A CLINICO – PATHOLOGICAL CORRELATION AND ANALYSIS OF OVARIAN TUMOURS WITH STUDY OF EXPRESSION PATTERN OF PANKERATIN

DISSERTATION

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CERTIFICATE

This is to certify that this dissertation entitled **"A CLINICO – PATHOLOGICAL CORRELATION AND ANALYSIS OF OVARIAN TUMOURS WITH STUDY OF EXPRESSION PATTERN OF PANKERATIN"** is the bonafide record work done by **DR.G. JEYANTHI** submitted as partial fulfillment for the requirements of **M.D Degree Examinations, Pathology** to be held in March 2009.

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CONTENTS

INTRODUCTION

Tumours of the ovary are common forms of neoplasms in women. The pathology of ovarian neoplsms is one of the most complex areas of gyneacology, because the ovary gives rise to the greater and larger variety of tumours than any other organ. While in other organs, tissue of origin is usually clear, tissue from which an ovarian tumour arises is often uncertain and most of the development of the presumptive tissue is often in disparity.[46]

Ovarian tumours account for a considerable proportion of clinically important problems in females and they are dangerous due to their silent growth.

Worldwide, ovarian tumuor is the sixth most common tumor in women. In the western countries, ovarian carcinoma is the fifth most common malignancy and ranks fourth in cancer mortality. In U.S women, ovarian cancer accounts for 5% of cancer deaths. In India, breast is the leading site of cancer, followed by cervix and ovary. In Chennai, ovarian cancer stands in the fourth position.[22,38,44]

About two thirds of ovarian tumours occur in women in the reproductive age group. In general the disease is most common in industrialized countries where parity is lower but there are notable exceptions such as Japan which has low parity and low rates of ovarian cancers.[8,22]

Evidence suggests that reproductive factors are important in ovarian cancer risk. Increase in parity and oral contraceptives offer protective effect for ovarian cancer. Some studies have demonstrated early menarche and late menopause as significant risk factors. High socioeconomic status contributes to increased ovarian cancer risk as a result of lower fertility rates in those women. Several risk factors have been identified, such as age at the birth of first child, breast feeding, weight, diet, talc, smoking, certain types of viral infections in childhood and ionizing radiation.[22]

Migration studies have shown that ovarian cancer rates approach those place of immigration rather than the place of emigration suggesting a significant environmental component to ovarian tumour risk. Genetic factors are an important ovarian cancer risk. Hereditary is responsible for approximately 10% cases due to the markedly increased risk conferred by the BRCA 1 and BRCA 2 tumour suppressor genes.[22,44]

Many patients present with later stages in ovarian cancer. This is because, unlike cervical cancer, effective early detective screening programmes are not available for ovarian cancer. Nowadays, for screening purpose, ultrasound and serum CA 125 level are used. Regarding prevention of ovarian cancer, preventive measures that could be recommended on a population wide basis, such as diet modifications, cessation of smoking and prophylactic oophorectomy is often performed in patients at high risk of ovarian cancer.[22]

Cytokeratins are a family of water insoluble, intracellular fibrous proteins present in almost all epithelia. Keratin represents an excellent marker for epithelial differentiation regardless of whether the tumour is of endodermal, neuroectodermal, mesenchymal or of germ cell origin.[35,42]

It is a useful marker for primary ovarian tumours and various types of metastatic tumours in the ovaries. Immunohistochemistry is done to demonstrate various patterns of cytokeratin expression in epithelial and non epithelial tumours.

This study is undertaken in view of evaluating the actual incidence of ovarian neoplasms in a semi urban area like Thanjavur with particular attention to age, clinical features, histopathological and immunohistochemical features. In

addition, the recent literatures, journals and research publications regarding ovarian tumors are also immensely reviewed.

AIM OF THE STUDY

1. To study the incidence of ovarian tumours in semi urban population, with clinical correlation.

2. To study and compare the incidence of malignant ovarian tumours in relation to female genital tract malignancies.

3. Application of histochemistry in selective cases.

4. Application of immuno histochemistry with study of cytokeratin expression in ovarian tumours.

MATERIALS AND METHODS

132 cases presented with ovarian neoplasms referred from Raja Mirasudhar Govt. Hospital (RMH), Thanjavur which is affiliated to Thanjavur Medical Collage (TMC) during 2006 to 2008 were included in this study.

We received ovariotomy specimen and also along with hysterectomy specimen. A detailed history with particular attention to clinical symptoms and signs were recorded and thorough gross examination of the specimen were also done. Specimen were fixed in toto in buffered 10% neutral formalin and processed routinely.

In cystic ovarian neoplasms, 4-5 bits were taken from the wall along with papillary excrescences if present. In solid tumours, 3-4 bits were taken if the tumors were less than 5cm. If more than 5 cm, one block per 1 cm of the tumour were taken across its greatest dimension, particularly if the appearance is variegated. 3-5 micro meter sections were cut and stained with haematoxylin and eosin (Appendix I).

Reticulin or PAS were applied in doubtful cases(Appendix II,III). In all types of malignant neoplasms, cytokeratin expression were also studied (Appendix IV) .

REVIEW OF LITERATURE

ANATOMY

The ovaries are paired ovoid structures, homologous with the testis, but smaller. They have an average volume of 11cm^3 in reproductively mature women. The ovaries are dull white in colour and consist of dense fibrous tissue in which ova are embedded. Before regular ovulation begins they have a smooth surface, but thereafter their surfaces are distorted by scarring that follows the degeneration of successive corpus luteum. The average size of the ovary is 3x2x1cm.[(2)]

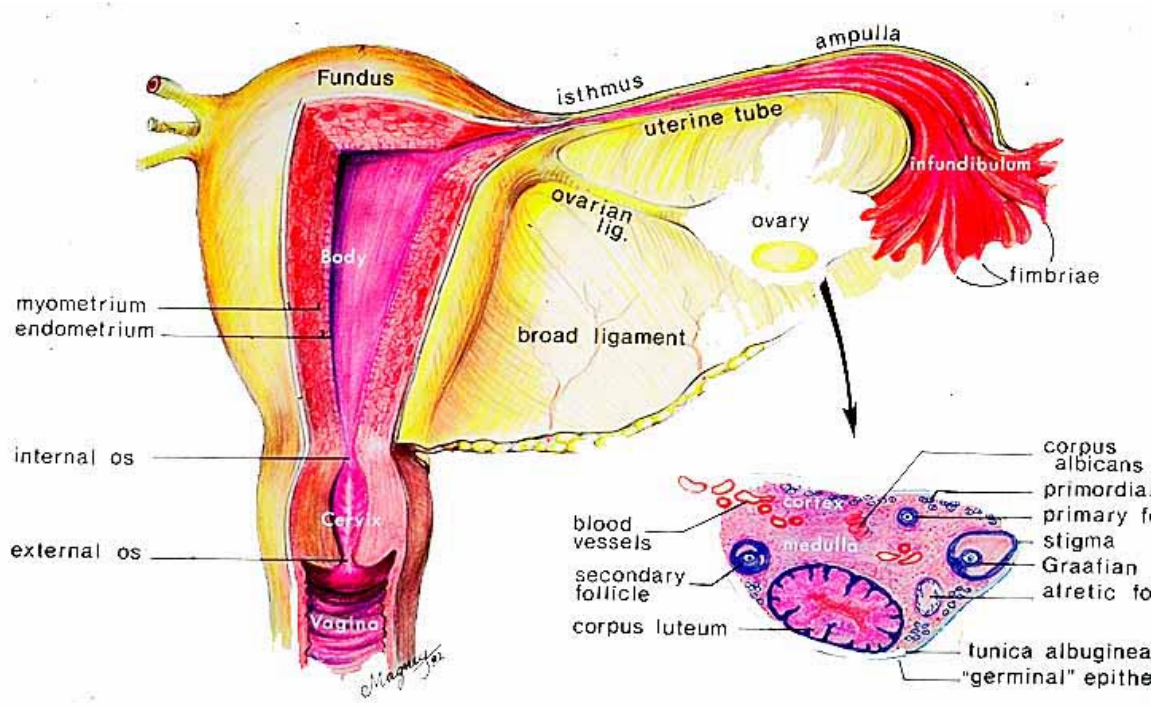


Diagram:1.Female reproductive tract.

DEVELOPMENT

Ovary is developed from coelomic epithelium on the medial side of the mesonephrons. The surface epithelium covering the ovaries are modified peritoneum called germinal epithelium. Cords of cells proliferate from this germinal epithelium and grow into the underlying mesoderm. Primordial germ cells, that are formed in relation to the yolk sac, migrate to the region of the developing ovary, and give rise to oocytes.

The sex cords become broken up into small masses. The cells of each mass surround one primordial germ cells or oocyte to form a primordial follicle, interstitial gland cells differentiate from the mesenchyme of the gonad. As no tunica albuginea is formed, the germinal epithelium may contribute to the ovary even in postnatal life.[53]

HISTOLOGY

The body of the ovary consists of spindle shaped cells, fine collagen fibres and ground substances that together constitute the ovarian stroma. Bundles of smooth muscle cells are also scattered throughout the stroma. In the peripheral zone of the stroma, known as the cortex, are numerous follicles that contain female gametes in various stages of development.

The central zone of ovarian stroma, the medulla, is highly vascular and contain hilar cells, ovarian artery, collagen rich meshwork containing elastic fibres and few clusters of interstitial cells.[2]

There are three main categories of primary ovarian tumors. Epithelial tumours which derive from the surface epithelium of ovary, sex cord-stromal tumours, which arise from the ovarian stroma and from the sex cord derivation or both. Germ cell tumour which originate from germ cells[42,43,62].

Generally, one out of eight ovarian tumours in patients <45years of age is malignant, by contrast in older women, the proportion is about one of three. Teratoma is encountered at all ages. Primitive germ cell tumour is never seen >50 years of age. The borderline surface epithelial tumour occur in women in their 30 years of age.[43]

The granulosa cell and Sertoli Leydig cell tumours are typically unilateral. Tumours that metastasize to the ovary are always bilateral.[1,14,43]

Finally accurate diagnosis of ovarian tumour depends on a knowledge of the wide range of microscopic patterns they may exhibit and the cell types they may contain.[1,43]

WORLD HEALTH ORGANIZATION – WHO HISTOLOGICAL CLASSIFICATION OF OVARIAN TUMOURS

1. Surface epithelial tumours
2. Sex cord – stromal tumours
3. Germ cell tumours
4. Gonadoblastoma
5. Germ cell sex cord – stromal tumour of nongonadoblastoma type
6. Tumours of Rete ovarii – adenoma, cystadenoma, adenocarcinoma
7. Mesothelial tumours – adenomatoid tumour, mesothelioma
8. Tumours of uncertain origin and miscellaneous tumours

   Small cell carcinoma

   Tumours of probable wolffian origin (FATWO)

   Hepatoid carcinoma

   Myxoma
9. Gestational trophoblastic diseases
10. Soft tissue tumours non specific to ovary
11. Malignant lymphomas, leukemias, and plasmacytoma
12. Unclassified tumours
13. Secondary (metastatic) tumours
14. Tumour like conditions

SURFACE EPITHELIAL TUMOURS

Epithelial tumours are classified according to the predominant pattern of differentiation of the neoplastic cells. Each of the tumour type subdivided into benign, borderline and malignant categories.[7]

HISTOLOGICAL TYPES OF SURFACE EPITHELIAL TUMOURS OF OVARY

1. Serous tumours
2. Mucinous tumours
    - Intestinal type
    - Endocervical type
3. Endometrioid
    - Adenosarcoma
    - Mixed mesodermal tumour
    - Endometrioid stromal sarcoma
4. Clear cell tumour
5. Transitional cell tumours (including Brenner)
6. Squamous cell tumours
7. Mixed epithelial tumours
8. Undifferentiated carcinoma

SEROUS TUMOURS

Serous tumours comprise about 25% of all ovarian neoplasms. They are the most common epithelial tumours, accounting for 20% of benign, 40% of malignant primary ovarian tumours. Of all serous tumours, 50% are benign, 15% are borderline and 35% are invasive carcinoma.[7,8,21,25,44]

BENIGN SEROUS TUMOURS

Benign serous tumours include serous cystadenomas, serous cystadenofibroma, serous adenofibromas and serous surface papillomas.

GROSS

Cystic, usually have a smooth pale-yellow (or) gray white exterior with a prominent vascular pattern. It can be either unilocular (or) multilocular. When solid and cystic portions are both prominent the tumour is designated as a cystadenofibroma.

HISTOPATHOLOGY

Consists of a mixture of tall ciliated and non ciliated columnar cells with elongated oval nuclei interspersed with a variable number of peg shaped cells and clear cells. Psammoma bodies are small whorled calcified structure. They are numerous in some serous tumours, and may be found (30%) in cellular as well as acellular areas.[7,25,44]

BORDERLINE SEROUS TUMOURS

Borderline are large, averaging about 8cm in maximum diameter. 30-40% are bilateral. Usually multicystic, numerous, coarse papillae form the cyst lining.

MICROSCOPIC PICTURE

The most characteristic microscopic feature of a borderline serous tumour is a complex branching papillary pattern of growth. The papillae typically branch into progressively finer fronds, a pattern that is referred as hierarchial branching. The cells are stratified into several layers and they form tufts from which single cells or small clusters of cell detach into the cyst lumen. There is mild to moderate nuclear atypia and mitotic activity is less than in serous carcinoma. [7,22,25,44]

Recently, a group of borderline serous tumour with particularly prominent cellular proliferation has been recognized. These tumours are called micropapillary serous tumours.[7]

The only universally accepted criterion for differentiation between a borderline serous tumuor and serous carcinoma is the presence of stromal invasion in the latter. Microscopic stromal invasion is detected in 5-10% of borderline serous tumours. Multiple foci of microinvasion each less than 3mm in maximum dimension are typically present.[2,32,33]

SEROUS CARCINOMA

Serous carcinoma is usually large, is often bilateral in about two thirds of all cases.[44]

GROSS

Serous carcinomas range from predominantly cystic papillary tumours to entirely solid, soft or hard masses, often having papillary surfaces.[7,22,43,44]

MICROSCOPIC FINDING

Microscopically, serous carcinoma is composed of low columnar cells. The degree of cytological atypia and mitotic activity is valuable. In high grade tumours which are the most common, the nuclei are markedly atypical and largely fill the cells. Bizzare and multinucleated cells are common, and very high mitotic rates are typical (often >50mf/hpf). The glands are often cleft like, rather than rounded, and they are lined by cuboidal or low columnar cells. The malignant cells diffusely infiltrate a fibrotic stroma and foci of necrosis are commonly present.[7,14,22,31,44,62]

MUCINOUS TUMOURS

Mucinous tumours account for 12-15% of all ovarian tumours. Approximately 75% of mucinous tumours are benign, 10% borderline, 15% carcinomatous.

BENIGN MUCINOUS TUMOUR

Mucinous cystadenomas are cystic neoplasm, that have a smooth, blue-white or gray external surface with numerous blood vessels. Most are >10cm in diameter. On cut surface reveals, thin walled mucin filled cysts ranging from a few mm to several cm in diameter. Benign are usually unilateral, only about 5% are bilateral.[6,7,22,44]

MICROSCOPIC FINDING

Mucinous cystadenomas are lined by a layer of columnar mucinous cells, most of which resemble endocervical or gastric mucinous cells. May have pale or clear cytoplasm and small bland basally situated oval nuclei.[7,22,44]

BORDERLINE MUCINOUS TUMOURS OF INTESTINAL TYPE

Intestinal type neoplasms constitute by far the most common type of borderline mucinous tumour. Borderline tumours average 15-20cm in diameter and fewer than 10% are bilateral.

GROSS

Borderline tumours tend to be multiloculated cystic neoplasms with variable amounts of fibrous stroma between the cysts.

MICROSCOPIC PICTURE

These tumours are composed of proliferating mucinous epithelium. Bland areas in which the cysts are lined by endocervical or gastric type of cells are typically present, but there are some areas in which cysts and glands are lined by intestinal type absorptive and goblet cells. The nuclei are basal, round to oval and mild to moderately atypical cells. The nuclei are typically stratified into two or three layers and scattered mitotic figures are present.[7,14,43,44]

BORDERLINE [ENDOCERVICAL LIKE] MUCIONOUS TUMOURS

Endocervical like mucinous borderline tumour have an architecture similar to that of serous borderline tumour, with both large, bulbous papillae and smaller papillae with prominent cellular budding. The papillae lined by slightly to moderately atypical epithelial cells. Mostly these cells have an abundant cytoplasmic mucin, but some may be mucin free and contain large amount of eosinophilic cytoplasm.

MALIGNANT MUCINOUS TUMOUR

Ovarian mucinous adenocarcinomas differ from borderline tumours having evidence of ovarian stromal invasion.

MACROSCOPY

Usually large, unilateral, smooth surfaced, multilocular, containing viscous mucoid material. Bilateral in approximately 5% of cases. Hemorrhagic, necrotic, solid or papillary areas are relatively frequent.[7,14]

HISTOPATHOLOGY

There are complex papillary areas or back-to-back arrangement of glands lined by malignant appearing cells with little or no discernible intervening stroma.

To qualify as frankly invasive, the invasion should be more than 5 mm. The invasion may be in the form of infiltrative glands, tubules, cords or cell nest with desmoplastic stroma.[14,25,43,44]

ENDOMETRIOID TUMOURS

Endometrioid epithelial tumours account for 2 to 4% of all ovarian tumours. Coexistent with endometriosis in 10-20%. Benign, borderline, and malignant endometrioid epithelial tumours occur most commonly in women in the older reproductive and post menopausal age groups, with mean ages of 56,51 and 56 years respectively.[44]

BENIGN ENDOMETRIOID TUMOUR

The histological diagnosis of endometrioid adenomas and cystadenomas is based on the presence of well differentiated, benign appearing glands or cysts lined by endometrial type cells with or without squamous, differentiation.[14]

BORDERLINE ENDOMETRIOID TUMOUR

Three pattern have been described. Islands of crowded endometrioid glands or cysts lined by cells displaying grade 1 to 3 cytological atypia proliferate in an adenofibromatous stroma. Stromal invasion is absent. Mitotic activity is low. Squamous metaplasia is common.The second is villoglandular papillary pattern. Third is combination of villoglandular and adenofibromatous pattern.[14,25,47]

MALIGNANT ENDOMETRIOID ADENOCARCINOMA

GROSS

The tumours, typically measuring 10-20cm in diameter, are solid, soft, friable or cystic with a fungating mass protruding into the lumen. They are bilateral in 28% of cases.

HISTOPATHOLOGY

Ovarian endometrioid carcinomas closely resemble endometrioid carcinomas of the uterine corpus. The well differentiated form shows round, oval or tubular glands lined by stratified nonmucin containing epithelium. Squamous differentiation occurs in 30-50% of the cases, often in the form of morules.[4,14,22,44,47,56]

CLEAR CELL TUMOURS

Benign clear cell tumours are rare and borderline forms account for less than1%. Clear cell carcinoma, however account for 6% of epithelial cancers. Most clear cell carcinomas are diagnosed during 5^{th} to 7^{th} decade. Benign, borderline clear cell tumours are almost invariably unilateral.

CLEAR CELL ADENOFIBROMA

GROSS

Adenofibroma has a median diameter of 12cm and smooth external surface. The sectioned surface has a fine honey comb appearance with minute cysts embedded in a rubbery stroma.

HISTOPATHOLOGY

It is characterized by tubular glands lined by one or two layers of epithelium that contains polygonal, hobnail cells. The cytoplasm may be clear, slightly granular or eosinophilic. Nuclear atypia and mitotic activity are minimal.[52]

BORDERLINE CLEAR CELL ADENOFIBROMATOUS TUMOUR

HISTOPATHOLOGY

Adenofibromatous tumours in which the glands are lined by malignant epithelium are best designated as “borderline clear cell adenofibromas with

intraepithelial carcinomas". Nuclear atypia is more marked with coarse chromatin clumping prominent nucleoli and increased mitotic activity.

CLEAR CELL ADENOCARCINOMA

The mean age of presentation is 57 years, tumours arise directly from the ovarian surface epithelium, from an inclusion cysts or from an endometriotic cyst.[14]

GROSS

The mean diameter of clear cell adenocarcinoma is 15cm. Tumour may be solid. Cut surface reveals a thick walled unilocular cyst with multiple yellow fleshy nodules, protruding into the lumen or multiloculated cysts containing watery or mucinous fluid.[14]

HISTOPATHOLOGY

Clear cell carcinoma is characterized by diffuse, tubulocystic, papillary and infrequently trabecular patterns. The most common clear cell types are clear, hobnail and flat. The clear cells are typically polyhedral, have distinct cell membranes contain abundant empty cytoplasm and eccentric nuclei. Hobnail cells, which are found in most of the tumours, are characterized by bulbous nuclei that protrude into the lumina of tubules and cysts, and line papillae. [43,50,52]

TRANSITIONAL CELL TUMOURS

Transitional cell tumours, most of which are benign account form 1 to 2% of all ovarian tumours. Approximately 95% of Brenner tumours are diagnosed in women between the ages of 30 and 70 years. It usually coexists with mucinous cystadenoma.[8,22,44]

BENIGN BRENNER TUMOUR

Typically small, <2cm in diameter 7-8% are bilateral. Gross examination reveals a sharply circumscribed, firm, nodular, smooth or slightly bosselated external surface. Cut surface shows white, but may be pale yellow colour. [44]

MICROSCOPIC FINDING

Solid and cystic nests of epithelial cells resembling transitional epithelium, surrounded by abundant stromal component. The epithelial cells are sharply outlined. These are flattened, cuboidal or columnar epithelium. The nuclei are small with distinct nucleoli, conspicuous grooves and clear cytoplasm.[25,44]

BORDERLINE BRENNER TUMOUR

Only 3-5% of Brenner tumours are borderline.[14]

GROSS

Borderline tumours are typically large with a median diameter of 16-20cm. May usually have a solid component.[7,14]

MICROSCOPIC FINDING

Tumour exhibits proliferative activity and nuclear atypia. The tumour cells grow in nests and sheets and line papillary fronds that project into cyst lumens. Mitotic figures are usually present but not numerous.[7]

MALIGNANT BRENNER TUMOUR AND TRANSITIONAL CELL CARCINOMA

Malignant Brenner tumour is almost always unilateral, size is 15cm in diameter. Most are partly cystic with solid, gray, yellow or tan areas often containing calcification.[7]

MICROSCOPIC FINDING

Malignant Brenner tumour has a component of invasive carcinoma that resembles a transitional cell carcinoma of bladder[45]. The tumour cells are polygonal and have eosinophilic cytoplasm. The nuclei are atypical and variably pleo-morphic. The degree of atypia and mitotic activity depend on the tumour grade. Benign or proliferating Brenner tumour must be identified adjacent to these carcinomas.[7,11,14]

SEX CORD - STROMAL TUMOURS

Neoplasms derived from the sex cords or ovarian mesenchyme comprise 5-12% of all ovarian neoplasms. A few tumours in this group such as benign fibromas are common, but most are uncommon.[7,14]

CLASSIFICATION OF SEX CORD - STROMAL TUMOURS OF THE OVARY

1. Granulosa cell tumour
    - Adult type
    - Juvenile type
2. Fibroma – thecoma group
    - Fibroma
    - Cellular fibroma
    - Fibrosarcoma
    - Thecoma
    - Fibroma or thecoma with minor sex cord elements
    - Sclerosing stromal tumour
3. Sertoli –Leydig cell tumour
    - Well differentiated
    - Intermediate differentiation
    - Poorly differentiated
    - Retiform
4. Sertoli cell tumour
5. Sex cord tumour with annular tubules
6. Steroid (lipid) cell tumor
    - Leydig cell tumour
    - Stromal luteoma
    - steroid cell tumour

7. Gynandroblastoma
8. Soft tissue tumours not specific to the ovary
9. Hematopoietic neoplasms (lymphoma, leukemia, plasmacytoma)

GRANULOSA CELL TUMOUR

Granulosa cell tumours are the most common malignant sex cord-stromal tumours. May constitute 1-2% of all ovarian tumours. Adult type granulosa cell tumour occur in peri or post menopausal women.[7,22] The average patient age is about 52 years. It is a slow growing tumour.

GROSS

The average diameter is about 10cm. Most are partly cystic and partly solid. The solid areas show tan, white, light yellow, or golden in colour. Intracystic hemorrhage is common.[43]

MICROSCOPIC FINDING

They are small with uniform round or oval hyperchromatic nuclei. The nuclear chromatin is finely granular, longitudinal nuclear grooves or folds are often present. Mitotic activity is low.

Granulosa cell tumours grow in a variety of histological patterns. These are microfollicular pattern with Call Exner bodies, macrofollicular, trabecular, insular, solid or diffuse, gyriform or watered – silk pattern.

JUVENILE GRANULOSA CELL TUMOUR

GROSS

Less than 5% occurs in children, less than 15 years of age, average 12cm in diameter, most often solid with cystic areas.

MICROSCOPIC FINDING

Macrofollicles and zones of diffuse solid growth. The tumour cells are large, have round dark nuclei with coarse chromatin. As a rule nuclear grooves are not present. Mitotic activity present (6/10hpf).[7,22,25,44]

FIBROMA AND RELATED NEOPLASMS

Fibroma is a benign tumour that accounts for 1-5% of all ovarian tumours. Average age is around 50 years. 30% associated with ascites.

GROSS

Usually small to medium, less than a centimeter to 10 cm in diameter, firm, solid with a tan or white cut surface.

MICROSCOPIC FINDING

Composed of fibroblastic cells that grow in whorls and interlacing fascicles. Mitotic figures are absent. Rarely small irregular nests or tubules of sex cord cells with small hyperchromatic nuclei and amphophilic cytoplasm are noted in fibroma or fibrothecoma. When there is mild to moderate nuclear atypia and

there are 3 or fewer mitotic figure /10 hpf , classified as cellular fibromas. If the degree of nuclear atypia is moderate to marked, with 4 or more mitotic activity/10hpf, classified as fibrosarcoma.[7,19]

THECOMA

It comprises 7% of sex cord- stromal neoplasms. The average age is between 50-55 years. 5% of patients have bilateral presentation.

GROSS

It is firm or hard, average 7cm in diameter, cut surface reveals gray or tan with focal to extensive yellow areas .[19,62]

MICROSCOPIC FINDING

Cells with uniform bland, oval and spindle shaped nuclei with abundant, pale, lipid-rich cytoplasm.[14]

SCLEROSING STROMAL TUMOURS

This tumour accounts for 2-6% of ovarian stromal tumours, >80% occurs in young women, presenting with menstrual abnormalities.

GROSS

Typically unilateral. Cut surface reveals, solid, gray-white with occasional yellow foci and cystic areas.

MICROSCOPIC FINDING

Pseudolobulation of the cellular areas separated by hypocellular areas of densely collagenous or edematous tissue with varying degrees of sclerosis

admixed with both spindle and lipid containing round cells that may simulate Krukenberg tumour. Lobular growth pattern with marked vascularity present.[25]

SERTOLI- LEYDIG CELL TUMOUR

Sertoli-Leydig cell tumours are rare and comprises less than 1% of ovarian tumour. Most occurs in young women. More than 50% are hormonally active, patients have menstrual disorders or virilization.[7]

MICROSCOPIC PATTERNS

1. Well differentiated, Meyer`s type I (11%)[54]

   Composed of tubules lined by Sertoli like cells, separated by variable number of Leydig cells.

2. Intermediate, Meyer`s type II (54%)

   Composed of cords, sheets and aggregates of Sertoli like cells, separated by spindle stromal cells and recognisible Leydig cells.

3. Poorly differentiated (sarcomatoid, undifferentiated Meyer's type III)

Composed of masses of spindle shaped cells arranged in a sarcomatoid pattern.

SERTOLI CELL TUMOUR

Pure Sertoli cell tumours are rare. They are most common in women of reproductive age. Sertoli cell tumours are unilateral and average 5-7cm diameter. Usually solid tumours, cut surface is tan or yellow.

MICROSCOPIC FINDING

Composed of Sertoli cells that line tubules or trabeculae or grow in nests or solid sheets. Cells are columnar or polygonal and have small, round to oval nuclei and granular or eosinophilic cytoplasm. Rarely Sertoli cell tumours are composed of lipid-rich and oxyphilic Sertoli cells. Nuclear atypia is minimal.[7,14]

GYNANDROBLASTOMA

Gynandroblastoma is a rare tumour, containing both Sertoli cell or Sertoli-Leydig cell and granulosa cell differentiation. Usually, unilateral with size ranging from 1cm to 18cm. Microscopically, tubules and trabeculae similar to those in well differentiated Sertoli or Sertoli-Leydig cell tumours mixed with nests and sheets of granulosa cells.

GERM CELL TUMOURS

Except benign cystic teratoma (dermoid cyst),germ cell tumours of the ovary are uncommon. Malignant germ cell tumours almost always occur in children and women less than 30 years of age.

CLASSIFICATION OF GERM CELL TUMOURS OF OVARY

- Dysgerminoma
- Yolk sac tumour (endodermal sinus tumour)
- Embryonal carcinoma
- Polyembryoma
- Choriocarcinoma
- Teratoma

    Mature teratoma
    Solid, cystic, immature teratoma
    Neuro ectodermal tumour

- Malignant tumour arising in a mature teratoma
- Monodermal teratoma

    Struma ovarii

    Carcinoid tumour

- Mixed germ cell tumour
- Gonadoblastoma
- Unclassified germ cell tumour

DYSGERMINOMA

Dysgerminoma is the most common malignant germ cell tumour of the ovary and it accounts for 1-2% of malignant ovarian tumours.[43]

The average age is 22 years. Dysgerminoma is the most common malignant tumour in patients with gonodal dysgenesis. It is usually unilateral.

GROSS

Dysgerminoma is a firm, solid tumour with smooth, nodular external surface. Cut surface is homogenous, fleshy and is tan or white.

MICROSCOPIC FINDING

Well defined nests separated by fibrous strands infiltrated by lymphocytes. The tumour cells are large polygonal cells with vesicular nuclei, abundant clear cytoplasm, and prominent nucleoli.(7)

YOLK SAC TUMOUR

Yolk sac tumours are most common in the second and third decades. The median age is between 16 and 19 years. Almost all the patients have an elevated serum levels of alpha feto protein.

GROSS

The median diameter of tumour is 15cm. External surface is smooth and glistening. 25% have capsular tears. Cut surface reveals solid with cystic, friable, yellow to gray tissue, with extensive areas of hemorrhage and necrosis are common.(44)

MICROSCOPIC FINDING

Yolk sac tumours exhibit a wide variety of microscopic patterns, but most tumours have atleast focally, a reticular pattern. It is characterized by a loose meshwork of communicating spaces lined by primitive tumour cells. With cytoplasm, that is clear, containing glycogen, occasionally lipid. Nuclei are large, hyperchromatic, irregular with prominent nucleoli. Mitotic figures are numerous. The presence of Schiller-Duval bodies is a characteristic feature of yolk sac tumour.[44] Also variable sized brightly eosinophilic PAS positive intracellular hyaline bodies are present in most of the yolk sac tumour.

EMBRYONAL CARCINOMA

The median age is 15, have precocious puberty with increased alpha feto protein.

GROSS

The external surface is smooth, glistening. Cut surface is solid with variegated appearance.

MICROSCOPIC FEATURE

Primitive cells are arranged in solid sheets, and nests, occasionally forming papillae and abortive glandular elements.[25]

CHORIOCARCINOMA

Extremely rare tumour. Most often seen in the ovary as a component of a mixed germ cell tumour.[7]

TERATOMA

It comprises 26% - 44% of all ovarian tumours. Most teratomas contain tissues from the various germ layers and consequently have a varied morphology. In some teratomas one germ cell derivative will predominate which is called as monodermal teratomas.[7]

MATURE (BENIGN) TERATOMA

The most common tumour in this category is a benign cystic teratoma or dermoid cyst. It is detected at any age, but 85% are between 20 and 50 yrs and 10% are bilateral.[17]

GROSS

Predominantly solid with small cystic areas, composed of all three germ cell layers.[25]

MICROSCOPIC FEATURE

Tumour exhibit 100% ectodermal derivatives, 93% mesodermal and 71% of endodermal structures.[25]

IMMATURE TERATOMA

Is a malignant teratoma in which the malignant elements have an embryonal appearance. Occurs predominantly in children and young adults. Histological grading is done by assessing the amount of immature tissue and neuroepithelium.

MIXED GERM CELL TUMOUR

This tumour contains varied mixture of malignant germ cell elements. It comprises 5-20% of all malignant germ cell tumours. The average age is 18 years.

GROSS

Usually larger size, 15cm in diameter. Apperance depends upon the elements that are present.

MICROSCOPIC FINDING

Mixed germ cell tumour contains atleast two malignant elements, commonly dysgerminoma and yolk sac tumour. Dysgerminoma is the most frequent element along with embryonal carcinoma, choriocarinoma, and polyembryoma. Also other combinations of both choriocarcinoma and polyembryoma may occur .[7,43,44]

GONADOBLASTOMA

A rare tumour found almost exclusively in abnormal gonads. It consists of a mixture of germ cells and sex cord cells.

Gonadoblastoma is benign unless a germinoma or some other type of malignant germ cell tumour arises from it.

GROSS

Small 2-3cm, 40% bilateral, cut surface shows tan or white and foci of calcification frequently seen.[7,44]

MICROSCOPIC FINDING

Contains nests of germ cells and sex cord cells surrounded by fibrous stroma. The stroma between the nests of tumour cells often contains luteinised cells as well as microcalcifications in post pubertal patients.

METASTATIC TUMOURS

Gastrointestinal, breast, and uterine carcinomas frequently metastasize to the ovaries. Metastatic cancer comprises 10% of all ovarian cancers.[7]

The characteristic features of metastatic disease are bilateral presentation with smaller size than primary ovarian tumours, nodular growth pattern, surface involvement, infiltrative growth, prior or synchronous extraovarian primary neoplasm of similar histologic appearance that is more microinvasive and involves other than just the ovary.[22,23,44]

The features characteristic of primary ovarian tumours are large unilateral, multicystic tumour without nodularity, surface involvement, capsular invasion, with confluent glandular expansile pattern, or even an atypical proliferative, [borderline] type growth pattern, apparently isolated involvement of the ovary.[23,25]

KRUNKENBERG TUMOUR

Is the form of metastatic cancer in which a signet ring cell carcinoma grows in abundant hypercellular stroma.[7] The Krukenberg tumour is almost always secondary to a gastric carcinoma.[14]

The features supportive of the diagnosis of a metastasis include bilaterality, histological surface involvement by epithelial cells, irregular infiltrative growth with desmoplasia, single cell invasion, signet-ring cells, vascular invasion, coexistence of benign-appearing mucinous areas, with foci of mitotic figures, nuclear hyperchromasia and histological surface mucin.[1,14]

CYTOKERATIN

Keratins are intermediate filament proteins that contribute to the cytoplasm of epithelial cells. As they are present in all epithelial cells, immunostains for cytokerain are useful as a screening test to identify a neoplasm as being of epithelial type.

Human cytokeratin have been classified according to their molecular weight and isoelectric Ph in the catalog published by Mollet al. 20 epithelial

cytokeratin polypeptides have been identified. Some of these have specific tissue distribution that can be exploited for the differential diagnosis of tumour. For screening purposes, a wide spectrum of antibodies that recognise many different CKs are most valuable, such as cocktail of AE1/AE3 and CAM5.2. [22,42,51]

CK7

CK 7 is a type II basic low molecular weight cytokeratin found in simple epithelium in a variety of organs including epithelial cells in female genital tract.

Epithelial tumours of ovary and fallopian tube all exhibit cytoplasmic and membrane staining for cytokeratin 7.

This characteristic staining pattern of female genital tract tumours can be used, usually in combination with staining for other keratin, such as CK 20, to differentiate primary female genital tract adenocarcinoma from adenocarcinoma arising in other organs.

A panel of immunostains needs to be evaluated because some primary ovarian neoplasms fail to stain for CK 7 and a proportion of metastatic carcinomas in the ovary are CK positive.

CK 20

CK 20 is a type I acidic, low molecular weight cytokeratin, that was initially described in 1992. It is found in normal tissues of stomach, intestine, urothelium and in Merkel cells.

It is found in most adenocarcinomas of large and small intestine, in mucinous tumours of the ovary, and in Merkel cell carcinomas, and it is frequently present in urothelial carcinomas and in adenocarcinoma of stomach, pancreas and bile duct.

It is a useful marker for primary mucinous tumours and for various types of metastatic tumours that are found in the ovaries. Most primary non-mucinous epithelial tumours are cytokerain negative.[42]

KEY DIAGNOSTIC POINTS : OVARIAN EPITHELIAL TUMOURS

- All common primary epithelial tumours of ovary express cytokeratin 7.
- If an epithelial tumours is CK 7 negative, consider a metastatic or one of the rare types of primary epithelial tumours.
- Most primary ovarian tumours are CK 20 negative, except the intestinal type of mucinous ovaries tumour are positive with CK 20 and CK 7 .
- The soft epithelial keratin intermediate filaments comprise approximately 20 different keratin polypeptides of the approximate 30 keratin polypeptides.
- The polypeptides numbered 1 through 20, comprise type II (basic) keratins and the type I (acidic) keratin.[42,44,51]

RETICULIN STAIN

The diffuse pattern of granulosa cell tumours may be confused with a benign thecoma, particularly when there is luteinsation. A reticulin stain is helpful, since granulosa cells typically grow in sheets, or aggregates bound by reticulin fibres, whereas thecomas contain an abundance of intercellular fibrils surrounding individual cells. The distinction is important since granulosa cell tumour have an aggressive potential, where as thecomas are with rare exceptions benign.[14]

PAS REACTION

Malaprade introduced periodic acid. Mcmanus first applied PAS Reaction. The basic principle is periodic acid oxidize compounds having free hydroxyl groups that are next to each other i.e., 1,2 glycol, bond between neighbouring carbon atoms is brokened and a dialdehyde structure is produced. This dialdehyde reacts strongly with Schiff reagent.[18]

PAS positive substances are many but it is positive with mucins of intestine, peptic gland, uterine cervical glands, salivary glands, bronchial glands, ovarian follicular cyst, prostatic gland secretion – corpora amylacea and renal hyaline casts. The positive substances are magenta in colour.[8,43]

In most of the Krukenberg tumours, PAS staining with or without diastase and alcian blue staining will be more extensively positive. PAS reaction will also be positive in ovarian origin of mucinous tumours.

OBSERVATION AND RESULTS

This prospective study covered a total number of 132 ovarian neoplasms during the period of Jun 2006 to May 2008.

I : INCIDENCE :

The following table shows the total number of ovarian neoplasm among female neoplasms .

Table 1 :

SL.NO	PERIOD	TOTAL NO. OF FEMALE NEOPLASMS	TOTAL NO. OF OVARIAN NEOPLASMS	%
1	Jun 06–Dec 06	451	33	7.3
2	Jan 07–May 07	329	39	11.8
3	Jun 07–Dec 07	546	28	5.0
4	Jan 08–May 08	290	32	11.0
	Total	1616	132	8.17

The average incidence of ovarian neoplasms (including benign and malignant) among females are 8.17 %.

II . AGE :

In this study ovarian neoplasms were in the age group ranging from 10 to 79 years. When the patients were divided into 7 groups according to their age, (i.e., 10 to 19 yrs, 20 to 29 yrs, 30 to 39 yrs, 40 to 49 yrs, 50 to 59 yrs, 60 to 69 years and 70 to 79 yrs), there was a high incidence of ovarian neoplasms in the age group of 40 – 49 yrs followed by 20 – 29 yrs and the low incidence is seen in more than 70 yrs of age.

The distribution of cases according to their age is given in the following table 2.

Table 2 :

SL.NO	AGE IN YEARS	TOTAL NO. OF CASES	%
1	10 – 19	13	9.8
2	20 – 29	31	23.5
3	30 - 39	24	18.2
4	40 – 49	39	29.5
5	50 – 59	20	15.2
6	60 – 69	4	3.0
7	70 – 79	1	0.85
	Total	**132**	

Likewise the neoplasms were also divided into benign, borderline and malignant categories as given in the following table.

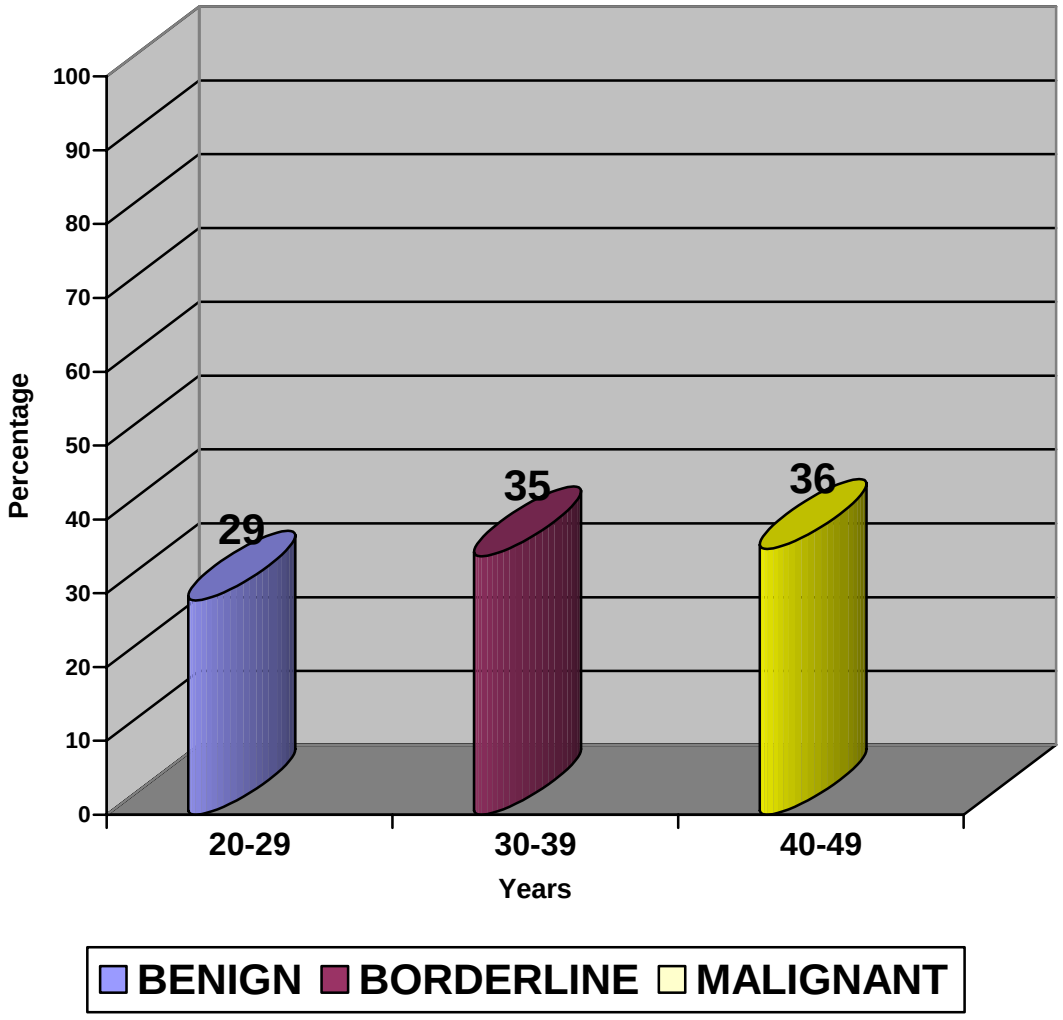
Table 3 :

SL.NO	AGE IN YRS	BENIGN	BORDERLINE	MALIGNANT
1	10 – 19	10	-	3
2	20 – 29	22	4	5
3	30 - 39	14	6	4
4	40 – 49	20	5	14
5	50 – 59	07		11
6	60 – 69	03	-	1
7	70 – 79	-	-	1
	Total	76 (57.5%)	17 (13%)	39 (29.5%)

The above table shows the highest incidence of benign neoplasm in 20 – 29 yrs (22 out of 76 cases, 29%), borderline neoplasm in 30 – 39 yrs (6 out of 17 cases, 35.2%) and malignant neoplasm in 40 – 49 yrs (14 out of 39 cases, 36%).

The table also shows that after 50 years, most of the ovarian masses are malignant, and malignant neoplasms are also encountered below 20 years of age(3 cases, 7.7%).

Diagram 2 : Frequency distribution of ovarian neoplasms, among different age groups



IV CLINICAL EVALUATION

All the cases were evaluated clinically at the time of admission along with basic investigations as in the following table 4.

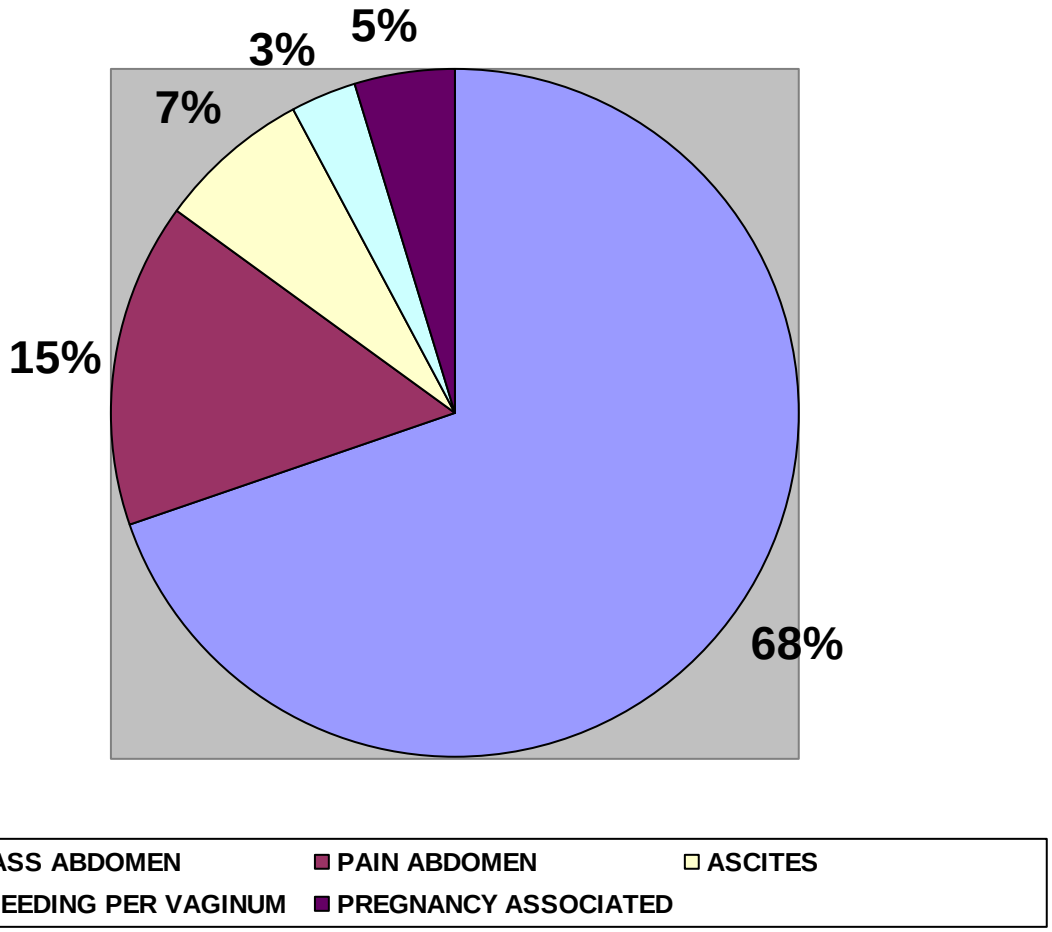
Table 4 : Clinical presentation

SL.NO	CLINICAL FEATURES	NO.OF CASES	%
1	Mass abdomen	86	65.15
2	Pain abdomen	20	15.15
3	Acute abdomen	2	1.52
4	Ascites	8	7.58
5	Bleeding Per vaginum	5	3.79
6	Associated with pregnancy	6	4.55
7	Asymptomatic	5	3.79

Abdominal mass is the most common clinical presentation (86 cases, 65.15%) followed by pain (20 cases, 15.15 %). Few cases presented as acute abdomen necessiating emergency laparotomy. Abnormal vaginal bleeding in the post menopausal period is also noticed in 5 cases. 6 cases were found to be

associated with pregnancy which was removed during LSCS. 5 cases were asymptomatic and detected during routine abdominal ultrasonography done for other causes.

Diagram 3 : Pie chart depicting the percentage of signs and symptoms among ovarian tumour patients



V.LATERALITY :

Likewise tumours were also categorised as with unilateral / bilateral ovarian involvement as in the given table.

Table 5 :

SL.NO	TUMOURS	UNILATERAL	%	BILATERAL	%
1	Serous				
	Benign Borderline Malignant	32 8 9		1 2 6	
	Total	49	37.1	9	6.8
2	Mucinous				
	Benign Borderline Malignant	26 6 4		1 1 2	
	Total	36	27.3	4	3.0
3	Endometrioid carcinoma	1	0.8	1	0.8
4	Transitional	1	0.8	0	
5	Sexcord- stromal tumor	6	4.5	0	
6	Germ cell tumor	18	13.6	1	0.8
7	Metastatic	-		5	3.8
8	Gonadoblastoma (Fig-17&18)	1	0.8	0	
	Grand Total	112		20	

Most of the Serous tumours (Fig1&2) were unilateral at the time of presentation (49 cases, 37.1%) , as in mucinous tumours (36 cases, 27.3 %) and in germ cell tumors(Fig3), (18 cases, 13.6%).Bilaterality in serous and mucinous tumours as a whole was less than 9.8%. (13 cases).

All cases of metastatic ovarian tumours were bilateral at the time of presentation (5 cases, 3.8 %).

VI.GROSS/HISTOMORPHOLOGY OF OVARIAN NEOPLASMS

The ovarian neoplasms were divided into following types as in table 6 according to Histomorphology.

Table 6 :

SL.No	GROSS MORPHOLOGY	NUMBER OF CASES
1	Pure Solid	10
2	Pure Cystic	83
3	Mixed Solid & Cystic	9
4	Cystic with Papillary excrescences	21
5	Solid with variegated appearance	05
6	Solid & Cystic with areas of calcification	04
	Total	132

VII. DISTRIBUTION OF OVARIAN NEOPLASMS ACCORDING TO HISTOLOGICAL CLASSIFICATION.

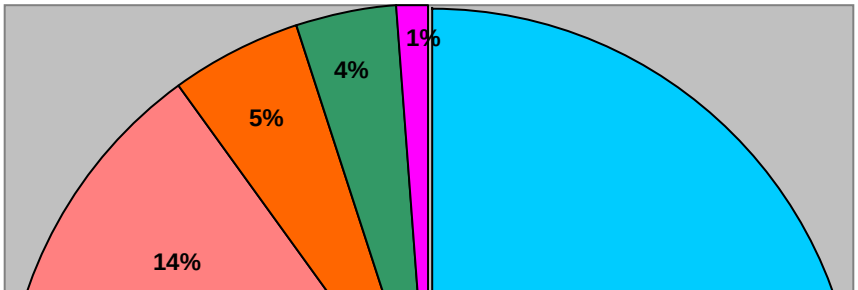
Table 7 :

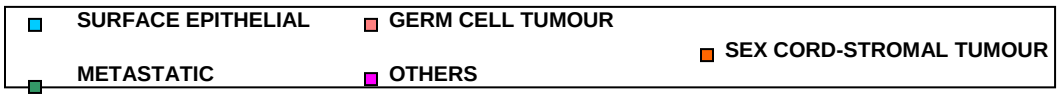
SL.No	CLASSIFICATION	No. OF CASES	TOTAL CASES	%

1	Surface epithelial Tumour			
	Benign Borderline Malignant	59 17 25	101	76.5
2	Germ-cell Tumour			
	Benign Malignant	14 4	18	13.6
3	Sexcord-stromal			
	Benign Malignant	1 6	7	5.3
4	Metastatic	5	5	3.7
5	Gonadoblastoma	1	1	0.76
	Total	**132**	**132**	

Out of 132 neoplasms surface epithelial tumours predominate with 101 cases (76.5 %), followed by germ cell tumours 18 cases (13.6 %) and sexcord- stromal tumours 7 cases (5.3 %).

Diagram 4 : Pie chart depicting the percentage of ovarian tumours according to histologic classification





VIII : SUB-CLASSIFICATION OF SURFACE EPITHELIAL TUMOURS

Surface epithelial tumours were also classified according to WHO classification as in the following table 8.

Table 8 : Sub-classification of surface epithelial tumours.

SL.No	CLASSIFICATION	No. OF CASES	%	AVERAGE %
1	Serous			
	Benign Borderline Malignant	29 7 17	54 13 22	
	Total	53		52.0
2	Mucinous			
	Benign Boderline Malignant	27 10 6	63 23 14	
	Total	43		43.0
3	Endometrioid			
	Malignant Total	2 2	50	 4.0
4	Clear cell tumour	-	-	-
5	Transitional			
	Benign Brenner	1		1.0
	Grand Total	**101**		

Serous tumours (Fig-7) predominate 53 cases, 52.4%) followed by mucinous tumours(Fig-8) (43 cases, 42.5%), 2 cases of endometrioid tumour and one case of transitional cell tumour were also observed.

IX. Sexcord-stromal Tumours

Likewise Sexcord-stromal tumours and germ cell tumours were also classified according to the following table 9 - A & B.

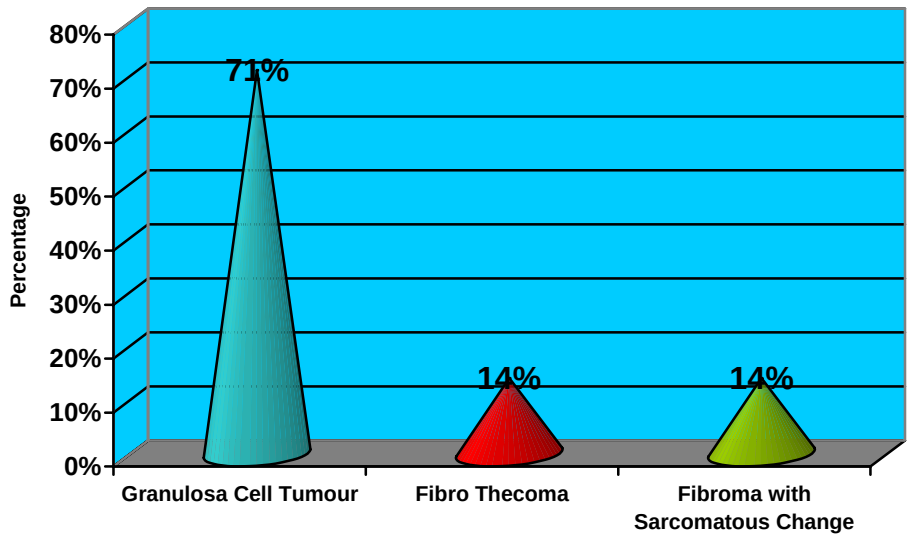
Table 9-A : Sexcord-stromal Tumours

SL.No	CLASSIFICATION	NO OF CASES	%
1	Granulosa cell tumour		

	Adult Juvenile	4 1	71.4
2	Fibrothecoma	1	14.3
3	Fibroma with sarcomatous change	1	14.3
4	Others	-	
	Total	7	

5 cases of granulosa cell tumours(Fig-5&11) (71.4 %) and one case of fibrothecoma(Fig-12) and one case of fibroma with sarcomatous changes were observed.

Diagram 5 :Bar chart ; percentage of sexcord – stromal tumour sub types



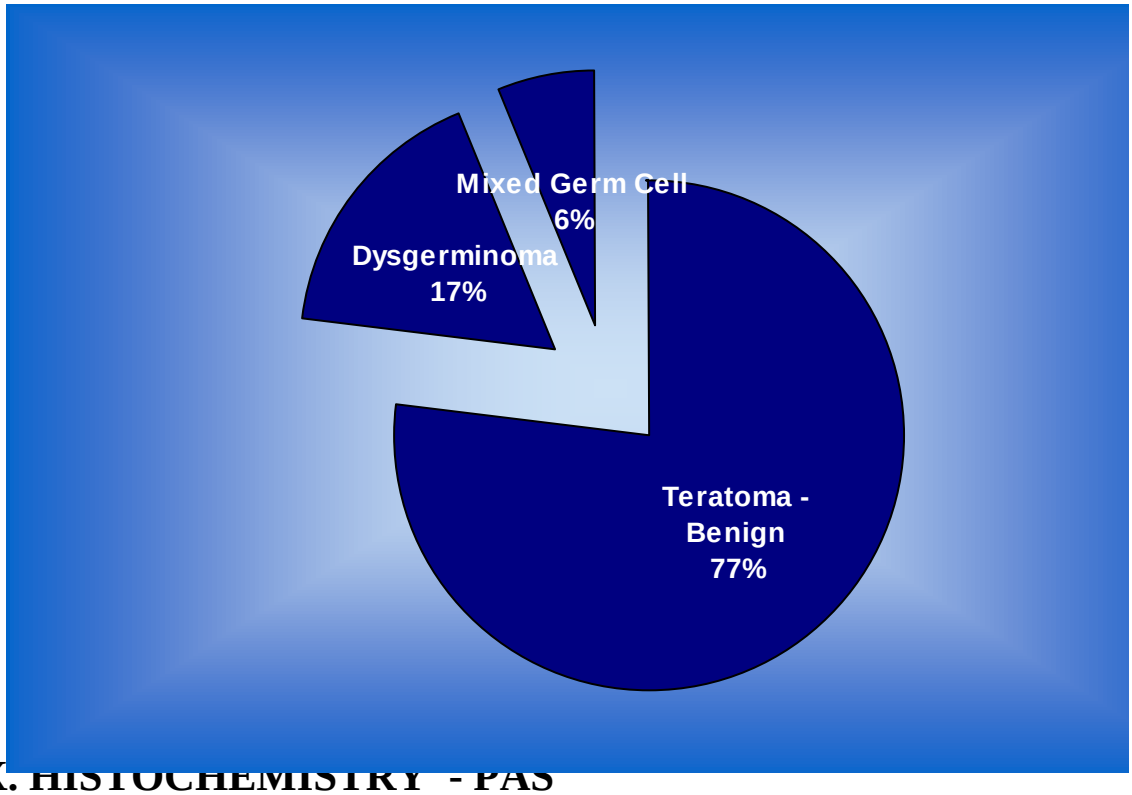
B: Germ Cell Tumours.
Table-9-B

SL.No	CLASSIFICATION	NO. OF CASES.	%
1	Teratoma Benign Malignant	14 -	77.7
2	Dysgerminoma(Fig-13)	1	5.5
3	Mixed Germ cell tumour	3	16.6

4	Others	-	
	Total	18	

In Germ cell tumours, most of the tumours were benign mature cystic teratomas (14 cases, 77.7 %) followed by mixed germ cell tumours(Fig-14&15) (3 cases, 16.6%).

Diagram 6 : Pie chart depicting the incidence of germ cell tumours



X. HISTOCHEMISTRY - PAS

In few doubtful cases of Krukenberg (Fig-6,16&21) and mucinous cystadenocarcinoma,(Fig -22) histochemical stain (PAS) was applied and results are given in the following table10.

Table 10 :

SL.No	PATH No	HPE DIAGNOSIS	PAS REACTION	PATTERN
1	G 692 / 66	Krukenberg tumour	Positive	Focal
2	G 1000/07	Mucinous cystadenocarcinoma	Positive	Diffuse
3	G 1279/07	Mucinous cystadenocarcinoma	Positive	Diffuse
4	G 1334/07	Mucinous cystaenocarcinoma	Positive	Focal
5	G 333/07	Krukenberg tumour	Positive	Focal

XI. HISTOCHEMISTRY - RETICULIN STAIN

Also in solid variants of sexcord-stromal tumours and fibrothecoma, reticulin was applied and the results are given in the following table 11.

Table 11 :

SL.No	HPE. No	HPE DIAGNOSIS	RETICULIN REACTION	PATTERN
1	G 516/06	Fibro Thecoma (Fig-22)	Positive	Investment of Individual Cells.
2	G1625/06	GranuIosa cell tumour (Fig-23)	Positive	Surrounding nests
3	G 91/06	Granulosa cell tumour	Positive	Surrounding nests
4	G1415/07	Granulosa cell tumour	Positive	Surrounding nests

XII. IMMUNOHISTOCHEMISTRY

The value of immuno histochemical marker, pancytokeratin was also evaluated in all malignant ovarian neoplasms as given in the table 12 and the results are expressed as positive (focal, diffuse) and negative. (Fig -24 to Fig - 30)

Table 12 :

S.NO	HPE NO	TUMOUR DIAGNOSIS	MARKER	PATTERN
1	G 973 A / 06	High grade papillary serous cystadeno carcinoma	Cytokeratin	Positive-Diffuse
2	G 1334/B/07	B/L mucinous cystadenocarcinoma	Cytokeratin	Positive-Diffuse
3	G 1439/B/07	B/L Krukenberg tumour	Cytokeratin	Positive-Diffuse
4	G 960 B / 07	Mixed germ cell - choriocarcinoma	Cytokeratin	Positive-Focal
5	G 960 / 07	Mixed germ cell – Embryonal cell component	Cytokeratin	Positive-Focal
6	G 333 / 07	Krukenberg tumour	Cytokeratin	Positive-Diffuse
7	G 239 / 06	Poorly differentiated serous cystadeno carcinoma	Cytokeratin	Focal-positive
8	G 221 / 08	Gonadoblastoma dysgerminoma component	Cytokeratin	Focal-Positive
9	G 221 / 08	Granulosa cell component	Cytokeratin	Focal-Positive
10	G 242 / 08	Fibroma with sarcomatoid change	Cytokeratin	Negative

DISCUSSION

Ovarian cancer has emerged as one of the most common malignancy affecting women. The absolute number of new cancer patients in India is increasing rapidly due to an increase in the size of the population as well as an

increase in the proportion of elderly persons due to improved life expectancy.[30] There is a wide variation in incidence between countries and also within any country for which several causes are cited. The increased diagnosis is partly due to more widespread screening programmes, improved certification and an alteration in registration procedures in certain countries.

Most ovarian cancers are environmental in origin. Hence increase in exposure to risk factors also plays a pivot role in incidence of ovarian cancer. Nandagudi Srinivasa Moorthy et al has observed that some of the very widespread changes in the incidence of ovarian cancer may be accounted for by the trends, in aspects of reproductive behavior such as progressively smaller family size, nulliparous women and proportion of unmarried women. Parity and combined oral contraceptive use have been consistently documented as the protective factors.[36]

In a review on epidemiology of ovarian cancer, cosmetic talc use and some aspect of diet (i.e. saturated fats, refined carbohydrates) may be associated with the increased risk of ovarian cancer .[36]

Women with a family history of ovarian and breast cancer in first degree relatives have also been reported to be at increased risk. [36] No such association has been found in our study. Nandakumar et al has observed that tubectomy as a method of family planning appeared to reduce the risk of development of ovarian cancer, but the follow up data is unavailable.

A COMPARATIVE ANALYSIS

In our study we observed that the ovarian malignancy accounted for 3.39% of total female malignancies.

The following table illustrates the incidence of malignant ovarian neoplasms observed in our study.

Table 13 :

SL.NO	PERIOD	NO OF MALIGNANCIES IN FEMALES	NO. OF MALIGNANT OVARIAN NEOPLASMS	%
1	**Jun 06 – Dec 06**	**372**	**17**	**4.6**
2	**Jan 07 – May 07**	**239**	**10**	**4.1**
3	**Jun 07 – Dec 07**	**330**	**7**	**2.2**
4	**Jan 08 – May 08**	**211**	**5**	**2.3**
	Total	**1152**	**39**	**3.39**

The incidence of ovarian carcinoma by various studies as per the literature and journals is given below :

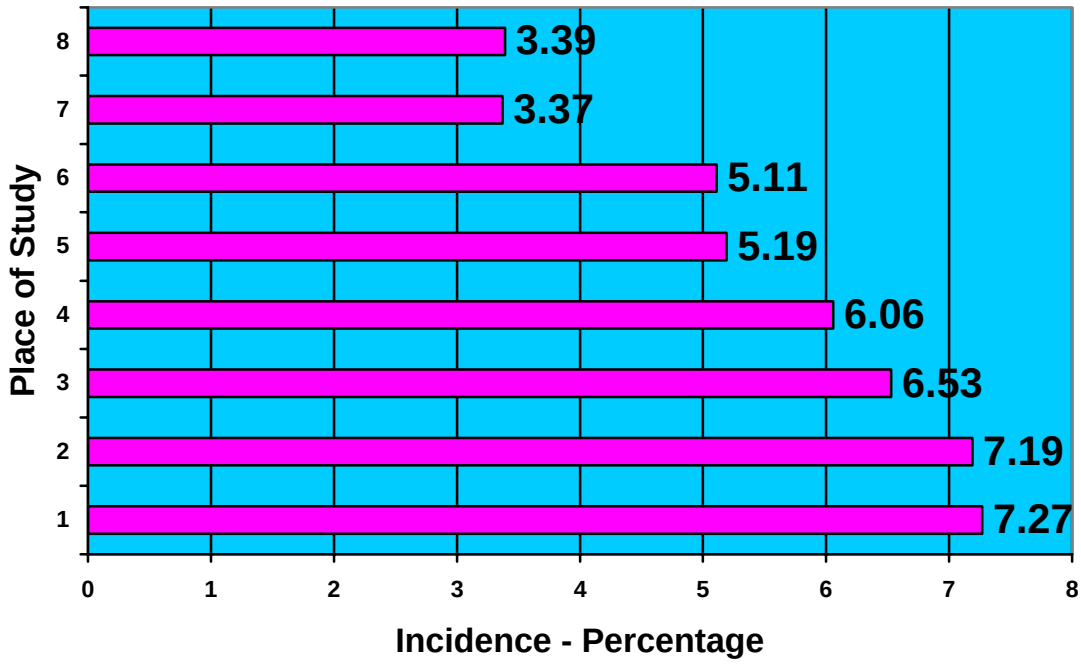
PLACE OF STUDY — INCIDENCE

1. Indian Cancer Society, Mumbai. 7.27%

2. Dr.B.R.Ambedkar Institute Rotary Cancer Hospital, All India Institute of Medical Sciences, New Delhi.	7.19%
3. Gandhi Medical College, Bhopal.	6.53%
4. The Gujarat Cancer and Research Institute, Ahamadabad.	6.06%
5. Kidwai Memorial Institute of Oncology, Bangalore	5.19%
6. Cancer Institute, WIA, Adyar Chennai.	5.11%
7. Nargis Dutt Memorial Cancer Hospital, Barshi.	3.37%
8. **PRESENT STUDY**	3.39%

Of all these studies, Mumbai holds the top ranking with the incidence rate of 7.27%, and the least is Barshi with the incidence rate of 3.37%. These observations suggest that the possible environmental and life style factors have an influence on the incidence rate. India is rapidly stepping towards industrialization. Hence in urban areas like Mumbai changes in life style factors such as increase in age of marriage, delay in age at first birth, reduction in parity and improved socio-economic conditions might have contributed to the increase in incidence in contrast with the rural area like Barshi with the lower incidence. In our study conducted in a semi urban area , the incidence of ovarian malignancy is in midway between rural area like Barsi and urban area like Chennai.

Diagram 7 : Bar chart depicting comparative analysis of incidence in ovarian cancer of our study with various other studies.



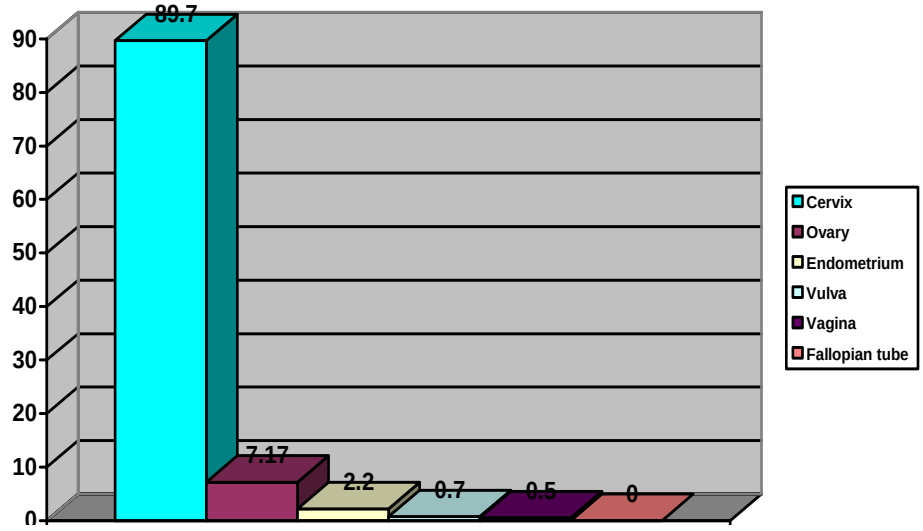
1. Indian Cancer Society, Mumbai. 2. Dr.B.R.Ambedkar Institute RotaryCancer Hospital, All India Institute of Medical Sciences, New Delhi.3. Gandhi Medical College,Bhopal 4. The Gujarat Cancer and Research Institute Ahamadabad.5. Kidwai Memorial Institute of Oncology, Bangalore.6. Cancer Institute, WIA, Adyar Chennai. 7. Nargis Dutt Memorial Cancer Hospital, Barshi. 8. PRESENT STUDY .

We also observed that incidence of ovarian malignant neoplasm among the female genital tract malignancies,as per the following table 14, is 7.17%, which is the second common female genital tract neoplasm.

Table 14 :

SL.No	SITE	NO OF FEMALE GENITAL TRACT MALIGNANCY	%
1	Cervix	488	89
2	Ovary	39	7.17
3	Endometrium	12	2.2
4	Vulva	4	0.7
5	Vagina	3	0.5
6	Fallopian tube	-	-
	Total	544	

Diagram 8: Bar chart depicting percentage of various female genital tract malignancies.



The age specific incidence of ovarian neoplasms ranges from 20 -70 years as per the studies, journals and literature and also show increased incidence at specific age groups for each category of benign, borderline and malignant tumours. The incidence of benign neoplasms peaks through 2nd to 4th decade in accordance with the literatures. As per the literature and studies conducted by

various authors, borderline forms are detected after the age of 40 years and 30-40% of them after the age of 65 years. [44] In contrast, in our study borderline tumours stand in peak at the 3rd decade.

Like, the age specific incidence of malignant ovarian neoplasms reaches peak in the 4th to 5th decade and in 6th decade it constitutes less than 3% in contrast to the studies of Nandagudi Srinivasa Murthy et al in which the ovarian cancers peak in the fifth and sixth decade of life. Serous carcinoma is exceedingly rare in Ist two decades according to the literature.[36] In contrast, in our study 7.6% of cases were noted in first two decades.

Seventy percent of women with the ovarian cancers are diagnosed with stage III or IV disease with 5 years survival of less then 15%. Late diagnosis is thought to be at least in part due to vague non specific symptoms which can often go unrecognized for a period of time.[10,48] So, efforts to improve disease outcome by detecting the disease at an early stage have focused on screening asymptomatic women.

According to the studies of BD Rufford et al 87% had abdominal symptoms, 41% had gastrointestinal,29% had constitutional symptoms and only 2% presented with mass abdomen[48]. In accordance in our study also 90% of the cases presented with abdominal symptoms. None of them had gastrointestinal or constitutional symptoms.

Due to non specific symptoms there was a significant delay in the referral for an ultrasound scan or CA 125 blood test. 67 percent of the cases presented with mass abdomen at a higher stage.

In future trials the delay in diagnosis, can be overcome with the use of patients information leaflets or symptoms questionnaires when women attend out patient department. Hence educating women about symptoms will result in earlier intervention by targeted screening and we can achieve a stage shift in survival improvement and mortality reduction.

Bilaterality is a common feature of tumour that has metastasized to the ovary and is an important diagnostic clue.[43] Certain primary ovarian neoplasms also exhibit the feature of bilaterality.

As per the literature bilateral presentation of serous cystadenoma is 7-20%, in contrast in our study it contributes only to 0.5% where as in borderline and malignant serous neoplasms it correlates well with the literature giving the percentage of 22.2% and 40% respectively.[44]

Like wise the incidence of bilateral presentation of mucinous cystadenoma and mucinous cystadenocarcinoma are 3.7% and 33.3% respectively in correlation with the literature, where as it is in contrast with the bilateral borderline mucinous tumour, it is 14.2% only. Endometrioid carcinoma shows bilateral presentation in

only one case of all the tumours. Metastatic tumours predominant with bilateral presentation of 100%.

In our study surface epithelial tumour observed in 101 cases (76.5%) stands as the most common ovarian neoplasms followed by germ cell tumour with 18 cases (13.6%) and sexcord – stromal 7 cases (5.3%), metastatic tumours contribute 5 cases (3.7%). Rare cases such as gonadoblastoma was also observed in this study.

Of the surface epithelial tumours serous tumours contribute to 52.4% of which 54% are benign serous cystadenoma, 13% are borderline and 17% are carcinomas in accordance with literature. [26,27,49]

Of the mucinous tumours, 63% are benign and 14% are malignant in accordance with the literature but, the borderline mucinous tumours contribute to 23% in contrast with the literature giving the frequency of 10%.

Low malignant potential (LMP) or borderline neoplasms derive from the so called surface epithelium of the human ovary, a modified mesothelium in continuity with the adjacent extra-ovarian peritoneum. These neoplasms represent an important category of ovarian common epithelial tumors usually associated with an excellent prognosis but rarely with a more aggressive and unpredictable behavior characterized by intraperitoneal seeding and frank malignant transformation.

The diagnostic challenge associated with LMP ovarian neoplasms begins at the exploratory laparotomy. At this time the gynaecologic surgeon must assess

several issues including (1) Ovarian or Para ovarian location and extent of problems. (2) Presence of adhesions between ovary and surrounding structures. (3) Indication for staging omentectomy, sub diaphragmatic smears and peritoneal washings.(4) Involvement of contralateral ovary and (5) Preservation of fertility. For accurate sampling the surgeon should indicate to the pathologist the presence and location of any adhesions.

Methodical sampling of the omentum may reveal small implants not visible to the un-assisted eye that would influence staging and treatment. If the exact degree of malignancy cannot be established intra -operatively, these women may be best treated conservatively with more extensive surgery carried out after a thorough study of the removed neoplasms, omentum and peritoneal washings. This approach appears justified in view of a reported lower rate of malignant transformation than previously thought of. [53]

According to Russel et al[49]low malignant potential ovarian neoplasms represented 15% of all ovarian surface epithelial tumours. This correlates well with the observation of 16% of borderline cases in our study. Likewise the low malignant potential forms also occur at a younger age in the 3rd to 4th decade than frankly malignant neoplasms in the 4th to 5th decade in correlation with the literature. [53]

In most series of studies by katsube et al, koonings et al and petterson et al,[26,27,41] mucinous borderline tumours are less common than serous borderline

tumours but in our study mucinous borderline tumours out number the serous borderline tumours in close correlation with the studies by isarangkul in Thailand. In Japan and Norway, both types of tumours are equally prevalent.[44]

As per the literature 42% of endometrioid tumours are associated with endometriosis in the same ovary or elsewhere in the pelvis.[14] In contrast in our study no such association has been found.

Brenner tumours are often associated with other tumours such as mucinous cystadenoma, mature teratomas and transitional cell carcinoma of bladder.[14,31] In our study one such association with mature cystic teratoma has been observed.

In our study 7 cases of sexcord - stromal tumours have been observed. Of which granulosa cell tumor predominates with 5 cases. One case of fibrothecoma and one case of fibroma with sarcomatous changes that typically has mitosis of more than 4/10 HPF, nuclear atypia and necrosis has also been observed .

Germ cell tumours constitute a heterogeneous group of tumours reflecting the capacity for multiple lines of differentiation of the main stem cell system. 14 cases of benign teratomas are observed in our study. According to Hurwitz et al,age at presentation with malignant transformation in a dermoid cyst is older than those with benign disease and is more common in post menopausal women.[33] In contrast in our study two cases of mature teratoma in post menopausal age group without any evidence of malignant transformation has been observed.

One case of dysgerminoma and 3 cases of mixed germ cell tumour with combination of (1) Dysgerminoma, Embryonal cell carcinoma (2) Yolk sac tumour, Embryonal cell carcinoma and choriocarcinoma (3) Yolk sac and Embryonal cell carcinoma has been observed.

Metastatic tumors to the ovary are common and occur in approximately 30% of women dying of cancer.General features of ovarian metastasis include bilaterality, small multinodular surface tumours, extensive extra ovarian spread, unusual patterns of dissemination, unusual histological features, blood vessel and lymphatic invasion and a desmoplastic reaction.[44]

Krukenberg tumour is the most common form of ovarian metastatic carcinoma in young women often found in fourth decade.[44]It is defined as ovarian neoplasms in which signet ring cells account for atleast 10% of the neoplasms. Mucin free epithelial cells, small glands with flattened lining cells, larger glands of typical intestinal and mucinous type, fibrous stroma ranging from densely cellular to edematous and extra cellular mucin may be prominent.[1,44]4 cases of krukenberg tumour and one case of small cell- neuroendocrine tumour of intestinal origin (Fig-19) have been observed in our study.

PAS (periodic acid schiff) stain is an extremely useful and esthetically pleasing technique. Substances containing vicinal glycol groups or their amino or alkyl amino derivatives are oxidized by periodic acid to form dialdehydes, which combine with schiff reagent to form an insoluble magenta

compound.This stain therefore demonstrates glycogen and neutral muco substances.[25]

In krukenberg tumors, intracellular material is PAS – positive, and diastase resistant. Mucin pools are positive in mucinous carcinoma of ovary.[44] In our study, mucinous carcinoma of ovary shows PAS positive mucin pools, and krukenberg tumour, show intracellular PAS positivity.

The diffuse pattern of granulosa cell tumors may be confused with a benign thecoma, particularly when there is luteinization. A reticulin stain is helpful, since granulosa cells typically grow in sheets or aggregates bound by reticulin fibrils, whereas thecomas contain an abundance of intercellular fibrils surrounding individual cells. The distinction is important since granulosa cell tumors have an aggressive potential, whereas thecomas are with rare exceptions benign.[14]

In this study, we applied reticulin stain for granulosa cell tumours and fibro thecoma. The reticulin stain shows fibrils surrounding nests and larger aggregates of granulosa cells. In thecoma, reticulin stain highlights an investment of individual cells by fibrils.

Expression of cytokeratin is present in all ovarian malignant tumours. Cytokeratins are a family of water insoluble, intracellular fibrous proteins present in almost all epithelia. Keratin represent an excellent marker for epithelial differentiation regardless of whether the tumour is of endodermal, neuroectodermal, mesenchymal or germ cell derivation.[25]

Antibodies to cytokeratin intermediate filament proteins have been used for many years to verify the epithelial origin of poorly differentiated carcinomas and to identify small volumes of tumor, often at matastatic sites including lymphnodes and meninges. More recently, the development of antibodies which react to specific cytokeratins in tissue that has been fixed in formalin and embedded in paraffin has permitted investigations to examine the cytokeratin profile of lesions including benign and malignant tumours.[35] Undifferentiated and poorly differentiated serous carcinoma show positivity for cytokeratin.[39] In this study, poorly differentiated carcinomas showed focal positivity.

The important immunohistochemical finding in adult granulosa cell tumours is the cytokeratin may be positive, typically with punctuate staining.[39] In this study, granulosa cell tumour showed the typical punctuate pattern of staining.

Dysgerminoma cells are, typically immuno reactive for cytokeratin.[39,40] In this study dysgerminoma also showed focal positivity for cytokeratin.In yolksac tumour, the cytoplasm of tumour cells are immuno reactive for cytokeratin. In our study, it did not show positivity. In embryonal cell carcinoma, the cytoplasm of the tumour cells is typically immuno reactive for cytokeratin.[39] In this study, in the mixed germ cell tumour, the embryonal cell component exhibited the focal positivity. Like wise, in choriocarcinoma, the syncytiotrophoblastic cells are typically immuno reactive with cytokeratin. Finally in this study, krukenberg tumours have shown diffuse positivity.

CONCLUSION

In the present prospective study of 132 ovarian neoplasms evaluated with clinical, histopathological, histochemistry and immunohistochemistry, the following conclusions are made and presented.

1. The incidence of ovarian neoplasms among the female neoplasms is 8.17%.

2. Ovarian malignancy ranks second among the female genital tract malignancies.

3. The ratio of benign and malignant ovarian neoplasm is 2.3:1.

4. The incidence of ovarian neoplasm is highest during the fifth decade followed by third decade.

5. Eighty five percentage of ovarian tumours are unilateral in presentation, in which benign neoplasms are predominantly cystic, whereas malignancies are predominantly solid and cystic or purely solid.

6. Surface epithelial tumours are the most common neoplasm, of which serous cystadenoma is the commonest.
7. Reticulin and PAS stain still have their value in the initial evaluation to distinguish Thecoma and Granulosa cell tumour as well as to demonstrate mucin filled signet ring cells in krukenberg tumour and mucinous nature of high grade mucinous cystadenocarcinoma.

8. The PANCYTOKERATIN exhibits varied pattern of positivity in various ovarian neoplasms.

9. The epithelial immunohistochemical marker - PANCYTOKERATIN also exhibits focal positivity in non epithelial tumours like granulosa cell tumour, mixed germ cell tumour and metastatic tumours.

Advanced diagnostic tools and awareness of screening periodically for malignancies helps early detection of ovarian neoplasms and thereby reduces the morbidity and mortality.

APPENDIX

I. HAEMATOXYLIN AND EOSIN

Preparation of the solution:

Distilled water	- 1000 ml
Ammonium alum	- 100 g
Haematoxylin	- 5 g
Absolute Ethyl Alcohol	- 50 ml
Mercuric Oxide	- 2.5 g

100 g of ammonium alum dissolved in 1000 ml of distilled water by heating and shaking at 60^{o}C.Add solution of 50 g of haematoxylin in 50 ml of ethyl alcohol and bring rapidly to boil.When it begins to boil,remove from flame and add 2.5 g of Mercuric oxide.Mix by swirling gently.

EOSIN STAIN

Eosin Y	- 1 g
Distilled water	- 20 ml
95% Ethanol	- 80 ml
Glacial acetic acid	- 0.2ml

Dissolve 1 g eosin Y in 20 ml of water and add 95% ethanol and glacial acetic acid.

Procedure:

1. Sections to water

2. Alum Hematoxylin (Harris)

3. Quick rinse in water

4. Dehydration- 1% acid alcohol- 3 to 4 times

5. Rinse in tap water-30 seconds

6. Stain 1 % aqueous eosin Y for ¼ to 2 minutes

7. Wash in water

8. Clear and mount

APPENDIX

II. PER-IODIC ACID SCHIFF STAINING

Preparation of solution:

Coleman's Feulgen reagent:

Basic Fuchsin	- 1.0 gm
Potassium metasulphite	- 2.0 gm
Normal Hydrochloric acid	- 10 cc
Distilled water	- 200 cc
Activated carbon	- 0.5 gm

Dissolve 1.0 gm Basic Fuschin in 200 cc of hot distilled water.Bring to boiling point.Cool and add 2.0 gm potassium metabisulphite and 10 cc normal hydrochloric acid.Let bleach for 24 hrs.

Add 0.5 gm of activated carbon,shake 1 mt and filter until colourless, store in refrigerator.

1% Per-iodic Acid solution:

Per-iodic Acid crystals	- 1 gm
Distilled water	- 100 cc

Normal Hydrochloric Acid solution:

Hydrochloric Acid Conc sp.Gr 1.19	-83.5 cc
Distilled water	-916.5 cc

Procedure:

1. Smear fixed in methanol for 20 mts

2. Air dried

3. Per-iodic acid for 10 mts(oxidant)

4. Rinse in distilled water

5.Place in Coleman’s Feulgen reagent (Schiff’s reagent) for 30 mts

6.Wash in tap water for 10 mts for pink colour to develop

7. Immerse in hematoxylin for 1 to 2 mts

8. Rinse in tap water

9. Differentiate in acid alcohol- 2 dips

10. Wash in water 30 sec

11.Two dips in ammonia water 2 %

12. Wash in tap water- 30 sec

13.Dehydrate in absolute alcohol

14.Clear with xylene.

APPENDIX

III RETICULIN STAINING

Preparation of solution

1 % Pottasium permanganate.

2 % Pottasium metasulphite.

2 % Ferric Ammonium Sulphate.

10 % Formalin neutral.

0.2 % Gold chloride.

2.5 % Sodium thio sulphate.

10% KOH

Ammoniacal silver solution.

Preparation of Ammoniacal silver solution.

10 % Ag No3 — 40 ml

10 % KOH —10 ml

- Add 40 ml of 10 % AgNo3 to 10 ml of 10 % KOH in a flask, cause silver to deposit.
- Remove the supernant fluid.
- Wash the deposit with distilled water several times.
- Add strong ammonia drop by drop until the solution takes a faint sheen.
- Make the solution to twice its volume by distilled water.

Procedure

- Section to water.
- Oxidize in potassium permanganate-2 minutes.
- Rince in water.
- Decolorize in potassium meta bisulphate-1 minute.
- Prolonged wash in water-5 minutes.
- Sensitise in ferric ammonium sulphate-1 minute.
- Prolonged wash in tape water followed by 2 changes of distilled water.
- Impregnate in ammoniacal silver solution – 1 minute

APPENDIX

IV - IMMUNO HISTOCHEMISTRY

Procedure

1. 5 microns thick sections were cut from the blocks received on slides coated with chrome alum gelatin.
2. Slides were dewaxed and dehydrated in graded alcohol.
3. Slides were immersed in 0.3 % Hydrogen peroxide for 20 minutes to block endogenous peroxidase activity.
4. Washed in phosphate buffered saline (PBS)
5. Incubated in primary antibody & Ki – 67.
6. Washed in PBS.
7. Biotinylated link was applied for 20 minutes.
8. Washed in PBS.
9. Incubated in streptavidin-biotin complex.
10. Washed in PBS
11. DAB was used as chromogen.

12. Washed and can be stained with haematoxylin.

13. Mounted with coverslip.

BIBLIOGRAPHY

1. Akako K, Robert YH, Robert SE. krukenberg tumours of the ovary clinicopathological analysis of 120 cases with emphasis on their variable pathological manifestations. AM J Surg Pathol. 2006; 30 (3): 277-282.
2. Barbara YAS. Lowe ASJ. Female genital organs. Wheater's functional Histology. Fifth edition, Elsevier press; 2006: 359-367.
3. Bchew S, Leifao M, Tornos C, Soslow RA. Invasion pattern in stage 1 endometrioid and mucinous ovarian carcinomas without destructive stromal invasion. Mod. Pathol. 2005; 18 (7) : 903-911.
4. Bellka, Kurman R J. A clinicopathological analysis of atypical proliferative (borderline) tumours and well differentiated endometrioid adenocarcinoma ovary. Am J Surg Pathol. 2001; 25: 1341-1342.
5. Castellvi Josep MD, Angel garco; et al. Ephrin B-expression in epithelial ovarian neoplasms correlates with tumour differentiation and angiogenesis. Hum pathol 2006; 37: 883-889.
6. Cathro HP, Stoler MH. Expression of cytokeratins 7 and 20 in ovarian neoplasia. Am J Surg Pathol. 2002; 9:14-18.
7. Charles Z, Brenda W. The ovary / fallopian tube. In:Steven SG, Donald DA, William FJ, Virginias A, Mark wick R. Silverberg's principles and practice of surgical pathology and cytopathology. Third edition. Elsevier press. 2006; 1987-2061.

8. Christopher CP. Female genital tract. In: Vinay kumar, Abdul AK, Nelson fausto, Robins and Cotran. Pathologic basis of disease. Seventh edition, Elsevier Inc press; 2004;1060-79.
9. Christopher HN, Marcus. Setechell E, John Hawkins. Shaw's text book of operative gynaecology. Sixth edition, Elsevier press; 2004: 352-373.
10. Deo SVS, Gobal Hemant. Neo adjuvant chemotherapy followed by surgical cytoreduction in advanced epithelial ovarian cancer. Indian Journal of cancer.2006; 43 : 117-121.
11. Eichorn JH, Young RH.Transitional cell carcinoma of the ovary.Morphological study of 100 cases with emphasis on differential diagnosis.AM J Surg Pathol.2004; 28: 453-463.
12. Elin A, Hbala VM.The activated nerve growth factor receptor Prk A is selectively expressed in advanced stage. Hum Pathol.2007; 38(1): 140-146.
13. Fabilia M, Micheal G, Yongee Lee, Elvin JA, Callahan MJ, Garbas JE, Coramer DW, Christopher p. The tubal fimbria is a preferred site for early adenocarcinoma in women with familial ovarian cancer syndrome. Am J Surg pathol. 2006; 30 (2): 230-238.
14. Fattench TA, peter devilee. WHO classification of tumours of female genital organs. IARC press; Lyon 2000: 113-202.
15. Fox H, Wells M. Ovarian tumours : Classifications, histiogenesis and eitiology. Harrold fox, Micheal Wells. Ovarian tumours in Haines and

Taylor. Obstetrical and gynaecological pathology. 5th edition, Churchill Livingston press; 2003: 693-899.

16. Glen W, Robert YH. Paraglioma of the ovary. Report of three cases of rare ovarian neoplasms, including two exhibiting inhibin positivity. AM J Surg Pathol.2006; 30 (5): 600-607.
17. Huswitz JL,Fenton A,Mcluggage G.Squamous cell carcinoma arising in a dermoid cyst of the ovary.a case series.BJOG.2007; 114: 1283-1287.
18. Ian Wilson,Marilyn gamble,Totty BA,Bancroft D.Theory and practice of histological techniques.Fifth edition,Elsevier press,2002:130-178.
19. Irving JA, Abdul mohsan Alkushi, Young RH, Philip B. Cellular fibromas of the ovary. a study of 75 cases including 40 mitotically active tumors emphasising their distinction from fibrosarcomas. AM J Surg pathol. 2006; 30 (8): 929-935.
20. Isarangkul W.Ovarian epithelial tumours in Thai Women. A histological analysis of 291 cases. Gynecol oncol 1984; 17: 321-329.
21. Ivan D, James Linder. Anderson pathology, Tenth edition, volume 2, Mosby year book.Press; 1996: 2235-2305.
22. Jeffray SD, Peter Russell, Robert KJ. Surface epithelial tumours of the ovary. In: Robert Kurman J. Blaustein's pathology of female genital tract, fifth edition. Springer – Verleg; 2002: 791-881.

23. Jeidman JD, Kurmar Robert BM. Primary and matastatic adenocarcinoma in the ovaries. Incidence in routine practice with a new approach to improve intraoperative diagnosis. AM J Surg Pathol. 2003; 27: 985-993.
24. Jonathan BS.Novak`s gynaecology. Thirteenth edition. LW&W press.2002:1245-1272.
25. Juan Ri, Rosai and Ackerman's surgical pathology. Nineth edition, Elsevier press; 2004: 1649-1707.
26. Katsube Y, Berg JW, Silverberg SG. Epidemiologic pathology of ovarian tumours. A histopathological review of primary ovarian neoplasms diagnosed in the Denver standard metropolitan stastical area, 1 july – 31 dec 1969 and 1july – 31 dec 1979. Int.J Gynaecol pathol. 1982; 1: 3-16.
27. Koonings PP, Campbell K, Mishell DR Jr, Grimes DA.. Relative frequency of primary ovarian neoplasms. A 10 year review. Obstet gynecol. 1984; 74: 921-6.
28. Larry CJ, John JF, Epethelial ovarian cancer Text Book of gynaecology.Second edition. Saunders press. 2000: 1333 -1373.
29. Leiteo Jr, Boyd J, Hummer A, et al. Clinicopathologic analysis of early stage sporadic ovarian carcinomas. AM J Surg pathol. 2004; 38 (2): 147-159.
30. Lerwill ME, Robert YH. Ovarian metastasis of intestinal type gastric carcinoma. A clinicopathological study of 4 cases with contrasting features

those of the krukenberg tumour. AM J Surg pathol. 2006 ; 30 (11): 1382-1390.

31. Manoj Sharma, Ruksha Arora, Reva Thripathi, Vijay zutsi. Department of radiation oncology and OBG in Maullana Azad Medical College, Hospital Delhi. Journal of postgraduate medical education and research. Recent advances in ovarian cancer. 2006; 1 (4): 158-165.
32. marjolijin AT, verbruggan B, Verheijen HM, Frank RW, et al. Serous borderline tumour of the ovary presenting with cervical lymphnode involvement. Am J Surg Pathol. 2006; 30 (6):739-745.
33. Meknney JK,Bonnie L,Longara A.Patterns of stromal invation in serous tumours of low malignant potential.a re-evaluation of the concept of stromal microinvation.Am J Surg Pathol.2006; 30 (10) : 1209-1217.
34. Micheal LR, Micheal DT, Elrio SG, Aneus morphia. Ovarian involvement by metastastic endothelial adenocarcinoma. Still a diagnostic challenge. AM J Surg Pathol. 2006; 30; 177-182.
35. Millward EJ. Heajley MK, Cytokeratin immunostainning profile in diagnostic pathology in Lowe DG, Underwood James CE, Recent advances in histopathology 20. Royal society of medicine press, 2003: 17-28.
36. Nandakudi SM, Muralidaran, Kishore Chaudry. Trends in incidence of ovarian carcinoma, Indian scenario. Obs & gynec today. 2007; 12 (2):82-87.

37. National Cancer Registery programme. Indian Council of medical research. Consolidated report of hospital based cancer registries HBCR: 2001-2003.
38. Petterson F. Annual report of the result of treatment in gynaecological cancer. Stock Holm International Federation of gynecology & obstetrics: 1991.
39. Philip EB, Robert YH, FRC Patho, Atlas of gyneacologic Surgical pathology. W. B.sanders press, 2000: 289-389.
40. Prasanth Kumar Deka, Ben DK, Dawka S. a rare case of pancreatic adenocarcinoma mimicking a early ovarian tumor. Obs & gynaec today. 2007; 12 (2) : 558-562.
41. Reddi P, Reddy Renjika. Chemotheraphy in epithelial ovarian cancer changing regimens. Obs & gynec today. 2007;12 (8):377-380.
42. Robert SA, Christina Isacson, Charles Zaloudex-Immunohistology of the female genital tract. In : Davis Dabbs. Diagnostic immunochemistry Second edition, Churchill Livingston 2006 : 637-697.
43. Robert SE, Philip CB, Robert Young H. ovarian tumours. In Stacey ME, Sternberg's diagnostic surgical pathology. Fourth edition, LWW 2004: 2543-2652.
44. Robert SE, Robert YH, Philip CB. Tumours of the ovary, maldeveloped gonads, fallopian tube, and broad ligament. published by armed force Institute of pathology. 1998; 27-445.

45. Roca JA,Thompson D,Lindes operative gynaecology. Eighth edition.Lippincott-Raven press.1997;1557-1567.
46. Rock A,Jones HW,Te lindes operative gynaecology.Ninth edition,LWW press ;2003:640-642.
47. Roth LM, Emerson RE, Albright TM. Ovarian Endometrioid tumours of the iow malignant potential, comparison with well differentiated endometrioid adenocarcinoma. AM J Surg Pathol.2007: 9: 1253-59.
48. Rufford BD, Menon V. Feasibility screening for ovarian cancer using symptoms as selection criteria.BJOG. 2007; 14 (1): 59-64.
49. Rusell p.The Pathological assessment of ovarian neoplasms. Introduction and analysis of benign “epithelial” tumours. Pathology. 1979; 11: 5-26.
50. Rusell V, Jefferey M, Michael DT. Current problems with staging lymphomas involving the ovary. AM J Surg Pathol. 2006; 3 (9): 1202-1210.
51. Russell V, Allen GM, Toded B, Darren WT, Anne, et al. Cytokeratin 7 and 20 in primary and secondary mucinous tumours of the ovary. Am J Surg Pathol. 2006; 30 (9): 1130- 36.
52. Sadako N, Hirosh T. Differential expression of Abc F2 protien ammy different histologic types of epithelial ovarian cancer and clear cell adenocarcinoma of different organ. Hum Pathol. 2007; 38 (1): 134-139.
53. Sadler TW. Langman’s medical embryology. Tenth edition. 22-25.

54. Santo NV. Ovarian and peritoneal borderline neoplasams. Histopathology, diagnostic pit falls. Cancer 2004; 161: 1-7.
55. Scott JR ,Philip J,Hammond CB,Spellary WN,Danforth`s obstetrics & gynaecology.Eighth edition.LW & W press.2004:865-907.
56. Silva EG, Deevars MT, Bordurka DC, Mrepica a. association of low grade endometrioid carcinomas of the uterus and ovary with undifferentiated carcinomas. Int J Gynecol Pathol.2006; 25 (1): 52-58.
57. Silva EG, Gershenson DM, Arai's malpica, micheal deavers. The recurrence and overall survival rates of ovarian serous borderline neoplasams with non-invasive implants in time dependent. Am J Surg Pathol. 2006;30 (11) : 1367-1373.
58. Sohei Y, Histoshi T, Shinsuka Aida. Immnuohistochemistry detection of hepatocyte nuclear factor in ovarian and endometrial clear cell adenocarcinoma and non neoplastic endometrium. Hum pathol. 2007; 38 (7): 1074- 1080.
59. Stearms AT, George WD. comparision of breast cancer mortality rates with those of ovarian & colorectal carcinoma. British journal of surgery. 2007; 94 (8): 957-965.
60. Susan S, Harold ellis, Jeramiah HC,et al. Gray 's anatomy. Thirty nineth edition, Elsevier press, 2005;1321-26.
61. Woodward ER, Considine AM, Williams S, Hugo JM, Guagor D. Annual surveillance by CA125 and transvaginal ultrasound for ovarian cancer in

both high risk and population risk in women. BJOG. 2007; 114 (12): 1500-1509.

62. Zaloudex C.Tumors of ovary. In : Chirstopher D M. Fleteher. Diagnostic histopathology of tumors. Second edition. Harcourt press; 2000 : 567-640.

MASTER CHART

S.No	HPE.NO.	AGE YEARS	IP NO	CLINICAL PRESENTATION	GROSS	
1.	G 238/06	30	6255	MASS ABDOMEN	UNILATERAL, CYSTIC	BENIGN S
2.	G 239/06	42	1943	MASS ABDOMEN	UNILATERAL, VARIEGATED	SEROUS C POORLY D
3.	G 253/06	20	5214	MASS ABDOMEN	UNILATERAL, CYSTIC	BENIGN M
4.	G 257/06	25	6256	PAIN/MASS ABDOMEN	UNILATERAL, VARIEGATED	MIXED GE (DYSGERM CARCINO
5.	G 299/06	30	7188	MASS ABDOMEN	UNILATERAL, CYSTIC	MATURE T
6.	G 327/06	28	7567	MASS ABDOMEN	UNILATERAL, CYSTIC	BENIGN M
7.	G 338/06	33	9288	PREGNANCY ASSOCIATED	UNILATERAL, CYSTIC	DERMOID
8.	G 359/06	56	7834	ASCITES	BILATERAL VARIEGATED	ENDOMET
9.	G 398/06	25	10409	MASS ABDOMEN	UNILATERAL, CYSTIC	SIMPLE SE
10.	G 418/06	55	8545	MASS ABDOMEN	UNILATERAL, CYSTIC	BENIGN M
11.	G 423/06	40	6684	PAIN/MASS ABDOMEN	UNILATERAL, CYSTIC	SIMPLE SE
12.	G 445/06	27	12515	PREGNANCY ASSOCIATED	UNILATERAL, CYSTIC	SIMPLE SE
13.	G 446/06	65	4358	MASS ABDOMEN	UNILATERAL, CYSTIC	ENDOMET
14.	G 447/06	40	8804	MASS WITH ASCITES	UNILATERAL, VARIEGATED	PAPILLAR CYSTADE
15.	G 473/06	22	11794	PAIN ABDOMEN	UNILATERAL, SOLID AND CYSTIC	BENIGN S
16.	G 480/06	24	10445	PAIN MASS ABDOMEN	UNILATERAL, CYSTIC	BENIGN S
17.	G 495/06	25	13735	MASS ABDOMEN	UNILATERAL, CYSTIC	BENIGN M
18.	G 505/06	16	14426	MASS ABDOMEN	UNILATERAL, CYSTIC	SEROUS C
19.	G 516/06	40	10831	MASS ABDOMEN	UNILATERAL - SOLID & CYSTIC	FIBRO TH
20.	G 625/06	50	17639	MASS AND PAIN	UNILATERAL - CYSTIC & SOLID	SEROUS C
21.	G 658/06	35	PRIVATE	MASS ABDOMEN	UNILATERAL, CYSTIC	BENIGN S
22.	G 692/06	33	21957	ACUTE PAIN ABDOMEN	BILATERAL - SOLID WITH FEW CYSTIC	BILATERA
23.	G 714 06	42	22236	MASS ABDOMEN	BILATERAL VARIEGATED	PAPILLAR CYSTADE
24.	G 807/06	14	24869	PAIN ABDOMEN	UNILATERAL - CYSTIC	SIMPLE SE
25.	G 818/06	70	23481	MASS ABDOMEN	UNILATERAL, VARIEGATED	SEROUS P CYSTADE
26.	G 908/06	60	26073	MASS ABDOMEN	BILATERAL - CYSTIC	BENIGN M SEROUS C
27.	G 937/06	45	5685	MASS ABDOMEN	UNILATERAL - CYSTIC	BENIGN D
28.	G 973/06	55	28278	MASS ABDOMEN ASCITES	BILATERAL - SOLID AND CYSTIC	HIGH GRA SEROUS C
29.	G 997/06	25	30757	PAIN AND MASS	UNILATERAL - CYSTIC	MUCINOU

				ABDOMEN	WITH SOLID	
30.	G 1018/06	36	306836	MASS ABDOMEN	UNILATERAL - CYSTIC	TORSION
31.	G 1086/06	45	30268	MASS ABDOMEN	UNILATERAL - CYSTIC	SEROUS P CYSTADE
32.	G 1100/06	40	29628	PAIN ABDOMEN	UNILATERAL - CYSTIC	SEROUS T MALIGNA
33.	G 1114/06	45	29905	MASS ABDOMEN	BILATERAL - SOLID & CYSTIC	MUCINOU
34.	G 1119/06	45	31556	MASS ABDOMEN	UNILATERAL, VARIEGATED	SEROUS C
35.	G 1169/06	40	30556	MASS ABDOMEN	UNILATERAL - SOLID & CYSTIC	SEROUS C
36.	G 1191/06	42	306893	PAIN /BLEEDING	UNILATERAL, VARIEGATED	SEROUS P CYSTADE GRADE
37.	G 1120/06	27	35047	MASS ABDOMEN	UNILATERAL - CYSTIC	MUCINOU
38.	G 1137/06	25	36047	MASS ABDOMEN	UNILATERAL - CYSTIC	SIMPLE SI
39.	G 1176/06	18	35663	BLEEDING PER VAGINUM	UNILATERAL - CYSTIC	DERMOID
40.	G 1341/06	19	40875	PREGNANCY	UNILATERAL - CYSTIC	SEROUS C
41.	G 1344/06	45	37067	MASS ABDOMEN	UNILATERAL - CYSTIC	MUCINOU
42.	G 1374/06	39	307372	MASS & PAIN ABDOMEN	UNILATERAL - CYSTIC	ENDOMET
43.	G 1392/06	40	307376	MASS ABDOMEN	UNILATERAL - CYSTIC	SEROUS C
44.	G 1425/06	23	44545	MASS ABDOMEN	UNILATERAL - CYSTIC	ENDOMET
45.	G 1446/06	47	38875	PAIN ABDOMEN	UNILATERAL - CYSTIC	SEROUS C
46.	G 1449/06	25	44098	MASS ABDOMEN	UNILATERAL - CYSTIC	MUCINOU
47.	G 1481/06	30	44099	MASS ABDOMEN	UNILATERAL - CYSTIC	MUCINOU
48.	G 1553/06	40	45799	MASS ABDOMEN	BILATERAL - CYSTIC	MUCINOU
49.	G 1543/06	18	49038	PREGNANCY	UNILATERAL - CYSTIC	TERATOM
50.	G 1604/06	36	48263	MASS ABDOMEN	BILATERAL - CYSTIC	MUCINOU MALIGNA
51.	G 1613/06	40	48143	MASS ABDOMEN	UNILATERAL - CYSTIC	MUCINOU MALIGNA
52.	G 1625/06	35	47738	MASS ABDOMEN	UNILATERAL, VARIEGATED	GRANULO TYPE
53.	G 1641/06	27	51135	PREGNANCY	UNILATERAL - CYSTIC	DERMOID
54.	G 1651/06	33	48734	MASS WITH PAIN	UNILATERAL - CYSTIC	BENIGN S
55.	G 1673/06	35	43529	MASS ABDOMEN	UNILATERAL - CYSTIC	SEROUS T MALIGNA
56.	693/06	52	878752	MASS WITH ASCITES	BILATERAL SOLID	SMALL CE CARCINO
57.	930/06	45	880075	MASS ABDOMEN	UNILATERAL - SOLID & CYSTIC	SEROUS C
58.	1245/06	60	885325	MASS ABDOMEN	BILATERAL CYSTIC	A) ONE OV SEROUS C CYSTADE
59.	1999/06	22	90442	MASS ABDOMEN	UNILATERAL - CYSTIC	BENIGN SE
60.	2018/06	20	903077	BLEEDING PER VAGINUM	UNILATERAL - SOLID	DYSGERM

61.	2122/06	36	903647	MASS ABDOMEN	UNILATERAL - SOLID	ENDOMET
62.	2719/06	11	38466	MASS ABDOMEN	UNILATERAL - CYSTIC	MATURE C
63.	2969/06	45	38595	MASS ABDOMEN	UNILATERAL - CYSTIC	BENIGN M
64.	3048/06	57	917599	ACUTE ABDOMEN	UNILATERAL - CYSTIC	MUCINOU
65.	3169/06	55	915265	MASS ABDOMEN	UNILATERAL, VARIEGATED	FIBROMA TRANS-- F
66.	G 19/07	49	48143	MASS ABDOMEN	UNILATERAL - CYSTIC	SIMPLE SE
67.	G 66/07	25	307396	MASS ABDOMEN	UNILATERAL - CYSTIC	MATURE C
68.	G 110/07	40	1565	MASS ABDOMEN	UNILATERAL - CYSTIC	BENIGN M
69.	G 117/07	40	2718	MASS ABDOMEN	UNILATERAL - CYSTIC	BENIGN S
70.	G 122/07	40	2266	MASS ABDOMEN	UNILATERAL - CYSTIC	MATURE C
71.	G 144/07	50	52279	MASS & ASCITES	UNILATERAL - SOLID	ADULT GI
72.	G 165/07	47	5056	MASS & ASCITES	BILATERAL - VARIEGATED	B/L PAPIL CARCINO
73.	G 174/07	30	30874	MASS ABDOMEN	UNILATERAL - CYSTIC	BENIGN M
74.	G 238/07	57	35995	MASS ABDOMEN	UNILATERAL - VARIEGATED	PAPILLAR CYSTDEN
75.	G 313/07	28	9215	MASS ABDOMEN	UNILATERAL - CYSTIC	BORDERL CYSTADE
76.	G 329/07	55	15273	MASS ABDOMEN	BILATERAL - VARIEGATED	PAPILLAR CYSTADE
77.	G 333/07	30	7690	MASS ABDOMEN	BILATERAL -SOLID	BILATERA
78.	G 334/07	14	6690	MASS ABDOMEN	UNILATERAL - CYSTIC	MATURE
79.	G 342/07	25	9960	PREGNANCY	UNILATERAL - CYSTIC	SEROUS C
80.	G 377/07	18	9955	MASS ABDOMEN	UNILATERAL - CYSTIC	MATURE
81.	G 438/07	34	8433	PAIN ABDOMEN	UNILATERAL - CYSTIC	BENIGN M
82.	G 449/07	23	10579	MASS ABDOMEN	UNILATERAL - CYSTIC	BENIGN M
83.	G 453/07	46	5558	MASS & ASCITES	UNILATERAL - CYSTIC	MUCINOU MALIGNAN
84.	G 462/07	62	9886	MASS & ASCITES	BILATERAL - SOLID	HIGH GRA CYSTDEN
85.	35/07	58	922616	MASS & ASCITES	UNILATERAL - CYSTIC & SOLID	MATURE T WITH BRE
86.	307/07	45	928123	MASS ABDOMEN	UNILATERAL - CYSTIC	BENIGN M
87.	G 539/07	50	13303	MASS ABDOMEN	UNILATERAL - CYSTIC	BENIGN M
88.	1362/07	40	944066	MASS ABDOMEN	BILATERAL VARIEGATED	BILATERA
89.	G 426/07	46	9096	MASS & ASCITES	BILATERAL - CYSTIC	a. ONE C CYSTA b. OTHE TUMO MALI
90.	G 680/07	43	12911	MASS ABDOMEN	UNILATERAL - CYSTIC	MUCINOU MALIGNAC
91.	G 748/07	40	20023	MASS ABDOMEN	UNILATERAL - CYSTIC	BENIGN C
92.	G 829/07	40	22214	MASS ABDOMEN	UNILATERAL - CYSTIC	MATURE T
93.	G 841/07	38	22751	MASS ABDOMEN	UNILATERAL - CYSTIC	BENIGN M
94.	G 881/07	53	233328	MASS ABDOMEN	UNILATERAL - CYSTIC	MUCINOU MALIGNA
95.	G 872/07	57	13353	MASS ABDOMEN	UNILATERAL - VARIEGATED	GRANULO

96.	G 890/07	38	22240	MASS ABDOMEN	BILATERAL - SOLID & CYSTIC	SEROUS T MALIGNA
97.	G 960/07	12	27245	MASS ABDOMEN	BILATERAL - CYSTIC & SOLID	MIXED GE (YOLKSAC NOM)
98.	G 1000/07	22	10375	MASS ABDOMEN	UNILATERAL - CYSTIC & SOLID	MUCINOU
99.	G 1002/07	27	30196	MASS ABDOMEN	UNILATERAL - CYSTIC	MATURE -
100.	G 1047/07	48	32291	MASS ABDOMEN	UNILATERAL - CYSTIC	BENIGN SE
101.	G 1088/07	55	33624	MASS ABDOMEN	UNILATERAL - CYSTIC	BENIGN M
102.	G 1268/07	50	33625	MASS ABDOMEN	UNILATERAL - CYSTIC	SEROUS MALIGNA
103.	G 1279/07	45	37375	MASS ABDOMEN	UNILATERAL - CYSTIC & SOLID	MUCINOU
104.	G 1302/07	35	311914	PAIN ABDOMEN	UNILATERAL - CYSTIC	BENIGN S
105.	G 1316/07	55	33431	MASS ABDOMEN	BILATERAL - VARIEGATED	BILATERA
106.	G 1317/07	41	40230	MASS ABDOMEN	UNILATERAL - CYSTIC	SEROUS T MALIGNA
107.	G 1334/07	40	41060	MASS ABDOMEN	BILATERAL - SOLID, CYSTIC, VARIEGATED	BILATERA CARCINO
108.	G 1356/07	20	43054	MASS ABDOMEN	UNILATERAL - CYSTIC	BENIGN S
109.	G 1377/07	42	311944	MASS ABDOMEN	UNILATERAL - CYSTIC	BENIGN M CYSTADE
110.	G 1382/07	35	311945	MASS ABDOMEN	UNILATERAL - CYSTIC	BENIGN S
111.	G 1387/07	50	43658	MASS ABDOMEN	UNILATERAL - CYSTIC	BENIGN S
112.	G 1405/07	23	311958	MASS ABDOMEN	UNILATERAL - CYSTIC	BENIGN P CYSTADE
113.	G 1415/07	21	46606	MASS ABDOMEN	UNILATERAL - VARIEGATED	JUVENILE
114.	G 1422/07	22	42939	MASS ABDOMEN BILATERAL – CYSTIC	BILATERAL – CYSTIC	RIGHT OV CYSTADE LEFT OVA BORDERL
115.	G 1438/07	48	46215	MASS ABDOMEN	UNILATERAL - CYSTIC	BENIGN M
116.	G 1439/07	50	311984	MASS ABDOMEN	BILATERAL – SOLID	BILATERA
117.	G 1480/07	27	47880	PAIN ABDOMEN	UNILATERAL - CYSTIC	BENIGN S
118.	G 1494/07	40	51573	MASS ABDOMEN	UNILATERAL - CYSTIC	BENIGN S FIBROMA
119.	G 31/08	27	1043	MASS ABDOMEN	UNILATERAL - CYSTIC	BENIGN S
120.	G 97/08	24	4640	MASS ABDOMEN	UNILATERAL - CYSTIC	SEROUS T MALIGNA
121.	G 103/08	35	3480	MASS ABDOMEN	UNILATERAL - CYSTIC	MUCINOU MALIGNA
122.	G 316/08	35	927735	MASS ABDOMEN	UNILATERAL - CYSTIC	MUCINO MALIGNA
123.	G 91/08	48	4075	MASS ABDOMEN	UNILATERAL - CYSTIC & SOLID	GRANULO TUMOUR
124.	G 127/08	21	5860	MASS ABDOMEN	UNILATERAL - CYSTIC	BENIGN M

125.	G 153/08	36	6570	MASS ABDOMEN	UNILATERAL - CYSTIC	BENIGN M
126.	G 179/08	27	9395	MASS ABDOMEN	UNILATERAL - CYSTIC	BENIGN M
127.	G 187/07	57	8647	PAIN ABDOMEN	UNILATERAL - CYSTIC	BENIGN M
128.	G 221/08	19	9148	MASS, PRIMARY AMANNORRHOEA	UNILATERAL - SOLID	GONADOB
129.	567/08	19	203108	MASS ABDOMEN	UNILATERAL - SLIDE FOR REVIEW	MIXED GE (YOLK SA COMPONE
130.	G 248/08	40	11460	MASS ABDOMEN	UNILATERAL - CYSTIC	MATURE -
131.	G 242/08	48	924	MASS ABDOMEN	UNILATERAL - VARIEGATED	PAPILLAR CYSTADE
132.	G 274/08	22	313989	PREGNANCY ASSOCIATED	UNILATERAL - CYSTIC	MUCINOU MALIGNA