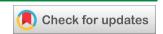
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(RESEARCH ARTICLE)



Histopathological analysis of ovarian cancer in Benghazi medical center (BMC) in Benghazi - Libya from the years 2020-2021

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Abstract

Ovarian cancer is a growth of cells that forms in the ovaries. The cells multiply quickly and can invade and destroy healthy body tissue. Tumors of the ovary are remarkably varied as they may arise from any of the three cell types in the normal ovary. A retrospective study was conducted on 48 cases of ovarian specimens diagnosed as ovarian tumors in the Oncology department at Benghazi Medical Center from January 2020 to December 2021. The files were conducted by the staff members of the Oncology department, and the students divided themselves into groups to obtain the data from the department, the data were age, type of ovarian cancer, histological and cytological reports (microscopic description) and diagnosis. Twelve patients were in the age range 51-60 years old as the highest number followed by the age range 61-70 years of age at 11 patients. Most of the ovarian tumors were seen in patient in postmenopausal age more than 45 years of age with a percentage of 78.7%. Surface epithelial tumors were the most found at followed by metastatic tumors while germ cell tumors were not found in our sample. The most common subtype of ovarian tumors observed in this study was serous cystadenocarcinoma low grade and endometrioid adenocarcinoma, while the least common tumor seen was papillary mucinous cystadenocarcinoma. Concerning the occurrence of bilateral versus unilateral tumors, most of the cases were bilateral. The aim of our research was to study the histological types of ovarian cancer in Benghazi Medical Center in Benghazi - Libya from the years 2020-2021.

Keywords: Histopathology; Ovarian cancer; Tumor; Ovary; Benghazi Medical Center

1. Introduction

Tumors of the ovary are remarkably varied as they may arise from any cell types in the normal ovary: the multipotent surface (coelomic) epithelium, the totipotent germ cells, and the sex cord-stromal cells. Neoplasms of epithelial origin account for the great majority of ovarian tumors and, in their malignant forms, account for almost 90% of ovarian Cancers (Kanpurwala *et al* 2016). Studies in Benghazi Libya area showed that ovarian cancer cases represented 13% (Alashger *et al* 2021). Germ cell and sex cord-stromal cell tumors are much less frequent; although they constitute 20% to 30% of ovarian tumors, they are collectively responsible for less than 10% of malignant tumors of the ovary. Important risk factors for ovarian cancer include nulliparity, family history, and germline mutations in certain tumor suppressor genes. There is a higher incidence of carcinoma in unmarried women and married women with low parity (Kuehnel. 2003). Around 5% to 10% of ovarian cancers are familial, and most of these are associated with mutations in the *BRCA1* or *BRCA2* tumor suppressor genes. The average lifetime risk for ovarian cancer is approximately 30% in *BRCA1* carriers; the risk in *BRCA2* carriers is somewhat lower. In contrast with familial ovarian cancer, mutations in *BRCA1* and *BRCA2* are found in only 8% to 10% of sporadic ovarian cancers, which appear to arise through alternative molecular mechanisms (Kumar *et al.*, 2018). The main risk factors for the ovarian cancers are: delayed childbearing, early menarche, endometriosis, estrogen replacement therapy for more than five years, family history suggesting

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genetic predisposition, genetic syndromes, High-fat diet and late menopause. On the other hand, the decreased risk factors are; breastfeeding for 18 months or more, early menopause, multiparity (risk decreases with each additional pregnancy), Hysterectomy, late menarche, low-fat diet, oral contraceptive use and tubal ligation. Hysterectomy and tubal ligation are likely associated with decreased risk of ovarian cancer because of decreased utero-ovarian blood flow, which limits local exposure to hormonal or potentially carcinogenic factors (Glance, A. 2009), causing vaginal bleeding in some cases (Abouzriq, et al., 2023). Ovarian cancer primarily spreads locally to the opposite ovary and the uterus, and then intraperitoneally. Distant metastases are rare, but may occur in the liver, lungs, pleura, adrenal glands, and spleen. The histologic grade of the tumors can also affect treatment and prognosis. Low-grade tumors with cells of low malignant potential (i.e., borderline tumors) have a more favorable prognosis than high grade tumors (Garg et al., 2017). The majority of ovarian tumors arise from the fallopian tube or epithelial cysts in the cortex of the ovary. Studies have shown that many of the tumors thought to arise from the coelomic epithelium that covers the surface of the ovary are now thought to arise from the fimbriated end of the fallopian tube. The epithelium lining the cortical cysts may be derived from displaced ovarian surface epithelium or the lining of fallopian tube. These can become metaplastic or undergo neoplastic transformation to give rise to a number of different epithelial tumors. Benign lesions usually are cystic (cystadenoma) and may have an accompanying stroma component (cystadenofibroma). Malignant tumors also may be cystic (cystadenocarcinoma) or solid (carcinoma). Some ovarian epithelial tumors fall into an intermediate category currently referred to as borderline tumors. Although the majority of borderline tumors behave in a benign manner they can recur and some can progress to carcinoma (Glance, A. 2009). Ovarian endometrioid tumor: 8-15% of all ovarian tumors. Endometrioid carcinomas of the ovary are a sub-type of epithelial ovarian tumors. The vast majority are malignant and invasive. On imaging, they are usually characterized as complex nonspecific solid-cystic masses and found associated with endometriosis. Endometrioid carcinomas account for 8-15% of all ovarian carcinomas. It is considered the second commonest malignant ovarian neoplasm. The typical gross appearance of these tumors is similar to that of other epithelial lesions, with variable cystic and solid components. Occasionally, it may be completely solid. Histologically, an endometrioid carcinoma is characterized by the appearance of tubular glands and bears a strong resemblance to the endometrium. Gross morphological appearance is that of a mass with both solid and cystic areas. Squamous differentiation can be present in more than a third of patients. A benign endometrioid carcinoma is relatively uncommon and when it is benign it tends to be an ovarian cystadenofibroma. Bilateral involvement can be seen in 25-40% of cases. Endometrioid histology may carry a slightly better prognosis than a serous or mucinous cystadenocarcinoma of the ovary. Metastases to the ovary with colon cancer could be considered especially if the ovarian lesion is bilateral or if there is a known colonic mass, especially due to strong histological similarity (Redondo et al., 2021). Differentiation from metastatic endometrial cancer can also sometimes be difficult. Endometrioid carcinomas of the ovary frequently have mutations in the PTEN tumor suppressor gene as well as mutations in other genes that also act by upregulating PI3K - AKT signaling (Kumar et al., 2018).

2. Material and methods

A retrospective study was conducted on 49 cases of ovarian specimens diagnosed as ovarian tumors in the Oncology department at Benghazi Medical Center from January 2020 to December 2021. The files were conducted by the staff members of the Oncology department, and the students divided themselves into groups to obtain the data from the department, the data were age, type of ovarian cancer, histological and cytological reports (microscopic description) and diagnosis. The age, histological pattern, character and diagnosis were reviewed and categorized according to the classification of the World Health Organization for ovarian tumors into surface epithelial tumors, metastatic tumors and sex cord tumors and others. Data were distributed on the basis of the year of diagnosis, age, histological types, and others. The data was then emptied in tables, calculated and analyzed by the use of Microsoft EXCEL 2016.

3. Results

A total number of 49 female cases of ovarian tumors were collected from the Oncology department at the Benghazi Medical Center in Benghazi, Libya. Two of the files were from the same patient so one of them was not used and one of the files had a normal histopathological diagnosis so it was also omitted. 30 cases were obtained from the year 2020 and 17 were from the year 2021, Figure 1 shows the percentage of cases taken from each year, they were 62% from year 2020 and 38% from the year 2021.

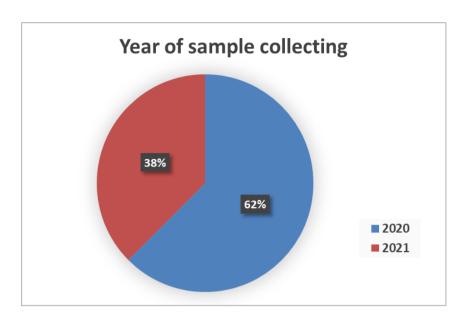


Figure 1 The percentage of cases taken from each year. 62% of the patients were from year 2020 while 38% were from year 2021

The age range of patients with ovarian tumors in our study was from 24 to 99 years old with a medium of 57 years old and a standard deviation of 15 years. The age distribution is clarified in Figure 2. Twelve patients were in the age range 51-60 years old as the highest number followed by the age range 61-70 years of age at 11 patients. On the other hand, there were no patients less than 21 years old.

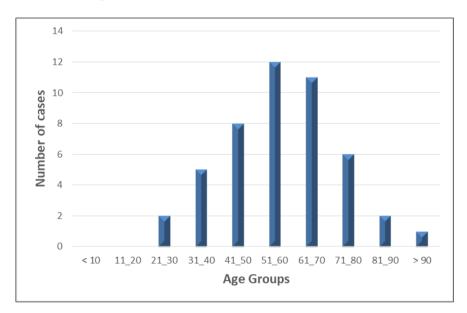


Figure 2 The age distribution. The highest percentage of ovarian tumors were seen between 51 to 70 years of age followed by 41 to 50 years. Least number of cases were seen in the ages older than 81 years old. No cases were recorded in age less than 20 years of age

According to the menopausal status, most of the ovarian tumors were seen in patient in postmenopausal age more than 45 years of age with a percentage of 78.7%. This is followed by perimenopausal age (ages between 35 – 46 years old) and premenopause with percentages of 14.9% and 6.4% respectively. There were no cases in prepubertal age group (Figure 3).

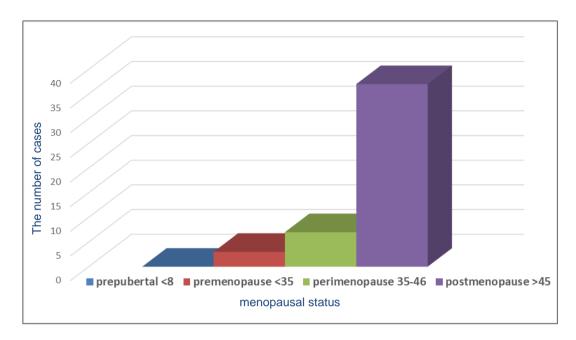


Figure 3 Distribution of patients according to menopausal status. There were no recorded cases of ovarian tumors in patients younger than 8 years of age. The number of cases in premenopausal age was 3 (6.4%) and the number of patients in perimenopause and post-menopause were 7 (14%) and 37 (78.7%) respectively

The total number of 47 cases of ovarian tumors were studied. The percentage of each tumor was as following, surface epithelial tumors were the most found at 81%, metastatic tumors were 15% and sex cord tumors were only 4% while germ cell tumors were 0% (figure 4).

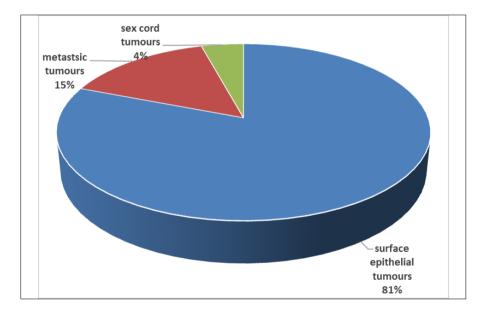


Figure 4 Percentage of tumors according to general histological type. Most common type was surface epithelial tumor 81%, followed by metastatic tumors 16%, and sex cord tumors 4%

The most common subtype of ovarian tumors observed in this study was serous cystadenocarcinoma low grade and endometrioid adenocarcinoma 13%. The least common tumor seen was papillary mucinous cystadenocarcinoma (1 out of 47 cases; 2%). The percentages of the rest of tumors were as following from less to more frequent, granulosa cell tumor, serous carcinoma and Krukenberg tumor were the same at 4%, serous adenocarcinoma and papillary serous cystadenocarcinoma at 6%, serous papillary adenocarcinoma and serous papillary carcinoma both at 8%, then serous cystadenocarcinoma high grade and mucinous cystadenocarcinoma at 10% and metastatic at 12% this is shown in Figure 5.

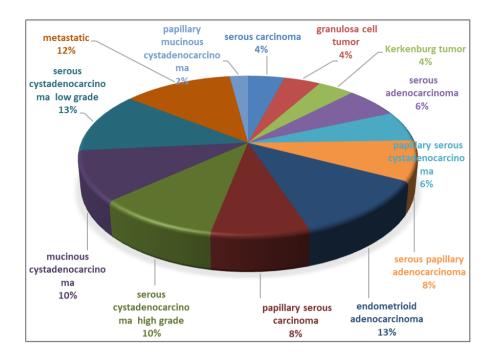


Figure 5 Percentage of tumors according to histological type. Most common type was serous cystadenocarcinoma low grade and endometrioid adenocarcinoma while the least common tumor detected was papillary mucinous cystadenocarcinoma

Regarding the occurrence of bilateral versus unilateral tumors, 29 out of 47 cases were bilateral (61.7%) and the rest of patients presented with unilateral ovarian tumors (38.3%) (Figure 6). The incidence of unilaterally among different types of ovarian tumor was shown in figure 7. The serous cystadenocarcinoma high grade, papillary serous carcinoma, serous carcinoma and kerkenburg tumor cases were all bilateral. However, the papillary serous adenocarcinoma and the papillary mucinous cystadenocarcinoma were found to be only unilateral. Meanwhile the other types were found in this study to be mixed.

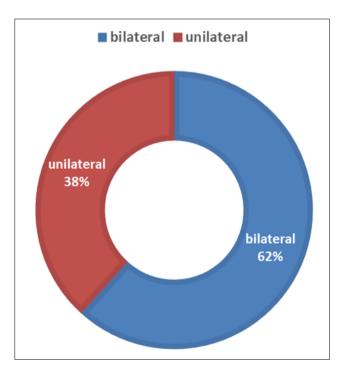


Figure 6 Percentage of laterality in overall ovarian tumor cases

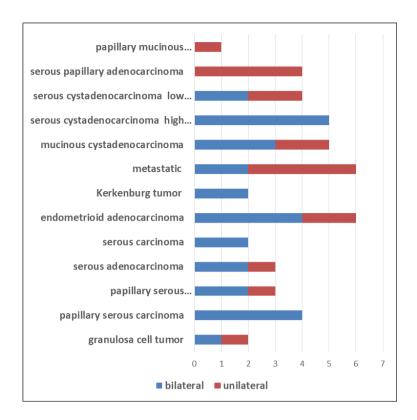


Figure 7 Laterality in ovarian tumors. Serous cystadenocarcinoma high grade, papillary serous carcinoma, serous carcinoma and Kerkenburg tumor cases were all bilateral. Nevertheless, the papillary serous adenocarcinoma and the papillary mucinous cystadenocarcinoma were found to be unilateral

4. Discussion

Ovarian cancer is considered one of the major clinical challenges in gynecologic oncology as most of the patients are asymptomatic until the disease has metastasized (Yassien and Ahmed, 2019). Ovarian cancer is the third type of gynecologic cancer in terms of prevalence after cervical and uterine cancer (Almisawi and Albajalan, 2021). Ovarian cancer is the second deadliest gynecological cancer worldwide with an estimated number of 207,252 deaths in 2020 (Elshami, *et al.*, 2022). About two-thirds of ovarian cancer patients are diagnosed in an advanced stage (Yassien and Ahmed, 2019). In our study of ovarian cancer cases in Benghazi Medical Center, Libya for the years 2020 and 2021, the median age of patients was estimated to be 57 years. While a study was conducted in America on ovarian cancer, and the median age of the cases was estimated at 63 years, whereas in another research conducted in India, the median age of the cases was estimated at 53 years (Takiar, 2019). Also, in Egypt were estimated to have a median age of 47 (Gharib *et al.*, 2018). Libya shows a low incidence of the disease while high mortality is noted in developed countries such as America, due to the lack of appropriate diagnostic and treatment options (Almisawi and Albajalan, 2021).

The highest ovarian cancer rate is reported from industrial countries with exception of Japan. United States and Denmark respectively have a higher incidence of ovarian cancer (Gharib *et al.*, 2018). The prevalence of ovarian cancer in developing countries such as Libya, Egypt and India is much lower than what is recorded in developed countries, and this is due to several reasons such as the spread of smoking, environmental pollution, overcrowding and the abundance of chemical elements in developed countries, although some of these causes are also starting to increase in developing countries such as smoking. Age status of ovarian cancer recorded recently in India were mostly found to be around the age of 32 years in 25% of the cases studied, and the cases established at perimenopause (about the age of 53 years) were 50%. As for cases in menopause at 77 years old the percentage was 95% and for the cases at the age after 77 years of age the percentage was 5% (Takiar, 2019). It was noted also, that the cases of ovarian tumors in Northern India, they found that in the period before menopause (30-39 years of age) the percentage was 24.3%, while the cases aged 50-59 years old their percentage was 24.3%, and cases after menopause their ages ranged from 70 to 79 their percentage was 7.2% (Puri *et al.*, 2018). In Assiut, Egypt, it was recently reported that the pre-menopausal cases were less than 50 years, their percentage was 27.8% and the postmenopausal cases were between 50-70, their percentage was 58.5%, and the postmenopausal cases were the cases were older than 70 years of age, their percentage was 13.8% (Gharib *et al.*, 2018). According to our study we found that most of the ovarian tumors were seen in patient in postmenopausal age more

than 45 years of age with a percentage of 78.7% this result is in accordance with the other mentioned studies. This is followed by perimenopausal age (ages between 35 – 46 years old) and premenopause with percentages of 14.9% and 6.4% respectively, this is furthermore in agreement with other studies.

In the United States in 2018, approximately 22,240 cases of ovarian cancer were detected and only 2% were sex cord, while germ cell was 3%, epithelial tumors are the most; constitutes 90% of all cases, and 26% are metastasis (Torre *et al.*, 2018). In another study in America 849 epithelial ovarian cancer cases, 451 (53%) were serous, 78 (9%) endometrioid, 38 (4%) mucinous, 27 (3%) clear cell, and 255 (30%) other epithelial carcinomas. In general, women with serous (mean=62.6 years), mucinous (63.5 years), and other epithelial carcinoma (63.9 years) subtypes were older while endometrioid (61.0 years) and clear cell (59.7 years) cases were younger. Differences were also observed across case groups in the distribution of tumor stage and grade, with endometrioid and mucinous cases more likely to be localized low grade tumors and the three other tumor types more likely to be high grade tumors and to have regional/distant metastas (Reid *et al.*, 2017).

Also in Pakistan between 1994 and 2003 the total number of cases was 544, only 22.4% reached to stage IV (metastatic) (Sarwar *et al.*, 2006). In Egypt, Assiut, statistics were done on the number of cases from 2010 to 2015 and there were 378 cases, including 205 cases 54%, epithelial tumors (which were the most), 42 Cases 11.1% sex cord tumors, germ cell only 2 cases 0.5%, 86 cases 22.8% metastatic tumors (Gharib *et al.*, 2018). A study in 10 provinces of Algeria, found that the most common histological subtypes was serous adenocarcinoma 52.45% followed by endometrioid 10.65%, mucinous 9.43% and clear cell carcinoma 4.09% (Cherbal *et al.*, 2018). While Sudan was the highest compared to other countries in detecting cancer in the late stage due to lack of sensitive early screening methods, around 43% of all ovarian cancer, which were 128 cases between 2015 and 2017 (Adam *et al.*, 2017). In this study we found: the total number of cases 49 of ovarian tumors. The percentage of each tumor is: surface epithelial tumors were 81%, metastatic tumors were 15%, and sex cord tumors were only 4%, while germ cell tumors were 0%, the smaller number of cases and different geographic stature could be a factor to not be comparable with other studies.

Ovarian cancer among Nigerian women was found to be the most common subtype of ovarian tumors observed was serous cystadenocarcinoma 41.10% and granulosa tumor 25.6%. The percentages of the rest of tumors were as following from less to more frequent, endometroid AC, Brenners tumor, Embryonal carcinoma Choriocarcinoma1.3%, malignant teratoma, endodermal sinus tumor, Dysgerminoma 2.6%, others 3.8%, immuture teratoma 6.4%, mucinous cyst AC 10.3% (Zyyan *et al.*, 2017).

A study was conducted in Libya in Benghazi University during the period from January 2019 to December 2020 on 76 ovarian cancer. The laterality in ovarian tumors were 50 unilateral 66% and 26 were bilaterality 34%). Granulosa cell tumor, sclerosing stromal tumor, fibroma and struma ovrii are presented in unilateral pattern only. All cases of mesenteric krukenberg tumors were bilateral. Borderline mucinous and serous adenoma show bilateral: unilateral ration of 5:1 and 3:1 respectively. Dermoid cyst and serious cystadenoma were seen more unilateral tumors (Saad et al., 2022). On the another hand, a study was done in India were a total of 157 cases of ovarian tumors from Jan 2007 to Sept 2010 found that 12.7% were bilateral and the rest of patients presented with unilateral ovarian tumors 87.2%. 12.6 %, 11.67% and 8.86% cases were bilateral in other studies conducted in various states of India. 17 out of 20 bilateral cases were surface epithelial tumors (9 serous, 7 mucinous and 1 transitional cell carcinoma). Among bilateral germ cell tumors (2 cases), both were mature cystic teratomas. 1 out of total 4 metastatic cases was bilateral while none of the sex cord stromal tumors presented were bilaterally. The most significant finding in this aspect of study was that 85% of bilateral tumors were Surface epithelial tumors (Kanpurwala et al., 2016). In our study 49 ovarian cancer cases from Benghazi Medical Center, Libya for the years 2020 and 2021 the occurrence of bilateral versus unilateral tumors were, 29 bilateral 61.7% and the rest of patients presented with unilateral ovarian tumors 38.3%. Serous cystadenocarcinoma high grade, papillary serous carcinoma, serous carcinoma and kerkenburg tumor cases were all bilateral. While, the papillary serous adenocarcinoma and the papillary mucinous cystadenocarcinoma were found to be unilateral.

5. Conclusion

Histopathological analysis of ovarian cancer is an important study to assess the multitude of the disease in the city of Benghazi. Benghazi medical center (BMC) in Benghazi is the largest hospital in the east side of Libya so it was chosen to conduct our research.

Forty-nine cases diagnosed as ovarian tumors from the Oncology Department of BMC were studied from the years 2020 to 2021. The age range of patients with ovarian tumors in our study was from 24 to 99 years, and the highest incidence of ovarian tumors seen was between 51 to 70 years. Most of the patients were postmenopausal (78.7%).

The percentage of surface epithelial tumors were the greatest found at 81%, while the ratio of tumors according to histological type, the most common type was serous cystadenocarcinoma low grade and endometrioid adenocarcinoma while the least common tumor detected was papillary mucinous cystadenocarcinoma. Laterality in ovarian tumors. Serous cystadenocarcinoma high grade, papillary serous carcinoma, serous carcinoma and kerkenburg tumor cases were all bilateral (61.7%). Nevertheless, the papillary serous adenocarcinoma and the papillary mucinous cystadenocarcinoma were found to be unilateral (38.3%). This research and similar others are key to maintain and sustain valuable information nationally and internationally.

Compliance with ethical standards

Acknowledgments

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Disclosure of conflict of interest

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

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