ORIGINAL ARTICLE

Histopathological Profile of Primary Ovarian Lesions in Nnewi, Nigeria: A 5 Year Retrospective Study

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ABSTRACT

Background: This is the first base line research on different primary ovarian lesions in Histopathology department, Nnamdi Azikiwe University Teaching Hospital (NAUTH) Nnewi since the institution of the hospital.

Objectives: To determine the different patterns of ovarian lesions in relation to age and histopathological features and compare these patterns with local and international studies. The study will also highlight the most common histologic variants in our environment and make recommendations depending on the outcome of the research.

Methodology: The pathology report forms of all the gynaecological lesions in histopathology department NAUTH, Nnewi, were studied. The processed tissue and the slides stained with regular histochemical stain (Haematoxylin and Eosin) technique in this 5-year study period were reviewed by the researchers using multi-headed microscope (CARL ZEISS®).

Results: Of the 130 cases that were analysed, 91 (70.0%)cases were neoplastic while 39(30.0%) cases were non-neoplastic lesions. Benign neoplasms were the most common neoplasm and accounted for 56.0% (51 cases) followed by invasive malignant neoplasms with 31.9% (29 cases) while borderline and indeterminate tumours, were 3.3% (3 cases) and 8.8% (8 cases). respectively. Among the benign neoplastic lesions, mature cystic teratoma was the most common tumour (no= 22, 16.9%) with the patients' mean age of 33.1 ±SD 13.0, followed by serous cystadenoma (no=15, 11.5%) with a mean age of 33.4 ±SD 12.9. However, high grade papillary serous cystadenocarcinomas (no=13, 9.8%) were the highest recorded invasive malignant lesions with a mean age of 49.8 ± SD 15.9) followed by choriocarcinoma (no.=5, 3.8%) with a mean age of 35.3 ±SD 9.7. Immature teratoma and mucinous cystadenocarcinoma were 4 (3.1%)cases each with mean ages of 20.8 ± SD 13.9 and 55.3 ± SD 14.3, respectively. Malignant germ cell tumours; immature teratoma and choriocarcinoma, formed only 28.1% of all germ cell tumours. Of the non-neoplastic lesions, corpus luteum cyst and follicular cyst were the most common with 11 cases (8.5%) and 10 cases (7.7%), respectively.

Conclusion: Ovarian neoplasia are quite diverse, and in our environment, benign lesions of the ovary were far more common than malignant cases and tend to occur at the reproductive age group. Surface –epithelial neoplasms were more common than germ-cell tumours with a ratio of 1.4:1. Majority of invasive malignant cases were high grade serous cystadenocarcinoma.

***Keywords**: Corpus luteum cyst, Follicular cyst, Teratoma, Cyst adenoma, Borderline tumour, Serous cystadenocarcinoma*

INTRODUCTION

Ovaries are paired pelvic organ that lie on either side of the uterus and attached to it by broad ligaments.[1] Its measurement and weight varies with age and reproductive status.[1] This organ of female genital system harbours numerous types of non-neoplastic and neoplastic lesions. Ovarian neoplasms have diverse clinical and biological behaviour as well as malignant potential. Although some literatures have found few associated risk factors in some of these neoplasms such as nulliparity, family history and heritable mutations, these neoplasms are still difficult to detect early. Hence, patients frequently present with advanced disease.[2]

World Health Organisation (WHO) classified these ovarian neoplasms based on tissue of origin. This includes Surface-Epithelial-Stromal, Sex-Cord Stromal, Germ-cell and Metastatic Cancer from non-ovarian primary.[1,2] Globally, malignant tumours of the ovary are more common in older women, borderline tumours occur at slightly older ages and majority of cases (80%) are benign diseases occurring mostly in young women between the ages of 20 and 45 years.[1] In a Caucasian series, most ovarian tumours were benign and constituted 75–80% while ovarian malignancy accounted for the remaining 20–25% of cases.[3] Again, ovarian cancer is more common in developed countries especially in Europe and the USA than in Asia and Africa.[4] African–Americans are reported to have a lower incidence of ovarian cancer but have a poorer prognosis compared to their white counterparts.[5]

The incidence rates of ovarian cancer in Japan and Asian countries is relatively low accounting for 2–6/100,000 women/year.[6] In United States of America ovarian cancer is the fifth most common cause of death in women, although recent data indicate a decline.[1,7] Ovary is the 3rd most common site of primary malignancy in female genital tract after cervix and endometrium.[2] It accounts for 30% of all cancers of female genital tract and 3% of all cancers in female.[1,2] In Nigeria, cervical cancer, still remains the most common gynaecological malignancies, however, ovarian cancers are the most common among teenage age group with advanced stage presentations.[8,9,10]

The World Cancer Research Fund reports that ovarian cancer is the seventh most common cancer in women worldwide and 18th most common cancer overall *i*n both males and females.[11] Ovarian cancer accounted for about 200,000 new cases and 100,000 deaths yearly, worldwide.[12] Globally, ovarian tumours of surface epithelium represent the most common tumour in an adult female while germ cell tumors are more common in adolescent and young females in their early twenties; 30% of these are malignant.[13] Odukogbe *et al.* in Ibadan Oyo state, Western Nigeria and Ugwu *E.O et al.* in Enugu South-East Nigeria reported that epithelial ovarian cancer constituted 76.2% and 68.0% of all ovarian cases respectively.[9,8]

This research therefore aims to determine the frequency, different histologic patterns, and age distributions of these lesions in Nnewi, South-East Nigeria as it compares with other parts of the world.

METHODOLOGY

The pathology request forms of all cases of gynaecological lesions seen at the Histopathology department of Nnamdi Azikiwe University Teaching Hospital Nnewi over a duration of 5 years from January 2011 to December 2015 inclusive, were retrieved. The demographic information such as clinical bio-data, anatomic sites, clinical diagnosis and nature of specimens which include oophorectomies, incisional biopsies and total abdominal hysterectomies with bilateral salpingo-oopherectomies were extracted.

A total of 923 gynaecological cases were obtained in the study period, out of which 139 cases were ovarian lesions but only 130 cases of ovarian specimens that fulfilled inclusion criteria were analysed. The processed tissues and the slides stained with regular histochemical stain (Haematoxylin and Eosin) technique were reviewed by the researchers using multi-headed light microscope (CARL ZEISS®). Ovarian tumours seen, were classified according to the World Health Organization (WHO) tumour book (edition 2016).[14] Data were analyzed using statistics software Statistical Product and Service Solutions(SPSS) Incorporated, version 21Chicago, Illinois, USA and results presented as tables, pie and bar charts.

RESULT

Of the 130 cases, 91 (70.0%) were neoplastic while 39(30.0%) were non-neoplastic lesions. The neoplastic cases include 29(31.9%) malignant neoplasm, 3(3.3%) borderline tumours, 8(8.8%)indeterminate and 51(56.0%)benign tumours (Figure 1**)**.

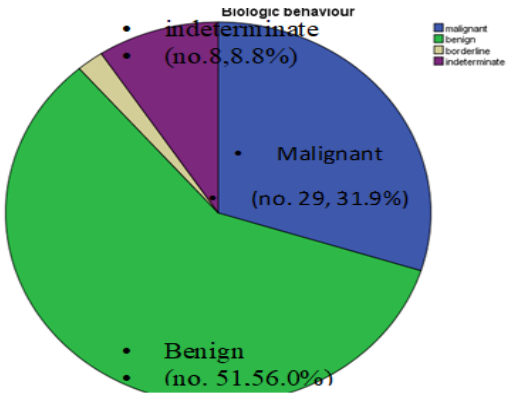
The non-neoplastic lesions accounted for 39 (30.0%) cases made up of 11(8.5%)corpus luteum cyst and 10 (7.7%)follicular cyst. Other non-neoplastic lesions also seen in this study include simple ovarian cyst 4 (3.1%), endometriosis 6 (4.6%), ovarian ectopic and tubo-ovarian abscess were 2 cases (1.5%) each while polycystic ovary, epithelial inclusion cyst, paramesonephric cyst or mesothelial cyst were the least represented with one case (0.8%) each (Table 1).

Mature cystic teratoma (no=22, 16.9%) cases was the most common benign tumour with a mean age of 33.1±SD 13.0 years followed by serous cystadenoma 15(11.5%) cases with a mean age of 33.4 ±SD 12.9. Other benign tumours observed were mucinous cystadenoma, 6 (4.6%) and benign Brenner's tumours, 3 (2.3%)cases (Figure 2**).**

Table 1. Frequencies of non-neoplastic & neoplastic ovarian lesions

Ovarian lesions	Freq(%)
Benign/Mature cystic teratoma	22 (16.9%)
Malignant-Immature teratoma	4 (3.1%)
Benign Struma Ovarii	1 (0.8%)
Choriocarcinoma	5 (3.8%)
Serous cystadenoma	15 (11.5%)
Borderline Serous cyst tumour	1 (0.8%)
Malignant-high grade Serous cystadenocarcinoma	13 (9.8%)
Mucinous cystadenoma	6 (4.6%)
Borderline mucinous cystadenoma	2 (1.5%)
Malignant-Mucinous cystadenocarcinoma	4 (3.1%)
Benign Brenner's tumour	3 (2.3%)
Transitional cell Carcinoma	1 (0.8%)
Fibroma	3 (2.3%)
Fibrothecoma	1 (0.8%)
Thecoma	1 (0.8%)
Fibrosarcoma	1 (0.8%)
Granulosa cell tumour	8 (6.2%)
Endometriosis	6 (4.6%)
Necrotizing granulomatous lesion	1 (0.8%)
Follicular cyst	10 (7.7%)
Haemorrhagic corpus luteum cyst	11 (8.5%)
Infected epithelial inclusion cyst	1 (0.8%)
Infarcted ovarian cyst	1 (0.8%)
Simple Ovarian cyst	4 (3.1%)
Paramesonephric cyst /Mesothelial cyst	1 (0.8%)
Ovarian ectopic gestation	2 (1.5%)
Polycystic Ovary-like lesion	1 (0.8%)
Tubo-ovarian abscess	2 (1.5%)
Total	**130 (100.0%)**

Figure 1. Showing biological behaviour of the ovarian lesions



Of the 29 (31.9%)malignant cases; high grade serous cystadenocarcinomas 13(9.8%) (Figure 3**)** was the highest recorded malignant lesions with the mean age of 49.7±SD15.9 years followed by choriocarcinoma with 5(3.8%) cases. Immature teratoma and mucinous cystadenocarcinoma were 4 (3.1%)cases each (Figure 4).

The total of both benign and malignant cases of surface-epithelial tumours was 45 (49.5%) outnumbering the total number of germ-cell tumours which accounted for 32 (35.2%) cases while the Sex Cord-Stromal Tumours was identified in 14 (15.4%)cases (Table 2).

The neoplastic lesions observed in this index study using WHO standard classification includes: (a)Surface epithelial tumours, (b) Sex-cord-stromal tumours; granulosa cell tumours 8(6.2%) (Figure 5) to (c) Germ-cell tumours which include, benign cystic teratoma 22(16.9%), choriocarcinoma 5(3.8%), malignant immature teratoma 4 (3.1%) and struma ovarii 1(0.8%)case (Table 2).

The age range at presentation of these lesions was between 10-90 years. Majority of non-neoplastic lesions occurred within the reproductive age groups of 21-30 and 31-40 years having 14 and 13 cases, respectively. Majority of benign ovarian neoplasm also occurred at the age groups of 21-30 and 31-40 years similar to that of non-neoplasm lesions with 17 and 16 cases respectively. (Figure 6) Approximately 80 cases of ovarian lesions out of 130 entire cases occurred at the reproductive age group. Germ cell tumours (Figure 7) occur mainly in the reproductive age group as well (21-40 years).

Mature cystic teratoma lesions occurred at a mean age of 33.1±SD 13.0 years while immature teratoma occurred at a mean age of 20.8±SD13.9 years. Serous cystadenoma occurred at a mean age of 33.4 ±SD 12.9years, mucinous cystadenocarcinoma had the highest mean age of 55.6±14.3 years and high grade papillary serous cystadenocarcinomas a mean age of 49.7±15.9 years

Figure 2. Photomicrograph showing Brenner's tumour coexisting with serous cystadenoma (arrow). The Brenner's tumour appears in nests of oval to polygonal epithelial cells (double arrow head) containing pale cytoplasm and cystic space containing eosinophilic secretions

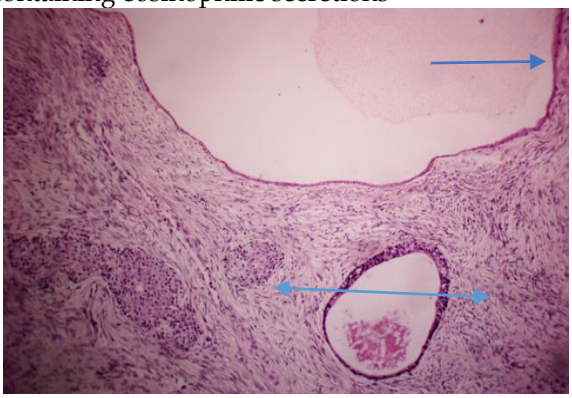
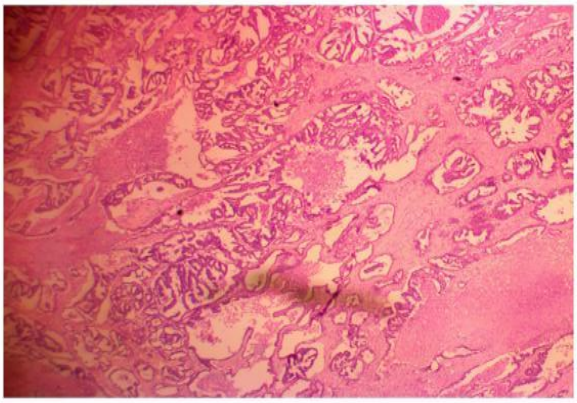


Figure 3. Photomicrograph displaying high grade serous cystadenocarcinomas showing cystic spaces with infolding complex papillae (arrow) and foci of necroses. High grade cellular details at higher magnification.



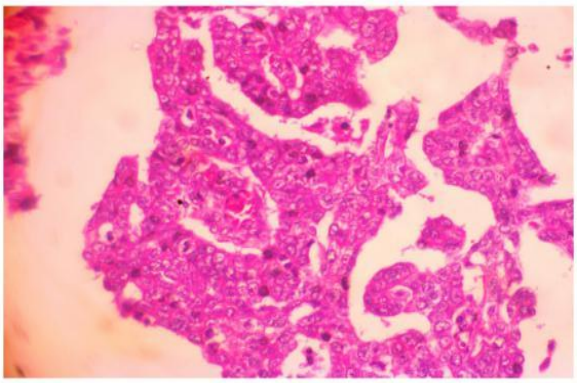


Figure 4. Photomicrograph showing Grade 2 immature teratoma displaying mature tissues such as skin appendages (arrow) and variable amounts of immature tissue like neuroepithelium cells in solid sheet (thick arrow head) in less than 3 low-power fields in any one slide of tumour

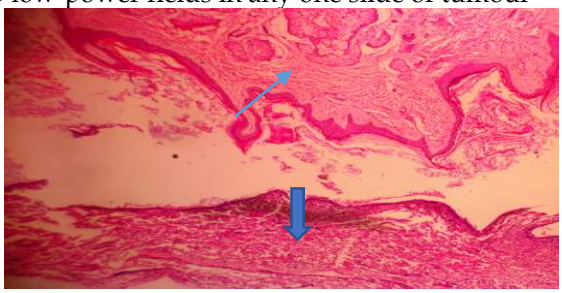


Figure 5. Photomicrograph showing adult granulosa cell tumour; a sex-cord stromal tumour displaying numerous Call-Exner bodies (arrows), focal area of necrosis with longitudinal nuclear grooves at high magnification (arrow heads).

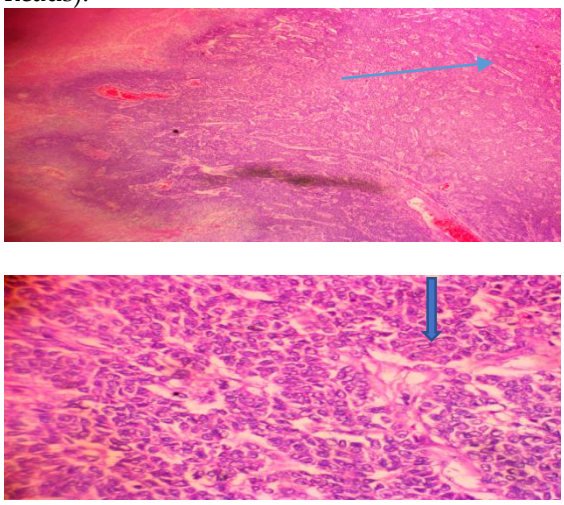


Table 2. Distribution of classes of neoplasm of ovary

Neoplasm of Ovary	Freq(%)
SURFACE-EPITHELIAL TUMOURS	
Serous tumours	0 (0.0)
Serous cystadenoma	15 (16.5)
Borderline serous cyst tumour	1 (1.1)
High grade Serous cystadenocarcinoma	13 (14.3)
Mucinous tumours, endocervical-like and intestinal type	0 (0.0)
Mucinous cystadenoma	6 (6.6)
Borderline Mucinous cyst tumour	2 (2.2)
Mucinous cystadenocarcinoma	4 (4.4)
Transitional cell tumours	0 (0,0)
Benign Brenner's tumour	3 (3.3)
Transitional cell carcinoma(non-Brenner type)	1 (1.1)
Total	**45 (49.5)**
GERM CELL TUMOURS	
Teratoma	0 (0.0)
Mature cystic teratoma	22 (24.2)
Malignant/ immature cystic teratoma	4 (4.4)
Monodermal (struma ovarii)	1 (1.1)
Choriocarcinoma	5 (5.4)
Total	**32 (35.2)**
SEX-CORD-STROMAL TUMOURS	
Granulosa cell tumour	8 (8.8)
Fibroma	3 (3.3)
Thecoma	1 (1.1)
Fibrothecoma	1 (1.1)
Fibrosarcoma	1 (1.1)
Total	**14 (15.4)**

Figure 6. Different age groups with different biological behaviours of ovarian lesions displaying majority of benign ovarian lesions at lesser age group

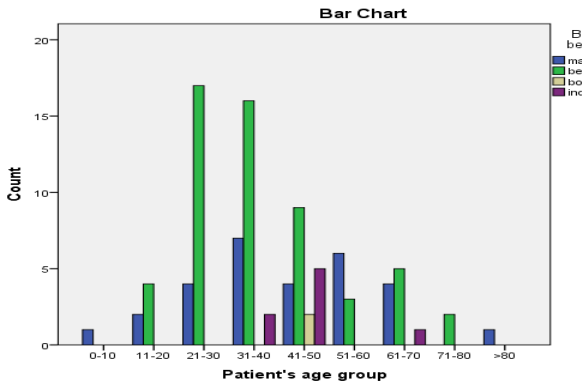
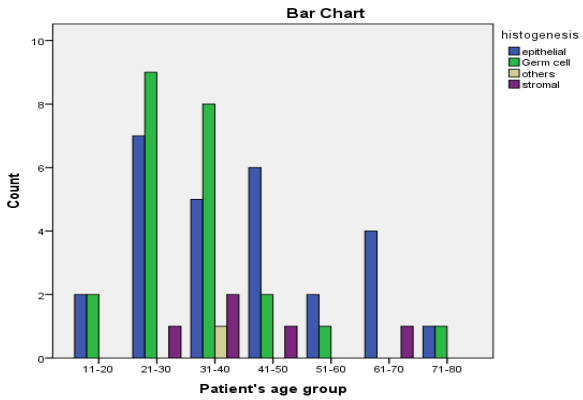


Figure 7. Preponderance of germ cell tumours and epithelial tumours at ~~a~~ reproductive age groups (21-30 years)



DISCUSSION

This study is a base line research of different primary ovarian lesions in the histopathology department of NAUTH Nnewi, South-East, Nigeria.

Histologically, overall benign ovarian lesions with the total frequency of 69.2% dominate the morphology whereas invasive malignant tumours were just 22.3%. This finding is in tandem with other studies elsewhere. In United kingdom Newson Louise *et al*., reported higher cases of benign ovarian lesions (94%) and only 6% of malignant ovarian neoplasm.[15] Abdulkareen *et al*. in university of Mosul Iraq had similar report of 87.3% of benign ovarian lesions and few cases of malignant neoplasm (5.6%).[16] In Nigeria, Forae *et al.* in Benin City as well as Udoye *et al.* in Niger Delta reported similar findings with 84.7% and 77.1% being benign ovarian lesions, while 15.0% and 22.9% were malignant ovarian neoplasms, respectively.[17,18]

The most common histologically diagnosed benign ovarian lesions in this study were benign germ cell tumour (mature cystic teratoma) followed by benign epithelial cell tumour (serous cyst adenoma), and then benign epithelial cysts; which includes corpus luteum cysts and follicular cysts. These findings are similar to the works done by Onyiorah *et al.* in Lagos State, Western Nigeria, Udoye *et al.* in Niger Delta, Forae *et al.* in Benin city, Akakpo *et al.* in Ghana tertiary Hospital, and Modi *et al.* in an Indian tertiary care centre where benign germ cell tumours predominate.[19,18,17,20,21] This is however, in contrast with studies done in the Middle East; Iran, Iraq, Saudi Arabia and Pakistan where physiological cysts such as follicular and corpus luteum cyst predominate.[22, 23,24,25]

Mature cystic teratomas occur due to abnormal differentiation of fetal germ cells that arise from the yolk sac while physiological cysts are formed in the ovary during the normal ovarian cycle. The difference may be attributed to the age group under study: most of middle east studies were within reproductive and pre-menopausal age groups where physiological cysts occur naturally, germ cell tumours although common at reproductive age group are not natural occurrence. Furthermore, our study encompassed 10 to 30 years post-menopausal where most physiological cysts are not attainable.

Further classification using World Health Organization (WHO) ovarian tumour book in this index study, revealed that combined malignant, borderline and benign cases of surface epithelial tumours formed the most common observed neoplasm with 45 cases (49.5%) (Table 2). Serous cystadenoma is the most predominant surface epithelial tumour in our environment. This finding is similar to some literatures in Nigeria where surface epithelial tumours were commonest; in Ilorin, Buhari *et al.* reported 43.9% (36 cases) of surface epithelial tumours while in Zaria, Zayyan *et al.* reported 53.9% (42 cases) with serous cystadenocarcinoma being the most common neoplasm in both studies.[26,27] Surface epithelial tumours also accounted for 90% of ovarian tumours in North America and Western Europe.[1] This is also similar to the work done in Iraq by Abdulkareem *et al.* but contrary to the other studies done in some part of Nigeria like in Benin City, in Niger Delta, and also in Ghana where germ cell tumours still top the list of all ovarian neoplasms followed by surface epithelial and then sex cord tumours. [16,17,18,20]

Germ cell tumours, however formed the second most common ovarian tumour in this study with 32(35.2%) cases, among which mature cystic teratoma were the most common type while choriocarcinoma and immature teratoma had 5 cases and 4 cases respectively. This is in contrary to the study done by Abduljabbar *et al.* in Saudi Arabia

where mature cystic teratoma was the third commonest tumour.[23]

The sex-cord stromal tumours observed in this research were 14 (15.4%)cases in all making it the 3rd most common neoplasm and include 8 cases of granulosa cell tumour, 3 cases of fibroma, and a case each for fibrothecoma, thecoma & fibrosarcoma. This finding is contrary to works done in Zaria and Ilorin where sex-cord-stromal tumours were the second most common ovarian lesions with 20 (25.6%)cases and 15 (18.5%)cases, respectively but with granulosa cell tumours being the most common.[26, 27]

Regarding the mean ages of benign lesions, mature cystic teratoma and serous cystadenoma were within the reproductive age group whereas malignant lesions such as high grade papillary serous cystadenocarcinoma and mucinous cystadenocarcinoma had higher age group of occurrence (49-55 years). However, immature teratoma which is a malignant counterpart of mature cystic teratoma had a lower mean age of 20.8±SD13.7. These findings are similar to numerous studies done in the literatures.[1,2,14]

Endometriosis is the presence of endometrial glands or stroma in ectopic locations beside the uterine corpus. This study showed six (4.6%) cases of endometriosis. This is similar to studies done by Abdulkareen *et al.* and Gupta *et al.* in India, but is contrast to European studies by Guerriero *et al.* and De Kroon *et al.*, who found higher cases.[16,28,29,30] This discrepancy may be attributed to the clinical diagnosis or the absence of the histological specimens of endometriosis in our studies.[16] In our environment the major attributes to low number of cases include, poor hospital policy regarding handling of specimens, patients are given samples to take to histopathology laboratory which in many cases might be misplaced, or not submitted because of financial constraints.

CONCLUSION

Ovarian neoplasia are quite diverse, and in our environment, benign lesions were more common than malignant cases and tend to occur at the reproductive age group. Surface-epithelial neoplasms were more common than germ-cell tumours Majority of invasive malignant cases were high grade serous cystadenocarcinoma.

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