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Original Research Article

Study of 92 cases of ovarian germ cell tumour at tertiary health care centre

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Abstract

Introduction: Ovarian germ cell neoplasm represents approximately 25 to 30 percent of ovarian tumours, which significantly varies with respect to their clinical presentation, histology, and biology. The main aim of this study is to evaluate frequency, incidence and histopathologic pattern with respect to age, sex and clinical presentation of tumor.

Materials and Methods: This work is a retrospective study of ovarian germ cell tumors carried out in department of pathology at tertiary health care center. All cases of germ cell tumors during the period from May 2008 to June 2018 were retrieved from the record files and analyzed. The tissues were routinely fixed with 10% formalin, and the slides were stained with hematoxylin and eosin stain and also with special stains whenever required.

Results: Out of 142 cases of GCTs, 15 cases (16.30%) ovarian GCT belonged to pediatric age group and 77 cases (83.69%) belonged to the adult age group (20-50Years). Out of 92 cases of ovarian neoplasm, most common histological types were mature teratoma 81.52%, followed by dysgerminoma 7.6%, immature teratoma 4 cases (4.34%) and mixed GCT 3.26%. There were 2 cases of yolk sac tumor and one case of choriocarcinoma. Abdominal pain followed by lump was the commonest Clinical presentation.

Conclusion: Mature teratoma is the most common germ cell tumor, most commonly occurring in the 3^{rd} decade. Dysgerminoma is the most common malignant germ cell tumor occurring in the 10-20 years age group.

Introduction

Germ cell tumors (GCTs) are a histologically diverse entity that can occur in a wide variety of locations and age groups. The majority of GCTs have a gonadal origin and comprise a large portion of tumors of the testicles and ovaries, with a 95% and 30% prevalence of neoplasms in these organs, respectively. However, a small number of Germ cell tumors can be extragonadal, reported as between 1% and 5%. 3,4 The mediastinum is the most common site outside the gonads for GCT, with lesions in the retroperitoneum, pineal gland, and sacral region constituting most other areas affected.¹

Germ cell tumors of the ovary form a group of neoplasms comprised of many individual and mixed entities. Approximately 25–30% of all ovarian tumors are of germ cell origin and of these 95% are benign and only 3–4% are malignant. They are relatively more frequent in children, as approximately 60 percent of ovarian tumors in patients less than 20 years of age are derived from germ cells and the younger the patient, the higher the likelihood that the tumor is malignant.²⁻⁴ Germ Cell Tumor (GCT) groups together a broad variety of neoplasms that significantly differ with regard to their clinical presentation, histology, and biology. Despite the profound differences between the histological

sub-entities of GCT, the common designation reflects the presumed common cell of origin of these tumors, the primordial germ cell.⁵ A female's risk at birth of having ovarian tumor sometime in her life is 6.0-7.0%, of having ovarian cancer is almost 1.5% and dying from ovarian cancer is 1.0%.⁶

As the histologic features and clinical behavior of these benign neoplasms are well known, only rarely do they present diagnostic problems such as identification or degree of maturity of particular tissue components, presence of secondary malignancies, or some unusual clinical manifestations. Some MOGCTs share a similar histologic profile with malignant testicular germ cell tumors (MTGCTs) of the adult, which occur far more frequently than their ovarian counterparts. MTGCTs exhibit genetic markers, such as a 12p isochromosome and chromosome 12 overrepresentation, 6 that are less frequently observed in MOGCTs. 8

Materials and Methods

This work is a retrospective study of germ cell tumors of the gonadal and extragonadal region carried out in department of pathology at tertiary health care center.

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Email: marshaltoppo@gmail.com http://doi.org/10.18231/j.ijpo.2019.089 All cases of germ cell tumors during the period from May 2015 to June 2018 were retrieved from the record files and analyzed. Ovarian germ cell tumor as salpingo-oopherectomy and extragonadal tumor were mainly received as tumor mass. The tissues were routinely fixed with 10% formalin, and the slides were stained with hematoxylin and eosin stain and also with special stains whenever required.

Results

Out of 142 cases of GCTs, 15 cases (16.30%) ovarian GCT belonged to pediatric age group with highest incidence in 10-15yrs age group (9.78%) and 77 cases (83.69%) belonged to the adult age group, highest in the 20-50 years age group. Only 06 cases were found in > 50 years age group. (Table 1)

In extragonadal GCTs, in pediatric, the incidence was highest in neonatal age group constituting 38.3% of cases, followed by 1 month – 1 year 10.63. In adults, it was commonly seen in the 20-30 years age group accounting 19.15% followed by 15-20 years group 8.5%. M:F ratio 1.1:6. (Table 1)

In our study of 142 cases of GCTs, the ovarian germ cell tumor had 64.79% incidence. Among extragonadal sites, sacrococcygeal was the commonest (7.04%) followed by head and neck region 4.93%, mediastinal and retroperitoneal 3.52% respectively. There were 06 (4.23%) cases of metastasis seen, two in intracranial region and two in urinary bladder and lung and two cases in duodenum. (Table 2)

Out of 92 cases of ovarian neoplasm, most common histological types were mature teratoma 81.52%, followed by dysgerminoma 7.6%, immature teratoma 4 cases (4.34%) and mixed GCT 3.26%. There were 2 cases of yolk sac tumor and one case of choriocarcinoma. (Table 3)

The incidence of ovarian GCTs was highest in the reproductive age group 20-50yrs, accounting for 63.04%, followed by the adolescence age group (10-20yrs) which comprised of 25.0% of all cases, out of which 10 cases were malignant. No tumor seen in 1-5 years age group, no Embryonal carcinoma seen in any age group. (Table 3)

Abdominal pain was the commonest Clinical feature seen in 63.3% of all cases. Abdominal lump was the presenting feature in 45.62% of cases; menstrual irregularities were also seen in 9.78%.

In ovary, out of 79 cases of teratoma, there were 9 cases of mature teratomas in pediatric age group, which presented with abdominal pain with a lump and the masses were solid, solid and cystic with size ranging from 5-20cms. All specimen received were of salpingo-oopherectomy. Whereas in adult 66 cases of mature teratoma were found, grossly majority of cases were solid cystic, size ranging from 2x2cms to 22x20cms. Only two cases of immature teratoma were seen in adult ovaries. They presented as abdominal pain with lump, the tumor masses were solid and cystic.

Extragonadal Teratoma in Pediatric Age

There were 8 cases of teratoma in pediatric age group, of which 4 cases were seen in retroperitonium with age range 1-1/2 years. The cases presented as abdominal lump and masses were solid and cystic, with size ranging from 7x6 to 21x12 cms. One cases CT was s/o Neuroblastoma revealed e/o immature teratoma, grade II, remaining 3 cases were mature teratoma. Three cases were seen in mediastinum and presented with mediastinal mass and cough with expectoration. Masses were sloid and cystic ranging from 5x5- 10x8 cms. One case seen in ilial mesentery presented with abdominal pain and lump.

Sacrococcygeal Teratoma in Pediatric Age

Out of cases of Sacrococcygeal teratoma, 7 were mature teratoma & 2 were immature teratoma (grade II). Masses were cystic or solid and cystic, ranging from 3x2 cms to 13x6 cms.

Extragonadal Teratoma in Adult Age

There were 7 cases of Extragonadal mature teratoma out of which 5 cases were in female and 2 in male. The age ranges from 16-54 yrs, with 85.71% cases occurred in second, third decade. Masses were solid, cystic or solid cystic with size ranging from 2.5x2cms to 9x6cms.

Dysgerminoma at Gonadal and Extragonadal Sites

There were 7 cases of dysgerminoma grade Ia, Ic & IIIa in our study, all of them were found in 10-20 years age group. They presented with abdominal pain with lump, and the masses were solid in all cases and size ranging from 5x3x3 cm to 20x20x12 cm. salpingo-oopherectomy performed in 6 cases. Only 3 cases of dysgerminoma were found in intracranial region grade II, all of them were seen in 10-15 years age group and presented with visual disturbance with headache, the masses were solid.

Yolk Sac Tumor at Gonadal and Extragonadal Sites

There were two cases of YST in the ovary with grade Ia & Ic, which were seen in 10-20 years age group, the tumor masses were solid and cystic of sizes 12x10cm to 14x12 cm and presented with abdominal pain with lump. Three cases of YST found at 2 cases at sacral region grade II and one case around lateral aspect of neck.

Mixed Germ Cell Tumor at Gonadal and Extragonadal Sites

In pediatric age group, two cases of mixed germ cell tumor were found in ovary grade Ia & IIc and one case each intracranial grade III and head and Neck region. Masses were solid or solid and cystic of sizes 1 cm to 20x16x10 cm. whereas in adults only one case found in ovary grade IIIa with metastasis in omentum and two cases were seen in mediastinum grade IIa & IVa.

Choriocarcinoma

There were three cases of gestational choriocarcinoma in of uterus grade Ic to grade Iva seen in 2nd to 3rd decade, masses

were solid of sizes 3x2x2 cm to 5x3x3 cm. one case each was found in ovary grade Ic, urinary bladder and duodenum grade IV stage. Only one case of uterus was alive.

duodenum grade IV with teratocarcinoma grade III, two cases in intracranial with grade II Malignant Mixed GCT, one case of each urinary bladder and lung with grade III and IV respectively. Masses were solid of sizes 2 cm to 4x4cm.

Metastasis of GCT

Out of 6 cases, 3 were in males and 3 were in females, all cases occurred in 20-40 years age group, two cases in

Table 1: Incidence of ovarian gonadal and extragonadal GCTs with respect to age and sex

A 000	Ova	Ovarian GCT		Extragonadal GCT		
Age	Ovary	Ovary Total %		Female	Total %	
Pediatric						
0-1 month	-	-	06	12	18 (36%)	
1 month- 1yrs	03	03 (3.26%)	01	04	05 (10%)	
1yr-5yrs	-	-	03	01	04 (8%)	
5yrs-10yrs	03	03 (3.26%)	-	02	02 (4%)	
10yrs-15yrs	09	09 (9.78%)	02	01	03 (6%)	
Adult						
15yrs-20yrs	14	14 (15.21%)	03	01	04 (8%)	
20yrs-30yrs	30	30 (32.60%)	03	06	09 (18%)	
30yrs-40yrs	15	15 (16.30%)	-	02	02 (4%)	
40yrs-50yrs	12	12 (13.04%)	01	-	01 (2%)	
50yrs-60yrs	06	06 (6.52%)	02	-	02 (4%)	
Total		92		29	50	

Table 2: Incidence of ovarian, extragonadal and metastatic GCTs with respect to site and behavior

Site	Pediatrics		Adults		Total no of cases %	
	Benign	Malignant	Benign	Malignant		
Gonadal	-		-	-		
Ovary	09	07	66	10	92 (64.79%)	
Extragonadal						
Sacrococcygeal	09	01	-	-	10 (7.04%)	
Presacral	01	01	-	-	02 (1.40%)	
Mediastinal	03	-	-	02	05 (3.52%)	
Lung	-	=	01	-	01 (0.70%)	
Abdominal Cavity						
Retroperitoneal						
Stomach	04	01	-	-	05 (3.52%)	
Mesenteric	01	-	01	-	02 (1.40%)	
Ileal						
Sigmoid	01	-	01	-	02 (1.40%)	
Genito-Urinary						
Uterus	-	-	01	03	04 (2.80%)	
Urinary Bladder	-	=	02	-	02 (1.40%)	
Intracranial	-	03	-	01	04 (2.80%)	
Head & Neck						
Lat Neck	-	01	01	-		
Nasopharyngx	02	-	-	-		
Epignathic	02	-	-	-	07 (4.93%)	
Orbital	01	-	-	-		
Metastatic	-	-	-	06	06 (4.23%)	
Total	33	14	73	22	142 (100%)	

Histologic types	Dysgerminoma	Yolk sac tumour	Chorio- carcinoma	Teratoma	Mixed malignant	Terato- carcinoma	Total
0-1mth							
1mth- 1yr				03			03
5-10yrs				02	01		03
10-15yrs	02	01		06	01		10
15-20yrs	05	01		07			13
20-30yrs				33			33
30-40yrs				12		01	13
40-50yrs			01	11			12
50-60yrs				05			05
Total %	07(7.6%)	02(2.17%)	01(1.09%)	79(85.86%)	02(2.17%)	01(1.09%)	92

Table 3: Distribution of various histologic types of Ovarian GCTs with respect to age

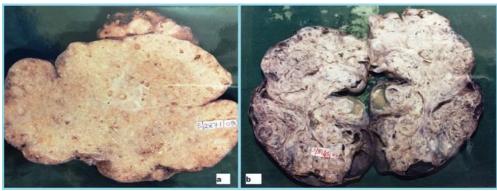


Fig. 1: Specimen of teratoma a) & b): Showing solid-cystic cut surface

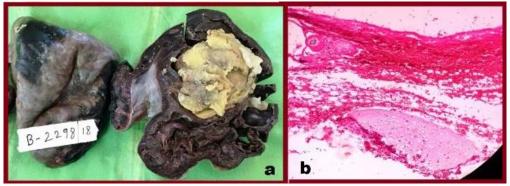


Fig. 2: Teratoma .a): Gross showing congestion, pultaceous material with hair. b): Showing hair follicle, cartilage, adipocytes and sebaceous gland.

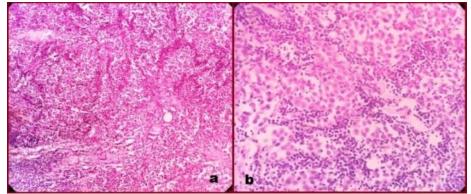


Fig. 3: Dysgerminoma. a): Low power view b): High power view showing large round or polygonal cells with vesicular nuclei, the cells were separated by fibrous septae containing lymphocytes

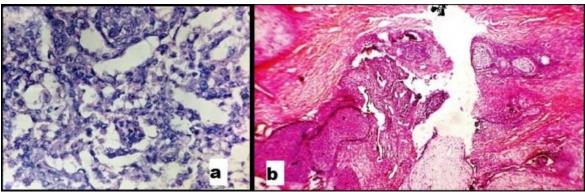


Fig. 4: a): High power view of yolk sac tumour showing characteristic Schiller– Duval bodies. b) Malignant mixed GCT showing hair follicle, neural tissue, sebaceous gland.

Discussion

In present study the most common site of tumor was ovary 92 (64.79%) cases, 31.52 % of OGCTs found among age less than 20 years, whereas the maximum incidence of tumor seen in age group 20-30yrs and extragonadal tumor comprised of 50 (35.2%) cases, sacrococcygeal was the commonest (7.04%) followed by head and neck region 4.93%, mediastinal and retroperitoneal 3.52% respectively. D.M. Patterson et al.⁹ analyzed similar study with 35 (95%) cases in ovary and the remaining two patients with extragonadal disease had their respective primaries in the anterior mediastinum and retroperitoneum. KAATSCH et al10 have shown the most common locations for the age groups 10-14 years were the CNS and gonads (ovaries) with mean age 11.6 years and Ovarian tumors accounted for 47% of all GCTs in girls (348 cases of 744) and extragonadal GCTs in CNS (27.9%), Pelvis (17.7%), Mediastinum (2.1%) and retroperitoneum (2%). Terenziani et al. 11 studied 77 patients with a median age of 11.8 years (range 1.8-17.2). Patients were staged as follows: 27 stage I (35%), 13 stage II (17%), 32 stage III (42%) and 5 stage IV (6%). Similar studies by Mondal, et al¹² have highlighted that most ovarian tumors are seen between 0-30 years. Jha R, Karki S⁶ have found that most ovarian tumors were seen between 21-50 years and in first three decades 72.7% tumors were germ cell tumors.

Out of 92 cases of OGCTs, 75 cases (81.5%) were benign and 17 cases (18.5%) were malignant. Abdominal pain was the commonest Clinical feature seen in 63.3% of all cases. Abdominal lump was the presenting feature in 45.62% of cases; menstrual irregularities were also seen in 9.78%. Cecchetto G¹³ found that 70% of neoplastic ovarian masses, being the most common ovarian neoplasms in children and teenagers. Benign and immature forms (teratomas) constitute about 80% of all ovarian GCTs, malignant forms represent 20% increasing during adolescence. Presentation is similar in malignant and benign lesions; abdominal pain (70-80%) and lower abdominal mass are common symptoms. De Backer et al¹⁴ presented in their study that out of 69 cases of OGCTs 54 (78.26%) were benign whereas 15 (21.73%) were malignant with predominant symptoms of pain and an abdominal/pelvic mass. A. Trama and F. Berrino¹⁵ stated incidence of

malignant ovarian GCT was low in all continents: $\le 0.9/100.000$ in Japan, $\le 0.7/100.000$ in Central and South America and in China, $\le 0.5/100.000$ in Australia and Asia, 0.4/100.000 in Canada and < 0.4/100.000 in Africa except Malawi where the incidence was 1.3/100.000.

Benign Germ Cell Tumors

Mature teratoma was the commonest benign germ cell tumor in our study, comprising 81.52% of all ovarian germ cell tumors. It presented as cysts of ovary or as solid and cystic masses (Fig. 1&2). The incidence of this tumor s ranged from 1 month to 60 years. S. P. Sah et al² highlighted in their study that 121 (43.36%) were diagnosed as germ cell tumors and of these, 113 (93.39%) cases were found to be benign and only eight (6.61%) cases were malignant. Patient age ranged from 8 to 65 years, with a median age of 31 years. The median age of benign cases was 32 years and that of malignant cases was 24 years. More than three quarters of the patients (78.51%) were under 40 years of age. Of these, 110 cases (90.90%) were benign mature teratoma (either solid or cystic) and presented with symptoms of abdominal pain or lump. Deka, et al³ found that the most common germ cell tumor was mature cystic teratoma (98/110 cases) comprising 88.18% of all germ cell tumors. Majority cases were cystic (65/110, 59.09%) followed by solid/cystic (35/110, 31.8%), the most common presenting complaint was abdominal mass (58/110, 52.7%). followed by abdominal pain (35/110, 31.8%). R Jha and S Karki⁶ highlighted the most germ cell tumors (95.6%) were benign and all of these benign germ cell tumors were mature cystic teratomas. Benign germ cell tumors constituted 48.2% (65/135) of all benign ovarian tumors and most of the tumors in 31-50 years age. Mondal, et al¹² highlighted that the mature teratoma was 69.54% (153/220) found to be most common benign GCTs, Most of the benign tumors occurred between 20 and 40 years of age. De Backer et al14 found mature teratomas were the commonest tumors (n=45), followed by immature teratomas (n=9), combined (mixed) malignant tumors (n=7), yolk sac tumors (n=3), dysgerminoma (n=2),gonadoblastoma (n=2),embryonal carcinoma (n=1). Predominantly symptoms were pain and an abdominal/pelvic mass. Giovanni Cecchetto¹³ found abdominal pain (70-80%) and lower abdominal mass

are the most common symptoms in patients with GCT. These tumor were solid and cystic components with cystic components are more frequent in benign forms. M. Zhang et al¹⁶ found 73.3% ovarian tumors are benign, with 60% cystic mass.

Dysgerminoma

Most common malignant GCT in our study dysgerminoma. There were 7 (7.6%)cases dysgerminoma grade Ia, Ic & IIIa in our study, all of them were found in 10-20 years age group. They presented with abdominal pain with lump, and the masses were solid in all cases and size ranging from 5x3x3 cm to 20x20x12 cm. Microscopically, the tumour was composed of aggregates of large round or polygonal cells with vesicular nuclei containing one/more nucleoli, clear pale cytoplasm and a prominent cell membrane (Fig. 3). The cells were separated by fibrous septae containing lymphocytes. Dysgerminoma is the most common malignant germ cell tumor of ovary and account for nearly half of all such tumors. 12 Deka, et al3 highlighted that there were 06 cases of dysgerminoma out of total 12 malignant germ cell tumors. All the cases were in 21-30 years age group, solid cystic. Sharma I, Chaliha T⁴ in their study found that benign cystic teratomas constituted highest numbers (26.47%), followed by dysgerminoma (1.96%), Immature teratoma (0.98%) and Yolk sac tumor (0.98%). Abdominal mass was the most predominant clinical presentation. Mondal, et al¹² stated dysgerminoma is predominant malignant germ cell group (2.6% of all ovarian tumors. Most of the malignant tumors presented as stage III (60%) or stage II (20%) disease. De Backer et al¹⁴ found combined (mixed) malignant tumors (n=7), dysgerminoma (n=2) of 69 cases of GCTs. Schultz et al. 17 studied 7 (7.4%) cases of dysgerminoma among age ranged from 7-18yrs, all were grade Ia, but there were recurrence in two cases.

Immature Teratoma

Immature teratoma represents 03% of teratomas, 01% of all ovarian cancers, and 20% of malignant ovarian germ cell tumors. 18 There were 4 cases (4.34%) of immature teratoma have been found in this study, the tumor masses were solid and cystic. Two cases of immature teratoma were seen in adult ovaries. Microscopically wide range of tissues having various degree of maturity was present. However combination of neural, squamous, respiratory & cartilage elements rarely seen. De Backer et al¹⁴ found 6 cases 13% of immature teratoma, solid cystic. Zynger et al¹ highlighted of the 10 cases containing IT, 4 cases found in ovary. Deka, et al³ studied 110 cases of GCT and found one case of immature teratoma. Majority cases were cystic (65/110, 59.09%) followed by solid/cystic (35/110, 31.8%). Sharma I, Chaliha T4 reported 1 (0.98%) of immature teratoma in ovary. R Jha and S Karki⁶ reported 2/26, 7.7% of ovarian GCT. Mondal et al¹² reported 15/170, 1.57% of immature teratoma. Schultz et al¹⁷ highlighted 11 (16.5%) of immature teratoma at an age 2-16 yrs with grade I-III.

Mixed GCT

Mixed germ cell tumors are composed of at least two different germ cell components, of which at least one is primitive. 18 (Fig. 4b) In our study it involves malignant mixed germ cell tumor and terato-carcinoma and comprised of 3.26% of all OGCTs. Two cases of mixed germ cell tumor were found in ovary grade Ia & IIc in pediatric age group, whereas in adults only one case found in ovary grade IIIa with metastasis in omentum. Histologically, the most common combination is the dysgerminoma and yolk sac tumor accounting for one-third of cases. 19 Deka, et al.3 studied 110 cases of GCT and found one mixed germ cell tumors (mature teratoma + embryonal carcinoma. Mondal et al¹² found 8/170, 0.83% cases of mixed GCT in ovary. De Backer et al14 found 7/69 cases of mixed GCT whereas Schultz et al¹⁷ reported 7 (10.5%) of MGCT having I-IV grades with ages varies between 3 to 16 yrs and TM Ulbright²⁰ reported <1% of MGCT of ovary.

Yolk Sac Tumour

Yolk sac tumors, also known as endodermal sinus tumor, is the second most common malignant germ cell tumors of the ovary.²¹ In present study there were two (2.17%) cases of YST in the ovary with grade Ia & Ic, which were seen in 10-20 years age group, the tumor masses were solid and cystic of sizes 12x10cm to 14x12 cm. Microscopically showing characteristic Schiller– Duval bodies. (Fig. 4a)

Zynger et al¹ studied 33 cases of YST four cases found in ovary, All YST components had GPC3 staining (33/33 [100%]). Deka, et al³ found two cases (2/110, 1.81%) of all ovarian germ cell tumours. Sharma I & Chaliha T4 reported One case of yolk sac tumour (1/31, 0.98%) was diagnosed in a 1 ½ year old girl who presented with lump abdomen and pain abdomen of 3 months duration. Whereas Gerohenson DM et al described in their study that it constitute 0.8 percent of all ovarian tumour and 2.8 percent of all malignant ovarian tumour (Saxena et al 1989). The age range is 14 months to 45 years, the median age is 19 years (Kurman, Norris 1976). Grossly, the tumour is predominantly solid, with multiple small cysts, haemorrhage and areas of necrosis.²² R Jha and S Karki⁶ reported 1/26, 3.8% YST of all ovarian GCT. Mondal et al¹² found (12/170, 1.25%) yolk sac tumor in the ovary, De Backer et al¹⁴ reported 3/69 cases and TM Ulbright²⁰ reported 1%. Schultz et al¹⁷ found 2 (3%) cases of YST in age group 15 and 16 yr, both cases had grade Ia, which are similar to our study.

Chorio-carcinoma

Choriocarcinoma is among the rarest of the gonadal germ cell tumors, one (1.09%) case was found in ovary grade Ic. Mondal et al¹² reported 4/170, (0.43%) of chorio carcinoma and TM Ulbright²⁰ reported <0.1%.

Conclusion

The main strength of this study is to give comprehensive picture of the current state of germ cell ovarian tumour incidence and histopathologic pattern. Benign cystic teratoma is found to be most common germ cell tumor in ovary accounting 81.52% cases. Majority of tumors occur during the reproductive age group (16-55 years), but may occur in the postmenopausal period or in childhood. Treatment of benign cystic teratoma should be according to further need of patient like desire for future fertility and presence of concomitant pelvic pathology. Malignant Germ cell tumors were seen in younger age group and most frequent type was dysgerminoma and found in 10-20 years age group. Choriocarcinoma is rare germ cell tumor in ovary.

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