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ORIGINAL RESEARCH

Pathological Features of Ovarian Tumors, Diagnosed at a Tertiary Care Hospital in Afghanistan: A Cross-sectional Study

Abdul Sami Ibrahimkhil, Haider Ali Malakzai, Ahmed Maseh Haidary, Nasrin Hussaini, Jamshid Abdul-Ghafar

Department of Pathology and Clinical Laboratory, French Medical Institute for Mothers and Children (FMIC), Kabul, Afghanistan

Correspondence: Jamshid Abdul-Ghafar, Tel +93 792 827 287, Email jamshid.jalal@fmic.org.af

Purpose: In Afghanistan, research work is still in its infancy and there is no national level tumor registry at the moment in the country that could elaborate the histopathological features of ovarian tumors in the country. The current study was conducted with the aim to describe pathological characteristics of ovarian tumors diagnosed at tertiary level in Afghanistan.

Patients and Methods: A descriptive cross-sectional study was conducted, including 198 cases diagnosed with ovarian tumors, that were consecutively included in the study from July 2017 to August 2020. All the cases were diagnosed at the Department of Pathology, French Medical Institute for Mothers and Children, Kabul, Afghanistan, that receives biopsy samples from all of the tertiary care institutions in Kabul.

Results: In the current study, majority of the ovarian tumors were benign and presented with nonspecific symptoms. The mean age at diagnosis was 34.4 (SD ±13.4). Benign tumors comprised 81.8%, borderline 1.5% and malignant 16.7% of the cases. Majority of the diagnosed tumors were from surface epithelium in origin, followed by germ cell tumors, sex cord stromal tumors, and a single metastatic tumor. The most common benign neoplasm was mature cystic teratoma, followed by benign serous cystadenoma. Considering the malignant tumors, serous cystadenocarcinoma and adult granulosa cell tumors were predominant, followed by endometrioid adenocarcinoma and mucinous cystadenocarcinoma. More than half of the ovarian tumors occurred between 21 and 40 years of age.

Conclusion: In the current study, the proportion of malignant ovarian neoplasms was significantly less than benign lesions. Although, many of the pathological features related to ovarian neoplasms were similar to the features demonstrated in other regions of the world, there were important findings that were exclusively noted in the cases diagnosed in Afghanistan.

Keywords: pathological features, ovarian neoplasms, benign, malignant, Afghanistan

Introduction

Cancer will be the leading cause of mortality and one of the most important causes of decreasing life expectancy all over the world in twenty-first century, that would be due to the rapid growth and aging of the population and socioeconomic development. Accordingly, it has been demonstrated that mortality rates from stroke and coronary heart disease have decreased considerably in comparison to cancers in many countries.[1]

Globally, the eighth most common cancer among women is ovarian cancer, that constitutes 4% of cancer in female population. The mortality and morbidity related to ovarian cancer, when compared to other reproductive system malignancies, is high. According to recent global estimates, 225,000 new cases are identified each year, and 140,000 patients die every year from ovarian cancer.[2]

American Cancer Society (ACS) has revealed that there were 22,530 new cases with 13,980 deaths reported due to ovarian cancers, in 2019 alone.[3] Even though ovarian tumors are not common among children and teenage girls they form a significant section of the gynecological malignancies in this age group, constituting 1% of all malignant

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neoplasms in children and 8% of the entire childhood abdominal neoplasms. Around 10–30% of all ovarian tumors occurring in girls less than 17 years of age are estimated to be malignant.[4]

The ovaries are pelvic organs located on both sides of the uterus adjacent to the lateral pelvic wall, behind the broad ligament and anterior to the rectum. The location of the ovary posterior to the broad ligament and a similar relationship of the ovarian ligament to the ipsilateral fallopian tube helps in the determination of the laterality of a salpingo-oophorectomy specimen.[5]

The ovary's sex and mesenchymal cells are totipotent and multipotent, respectively, thus resulting in a wide spectrum of neoplastic transformations. Therefore, accurate diagnosis of ovarian neoplastic and non-neoplastic lesions is crucial but challenging.[6] Ovarian malignant tumors constitute the third most common type of malignancy in women, surpassed only by cervical and endometrial cancers.[7]

On the basis of tumor origin, ovarian neoplasms have been classified by World Health Organization (WHO) into surface epithelial, germ cell, sex cord – stromal and metastatic tumors. The most frequently occurring malignant tumors comprise surface epithelial tumors, which are further classified based on the cell type as serous, mucinous, and endometrioid carcinomas. Considering tumor behavior, ovarian neoplasms can be sub-classified into benign, borderline, and malignant.[8]

It must be noted, that around 90% of ovarian neoplasms are benign.[9] Benign ovarian tumors may arise at any age, however, they are commonly found during the childbearing ages, especially between 20 and 45 years of age. Conversely, malignant tumors are more common in advanced ages, usually between 40 and 65 years of age.[10]

Although, the risk of developing ovarian cancer during a woman's lifetime is pretty low with one in every 71 women, most of the deaths occur from complications of the disease. Luckily, 75% of ovarian cancer patients survive at least one year after diagnosis. Sadly, same percentage of patients die from the disease within five years of diagnosis. In general, lifetime chance of dying from invasive ovarian malignant tumor is nearly 1 in 95.[2] In 2012, Afghanistan's estimated ovarian cancer incidence was 346 while mortality rate was 1.6 (per 100,000) for all ages.[2] Ovarian tumors have various histopathological patterns and considering their prognostic implications, correct diagnosis guides in better treatment plans.[11]

To the best of our knowledge, there is no published data available for ovarian neoplasms in Afghanistan. Identification of common benign and malignant neoplasms is essential before appropriate health guidelines for management and funding for the disease are ever planned by the country's health sector. Pathology and Clinical Laboratory of French Medical Institute for Mothers and Children (FMIC) is one of the country's very few diagnostic centers, which receives notable numbers of pathological specimens, including those of ovarian origin, from almost every region of the country. Our study provides baseline data for the future research related to ovarian neoplasms in Afghanistan that can be used for further planning of health policies.

Materials and Methods

A descriptive cross-sectional study was conducted to determine the histopathological patterns of ovarian neoplasms diagnosed at FMIC, Kabul, Afghanistan. The study was approved by the Ethical Research Committee (ERC) of FMIC (64-FMIC-ER-19) and 198 patients diagnosed with ovarian tumors were consecutively included in the study from July 2017 to August 2020. Formal consents were taken upon participation from the patients and a well-organized questionnaire was developed that consisted of all the variables with well-defined inclusion criteria for the study. The consents were taken from the patients' legal guardians when they were younger than 18 years old or were not able to give consent due to cultural concerns.

Histopathological reports were retrieved from medical records of the Department of Pathology of FMIC. All the cases were diagnosed through histopathological examination by qualified and credentialed histopathologists. Biopsy tissues were submitted in 10% formalin solution prior to further processing. The tumor specimens less than 3 cm in the greatest dimension were entirely submitted, however, the solid tumors larger than 3 cm were sliced in 1 cm intervals and random sections per 1 cm of the greatest dimension of the tumors were taken in separate blocks. Paraffin embedded tissue sections were stained with hematoxylin and eosin (H&E) and then the slides were examined under a microscope

for diagnosis. The cases were diagnosed and subclassified in accordance with the fourth edition of WHO Classification of Female Genital Tumors.

Statistical Package for Social Sciences (SPSS) application, version 25, was used for data analysis. Considering the type of data, frequencies and proportions were used for calculating categorical variables, while mean, median and standard deviation were used to describe continuous variables.

Results

A total of 198 cases were included in our study with the mean age of 34.4 (±SD=13.4) at diagnosis. Abdominal mass was the main complaint and almost half of the participants were multiparous, as shown in Table 1. A considerable number of neoplasms were seen in the right side and most of the benign tumors were cystic. Most of the tumors were benign

Table 1 Demographics and Clinical Characteristics of Women with Ovarian Neoplasms (n=198)

Characteristics	Frequency	Percentage (%)
Age (in years)		
Mean ±standard deviation	34.42±13.4 1	
Age groups (in years)		
Less than 20	21	10.6
21 to 40	116	58.6
41 to 60	55	27.8
Above 61	6	3
Ethnicity		
Pashtun	55	27.8
Tajik	95	48.0
Hazara	47	23.7
Uzbek-Turkmen	1	0.5
Signs and Symptoms		
Abdominal pain	76	38.4
Abdominal mass	106	53.5
Abdominal distension	8	4.0
Ascites	2	1.0
Menstrual irregularities	1	0.5
Asymptomatic	5	2.5
Menarche in years (n=195)		
Mean ±standard deviation	36.6 ± 1.02	
Menopause in years (n=40)		
Mean ±standard deviation	48.7 ± 2.46%	

(*Continued*)

Table 1 (Continued).

Characteristics	Frequency	Percentage (%)
Parity		
Uniparous	38	19.2
Multiparous	113	57.1
Patient with no childbearing age or has no children	47	23.7
Survival status		
Dead	1	0.5
Alive	197	99.5

followed by malignant and borderline. Mature cystic teratoma and serous cystadenocarcinoma were the frequently occurring benign and malignant tumors respectively.

Considering the surgical procedures, total abdominal hysterectomy, and bilateral salpingo-oophorectomy (n=21, 10.6%) was the most common procedure applied for resection of ovarian tumor, followed by bilateral salpingo-oophorectomy (n=11, 5.6%), right salpingo-oophorectomy (n=47, 23.7%), left salpingo-oophorectomy (n=30, 15.2%), right oophorectomy (n=30, 15.2%) and left oophorectomy (n=27, 13.6%). However, there were no surgical information available for (n=32, 16.2%), as shown in Table 2.

Table 2 Surgical Procedure, Laterality, Size and Consistency of Ovarian Neoplasms

Characteristics	Frequency	Percentage (%)
Surgical procedure		
Total abdominal hysterectomy and bilateral salpingo-oophorectomy	21	10.6
Bilateral salpingo-oophorectomy	11	5.6
Right salpingo-oophorectomy	47	23.7
Left salpingo-oophorectomy	30	15.2
Right oophorectomy	30	15.2
Left oophorectomy	27	13.6
Unknown surgical procedure	32	16.2
Laterality		
Right	84	42.4
Left	66	33.3
Bilateral	15	7.6
Unknown laterality	33	16.7
Tumor size (in cm)		
Less than 5	16	8.1

(*Continued*)

Table 2 (Continued).

Characteristics	Frequency	Percentage (%)
5–10	60	30.3
10–20	103	52.0
More than 20	16	8.1
Tumor size cannot be assessed	3	1.5
Tumor consistency		
Cystic	144	72.7
Solid	22	11.1
Complex	31	15.7
Diffuse pattern (metastatic tumor)	1	0.5
Association with endometriosis		
Yes	2	1.0
No	196	99.0

A considerable number of the neoplasms were seen in the right side (n=84, 42.4%), followed by left side (n= 66, 33.3%), bilateral (n=15, 7.6%); and for 33 (16.7%) cases, the tumor laterality was unknown, as shown in Table 2. The tumor size was as small as 0.3 cm and as large as 35 cm and was categorized into four groups. Tumors less than 5 cm constituted 8.1% (n=16), 5 cm to 10 cm, 30.3% (n=60), 10 cm to 20 cm, 52% (n=103) and tumor size more than 20 cm formed 8.1% (n=16). In three of the cases (1.5%), the tumor had either diffuse pattern or the tumor found incidentally where their gross size could not be assessed, as shown in Table 2.

In consideration of tumor consistency, 72.7% (n=144) were cystic, 11.1% (n=22) solid, 15.7% (n=31) complex and in one case, tumor consistency showed diffuse pattern which could not be assessed grossly. Only one patient died of the disease and two patients had concomitant ovarian endometriotic cysts, a precursor lesion to ovarian cancer, as shown in Table 2.

Table 3 describes tumor type and frequency of ovarian neoplasms. Benign tumors were 81.8% (n=162), borderline 1.5% (n=3) and malignant 16.7% (n=33) cases.

As shown in Table 4, the majority of the diagnosed cases were of surface epithelial in origin, consisting of 52% (n=103) of cases, followed by germ cell tumors 39.9% (n=79), sex cord stromal tumors 7.1% (n=14), and finally, there was only one metastatic tumor (0.5%) and a single poorly differentiated neoplasm (0.5%), for which, histologic classification was not possible without performing immunohistochemical stains. Out of 162 benign tumors, the most common diagnosis was mature cystic teratoma, constituting 34.8% (n=69) of cases, followed by serous cystadenoma

Table 3 Natural Behavior and Frequency of Ovarian Neoplasms

Characteristics	Frequency	Percentage (%)
Benign	162	81.8
Borderline	3	1.5
Malignant	33	16.7

Table 4 Histologic Types, Classification and Diagnostic Category of Ovarian Neoplasms

Classification	Benign (n=162/81.8%)	Borderline (n=3/1.5%)	Malignant (n=33/16.7%)	Total (%)
Surface epithelial cells	Serous cystadenoma (50/25.2%), mucinous cystadenoma (29/14.6%), benign Brenner tumor (2/1%)	Mucinous borderline tumor (1/0.5%), serous borderline tumor (2/1%)	Serous cystadenocarcinoma (6/3%), mucinous cystadenocarcinoma (4/2%), clear cell carcinoma (1/0.5%), malignant Brenner tumor (1/0.5%), endometroid adenocarcinoma (5/2.5%), adenocarcinoma (1/0.5%), squamous cell carcinoma arising in mature teratoma (1/0.5%)	103 (52)
Germ cell	Mature cystic teratoma (69/34.8%) stroma ovarii (4/2%)		Dysgerminoma (3/1.5%), Immature teratoma (1/0.5%), malignant mixed germ cell tumor (2/1%)	79 (39.9)
Sex cord stromal cells	Fibroma (2/1%), fibro-thecoma (5/2.5%), leiomyoma (1/0.5%)		Adult granulosa cell tumor (6/3%)	14 (7.1)
Metastatic			Krukenburg tumor (1/0.5%)	1 (0.5)
Unclassified			Malignant neoplasm (1/0.5%)	1 (0.5)

25.2% (n=50). Out of 33 malignant cases, serous cystadenocarcinoma, and adult granulosa cell tumors each comprised 3% (n=6), were the commonest malignant neoplasms followed by endometrioid adenocarcinoma 2.5% (n=5) and mucinous cystadenocarcinoma 2% (n=4).

Discussion

The findings of our study were similar to studies conducted in international and regional countries and described the histopathological patterns of ovarian neoplasms in Afghanistan. In the current study, we attempted to fill an important literature gap regarding the patterns and proportions of ovarian neoplasms diagnosed based on histopathology in Kabul, Afghanistan.

One hundred and ninety-eight subjects with histopathological diagnosis of ovarian neoplasms with an age range from 4 to 80 years were included in the study.

The mean age at diagnosis was 34.4 years and most of the cases occurred between 21 and 60 years of age which was similar to studies carried out in Lahore, Pakistan, and in Ahmedabad, India.[12,13]

The current study revealed that 81.8% of the neoplasms were benign, while only 16.7% malignant and 1.5% borderline tumors. This finding was in concordance with the studies conducted in western region of Saudi Arabia, Pakistan, and in eastern India.[14–16]

In our study, surface epithelial tumors accounted for 52%, germ cell tumors were 39.9%, sex cord stromal tumors were 7.1% and metastatic tumors constituted only 0.5% of the cases. This finding was similar to studies conducted in Iraq, Pakistan and Iraq.[15,17,18] However, a study conducted in Ghana showed that germ cell tumors were slightly more than surface epithelium.[19]

The most common benign neoplasm was mature cystic teratoma (34.8%). This finding was inconsistent with previous studies where serous cystadenoma was demonstrated to be the commonest benign tumor.[6,13,16] However, studies conducted in Nepal, Ghana and Nigeria showed that mature cystic teratoma was the commonest benign ovarian neoplasm.[19–21]

The most common malignant tumor was serous cystadenocarcinoma and adult granulosa cell tumor, each constituting 3% of the all malignant cases followed by endometrioid adenocarcinoma (2.5%) and mucinous cystadenocarcinoma (2%) which apart from relatively higher incidence of adult granulosa cell tumor in our study, shows a concordance with the literature[20,22] that could be explained related to our study's small sample size, genetic or environmental factors.

In this study, information for laterality for 33 cases was not available. One-sided (75.7%) tumors were more common than bilateral (7.3%) and right ovarian involvement (42.4%) was more common than the left (33.3%), which was in concordance with findings of studies conducted in India, Iraq, and Bangladesh.[10,17,22,23]

In terms of tumor consistency, 72.7% were cystic, 11.1% solid and 15.7% complex and only one case (0.5%) was not assessable due to diffuse pattern of the tumor. Tumors with cystic consistency were mostly benign constituting 88.3%, while malignant tumors were either solid or complex, each being 42.4% and 51.5%, respectively. These finding are in concordance with studies conducted in Bangladesh and India.[23,24]

Our study revealed that 53.4% of the patients presented with abdominal mass, which was the most common presenting symptom followed by abdominal pain. These findings were in line with a study carried out in India, showing abdominal mass followed by abdominal pain as the major presenting symptoms in patients suffering from ovarian tumors.[6]

Although the ovarian tumors were subclassified in accordance with fourth edition of the WHO Classification of Female Genital Tumors at the time of diagnosis in our study, the updated fifth edition comprises five principal histological types: high-grade serous carcinoma, low-grade serous carcinoma, mucinous carcinoma, endometrioid carcinoma, and clear cell carcinoma.[25]

In addition to that, although the identification of *TP53* mutation in high grade serous carcinomas and missense point mutation in *FOXL2* in granulosa cell tumors is vital for confirmative diagnosis of these tumors,[26,27] the cases in our study were exclusively diagnosed on the basis of morphological findings with the help of H&E stains. No immunohistochemical and molecular studies were done for the diagnosis in the current study.

In Afghanistan, research work is still in its infancy with no reliable tumor registry at national level that could provide a good picture of prevalence and distribution of various tumors and their possible linked factors to the environment, lifestyle and genetics of the Afghan population.[28,29] In addition, low level of education, poverty and lack of specialized diagnostic and therapeutic facilities for neoplastic disorders adds to predicaments of the issue.[30]

Strengths and Limitations of the Study

To the best of the researcher's knowledge, this study was the first of its kind to be conducted in Afghanistan. Due to the decades of continuous war in the country, research is still in its infancy in Afghanistan; and the researchers do believe that the current study will pave the way for large scale studies in the future, regarding ovarian tumors.

Despite the abovementioned strengths, the present study was conducted at a private tertiary care hospital setting; therefore, it extrapolated the study findings and hence the generalizability of study is questionable. Moreover, due to the lack of immunohistochemical stains, a considerable number of cases were excluded from the study which might have affected the internal validity of research.

Conclusion

The current study demonstrated significant information regarding demographic, histopathological patterns, and clinical characteristics of ovarian tumors in Afghanistan. The study revealed that ovarian neoplasms had nonspecific signs and symptoms, occurring mainly in reproductive age groups and the majority of them were benign. The proportion of malignant ovarian neoplasms was far less than benign ones. While many of the patterns related to ovarian neoplasms in Afghanistan were similar to the patterns demonstrated in other regions of the world, there were peculiar differences that need further elaboration. Furthermore, considering the study setting, our data represented only the tip of the iceberg and it is indispensable to conduct further multi-institutional studies, targeting larger sample size, for detailed scrutiny into the subject, that will eventually lead to the development of effective health policies.

Data Sharing Statement

The data generated and analyzed in this article data are not publicly available due to the privacy and confidentiality of the patients, however, it can be shared by the corresponding author upon reasonable request.

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Disclosure

All the authors report no conflicts of interest in this research work.

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