovarian cancer diagnosis and death rates range from 1% to 1.5% throughout the course of a lifetime. The average age at which invasive epithelial ovarian cancer first manifests is around 60 years. Only around 7% of ovarian epithelial tumors in premenopausal females are malignant, compared to about 30% of ovarian neoplasms in postmenopausal women. The average age of individuals with borderline tumors at diagnosis is roughly 46 years old. (3)

Evidence points that fallopian tube cancer, epithelial ovarian cancer and primaryperitoneal carcinomatosis are derived from Müllerian epithelium. Hence, they have a similar management. As with mucinous subtypes, clear cell and endometrioid ovarian tumors associated with endometriosis have distinct patterns of gene expression. (7)

➤ Anatomy

The body of the uterus is located under a layer of peritoneum. Fallopian tube arises from the cornual end of uterus. The fimbriated ends of the fallopian tubes are inclose apposition to the ovaries and in the peritoneal space. (7)

- Risk Factors (7)
- Increasing age
- Family history of ovarian cancer. A first-degree relative (e.g., mother, daughter, or sister) with the disease.
- Inherited risk. BRCA1 or BRCA2 gene mutations.
- Other hereditary conditions such as hereditary nonpolyposis colorectal cancer(HNPCC; also called Lynch syndrome).
- Endometriosis.
- Hormone therapy-Postmenopausal hormone replacement therapy.
- Obesity High body mass index.
- Tall Height
- Low parity and infertility
- Clinical Presentation (7)

Ovarian, fallopian tube, or peritoneal cancer may not cause early signs or symptoms. Signs or symptoms develop when the cancer is advanced.

- Pain, swelling, or a feeling of pressure in the abdomen or pelvis.
- Urinary urgency or frequency.
- Difficulty eating or feeling full.
- A lump in the pelvic area.
- Gastrointestinal problems such as gas, bloating, or constipationScreening of ovarian cancers

In detecting ovarian cancer gynecologic assessment, vaginal ultrasound, and cancer antigen 125 (CA-125) assay have low predictive value only. (7)

Diagnostic and Staging Evaluation (7)

- Physical exam and history.
- Pelvic exam.
- CA-125 assay.
- Ultrasonography (pelvic or transvaginal).
- Computed tomography (CT) scan.
- Positron emission tomography (PET) scan.
- Magnetic resonance imaging (MRI).
- Chest x-ray.
- Biopsy.

CA-125 and transvaginal ultrasonography cannot be used routinely to screen women for ovarian cancer due to the falsepositive results particularly in premenopausal women, and the lack of evidence from randomized trials that screening with CA-125 and TVUS reduces the mortality of ovarian cancer. (3)

➢ IOTA the original Simple Rules (2008) (12)

Used to diagnose ovarian cancer in women who have at least one persistent adnexal(ovarian, para-ovarian, and tubal) tumor and are considered to require surgery.

- Benign features
- Unilocular cyst
- Smooth multilocular tumor <10 cm
- Solid components <7 mm in diameter
- Presence of acoustic shadows
- No detectable Doppler signal
- Malignant features
- Irregular solid tumor
- Irregular multilocular-solid mass >10 cm in diameter
- \geq 4 papillary structures
- Ascites
- High Doppler signal (color score 4)

> Tumors are Classified as Benign, Malignant or Inconclusive

- Benign Only Benign features apply
- Malignant Only Malignant features apply
- Inconclusive No features apply or both Benign and Malignant features apply
- Prognostic Factors (7)
- Younger age.
- Good performance status.
- Cell type other than mucinous or clear cell.
- Well-differentiated tumor.
- Early-stage disease.
- Absence of ascites.
- Lower disease volume before surgical debulking.
- Smaller residual tumor after primary cytoreductive surgery.
- BRCA1 or BRCA2 mutation carrier.

→ Histological Types of Ovarian Cancer and Cellular Origin (3)

- Serous Endo salpingeal
- Mucinous Intestinal, endocervical
- Endometrioid Endometrial
- Clear cell Müllerian
- Brenner Transitional
- Mixed epithelial Mixed
- Undifferentiated May be anaplastic
- Unclassified

Table 1 FIGO Staging for Primary Carcinoma of the Ovary, Fallopian Tube, or Primary Peritoneal Cancer (13)

| Stage 1 | Growth Limited to the Ovaries or Fallopian Tubes |
|----------|--|
| IA | Growth limited to one ovary or fallopian; no ascites containing malignant cells, No tumor on the external surface; |
| | capsule intact |
| IB | Growth limited to both ovaries or fallopian tubes; no ascites |
| | containing malignant cells, No tumor on the external surface; capsule intact |
| IC | Tumor limited to one or both ovaries or fallopian tubes with any of the following: |
| 1C1 | Surgical spill |
| 1C2 | Capsule ruptured before surgery or tumor on ovarian or fallopian tube surface |
| 1C3 | Malignant cells in the ascites or peritoneal washings |
| Stage II | Growth involving one or both ovaries or fallopian tubes with pelvic extension (below the pelvic brim) |
| IIA | Extension and/or metastases to the uterus and/or fallopian tubesand/or ovaries |

| IIB | Extension to other pelvic tissues |
|-----------|--|
| Stage III | Tumor involving one or both ovaries or fallopian tubes or peritoneal cancer with cytologically or histologically |
| | confirmed spread to the peritoneum outside the pelvis and/or metastasis to the retroperitoneal lymph nodes |
| IIIA | Positive retroperitoneal lymph nodes and/or microscopic metastasis beyond pelvis |
| IIIA1(i) | Positive retroperitoneal lymph nodes with metastasis up to 10 mmin greatest dimension |
| IIIA1(ii) | Positive retroperitoneal lymph nodes with metastasis more than 10 mm in greatest dimension |
| IIIA2 | Microscopic extra pelvic (above the pelvic brim) peritoneal involvement, with or without positive |
| | retroperitoneal lymph nodes |
| IIIB | Macroscopic peritoneal metastasis beyond pelvis up to 2 cm in greatest dimension, with or without positive |
| | retroperitoneal nodes |
| IIIC | Macroscopic peritoneal metastasis beyond pelvis more than 2 cm in greatest dimension |
| Stage IV | Distant metastasis (excludes peritoneal metastasis) |
| IVA | Pleural effusion is present, there must be positive cytologic test results |
| IVB | Parenchymal metastases and metastases to extra-abdominal organs (including lymph nodes and lymph nodes |
| | outside the abdominalcavity) |

➤ Treatment

Stages I and II are considered early stages, whereas stages III and IV are considered advanced stages of ovarian cancer. Prior to attempting interval cytoreductive surgery, two to three cycles of neoadjuvant chemotherapy are given to patients who are determined to have a poor performance status, a high perioperative risk, or a low probability of achieving optimal cytoreduction to no visible, or palpable residual disease, or at least cytoreduction to less than 1 cm of residual disease. Primarycytoreductive surgery should be offered to patients with advanced ovarian cancer whoare medically fit for major surgery and have resectable disease. The pathological diagnosis of ovarian, fallopian tube, or peritoneal cancer must be made on biopsy before beginning neoadjuvant chemotherapy. (3)

Carboplatin and paclitaxel (CP) combination chemotherapy is recommended for patients with high-risk, low-stage disease. The decision between intravenous (IV) versus intraperitoneal (IP) platinum and taxane treatment with the addition of bevacizumab for advanced-stage epithelial ovarian cancer should be made individually. 3-weekly regimens remain the standard of care. BRCA-associated ovarian cancers haveincreased sensitivity to platinum chemotherapy and to poly (ADP-ribose) polymerase (PARP) inhibitors. In the recurrent setting, PARP inhibitors are approved to treat selected patients with recurrent ovarian cancer and for maintenance therapy following response to platinum-based chemotherapy. Regardless of BRCA status, these agents increase progression-free survival. (3)

Nearly 70% of ovarian tumors in the first two decades of life have germ cell origin, with one-third of these being malignant. The most prevalent malignant germ celltumors are dysgerminomas, immature teratomas, and endodermal sinus tumors. Germ cell malignancies spread quickly (EST). In the majority of patients, fertility preservation should be norm. Bleomycin, etoposide, and cisplatin constitute the most effective chemotherapy drugs (BEP). (3)

Adult granulosa cell tumors are a subtype of stromal tumors and are low-grademalignancies. 70% of ovarian sex cord-stromal cancers are adult granulosa cell tumor. The most prevalent variety of malignant ovarian sex cord-stromal tumors are granulosacell tumors. They are amenable to conservative treatment in premenopausal women. The value of adjuvant chemotherapy is unknown. (3)

Eileen Lalrinpuii et al(11) conducted a study among 93 patients and found that 72% of the ovarian malignancies younger than 40 years were epithelial in origin. Serous cystadenocarcinoma was the most prevalent malignancy (33.3%). 23% of cases had germ cell tumors, the most prevalent of which was mixed malignant germ cell tumor. Of the epithelial ovarian malignancies, 46.3% had serous histology, 34.3% had mucinous histology, 16.4% were endometrioid, and 3.0% were clear cell tumors. Malignant germ cell tumors included 14.3% dysgerminomas, 23.8% immature teratomas, 19.0% yolk sac tumors, and 42.9% mixed germ cell tumors. Among the advanced ovarian cancer, 80.1% patient belonged to the epithelial group and 19.5% patients belonged to non-epithelioid group. 23.7% of patients underwent fertility- sparing surgery, while 76.3% of patients had optimum debulking. In the epithelial group, 44.23% of patients experienced recurrence, compared to 20.83% of patients in the non- epithelial group. The time to recurrence for epithelial tumors was 3.8 years and for non- epithelial tumors was 5.3 years.

In a study by Purti Agrawal et al(5) Ovarian tumor incidence peaked in the third and fifth decades, accounting for 22.6% and 26.5% of cases, respectively. Germ cell tumors were prevalent in the 11–30 age range, benign tumors predominated in the 21–40 age range, and malignant tumors predominated in the above 40 age group. In the first two decades, 60% of germ cell cancers occurred. The third and fourth decades had the highest frequency of mature cystic teratoma. Regardless of the kind of tumor, abdominal pain was the most frequent presenting complaint in 50.9% of patients and an abdominal lump in 29.2% of patients. The signs of borderline and malignant tumors were ascites, anorexia, and weight loss. The CA 125 test had a sensitivity of 90.9%, a specificity of 40%, and a diagnostic precision of 81.5%. Cystectomy made up 57.3% and 43.8% of the surgical specimen for

benign and borderline ovarian tumors. 80.6% of the surgical specimen for malignant ovarian tumors, was transabdominal hysterectomy with bilateral salphingo-oophorectomy (TAH + BSO) with or without omentum. 3-30 cm, 7-32 cm, and 4-25 cm were the size range of benign, borderline, and malignant tumors, respectively. Bilaterality was common in malignant tumors. The majority of benign and borderline tumors were unilateral. Among unilateral tumors right and left sides were equally affected. 10.6% of cases involved both ovaries.

In a study by SK Mondal et al(4) Most benign tumors developed between the ages of 20 and 40, while most malignant lesions developed between the ages of 41 and 50. The median age at which all ovarian tumors presented was 35 years, while the median age at which all malignant lesions presented was 48 years. Under the age of 20,germ cell cancers were more common. 72% of metastatic tumors, 49.5% of malignant serous tumors, and 28.1% of malignant mucinous tumors affected bilateral ovaries. Bilateral involvement was seen more frequently in borderline serous tumors (27.4%) than in borderline mucinous tumors (15.7%). Stage III (60%) or stage II (20%) diseasewas the most common presentation for malignant tumors.

In a study by N Gupta et al(6) both benign (94.1%) and malignant (78.8%) tumors tended to develop unilaterally. Of all tumors, 87.7% were unilateral and 12.3% were bilateral. 86.8% of epithelial tumors were unilateral and 13.2% were bilateral. 87.2% of germ cell tumors were unilateral and 12.8% were bilateral. Only unilateral sex cord stromal and metastatic tumors were observed. In 56% of cases, the tumor was cystic, in 32.1% of cases it was solid-cystic, and in 11.9% of cases it was solid. Cystic epithelial tumors made up 63.7% of all cases, solid-cystic epithelial tumors made up 28.1%, and solid epithelial tumors made up 8.2%. 43.5% of germ cell tumors were cystic, 45.6% were solid-cystic, and 10.9% were solid. 33.3% of sex cord-stromal tumors were cystic + solid, while 66.7% were solid. 25% of other category tumors were solid-cystic, and 75% were solid. 14.7% were in size range of up to 5 cm, 41.8% werein range of 5–10 cm, 24.1% in range of 10–15 cm, 10.6% in 15–20 cm, 5.9% in 20–25 cm, 2.9% in 25–30 cm size range.

In a study by Basu P et al(9) the patients with germ cell malignancies were on average 26.0 + 12.9 years old. 80% of all malignant ovarian tumors had epithelial origins. At the time of diagnosis, more than 80% of the patients were in stages III or IV. Serous adenocarcinoma and dysgerminoma were the most prevalent histological forms among epithelial malignancies and germ cell cancers, respectively. In comparison to patients with substantial residual disease, those with less than 2 cm of residual disease after surgery had considerably improved overall survival.

In a study by Shabir et al(10) Ovarian cancer risk was 30% greater in endometriosis-positive women. Ovarian tumors with epithelial origin accounted for 90% of cases. The following subtypes of epithelial ovarian cancer are present: serous (80% of non-mucinous), endometrioid (10%), clear cell (10%), mucinous (3%), and unidentified subtypes (5%). Compared to epithelial malignancies, non-epithelial cancers are less invasive. Before surgery, a woman who has been diagnosed with ovarian cancer is tested for CA125, which is elevated in more than 80% of women with advanced epithelial ovarian cancer. In serous, Stage 1 and mucinous EOC, the sensitivity of CA125 is higher, lower, and lowest, respectively. One or both ovaries are affected in ovarian cancer in 25% of women with pelvic involvement.

In a study by MA Sofi et al(14) while 58% of malignant ovarian neoplasms were found in individuals over 40, 58.2% of benign ovarian neoplasms were found in patients under 40. In the 20 to 40year age range, non-neoplastic lesions made up 68.6% of the total tumors. Abdominal pain or discomfort was the most common symptom (64.7%). 53.8% of patients had abdominal bloating or distension. 21.8% of people hadascites. Ascites was exhibited by malignant tumors, with the exception of one benign mucinous cyst adenoma that ruptured. The majority (42.6%) of non-neoplastic cases had no symptoms. Ovarian tumors were more common in nulliparous people (25.2%) and those with parities of lower than three (49.6%), compared to people with parities of three or more (25.2%).84.9% of cases only included one ovary. Right-sided tumors made up 59.7% of cases, whereas left-sided tumors made up 35.7%. 94.0% of the benign tumors had a unilateral involvement. The majority of cases (88.6%) with non-neoplastic lesions were unilateral. In total, 28.6% of the non-neoplastic tumors were on the right. 11.4% of the overall non-neoplastic lesions were bilateral tumors.

On a gross inspection, 63.8% were found to be between 1 and 10 cm in size. 49.6% of neoplastic lesions had cystic neoplasms, 16.8% had solid lesions, and 33.6% had mixed lesions. 94.3% of the cysts in non-neoplastic tumors had a size between 1 and 10 cm. Out of the neoplastic lesions, 16.8% had solid consistency, 49.6% had cystic consistency, and 33.6% had mixed consistency. Among non-neoplastic tumors, 94.3% of the cysts had a size between 1 and 10 cm. A total of 74.8% of ovarian neoplasms were surface epithelial tumors, followed by germ cell tumors (16.0%), sex cord stromal tumors (1.7%), and metastatic ovarian cancers (5.9%). 73.1% of all benign neoplasms were benign surface epithelial tumors, and 76.0% of all malignant neoplasms were epithelial tumors. (13)

In a study by U Singh et al(1) the mean age for benign ovarian neoplasms was 23, for borderline ovarian neoplasms it was 34.4, and for malignant ovarian neoplasms it was 41.2. In the age range under 40 years, a new trend of increased serous cystadenocarcinoma frequency was observed. Maximum number of neoplasms were seen in age group 31–40 years.

NS Murthy et al(2) conducted a study and found that although it has been observed that women with a family history of ovarian and breast cancer in first-degree relatives are at increased risk of developing the disease, family history may only be a factor in 4-5% of cases. The progressive rise in the prevalence of ovarian cancer in India may have been caused by variables related to a change in lifestyle, such as an increase in the age at marriage, a delay in the age at the first birth, a reduction in parity, and improved socioeconomic situations.

In a study by K Chandra et al(15) in 92.5% of cases, abdominal discomfort was the most prevalent symptom, followed by abdominal distension in 89.2% of cases, menstrual irregularities in 54.2%, pelvic pain in 26.4% of cases, constipation in 9.4% of cases, intermittent intestinal obstruction in 2.3% of cases, and ascites in 2.3% of cases. Abdominal discomfort is the most typical symptom of both benign and malignant tumors. Torsion was the main cause of acute pain in benign tumors, but persistent pain in larger tumors have a higher risk of malignancy.

R Jha et al(16) conducted a study and up to 30 years, serous carcinomas were not observed. Only 16.6% of serous carcinomas were seen in people under 40 years. In the third and fourth decades, 60.3% of all germ cell tumors were diagnosed. For the first 30 years, only germ cell tumors were malignant; all other tumors were benign. Allgerm cell cancers older than 30 years were benign. Only 3.1% of the ovarian cancers were sex cord stromal tumors. They were never seen before the age of 15.

In a study conducted by Engeland A et al(17) women who were overweight orobese in adolescence or young adulthood had a higher risk of ovarian cancer compared to those with a medium BMI (18.5-24.9 kg/m2). In comparison to women with medium BMI, those with very high BMI in adolescence had a relative risk of 1.56. In women under the age of 60, there was a correlation between height and ovarian cancer risk, particularly endometrioid ovarian cancer.

F Parazzini et al(18) conducted a study and found that women having a familyhistory of breast cancer were more susceptible for developing ovarian cancer, while a family history of endometrial cancer did not significantly increase the risk.

In a study by Wan Q et al(19) cases of mucinous epithelial ovarian cancer, CEA is significantly expressed. Patients in the recurrent group and the metastatic grouphad significantly higher levels of CEA, indicating that prognosis and treatment decisions can be made based on changes in CEA levels. The sensitivity of CEA in diagnosing EOC was only 51.64%.

In a study by Deeba F et al(20) the validity of LDH in detecting malignant ovariantumors were sensitivity 57.1%, specificity 84.1%, accuracy 78.7%, positive predictivevalues 47.1% and negative predictive values 88.8%.

In a study by N Nunes et al(21) sensitivity of IOTA simple rules was 96.2% and specificity was 88.6% and they discovered that in the study populations with the highest occurrence of malignant tumors, sensitivity was higher and specificity was lower.

In a study by Tantipalakorn C et al (22) the simple rules yielded inconclusive results in 19.9% masses. sensitivity was 82.9% and specificity 95.3%. In identifying benign from malignant adnexal tumors, the IOTA simple guidelines have a high diagnostic performance.

In a study by Smith-Bindman R et al(23) based-on patient age and ultrasound results, women with complicated cysts or solid masses had a considerably increased chance of developing cancer. When compared to women with normal ovaries, the risk of ovarian cancer was not noticeably higher in 23.8% of women under 50 years and 13.4% of women 50 years or older with simple cysts.

Szender J B et al(24) conducted a study and found that the presence of ascites was inversely related to the capacity to perform optimum cytoreductive surgery and the amount of ascites at the time of the initial diagnosis of ovarian cancer was associated with worse survival.

In a study conducted by C.K. Lee et al(25) Women under 40 years tended to have diseases that were in less advanced stages. 65% of women under the age of 40 were still alive at five years. Progression-free interval is better, and at the most recent time of observation, more than 58% of women under the age of 40 remained free of disease. After 18 months, no women under the age of 40 experienced a relapse.

In a study by Uma Devi K et al(26) fertility-sparing surgery, salphingo- oophorectomy, omentectomy, peritoneal cytology, and retro peritoneal lymphadenectomy are performed in younger women. Other than patients with stage IA illness, all other patients need adjuvant chemotherapy in addition to fertility-preservingsurgery.

In a study conducted by Neeyalavira V et al(27) 80.3% of patients with germ cell tumors got conservative surgery, and 39.4% of them underwent conservative surgical staging. Just 18.4% of patients underwent non-fertility-sparing surgery. 71% received chemotherapy after surgery. 11.1% of patients had a partial response, while 73.3% had a complete response. By increasing tumor marker levels in 3 patients, recurrence was identified, and advanced stage represents a separate risk factor for

recurrence.

Bouchard-Fortier G et al(28) conducted a study and the women with endometrioid cancer had a five-year overall survival rate of 80.6%, while those with serous ovarian cancer had a survival rate of 35.0%. For endometrioid and serous histology, the 10-year overall survival rates were 68.4% and 18.4%, respectively.

CHAPTER THREE MATERIALS AND METHODS

Study Design

Prospective cohort study

➤ Study Setting

Department of Obstetrics and Gynecology, Government Medical College, Kozhikode.

Study Period

1st APRIL 2021 TO 1st APRIL 2022

> Study Population

Cases of ovarian malignancies in women 15 years to 40 years of age, those who undergo surgery in govt medical college hospital, Kozhikode during the time period of1st APRIL 2021 to 1st APRIL 2022

Sample Size:

From a study by Manzoor Ahmad Sofi et al (14) 64.7% of the patients presented with abdominal pain or discomfort. Expecting similar results, the sample size required by the formula n=4pq/d2 where d=20% of p is 47. Hence, I will be studying 50 patients.

> Study Subjects

➢ Inclusion Criteria

- Patients diagnosed with ovarian neoplasms who underwent surgery either laparoscopy or laparotomy at government medical college Kozhikode between age15 years to 40 years will be included in the study
- Patients undergoing primary surgery, those undergoing interval cytoreduction after neoadjuvant chemotherapy and those undergoing 2nd look surgery will be included in the study.
- ➢ Exclusion Criteria
- Patients who underwent definitive surgery outside government medical collegeKozhikode.

> Methodology

Consecutive patients diagnosed with ovarian tumors satisfying the inclusion criteria during the study period were selected for the study. A proforma designed withhistory, examination, investigations, ultrasonography, serum tumor markers, CECT and details of surgery is recorded. Patients who underwent surgery were followed up to 6 months after the surgery. Histopathological findings collected. Details of further treatment and recurrence was obtained. Tumor markers and USG done 6 months after surgery. Data collected were analyzed.

CHAPTER FOUR RESULTS AND ANALYSIS

| Table 2 Age Wise Distribution | | | | |
|-------------------------------|-----------|------------|--|--|
| Age (Years) | Frequency | Percentage | | |
| 15-20 | 13 | 21.7 | | |
| 20-30 | 22 | 36.7 | | |
| 30-40 | 25 | 41.7 | | |
| Total | 60 | 100.0 | | |

41.7% of patients belong to the age group between 30-40 years.





| | Frequency | Percentage |
|-------|-----------|------------|
| NO | 56 | 93.3% |
| YES | 4 | 6.7% |
| Total | 60 | 100.0% |



Fig 2 History of Treatment for Ovarian Factor Infertility

Among 4 patients 3 took Ovulation induction drugs.2 patients took Letrozole. 1 patient took it for 6 months and another patient for 2 months.1 patient took Clomiphene Citrate for 3 months.

IJISRT23DEC116

www.ijisrt.com

Table 4 Parity and Incidence of Ovarian Tumors

| | Frequency | Percentage |
|--------------|-----------|------------|
| NULLI PAROUS | 29 | 48.3% |
| PAROUS | 31 | 51.7% |
| Total | 60 | 100.0% |



Fig 3 Parity and Incidence of Ovarian Tumors 51.7% of Patients were Parous Women

| Procedure | Туре | No of Cases | Treatment Given |
|-----------------|---------------------------------|-------------|-------------------------------------|
| True cut biopsy | Malignant OvarianAdenocarcinoma | 1 | 6 Cycles of cisplatin andpaclitaxel |
| True cut biopsy | Poorly DifferentiatedCarcinoma | 2 | 6 cycles of cisplatin andpaclitaxel |

3 patients had history of advanced stage of disease and underwent true cut biopsy and diagnosed to have malignancy. They were given 6 cycles of cisplatin and paclitaxel and now they admitted for interval cytoreduction.

Table 6 Previous Gynecological Procedures done for Therapeutic Purpose

| Procedure | Туре | No of Cases |
|-------------------------------|--|-------------|
| Cystectomy | Mucinous Cyst Adenocarcinoma | 1 |
| Laparotomy | Stage 3 Endometriosis, Frozen Pelvis | 1 |
| Cystectomy | Right Mucinous Cyst Adenoma & Left Serous Cyst Adenoma | |
| Laparotomy | Mature Cystic Teratoma | |
| Cystectomy Serous Cystadenoma | | 1 |
| Cystectomy | Mucinous Borderline TumourWith Foci Of Microinvasion | 1 |

. . .

For 1 case of mucinous cystadenocarcinoma only cystectomy was done. •

| Table / Symptoms | | |
|--|-----------|------------|
| Symptoms | Frequency | Percentage |
| DYSPEPSIA | 3 | 5 |
| ABDOMINAL LUMP/DISTENSION | 30 | 50 |
| ABDOMINAL PAIN | 33 | 55 |
| IRREGULAR MENSES-AMENORRHEA/MENORRHAGIA | 4 | 6.67 |
| NAUSEA/ANOREXIA/EARLY SATIETY/CONSTIPATION | 5 | 8.33 |

T-1-1-7 C-

Most common symptoms were abdominal pain and abdominal lump/distension.

URINARY SYMPTOMS- RETENSION OF URINE/INCREASED FREQUENCY

LOSS OF APPETITE AND WEIGHT

Many patients have more than 1 symptom at the time of presentation.

1.67

1.67

1

1



Fig 4 Symptoms

Table 8 Family History of other Cancers

| | Frequecy | Percentage |
|----------------------|----------|------------|
| NO FAMILY HISTORY | 57 | 95.0 |
| CARCINOMA ENDOMETRUM | 1 | 1.7 |
| CARCINOMA BREAST | 2 | 3.3 |
| Total | 60 | 100.0 |

• 95% of the patients had no family history of carcinoma breast or carcinoma endometrium No patients had family history of carcinoma colon.

Table 9 BMI and Incidence of Ovarian Tumors

| | Frequency | Percentage |
|----------|-----------|------------|
| <18.5 | 5 | 8.3% |
| 185-22.9 | 24 | 40.0% |
| 23-24.9 | 13 | 21.7% |
| 25-29.9 | 13 | 21.7% |
| >30 | 5 | 8.3% |
| Total | 60 | 100.0% |



Fig 5 BMI and Incidence of Ovarian Tumors

- 40% of patients have BMI of 18.5kg/m² to 22.9kg/m². BMI less than 18.5kg/m² andmore than 30 kg/m² is seen only in 8.3% ٠ of patients.
- Tumor Markers \geq

| Table 10 CA 125 Frequency | | | |
|---------------------------|-----------|------------|--|
| CA 125 Levels (U/ml) | Frequency | Percentage | |
| <35 | 37 | 61.7% | |
| >35 | 23 | 38.3% | |
| Total | 60 | 100.0 | |

CA 125 levels are elevated in 38.3% of tumors.

Table 11 CEA Frequency

| CEA Levels (ng/ml) | Frequency | Percentage |
|--------------------|-----------|------------|
| NOT DONE | 5 | 8.3% |
| <2.5 | 49 | 81.7% |
| >2.5 | 6 | 10.0% |
| Total | 60 | 100.0 |

CEA levels are elevated in only 10% of patients.

Table 12 LDH Frequency

| LDH (U/L) | Frequency | Percentage | |
|-----------|-----------|------------|--|
| NOT DONE | 19 | 31.7% | |
| <280 | 11 | 18.3% | |
| >280 | 30 | 50.0% | |
| Total | 60 | 100.0 | |

In almost 50% of patients LDH levels are elevated.

Table 13 AFP Frequency

| AFP (ng/ml) | Frequency | Percentage |
|-------------|-----------|------------|
| NOT DONE | 25 | 41.7% |
| <400 | 33 | 55% |
| >400 | 2 | 3.3% |
| Total | 60 | 100.0 |

AFP levels are elevated only in 2 patients

Table 14 BHCG Frequency

| | 1 2 | |
|---------------|-----------|------------|
| BHCG (mIU/ml) | FREQUENCY | PERCENTAGE |
| NOT DONE | 24 | 40.0 |
| <5 | 35 | 58.3 |
| >5 | 1 | 1.7 |
| Total | 60 | 100.0 |
| | | |

S.BHG is elevated only in 1 tumor.

Table 15 IOTA Simple Rules

| Score | Frequency | Percentage |
|--------------|-----------|------------|
| BENIGN | 32 | 53.33% |
| MALIGNANT | 13 | 21.67% |
| INCONCLUSIVE | 15 | 25.0% |
| Total | 60 | 100.0 |

According to IOTA simple rules, 25% were inconclusive. 21.67% were suggestive ofmalignancy.

> USG Findings

| Table 16 Echogenicity | | |
|-----------------------|-----------|------------|
| Туре | Frequency | Percentage |
| SOLID | 11 | 18.3 |
| CYSTIC | 36 | 60.0 |
| COMPLEX | 13 | 21.7 |

In USG findings most of the ovarian tumors were cystic in echogenicity.

Table 17 Locularity

| Туре | Frequency | Percentage |
|--------------|-----------|------------|
| UNILOCULAR | 33 | 55.0% |
| MULTILOCULAR | 27 | 45.0% |
| Total | 60 | 100.0 |
| | | |

In USG most of the tumors were unilocular.

| Table | 185 | Sept | tations |
|-------|-----|------|---------|
|-------|-----|------|---------|

| Septations | Frequency |
|------------|-----------|
| THICK | 9 |
| THIN | 18 |

Among the 27 tumors which are multilocular, 18 tumors had thin septations.

| Table 19 Vascularizatio |
|-------------------------|
|-------------------------|

| TYPES OF TUMORS | FREQUENCY |
|-----------------------------------|-----------|
| HIGH GRADE SEROUS CARCINOMA | 2 |
| LOW GRADE SEROUS CARCINOMA | 1 |
| MUCINOUS CARCINOMA | 1 |
| ENDOMETRIOD CARCINOMA | 3 |
| GRANULOSA CELL TUMOR | 1 |
| YOLK SAC TUMOR | 2 |
| METASTASIS FROM SIGNET RING CELLS | 1 |
| BORDERLINE MUCINOUS TUMOR | 1 |
| SEROUS BORDERLINE TUMOR | 1 |
| | |

13 patients had neovascularization in USG findings.

Table 20 Types of Surgery

| Types of Surgery | Frequency | Percentage |
|--------------------------------------|-----------|------------|
| STAGING LAPAROTOMY+HYSTERECTOMY | 19 | 31.7% |
| INTERVAL CYTOREDUCTION +HYSTERECTOMY | 3 | 5.0% |
| OVARIAN CYSTECTOMY | 11 | 18.3% |
| OVARIOTOMY | 23 | 38.4% |
| PARAOVARIAN CYSTECTOMY | 3 | 5.0% |
| LAPAROSCOPIC OVARIAN CYSTECTOMY | 1 | 1.7% |

Staging laparotomy with hysterectomy and interval cytoreduction with hysterectomydone in 36.7% cases. Fertility preserving surgeries were done in 63.33% cases.

Intraoperative Findings

• Ascitic Fluid

| Table 21 Ascitic Fluid | | | |
|------------------------|-----------|------------|--|
| | Frequency | Percentage | |
| NIL | 40 | 66.7% | |
| MILD | 12 | 20.0% | |
| MODERATE | 4 | 6.7% | |
| LARGE | 4 | 6.7% | |
| Total | 60 | 100.0 | |

Most of the tumors had no ascitic fluid Only 6.7% of patients had large volume of ascites.

• Capsule of Tumors

| Table 22 Capsule of Tumors | | | |
|----------------------------|-----------|------------|--|
| Capsule | Frequency | Percentage | |
| INTACT | 51 | 85.0 | |
| RUPTURED | 2 | 3.3 | |
| RUPTURED DURING SURGERY | 7 | 11.7 | |

For most of tumor's capsule were intact during surgery.

• Size of Tumor

| Size of Tumor | Frequency | Percentage |
|---------------|-----------|------------|
| <5 CM | 2 | 3.3% |
| 5-10 CM | 21 | 35.0% |
| 10-15 CM | 23 | 38.3% |
| 15-20 CM | 8 | 13.3% |
| 20-25 CM | 2 | 3.3% |
| 25-30 CM | 2 | 3.3% |
| >30 CM | 2 | 3.3% |
| Total | 60 | 100.0 |

Most of the tumors were in the size range of 5cm to 15 cm.



Laterality of Tumors

•

| Laterality | Frequency | Percentage |
|------------|-----------|------------|
| LEFT | 29 | 48.3 |
| RIGHT | 20 | 33.3 |
| BOTH | 11 | 18.3 |
| | | |

81.6% of all tumors were unilateral.

• Consistency of Tumors

| Table 25 Consistency of Tumors | |
|--------------------------------|--|
|--------------------------------|--|

| Consistency | Frequency | Percentage |
|-------------|-----------|------------|
| SOLID | 12 | 20.0 |
| CYSTIC | 34 | 56.7 |
| MIXED | 14 | 23.3 |

Most of the tumors were cystic in consistency

Table 26 Types of Tumors

| Type Of Tumors | Frequency | Percentage |
|----------------|-----------|------------|
| BENIGN | 43 | 71.67% |
| BORDERLINE | 5 | 8.3% |
| MALIGNANT | 12 | 20% |

Most of the ovarian tumors were benign which constitutes 71.67% of allovarian tumors and it was followed by malignant tumors.



Fig 7 Types of Tumors

| Туре | Frequency | Percentage Among Benign Tumors | Percentage Among AII Tumors |
|------------------------|-----------|-----------------------------------|--------------------------------|
| SEROUS CYSTADENOMA | 16 | 37.2% | 26.66% |
| MATURE CYSTIC TERATOMA | 15 | 34.88% | 25% |
| MUCINOUS CYSTADENOMA | 10 | 23.25% | 16.66% |
| FIBROMA | 2 | 4.6% | 3.33% |

Most common benign ovarian tumors were serous cystadenoma and its wasfollowed by mature cystic teratoma and mucinous cystadenoma.



| Туре | Frequency | Percentage Among Borderline Tumors | Percentage Among AllTumors |
|----------|-----------|------------------------------------|----------------------------|
| SEROUS | 3 | 60% | 5% |
| MUCINOUS | 2 | 40% | 3.33% |

Table 28 Borderline Ovarian Tumors

There were only 5 cases of borderline ovarian tumors and serous tumors were3 in number.



Fig 9 Borderline Ovarian Tumors

| Table | 29 | Malignant | Ovarian | Tumors |
|--------|----|-----------|---------|-----------|
| 1 uore | | mangnanc | Ovurium | 1 unior 5 |

| Туре | Frequency | PercentageAmong Malignant Tumors | PerecentageAmong All Tumors |
|------------------|-----------|----------------------------------|-----------------------------|
| EPITHELIAL | 8 | 67% | 13.33% |
| GERM CELL | 2 | 17% | 3.33% |
| SEX CORD STROMAL | 1 | 8% | 1.66% |
| METASTASIS | 1 | 8% | 1.66% |

Epithelial cancer forms majority of ovarian cancer and forms only 13.3% of all ovarian tumors.



Fig 10 Malignant Ovarian Tumors

| Туре | Frequency | PercentageAmong Malignant Epithelial Tumors | PercentageAmong Malignant Tumors | PercentageAmong All Tumors |
|--------------------------------|-----------|--|-------------------------------------|-------------------------------|
| SEROUS HIGH GRADE LOW GRADE | 4 | 50% | 33.3% | 6.66% |
| | 3 | | | 5% |
| | 1 | | | 1.66% |
| ENDOMETROID | 3 | 37.5% | 25% | 5% |
| MUCINOUS | 1 | 12.5% | 8.33% | 1.66% |

Table 30 Epithelial Ovarian Cancers

Serous epithelial tumors form majority of surface epithelial tumors and therewere 3 cases of high-grade serous carcinoma.



| Table 31 | Types | of Ovarian | Tumors |
|----------|-------|------------|--------|
|----------|-------|------------|--------|

| | ** | |
|---------------------------|-----------|------------|
| Types | Frequency | Percentage |
| SURFACE EPITHELIAL TUMORS | 39 | 65% |
| GERM CELL TUMORS | 17 | 28% |
| SEX CORD STROMAL TUMORS | 3 | 5% |
| METASTASIS | 1 | 2% |

Among all the tumors surface epithelial tumors form majority and among the surface epithelial tumors benign tumors were more common.



Fig 12 Types of Ovarian Tumors

| Table 32 Types of Tumors and Age Wise Distribution |
|--|
|--|

| | 15yrs-20yrs | 20yrs-30yrs | 30yrs-40yrs | TOTAL |
|-----------------------------|-------------|-------------|-------------|--------|
| SEROUS CYSTADENOMA | 5 | 7 | 4 | 16 |
| | 31.25% | 43.75% | 25.0% | 100.0% |
| MUCINOUS | 1 | 5 | 4 | 10 |
| CYSTADENOMA | 10.0% | 50.0% | 40.0% | 100.0% |
| MATURE CYSTICTERATOMA | 5 | 5 | 5 | 15 |
| | 33.3% | 33.3% | 33.3% | 100.0% |
| FIBROMA OF OVARY | 0 | 1 | 1 | 2 |
| | 0.0% | 50.0% | 50.0% | 100.0% |
| SEROUS BORDERLINETUMOUR | 0 | 0 | 3 | 3 |
| | 0.0% | 0.0% | 100.0% | 100.0% |
| MUCINOUS | 1 | 0 | 1 | 2 |
| BORDERLINETUMOUR | 50.0% | 0.0% | 50.0% | 100.0% |
| YOLKSAC TUMOUR | 0 | 2 | 0 | 2 |
| | 0.0% | 100.0% | 0.0% | 100.0% |
| HIGH GRADE SEROUSCARCINOMA | 0 | 0 | 3 | 3 |
| OVARY | 0.0% | 0.0% | 100.0% | 100.0% |
| SEROUS CARCINOMALOW GRADE | 0 | 0 | 1 | 1 |
| | 0.0% | 0.0% | 100.0% | 100.0% |
| MUCINOUS | 0 | 1 | 0 | 1 |
| CARCINOMA | 0.0% | 100.0% | 0.0% | 100.0% |
| ENDOMETROID ADENOCARCINOMA | 0 | 1 | 2 | 3 |
| | 0.0% | 33.3% | 66.7% | 100.0% |
| GRANULOSA CELLTUMOUR | 0 | 0 | 1 | 1 |
| | 0.0% | 0.0% | 100.0% | 100.0% |
| METASTASIS FROM SIGNET RING | 1 | 0 | 0 | 1 |
| CELLS | 100.0% | 0.0% | 0.0% | 100.0% |
| TOTAL | 13 | 22 | 25 | |
| PERCENT | 21.7% | 36.7% | 41.7% | |

Serous cystadenoma and mucinous cystadenoma were more commonly seen in 20 years to 30 years of age. Mature cystic teratoma is equally distributed in all age groups.

| Table 33 | Parity a | and Type | e of Ova | rian Tumo | ors |
|----------|----------|----------|----------|-----------|-----|
| | | | | | |

| | No of Parous Women | Percentage Among the Type of Tumor |
|---------------------------|--------------------|------------------------------------|
| SURFACE EPITHELIAL TUMORS | 21 | 53.8% |
| GERM CELL TUMORS | 8 | 47% |
| SEX CORD STROMAL TUMORS | 2 | 66.6% |
| METASTASIS | 0 | 0 |

Even though parity is a protective factor for epithelial ovarian cancer, 53.8% of surface epithelial tumors were seen in parous women. 66.6% of Sex cord stromal tumors seen in parous women.

| Table 34 CA 125 and Type of Tumors | | | |
|------------------------------------|----------|----------|--|
| Type of Tumors | <35 U/ML | >35 U/ML | |
| HIGH GRADE SEROUS CARCINOMA OVARY | 0 | 3 | |
| MATURE CYSTIC TERATOMA | 12 | 3 | |
| SEROUS CARCINOMA LOW GRADE | 0 | 1 | |
| SEROUS BORDERLINE TUMOUR | 1 | 2 | |
| FIBROMA OF OVARY | 2 | 0 | |
| YOLKSAC TUMOUR | 1 | 1 | |
| SEROUS CYSTADENOMA | 13 | 3 | |
| MUCINOUS CYSTADENOMA | 6 | 4 | |
| MUCINOUS BORDERLINE TUMOUR | 1 | 1 | |
| GRANULOSA CELL TUMOUR | 0 | 1 | |
| ENDOMETROID ADENOCARCINOMA | 0 | 3 | |

ISSN No:-2456-2165

| METASTASIS FROM SIGNET RING CELLS | 1 | 0 |
|-----------------------------------|---|---|
| MUCINOUS CARCINOMA | 0 | 1 |

CA 125 levels were elevated in 38.33% of tumors

| CA 125 Levels | Non-Malignant | Malignant | Total |
|---------------------|---------------|-----------|-------|
| NEGATIVE (<35 U/ml) | 35 | 2 | 37 |
| POSITIVE (>35U/ml) | 12 | 11 | 23 |

Table 35 CA 125 Levels and Malignant Tumors

Sensitivity and specificity of CA 125 was 83% and 75% for diagnosing malignancy.

• ROC Curve of CA 125 Levels



• It Points that Predictive Ability of the Test is Poor.

| Type of Tumors | CEA >2.5 ng/ml |
|------------------------|----------------|
| MATURE CYSTIC TERATOMA | 4 |
| YOLKSAC TUMOUR | 1 |
| MUCINOUS CYSTADENOMA | 1 |
| | |

CEA levels are above the normal range in 4 cases of mature cystic teratoma.

Table 37 LDH Levels and Types of Tumors

| Types of Tumors | >280 U/L |
|-----------------------------------|----------|
| YOLK SAC TUMOUR | 1 |
| HIGH GRADE SEROUS CARCINOMA OVARY | 1 |
| MATURE CYSTIC TERATOMA | 5 |
| SEROUS CARCINOMA LOW GRADE | 1 |
| SEROUS CYSTADENOMA | 13 |
| MUCINOUS CYSTADENOMA | 4 |
| MUCINOUS BORDERLINE TUMOUR | 1 |
| GRANULOSA CELL TUMOUR | 1 |
| ENDOMETROID ADENOCARCINOMA | 3 |

- ✓ LDH levels were elevated in 1 germ cell tumor & 5 cases of surface epithelial tumors. AFP levels are elevated in 2 cases of yolk sac tumor.
- ✓ Serum BHCG levels were elevated only in 1 case, which is yolk sac tumor.

| Types Of Tumors | Benign | Malignant | Inconcl Usive | Total |
|-------------------------------|--------|-----------|---------------|--------|
| HIGH GRADE SEROUS | 1 | 2 | 0 | 3 |
| CARCINOMA OVARY | 3.33% | 66.67% | 0.0% | 100.0% |
| MATURE CYSTIC | 9 | 0 | 6 | 15 |
| TERATOMA | 60.0% | 00.0% | 0.0% | 100.0% |
| SEROUS CARCINOMA | 0 | 1 | 0 | 1 |
| LOW GRADE | 0.0% | 100.0% | 0.0% | 100.0% |
| SEROUS BORDERLINE | 1 | 1 | 1 | 3 |
| TUMOUR | 33.3% | 33.3% | 33.3% | 100.0% |
| FIBROMA OF OVARY | 2 | 0 | 0 | 2 |
| | 100.0% | 0.0% | 0.0% | 100.0% |
| YOLKSAC TUMOUR | 0 | 2 | 0 | 1 |
| | 0.0% | 100.0% | 0.0% | 100.0% |
| SEROUS | 14 | 0 | 2 | 16 |
| CYSTADENOMA | 87.5% | 0% | 12.5% | 100.0% |
| MUCINOUS | 5 | 0 | 5 | 10 |
| CYSTADENOMA | 50.0% | 0.0% | 50.0% | 100.0% |
| MUCINOUS | 0 | 1 | 1 | 2 |
| BORDERLINE TUMOUR | 0.0% | 50.0% | 50.0% | 100.0% |
| GRANULOSA CELL | 0 | 1 | 0 | 1 |
| TUMOUR | 0.0% | 100.0% | 0.0% | 100.0% |
| ENDOMETROID ADENOCARCINOMA | 0 | 3 | 0 | 3 |
| | 0.0% | 100.0% | 0.0% | 100.0% |
| METASTASIS FROM | 0 | 1 | 0 | 1 |
| SIGNET RING CELLS | 0.0% | 100.0% | 0.0% | 100.0% |
| MUCINOUS | 0 | 1 | 0 | 1 |
| CARCINOMA | 0.0% | 100.0% | 0.0% | 100.0% |
| | 32 | 13 | 15 | |
| | 1 | | | |

Table 38 IOTA Simple Rules and Types of Tumors

15 results were inconclusive.

Table 39 IOTA and Malignancy

| IOTA Rules | Non-Malignant Tumors | Malignant Tumors |
|---------------|----------------------|------------------|
| NON-MALIGNANT | 31 | 1 |
| MALIGNANT | 2 | 11 |
| | | |

Sensitivity of IOTA SIMPLE RULE - 91.67% Specificity of IOTA SIMPLE RULE - 93.9%

• Intra Operative Findings

| Type of Tumors | Size | Frequency | Percent |
|----------------|----------|-----------|---------|
| BENIGN | 5-10 CM | 17 | 39.5% |
| | 10-15 CM | 17 | 39.5% |
| | 15-20 CM | 5 | 11.6% |
| | 20-25 CM | 2 | 4.7% |
| | 25-30 CM | 1 | 2.3% |
| | >30 CM | 1 | 2.3% |
| | Total | 43 | 100.0 |
| BORDER LINE | <5 CM | 1 | 20.0% |
| | 5-10 CM | 1 | 20.0% |
| | 10-15 CM | 2 | 40.0% |
| | >30 CM | 1 | 20.0% |
| | Total | 5 | 100.0 |

Table 40 Size of Tumors and Types of Tumors

International Journal of Innovative Science and Research Technology

ISSN No:-2456-2165

| MALIGNANT | <5 CM | 1 | 8.3% |
|-----------|----------|----|-------|
| | 5-10 CM | 3 | 25.0% |
| | 10-15 CM | 4 | 33.3% |
| | 15-20 CM | 3 | 25.0% |
| | 25-30 CM | 1 | 8.3% |
| | Total | 12 | 100.0 |

Most of the tumors were 5cm to 10 cm in size among benign tumors, 10 cm to 15 cm among borderline tumors and 5 cm to 20 cm among malignant tumors. Size more than 30 cm is seen only in 2 patients.

| Types of Tumors | Laterality | Frequency | Percent |
|-----------------|------------|-----------|---------|
| BENIGN | LEFT | 21 | 48.8% |
| | RIGHT | 15 | 34.9% |
| | BOTH | 7 | 16.3% |
| BORDER LINE | LEFT | 2 | 40.0% |
| | RIGHT | 2 | 40.0% |
| | BOTH | 1 | 20.0% |
| MALIGNANT | LEFT | 6 | 50.0% |
| | RIGHT | 3 | 25.0% |
| | BOTH | 3 | 25.0% |

Table 41 Types of Tumors and Laterality

Among the malignant tumors only 25% were bilateral.

Table 42 Types of Tumors and Consistency

| Types of Tumors | Consistency | Frequency | Percent |
|-----------------|-------------|-----------|---------|
| BENIGN | SOLID | 6 | 14.0 |
| | CYSTIC | 28 | 65.0 |
| | COMPLEX | 9 | 20.9 |
| BORDER LINE | SOLID | 1 | 20.0 |
| | CYSTIC | 4 | 80.0 |
| | COMPLEX | 0 | 0.0 |
| MALIGNANT | SOLID | 6 | 50.0 |
| | CYSTIC | 3 | 25.0 |
| | COMPLEX | 3 | 25.0 |

Most of the tumors were cystic in consistency. 50% malignant tumors were solid inconsistency.

| Table 43 | Stage of | Ovarian | Malignanc | cy |
|----------|----------|---------|-----------|----|
| | 0 | | 0 | ~ |

| Stage of Malignancy | Frequency | Percent | | | |
|---------------------|-----------|---------|--|--|--|
| 1A | 2 | 16.66% | | | |
| 1B | 3 | 25% | | | |
| 1C1 | 3 | 25% | | | |
| 1C3 | 1 | 8.3% | | | |
| 3A1(ii) | 1 | 8.3% | | | |
| 3B | 1 | 8.3% | | | |
| 3C | 1 | 8.3% | | | |

Most of the tumors were limited to the Ovaries or Fallopian Tubes.

| Treatment after Surgery | Frequency | Percent | | |
|-------------------------|-----------|---------|--|--|
| On Follow up | 50 | 83.3 | | |
| BEP*3 CYCLES | 3 | 5.0 | | |
| CP*4 CYCLES | 1 | 1.7 | | |
| CP*6 CYCLES | 6 | 10.0 | | |

Most of the patients were kept on follow up, chemotherapy was given in 10 patients

CHAPTER FIVE DISCUSSION

Ovarian tumors are one of the most serious health concerns. Due to the wide range of pathologic diseases that can affect the ovaries, diagnosis can be challenging. The diagnosis can be improved with knowledge about morphology and age-specific traits. Both pathogenic and functional abnormalities can be found in ovarian tumors. Lesions developing in them are often associated with the mildness of symptoms. Hence, they grow to be quite large before being found and treated. Diverse pathologic diseases that can affect the ovaries and appear with comparable clinical and radiologic signs make it difficult to diagnose ovarian cancers. Knowing the morphology and age-specific traits can help with the diagnosis. (15)

Among the 60 cases, patients are classified in to different age groups. 41.7% patients belong to 30-40 years, 36.7% patients belonged to 20-30 years and 21.7% patients belonged to 15-20 years.

31 patients were parous and among that 7 were sterilized. In a study by Kjaer SK et al(29) following tubal sterilization, women had a lower risk of acquiring ovarian cancer. Since only 6 months follow up is done, reduction in risk of developing ovariancancer is yet to be studied.

Among the 29 nulliparous women 4 women took treatment for female factor infertility in our study. 3 took Ovulation induction drugs.2 patients took Letrozole. 1 patient took it for 6 months and another patient for 2 months.1 patient took Clomiphene Citrate for 3 months. Based on the updated version of the original Cochrane Review done by Rizzuto I, et al(30) compared to the general population or sub fertile women who are not treated, infertility drugs increase the risk of ovarian cancer in sub fertile women who are treated. When using infertility medications, nulliparous women are at a larger risk than multiparous women. Due to the tiny sample size, information regarding the dosage or type of fertility drugs used is lacking. Since follow up is only 6 months in our study, and sample size is small reliable data could not be made out.

The most common presenting complaint was abdominal pain (55%) followed by abdominal lump or distension (50%), nausea/anorexia (8.33%) and menstrualirregularities (6.66%) in our study. In a study done by Purti Agarwal et al(5) also most common complaint was pain in the abdomen (50.9%) irrespective of the nature of the ovarian tumor, Menstrual irregularities, excessive bleeding, and postmenopausal bleeding were the presenting complaints in the 11.9% cases. In a study by Lalrinpuii E et al(11) commonest clinical presentation was abdominal pain in 46%. In a study by MA Sofi et al(14) the commonest symptom was abdominal pain/discomfort-64.7%. Abdominal swelling/distension in 53.8% patients, menstrual disturbances in the form of amenorrhea, polymenorrhagia, dysmenorrhea and metrorrhagia were seen in 8.4% of cases. Almost in all studies the most common presentation was abdominal pain, which is comparable to my study.

2 patients had family history of breast cancer, 1 patient had history of endometrial cancer and no patient had family history of colon cancer in my study. None were evaluated for BRCA/Lynch Syndrome. In a study by F Parazzini et al(18) although the chance of developing ovarian cancer is increased in families with the disease, only a small portion of cases are attributable to family history. In this study, less than 1% of observed cases may be linked to this family risk factor.

40% of patients belong to BMI range of 18.5 to 22.9 kg/m2. BMI was less than 18 and more than 30 kg/m2 in 8.3% patients. In a study by Anders Engeland et al(17) in comparison to women with a medium BMI, those who were overweight or obese as adolescents or young adults had a higher relative risk of 1.56. In women under the age of 60, there was a correlation between height and ovarian cancer risk, particularly endometrioid ovarian cancer.

Staging laparotomy with hysterectomy was done in 30% of patients. 5% of patients underwent interval cytoreduction with hysterectomy. Ovariotomy in 38.4% of patients. 18.3% patients underwent ovarian cystectomy and 5% patients underwent para ovarian cystectomy. Fertility preserving surgeries were done in 63.33% cases

Out of the 60 patients 39 are surface epithelial tumors (65%), germ cell tumors 17(28%), sex cord stromal tumors 3(5%) and metastasis 1(2%). Among the 60 patients

71.67 % were benign, 20% were malignant and 8.3% borderline in our study. In a studyconducted by Purti Agarwal et al(5) Benign tumors were most common which constitutes 61.1%,7.1% belongs to borderline category and 31.9% belongs to malignant ovarian tumors, this may be due to the difference in the study age group. In a study by R Jha et al(16) below 40 years of age, 91.9% of the tumors were benign.

Benign surface epithelial tumors constitute 60.4% of benign tumors and malignant surface epithelial neoplasms constitute 66.7% of all malignant neoplasms in the present study. In a study by MA Sofi et al(14) Benign surface epithelial tumors constituted 73.1% of all benign neoplasms and its malignant counterpart constituted 76.0% of all malignant neoplasms. In a study by R Jha et al(16) Benign surface epithelial tumors comprised 48.9% of all benign tumors whereas their malignant counterpart formed 69.2% of all malignant tumors. The results were not comparable toour study and it may be due to small sample size and

due to heterogenicity in the studygroup.

Serous cystadenoma was the majority and constitute 26.66% of all tumors and 37.25% among benign tumors, Followed by mature cystic teratoma 34.88% of all tumors and 25% among benign tumors in our study. This is comparable to the study bySK Mondal et al(4) most common histological types were serous cystadenoma (29.9%), followed by mature teratoma (15.9%) and mucinous cystadenoma (11.1%). In another study by Purti Agarwal et al(5) mucinous cystadenoma (30.4%) was the most common.

Epithelial ovarian cancer constitutes among 13.33% of all ovarian tumors (67% of malignant tumors), followed by germ cell cancers 3.33% (17% of all malignant tumors), sex cord stromal cancers and metastasis 1.66% (8%) each in our study. The commonest histological type was serous cystadenocarcinoma which is 33.3% among all malignant tumors in our study. This is similar to study by Lalrinpuii E et al(11) in which commonest histological type was serous carcinoma, 33.3% among all malignant tumors. Serous carcinoma constitutes 50% of malignant epithelial tumors and endometroid carcinoma-37.5% of malignant epithelial tumors in our study. How-ever in Lalrinpui et al(11) among the epithelial ovarian cancers, 46.3% had serous histology, 34.3% had mucinous tumor, 16.4% had endometroid and 3.0% had clear cell tumors. In a study by R Jha et al(16) no cases of serous and mucinous carcinoma in people under 30 years old have been documented.

In our study there were only 2 germ cell tumors, both were yolk sac tumors (3.33% of all ovarian tumors and 17% of all ovarian cancers). In a study by LalrinpuiiE et al(11) Germ cell tumors constituted 23% of all malignant cases. Of the malignant germ cell tumors, 42.9% were mixed germ cell tumors, 23.8% were immature teratoma, 19.0% were yolk sac tumors and 14.3% were dysgerminomas in their study. This difference may be due to the small study sample.

1 case of mature cystic teratoma have taken OCP during her life for 6 months. In a study by Beral V et al(31) the longer a woman used oral contraceptives, the risk of ovarian cancer was reduced. After the usage of oral contraceptives had ended, this decrease in risk continued for more than 30 years.

CA 125 is elevated in 38.3% of patients. Highest value of CA 125 was 3630 and it was in a case of high-grade serous carcinoma. Values >1000 were seen in 3 cases and all 3 were high grade serous carcinoma. Among the 12 malignant ovarian tumors metastasis from signet ring cells had CA 125 less than 35 and all others had values morethan 35. The sensitivity of CA 125 for value of more than 35 IU/ml was 83% and specificity was 75%. AUC for CA 125 levels in detecting ovarian malignancies was only 0.532. It points that predictive ability of CA 125 in diagnosing malignancy is poor.

In a study conducted by Purti Agarwal et al(5), sensitivity of CA 125 was 90.9%, specificity 40% and diagnostic accuracy was 81.5%. In a study by Shabir S et al(10) Over 80% of individuals with advanced epithelial ovarian cancer had elevated CA125 levels. Serous tumors had a higher CA125 sensitivity than Stage 1 cancers, while mucinous cancers had the lowest sensitivity. Pelvic inflammatory illness, endometriosis, leiomyomas, pregnancy, menstruation and other common benign reasons may all contribute to the increased value (false-positive).32

CEA is elevated in 6 cases. Out of which only 1 is malignant. Hence in our study the sensitivity is very poor. In a study by Wan Q et al(19) the sensitivity of CEA in diagnosing EOC was only 51.64%. in our study this may be due to the small sample size and according to my study CEA is not accurate enough to detect epithelial ovariancancer.

LDH was elevated in 50% cases. LDH is elevated in malignant germ cell tumorof ovary particularly dysgerminoma. 58% of malignant tumors have elevated LDH. Inour study sensitivity was 43.75% and specificity was only 28.1%. In a study by DeebaF et al(20), the validity of LDH in detecting malignant ovarian tumors were sensitivity 57.1%, specificity 84.1%, accuracy 78.7%, positive predictive values 47.1% and negative predictive values 88.8%. The difference in observation may due to the small sample size.

AFP was elevated in 2 cases and both were yolk sac tumor and the values were 2595 and 1500. BHCG is elevated only in 1 case.7.5 IU/ml in yolk sac tumor. Literature shows that differentiated germ cell tumors, such as yolk sac tumor secretes AFP. HCG secreted by choriocarcinoma3

According to IOTA simple rules, 25% were inconclusive. Sensitivity of IOTA simple rule was 91.67% and Specificity of IOTA simple rule was 93.9% in our study. In a study by N Nunes et al(21) sensitivity of IOTA simple rules was 96.2% and specificity was 88.6% and they discovered that in the study populations with the highestoccurrence of malignant tumors, sensitivity was higher and specificity was lower. In a study by Tantipalakorn C et al (22) the simple rules yielded inconclusive results in 19.9% masses. sensitivity was 82.9% and specificity 95.3%. In identifying benign frommalignant adnexal tumors, the IOTA simple guidelines have a high diagnostic performance. This difference in results could be due to small sample size and heterogenicity in the study population.

In USG, 55% of the tumors were unilocular and 45% were multilocular. 6 malignant tumors were having multilocularity. All the 5 borderline tumors were multilocular. Among the 6 malignant tumors 5 were having thick septations. 2 borderline tumors

were also having thick septations. In a study by Rebecca Smith- Bindman, Liina Poder et al(23) based-on patient age and ultrasound results, the risk of cancer over the next three years ranges from 9 to 430 cases per 1000 women in women with complex cysts or solid masses. When compared to women with normal ovaries, the risk of ovarian cancer was not noticeably higher in 23.8% of women under 50 and 13.4% of women 50 years or older with simple cysts.

Most common procedure in benign tumors was ovariotomy (48%). Ovariotomy was done in 66% of borderline tumor. The most common surgery done in malignant ovarian tumors was total abdominal hysterectomy+ bilateral salphingo-oophorectomy and infra-colic omentectomy (91.66%) in our study. In the study by Purti Agarwal et.al

(5) In which ovariotomy was done in 57.3% of benign tumors, 43.8% of borderline tumors. TAH+BSO+Omentectomy was done in 80.6% of malignant tumors.

In our study 50% of malignant germ cell tumors underwent conservative surgery. In a study by Neeyalavira V et al(27) malignant germ cell tumor patients underwent conservative surgery in 80.3% of cases, with conservative surgical staging performed in 39.4% of cases. Only 18.4% of patients underwent non-fertility-sparing surgery. The difference may be due to the small sample size of malignant germ cell tumors.

Intraoperatively 66.7% have no ascitic fluid. 20% have mild ascitic fluid, 6.7% have moderate or large amount of ascites. Large amount of ascitic fluid was seen in 2 malignancies-mucinous carcinoma, granulosa cell tumour 1 case of serous borderline tumour and 1 mucinous cystadenoma. None of the cases of fibroma of ovary had ascites. In a study by J Brian Szender, Tiffany Emmons et al(24) ability to perform appropriate cytoreductive surgery was inversely related to the presence of ascites.

Most of the tumors have size of 10-15 cm, which constitute 38.3%. 35% were between 5-10 cm. 13.3% were between 15-20 cm in size. Size >30 cm was seen in 2 cases-mucinous borderline tumour and serous cystadenoma. Size 25-30 cm were seen in 2 cases -mature cystic teratoma and high-grade serous carcinoma in our study. In a study by Gupta N et al(6) 14.7% were in size range of up to 5 cm, 41.8% were in rangeof 5–10 cm, 24.1% in range of 10–15 cm, 10.6% in 15–20 cm, 5.9% in 20–25 cm, 2.9% in 25–30 cm size range. In a study by MA Sofi et al(14) majority 63.8% was in the sizerange of 1-10 cm. The difference in the statistics may be due to heterogenicity of the study population.

Most of the ovarian tumors were unilateral. Bilateral tumors were seen only in 11(18.3%) cases. 4 malignant tumors showed bilaterality (36.66% of bilateral tumors and 33.3% of all malignant tumors). 20% of borderline tumour are bilateral and 13.9% of benign tumors are bilateral. Among unilateral tumors, 48% were on left side and 33.3% were right side in our study. In a study by Purti Agarwal et al(5), 66.7% of malignant tumors exhibited bilaterality. The majority of benign and borderline tumors were unilateral. In a study by Gupta N et al(6) 12.3% of tumors were bilateral, whereas 87.7% of them were unilateral. 5.9% of benign tumors, 21.1% of malignant tumors, and 36.4% of borderline tumors were bilateral. Only 6.7% of benign tumors and 42.3% of malignant tumors were bilateral in research by R. Jha et al(16). Most of the studies are not comparable to my study, it may be attributed to the heterogenicity in the study population.

Out of 60 patients, Epithelial tumors (20.5%) were bilateral, germ cell tumors (17.6%) were bilateral and all cases of sex cord stromal tumors and metastasis were unilateral. In a study by Gupta N et al(6), Epithelial tumors-13.2% were bilateral, germ cell tumors-12.8% were bilateral. Sex cord–stromal and metastatic tumors were only unilateral. This finding was almost comparable to our study.

Out of 60 patients, 56.7% of tumors were cystic,20% was solid and 23.33% were mixed. Among the benign tumors 65%-cystic, 14%-solid and 21%-complex in consistency. Among the borderline tumors, 80%-cystic and 20%-solid. In the malignant tumors cystic-25%, complex-25% and solid-50%. According to a study by PurtiAgarwal et al(5), 100% of borderline tumors and 83.3% of benign tumors were cystic. The majority of malignant tumors (65.2%) had mixed consistency. In research by GuptaN et al(6), 56% of tumors were cystic, 32.1% were solid-cystic, and 11.9% were solid. In research by MA Sofi et al(14), 49.6% of the tumors were cystic, 16.8% were solid, and 33.6% had a mixed consistency.

Para aortic lymph node was involved in a case of yolk sac tumour. Retroperitoneal lymph node was involved in a case of high-grade serous carcinoma. Omental deposits were seen in 2 cases of high-grade serous carcinoma and 1 case of serous borderline tumour. Other metastasis seen were a) under surface of liver- 1 case of endometrial carcinoma, b) anterior abdominal wall- 1 case of mucinous carcinoma, c) peritoneal deposits-2 cases of high-grade serous carcinoma, 1 case of metastasis fromsignet ring cells, 1 case of serous borderline tumor, d) peritoneal deposits and retroperitoneal deposits in 1 case of high-grade serous carcinoma.

After surgery 6 patients took 6 cycles of chemotherapy with carboplatin and paclitaxel,1 patient took 4 cycles of carboplatin and paclitaxel,3 patients took 3 cycles of bleomycin, etoposide and cisplatin. In a study by C K Lee et al(25) 65% of women under the age of 40 were still living at five years. Women under 40 had a much higher overall survival rate, and more than 60% of women were still living as of the most recent data (116.5 months). Better is the progression-free interval, and at the time of the

most recent observation, more than 58% of women under the age of 40 were still disease-free (116.5 months). After 18 months, no women under 40 years old experienced a relapse. In a study by Neeyalavira V et al(27) malignant germ cell tumorpatients received adjuvant treatment in 71% of cases. 11.1% of patients had a partial response, while 73.3% had a complete response. According to a study by Bouchard- Fortier G et al(28), women with endometrioid cancer had a five-year overall survival rate of 80.6%, while women with serous ovarian cancer had a five-year overall survivalrate of 35.0%. For endometrioid and serous histology, the 10-year overall survival rateswere 68.4% and 18.4%, respectively.

On follow up for 6 months, 2 patients had recurrence-1 mucinous carcinoma (stage 3B) of age 26 years & 1 case of highgrade serous carcinoma (stage 3C) of age 35 years. Tumor markers were done after 6 months and CEA, LDH & SBHG were found to be normal. CA 125 was found to be elevated in only in 11 cases. 6 malignant tumors, 3 borderline tumors and 2 benign tumors shows CA 125 levels more than 35 IU/ml. CEA was found to be 2.7 & 2.9 in yolk sac tumors.

CHAPTER SIX SUMMARY

➤ In this Prospective Cohort Study

- 41.7% patients belong to 30-40 years, 36.7% patients belonged to 20-30 years and 21.7% patients belonged to 15-20 years.
- 48.3% were nulliparous and 51.7% of patients were parous women.
- Most common symptoms were abdominal pain and abdominal lump/distension. Many patients have more than 1 symptom at the time of presentation.
- 40% of patients have BMI of 18.5kg/m2 to 22.9kg/m2. BMI less than 18.5kg/m2 and more than 30 kg/m2 is seen only in 8.3% of patients.
- CA 125 is elevated in 38.3% of patients, CEA is elevated in 6 cases, LDH was elevated in 50% cases, AFP was elevated in 2 cases and BHCG is elevated only in 1 case.
- According to IOTA simple rules, 25% were inconclusive.
- In USG, 60 % were cystic in echogenicity, 45% were multilocular cysts, 9 were having thick septations and 13 patients had neovascularization.
- Staging laparotomy with hysterectomy was done in 30% of patients. 5% of patients underwent interval cytoreduction with hysterectomy. Ovariotomy in 38.4% of patients. 18.3% patients underwent ovarian cystectomy and 5% patients underwent para ovarian cystectomy.
- Intraoperatively 66.7% have no ascitic fluid. 20% have mild ascitic fluid, 6.7% havemoderate or large amount of ascites.
- Capsule was intact in 85% of tumors
- Most of the tumors have size of 10-15 cm, which constitute 38.3%. 35% werebetween 5-10 cm. 13.3% were between 15-20 cm in size.
- Most of the ovarian tumors were unilateral. Bilateral tumors were seen only in11(18.3%) cases
- 56.7% of tumors were cystic in consistency
- 71.67 % were benign, 20% were malignant and 8.3% borderline
- Serous cystadenoma was the majority and constitute 26.66% of all tumors and 37.25% among benign tumors, Followed by mature cystic teratoma 34.88% of all tumors and 25% among benign tumors
- Serous cystadenocarcinoma is the most common malignant tumor which is 33.3% among malignant ovarian tumors.
- Epithelial ovarian cancer constitutes among 13.33% of all ovarian tumors (67 % of malignant tumors), followed by germ cell cancers 3.33% (17% of all malignant tumors), sex cord stromal cancers and metastasis 1.66% (8%).
- Benign surface epithelial tumors constitute 60.4% of benign tumors and malignant surface epithelial neoplasms constitute 66.7% of all malignant neoplasms
- only 2 germ cell tumors were diagnosed and both were yolk sac tumors
- Among the 12 malignant ovarian tumors metastasis from signet ring cells had CA 125 less than 35 and all others had values more than 35. The sensitivity of CA 125 for value of more than 35 IU/ml was 83% and specificity was 75%. AUC for CA 125 levels in detecting ovarian malignancies was only 0.532. It points that predictiveability of CA 125 in diagnosing malignancy is poor.
- CEA is elevated in 6 cases. Out of which only 1 is malignant.
- AFP was elevated in 2 cases and both were yolk sac tumor. BHCG is elevated onlyin 1 case in yolk sac tumour.
- Sensitivity of IOTA simple rule was 91.67% and Specificity of IOTA simple rule was 93.9%.
- In USG, 6 malignant tumors were having multilocularity. All the 5 borderline tumors were multilocular. Among the 6 malignant tumors 5 were having thick septations. 2borderline tumors were also having thick septations.
- Most common procedure in benign tumors was ovariotomy (48%). Ovariotomy was done in 66% of borderline tumour. The most common surgery done in malignant ovarian tumors was total abdominal hysterectomy+ bilateral salphingo-oophorectomy and infra-colic omentectomy (91.66%)
- Fertility preserving surgeries were done in 63.33% cases.
- Large amount of ascitic fluid was seen in 2 malignancies-mucinous carcinoma, granulosa cell tumour. None of the cases of fibroma of ovary had ascites.
- Size of tumor more than 30 cm was seen in 2 cases-mucinous borderline tumour and serous cystadenoma. Size 25-30 cm were seen in 2 cases -mature cystic teratoma and high-grade serous carcinoma
- Intraoperatively, 4 malignant tumors showed bilaterality (36.66% of bilateral tumors and 33.3% of all malignant tumors). 20% of borderline tumour are bilateral and 13.9% of benign tumors are bilateral. Among unilateral tumors, 48% were on left side and 33.3% were right side in our study
- Epithelial tumors-20.5% were bilateral, germ cell tumors-17.6% were bilateral and all cases of sex cord stromal tumors and metastasis were unilateral.
- Among the benign tumors 65%-cystic, 14%-solid and 21%-complex in consistency. Among the borderline tumors, 80%-cystic and 20%-solid. In the malignant tumors cystic-25%, complex-25% and solid-50%

- After surgery 6 patients took 6 cycles of chemotherapy with carboplatin and paclitaxel, 1 patient took 4 cycles of carboplatin and paclitaxel, 3 patients took 3 cycles of bleomycin, etoposide and cisplatin.
- On follow up for 6 months, 2 patients had recurrence-1 mucinous carcinoma (stage3B) of age 26 years & 1 case of high-grade serous carcinoma (stage 3C) of age 35 years

CHAPTER SEVEN CONCLUSION

In this study on ovarian neoplasms among women 15 to 40 years of age, mostcommon presenting symptoms was abdominal pain/abdominal distension. Size of tumor, echogenicity and bilaterality has no predictive value in diagnosing ovarian malignancy in this study. IOTA simple rule has sensitivity of 91.67% and specificity of 93.9% in predicting malignant tumors from benign tumors. Tumor markers has no predictive ability in diagnosing malignant ovarian neoplasm in this study. Staging laparotomy with hysterectomy and interval cytoreduction with hysterectomy done in 36.7% cases. Fertility preserving surgeries were done in 63.33% cases and they were benign. Surface epithelial tumors is the most common type of tumor, followed by germcell tumors. Benign tumors (71.67%) are more common than malignant tumors (20%). Most common tumor was serous cystadenoma. Most common malignant tumor was serous epithelial tumors. On follow up 2 patients had recurrence within 6 months and they were having stage 3 disease.

LIMITATIONS

In the present study 60 consecutive patients were identified in a time period of 1 year and they were followed up for 1 year. Since the sample obtained is only 60, the findings cannot be compared to the general population. Clinicopathological outcomes could not be compared between benign and malignant tumors and between epithelial and non-epithelial tumors due to small sample size. The number of sex cord stromal tumors were very low for meaningful statistical analysis.

REFERENCES

- Singh U, Solanki V, Prakash B, Mehrotra S, Verma ML, Solanki V. Clinicopathological spectrum of ovarian tumors in northern India: Changing trends over 10 years. Indian j gynecol oncol [Internet]. 2020;18(2). Available from: http://dx.doi.org/10.1007/s40944-020-00405-8
- [2]. Murthy NS, Shalini S, Suman G, Pruthvish S, Mathew A. Changing trends in incidence of ovarian cancer the Indian scenario. Asian Pac J Cancer Prev. 2009;10(6):1025–30.
- [3]. Berek JS. Berek & Novak's Gynecology. 16th ed. Baltimore, MD: Wolters KluwerHealth; 2019.
- [4]. Mondal SK, Banyopadhyay R, Nag DR, Roychowdhury S, Mondal PK, Sinha SK. Histologic pattern, bilaterality and clinical evaluation of 957 ovarian neoplasms: a 10-year study in a tertiary hospital of eastern India. J Cancer Res Ther [Internet]. 2011;7(4):433–7. Available from: http://dx.doi.org/10.4103/0973-1482.92011
- [5]. Agrawal P, Kulkarni D, Chakrabarti P, Chourasia S, Dixit M, Gupta K. Clinicopathological spectrum of ovarian tumors: A 5-year experience in a tertiary health care center. J Basic Clin Reprod Sci [Internet]. 2015;4(2):90. Available from: http://dx.doi.org/10.4103/2278-960x.161062
- [6]. Gupta N, Yadav M, Gupta V, Chaudhary D, Patne SCU. Distribution of various histopathological types of ovarian tumors: A study of 212 cases from a tertiary carecenter of Eastern Uttar Pradesh. J Lab Physicians [Internet]. 2019;11(1):75–81. Available from: http://dx.doi.org/10.4103/JLP.JLP_117_18
- [7]. (Guideline) Epithelial O. Fallopian Tube, and Primary Peritoneal Cancer Treatment (PDQ®)-Health Professional Version.
- [8]. [Guideline] National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology, Ovarian Cancer Including Fallopian Tube Cancer and Primary Peritoneal Cancer. Availableat http://www.nccn.org/professionals/physician _gls/pdf/ovarian.pdf. Version1.2020 March 11, 2020;
- [9]. Basu P, De P, Mandal S, Ray K, Biswas J. Study of 'patterns of care' of ovarian cancer patients in a specialized cancer institute in Kolkata, eastern India. Indian J Cancer. 2009 Jan-Mar;46(1):28-33. doi: 10.4103/0019-509x.48592. PMID: 19282563.
- [10]. Shabir S, Gill PK. Global scenario on ovarian cancer Its dynamics, relative survival, treatment, and epidemiology. Adesh University Journal of Medical Sciences & Research [Internet]. 2020;2(17):17–25. Available from: http://dx.doi.org/10.25259/aujmsr_16_2019\
- [11]. Lalrinpuii E, Bhageerathy PS, Sebastian A, et al. Ovarian Cancer in Young Women. Indian Journal of Surgical Oncology. 2017 Dec;8(4):540-547. DOI:10.1007/s13193-017-0680-z. PMID: 29203987; PMCID: PMC5705514.
- [12]. IOTA Simple Rules and SRrisk calculator to diagnose ovarian cancer by International Ovarian Tumor Analysis (2018) guidelines.
- [13]. FIGO ovarian cancer staging guidelines (January 2014)
- [14]. Manzoor Ahmed Sofi et al. Histopathological pattern of ovarian tumors-An experience: International journal of current research and review DOI: 10.31782/IJCRR.2018.10905
- [15]. Chandra K, Arora N. Clinicopathological analysis of ovarian tumors: a two year retrospective study. Int J Reprod Contracept Obstet Gynecol [Internet]. 2019;8(8):3015. Available from: http://dx.doi.org/10.18203/2320-1770.ijrcog20193163
- [16]. Jha R, Karki S. Histological pattern of ovarian tumors and their age distribution. Nepal Med Coll J. 2008;10(2):81–5.
- [17]. Engeland A, Tretli S, Bjørge T. Height, body mass index, and ovarian cancer: a follow-up of 1.1 million Norwegian women. J Natl Cancer Inst [Internet]. 2003;95(16):1244–8. Available from: http://dx.doi.org/10.1093/jnci/djg010
- [18]. Parazzini F, Negri E, La Vecchia C, Restelli C, Franceschi S. Family history of reproductive cancers and ovarian cancer risk: an Italian case-control study. Am J Epidemiol [Internet].1992;135(1):35–40. Available from: http://dx.doi.org/10.1093/ oxfordjournals.aje.a116199
- [19]. Wan Q, Liu Y, Lv B, Chen X. Correlation of molecular tumor markers CA125, HE4, and CEA with the development and progression of epithelial ovarian cancer. Iran J Public Health [Internet]. 2021;50(6):1197–205. Available from: http://dx.doi.org/10.18502/ijph.v50i6.6418
- [20]. Deeba F, Khatun S, Alam MM, Shahida SM. Serum LDH and CA-125: Markers for diagnosis of ovarian malignancy. Mymensingh Med J. 2015;24(2):334–40.
- [21]. Nunes N, Ambler G, Foo X, Naftalin J, Widschwendter M, Jurkovic D. Use of IOTA simple rules for diagnosis of ovarian cancer: meta-analysis. Ultrasound Obstet Gynecol [Internet]. 2014;44(5):503–14. Available from: http://dx.doi.org/10.1002/uog.13437
- [22]. Tantipalakorn C, Wanapirak C, Khunamornpong S, Sukpan K, Tongsong T. IOTA simple rules in differentiating between benign and malignant ovarian tumors. Asian Pac J Cancer Prev [Internet]. 2014;15(13):5123–6. Available from: http://dx.doi.org/10.7314/apjcp.2014.15.13.5123
- [23]. Smith-Bindman R, Poder L, Johnson E, Miglioretti DL. Risk of malignant ovariancancer based on ultrasonography findings in a large unselected population. JAMA Intern Med [Internet]. 2019;179(1):71–7. Available from: http://dx.doi.org/10.1001/jamainternmed.2018.5113
- [24]. Szender JB, Emmons T, Belliotti S, Dickson D, Khan A, Morrell K, et al. Impact of ascites volume on clinical outcomes in ovarian cancer: A cohort study. Gynecol Oncol [Internet]. 2017;146(3):491–7. Available from: http://dx.doi.org/10.1016/j.ygyno.2017.06.008

- [25]. Lee CK, Pires de Miranda M, Ledermann JA, Ruiz de Elvira MC, Nelstrop AE, Lambert HE, et al. Outcome of epithelial ovarian cancer in women under 40 years of age treated with platinum-based chemotherapy. Eur J Cancer [Internet]. 1999;35(5):727–32. Available from: http://dx.doi.org/10.1016/s0959- 8049(99)00011-8
- [26]. Uma Devi K, Purushotham N, Jayashree N. Management of ovarian cancer in younger women. Rev Recent Clin Trials [Internet]. 2015;10(4):263–9. Available from: http://dx.doi.org/10.2174/1574887110666150923112047
- [27]. Neeyalavira V, Suprasert P. Outcomes of malignant ovarian germ-cell tumors treated in Chiang Mai University Hospital over nine year period. Asian Pac J Cancer Prev [Internet]. 2014;15(12):4909–13. Available from: http://dx.doi.org/10.7314/apjcp.2014.15.12.4909
- [28]. Bouchard-Fortier G, Panzarella T, Rosen B, Chapman W, Gien LT. Endometrioid Carcinoma of the Ovary: Outcomes Compared to Serous Carcinoma After 10 Years of Follow-Up. J Obstet Gynaecol Can. 2017 Jan;39(1):34-41. doi: 10.1016/j.jogc.2016.10.006. Epub 2016 Dec 10. PMID: 28062021.
- [29]. Kjaer SK, Mellemkjaer L, Brinton LA, Johansen C, Gridley G, Olsen JH. Tubal sterilization and risk of ovarian, endometrial and cervical cancer. A Danish population-based follow-up study of more than 65 000 sterilized women. Int J Epidemiol [Internet]. 2004;33(3):596–602. Available from:http://dx.doi.org/10.1093/ije/dyh046
- [30]. Rizzuto I, Behrens RF, Smith LA. Risk of ovarian cancer in women treated withovarian stimulating drugs for infertility. Cochrane Database Syst Rev [Internet]. 2019;6:CD008215. Available from: http://dx.doi.org/10.1002/14651858.CD008215.pub3
- [31]. Collaborative Group on Epidemiological Studies of Ovarian Cancer, Beral V, DollR, Hermon C, Peto R, Reeves G. Ovarian cancer and oral contraceptives: collaborative reanalysis of data from 45 epidemiological studies including 23,257 women with ovarian cancer and 87,303 controls. Lancet [Internet]. 2008;371(9609):303–14. Available from: http://dx.doi.org/10.1016/S0140-6736(08)60167-1
- [32]. Hoffman BL, Schorge JO, Bradshaw KD, Halvorson LM, Schaffer JI, Corton MM.Williams Gynecology, Third Edition. 3rd ed. New York, NY: McGraw-Hill Professional; 2016.
- [33]. Toufakis V, Katuwal S, Pukkala E, Tapanainen JS. Impact of parity on the incidence of ovarian cancer subtypes: a population-based case-control study. Acta Oncol [Internet]. 2021;60(7):850–5. Available from:http://dx.doi.org/10.1080/ 0284186X.2021.1919754
- [34]. DiSilvestro P, Colombo N, Scambia G, Kim BG, Oaknin A, Friedlander M, et al. Efficacy of Maintenance Olaparib for Patients With Newly Diagnosed Advanced Ovarian Cancer With a BRCA Mutation: Subgroup Analysis Findings From the SOLO1 Trial. J Clin Oncol. 2020 Aug 4. JCO2000799. [Medline].
- [35]. Armstrong DK, Alvarez RD, Bakkum-Gamez JN, Barroilhet L, Behbakht K, Berchuck A, et al. Ovarian cancer, version 2.2020, NCCN clinical practice guidelines in oncology. J Natl Compr Canc Netw [Internet]. 2021;19(2):191–226.Available from: http://dx.doi.org/10.6004/jnccn.2021.0007

ANNEXURE

➤ Consent Form

I confirm that I have freely agreed to participate in the study conducted by Dr. Vismaya J, Junior Resident, Department of Obstetrics and Gynecology, Calicut Medical College entitled "CLINICOPATHOLOGICAL PATTERN AND SURGICAL OUTCOMES IN OVARIAN NEOPLASMS DIAGNOSED IN WOMEN AGED LESS THAN 40 YEARS IN A TERTIARY CARE CENTRE" I agree to cooperate with the study and provide necessary information and investigations for the same under the following conditions. The details disclosed by me for the study will not be misused andnot used in ways which can be detrimental to me. I don't have any financial burden in participating in the study. I may withdraw and discontinue participation at any stage of the study without penalty. Participation in the study will not affect the services entitled to me. Study does not include any procedures harmful to my health. I have read and understood the above information. I consent to participate in the study.

Signature:

Name of the patient:

Signature

Name of the relative :

Address:

Principal Investigator: Dr. Vismaya J

Department of Obstetrics and Gynecology, Calicut Medical College.Signature: