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Original Article

Histopathological Types of Ovarian Cancer in Different Age Group of Patients; A Single Institution Experience

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ABSTRACT

Objective: To see the relationship between age and histological types among patients presenting with ovarian cancer at tertiary care hospital, of Karachi Pakistan.

Study Design: Cross-sectional study.

Place and Duration of study: Department of medical oncology, Jinnah Postgraduate Medical Centre, Karachi Pakistan from Mar 2019 to May 2020.

Methodology: Three fifty women presenting with confirmed diagnosis of ovarian carcinoma were included irrespective of their age. The information regarding socio-demographics and family history were noted on pre-designed proforma. Pathology reports were obtained from all the patients and information regarding age, stage and histological type were noted. World Health Organization classification was used to classify the histological type of tumours. All data was entered and analyzed using SPSS version 23.

Results: The mean age of the study sample was estimated as 44.27±12.7 years ranging from 14-92 years. According to histological type, most of the females had surface epithelial tumors 307(87.71%), followed by sex cord-stromal tumors 20(5.7%) and germ cell tumors tumors 19(5.43%) respectively. The statistically significant difference was observed between age and histological types and subtypes of ovarian cancer (p<0.05).

Conclusion: It is concluded that age is an important factor in determining risk of developing different types of ovarian cancers. Serous type of epithelial ovarian cancer is the most common type and commonly present in 4th to 5th decade of life. Germ cell ovarian tumor is second most common type and present in 2nd decade of life.

Keywords: Age, epithelial tumors, histological types, germ cell tumors, ovarian cancer.

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INTRODUCTION

Ovarian cancer is the most commonly prevalent fatality causing gynaecological tumour in the United States. Worldwide, it exists as 3.6% among all malignancies and responsible for around 4.3% of mortalities in females.[1] Annually, almost 2.5 lac cases are diagnosed and every year half of the recently diagnosed lose their lives.[2] It is sixth most commonly occurring malignancy in females with discrepancy among their histological variant. The histopathological variant is quite distinguishable between Asian and western population. The classification of ovarian cancer on the basis of histology helps differentiate between benign and malignant tumour. According to WHO, there are five types of ovarian cancer histologically, namely, surface epithelial tumour, germ cell tumours, stromal cell tumour, mixed cell tumour and metastatic tumour. The incidence of malignant tumours in Pakistan is at peak. Cancer of ovary is found to be the fifth commonly prevalent tumour in Pakistan.[3] And unfortunately, Pakistan carries peak mortality rates (crude rate 3.1) of ovarian cancer.[4]

The signs and symptoms of ovarian cancer are not apparent at an initial stage until the cancer progresses further. The most frequent symptoms are nausea, pain in pelvis, bloating and abdominal swelling.[5] The ovarian cancer is a silent killer. Therefore, early diagnosis is required as it contributes to worst prognosis and lower survival rate.[6] There is 6-7% risk of developing benign ovarian cancer since birth to death and almost 1.5% risk of developing malignant ovarian cancer wherein 1% female die from this cancer. During the early menarche and late menopause, the incidence of ovarian cancer is highest.[7] The evidence shows that benign ovarian cancer can occur at any age. However, the malignant tumour is commonly found in elder females. The epidemiological data shows that the different types of ovarian cancer are commonly age related. It has been frequently seen that benign serous tumours and mucinous cystadenoma occur in between 4th and 6th decade (41-69 years). However, it could also

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occur in younger females of age less than 20 years or very older females of age more than 80 years.[8]

The risk of ovarian cancer rises with null parity, ovulation induction treatment, being ovulate at a younger age, women on hormonal replacement therapy or reaching menopause at an older age whereas the risk declines with use of oral contraceptives, ligation of tube and breastfeeding. In addition, sometimes genetic involvement is one of the primary reason of ovarian cancer in women having BRCA1 and BRCA2 genes.[9] The risk factors are not modifiable. Nevertheless, detection of different histological types of ovarian cancer subjective to different age groups will help clinicians to execute early screening of ovarian cancer in order to reduce poor prognosis and outcomes of detecting at late stage. Therefore, the aim of the study is to see the relationship between age and histological types among patients presenting with ovarian cancer at tertiary care hospital of Karachi.

METHODOLOGY

The cross-sectional study was conducted at the department of medical oncology, Jinnah Postgraduate medical center, Karachi Pakistan from May 2018-March 2020. Sample size of 343-350 was estimated using Raosoft online sample size calculator by taking statistics of epithelial tumour as 17.6%, margin of error 4% and 95% confidence interval.[10]

Inclusion Criteria: All of women presenting with confirmed diagnosis of ovarian carcinoma were included in the study irrespective of their age.

Exclusion Criteria: Pregnant women and women with history of platinum based agent exposure were excluded from the study.

Approval from ethical review committee (Approval no. F.2-81-IRB/2019-GENL/17552/JPMC) was obtained before start of the study. The written informed consent was taken from the patients before starting data collection. The information regarding socio-demographics and family history were noted on pre-designed questionnaire. The reports on pathology were obtained from all the patients and information regarding stage, histological type and subtype were abstracted by the consultant pathologist. WHO classification was used to classify the histological type of tumours.

All data was entered and analyzed using SPSS version 23. Descriptive analysis was done for all the numeric and categorical variables. Chi-square was used to see the association between age and histological types and subtypes. $p \leq 0.05$ was taken as statistically significant.

RESULTS

Total 350 patients were included with mean age estimated as 44.27±12.7 years ranging from 14-92 years. Majority of the females were from urban area 180(51.4%), Urdu speaking 164(46.9%), illiterate

Table-I: Baseline Characteristics (n=350)

Variables	Mean±SD
Age (years)	44.27±12.70
	n(%)
Residence	
Rural	170(48.6%)
Urban	180(51.4%)
Ethnicity	
Urdu	164(46.9%)
Punjabi	59(16.9%)
Balochi	18(5.1%)
Sindhi	79(22.6%)
Pashto	11(3.1%)
Others	19(5.4%)
Education	
Illiterate	167(47.7%)
Matric	102(29.1%)
Matric	52(14.9%)
Intermediate	16(4.6%)
Graduate	10(2.9%)
Postgraduate	3(0.9%)
Monthly income (PKR)	
<15,000	72(20.6%)
15,000-30,000	208(59.4%)
>30,000	70(20%)

Variables	n(%)
Marital Status	
Single	42(12%)
Married	268(76.6%)
Widow	31(8.9%)
Divorced	9(2.6%)
Family History of Breast Cancer	
Yes	22(6.3%)
No	328(93.7%)
Family History of Ovarian Cancer	
Yes	12(3.4%)
No	338(96.6%)
Family History of Other Cancer	
Yes	14(4%)
No	336(96%)
Clinical Stage	
I	105(30%)
II	35(10%)
III	135(38.6%)
IV	75(21.4%)
Pathological Stage	
I	105(30%)
II	38(10.9%)
III	139(39.7%)
IV	68(19.4%)

167(47.7%), 208 had monthly income 15,000-30,000 PKR (59.4%) and 268 were married (76.6%). About 6.3% of the females had positive family history of breast cancer, 3.4% had positive family history of ovarian cancer and 4% had positive family history of other cancers. Most of the females had clinical and pathological stage I of tumour followed by stage III. (Shown in above Mentioned Table-I).

According to histological type, most of the females had surface epithelial tumors 307(87.71%), followed by sex cord-stromal tumours 20(5.7%) and germ cell tumors tumors 19(5.43%) respectively (Figure).

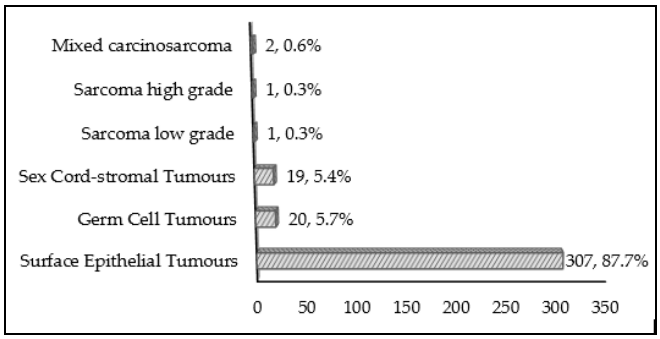

Figure: Frequency Distribution of Histological Types of Ovarian Cancer (n=350)

The distribution of various histological subtypes of ovarian cancer are displayed in Table-II.

According to age distribution, more than half of the patients were of middle age (54.1%) followed by Adults (29.4%) and old age (14.3%). Only 2% of the patients were in childhood to adolescence category. Among the patients with surface epithelial tumours, 58.5% were of age 40-60 years and 25.5% were of age 18-40 years. Among germ cell tumors, most of the patients were adults (45%) and 40% were middle age. Among sex cord-stromal tumours, 1 patient was in adult age group and 1 patient was in middle age group whereas 2 patients belonged from old age. The statistically significant difference was observed between frequency of histological types and age (p<0.05). (Table-III).

The statistically significant difference was observed in frequency of subtypes of ovarian cancer with respect to age (p<0.05). The serous high grade was the most frequent subtype and among them most of the patients were of middle age (69%). The second and third most frequent subtypes were endometrial high grade and mucinous high grade. Among endometrial high grade, majority of the females were of middle age (43.3%) whereas in mucinous high grade, most of the females were adults (43.3%). The distribution of all subtypes of ovarian cancer with respect to age is given in Table-IV.

Table-II: Frequency Distribution of Histological Subtypes of Ovarian Cancer (n=350)

Histological type	Subtype	n(%)
Surface Epithelial Tumours	Serous high grade	174(49.7%)
	Serous low grade	24(6.9%)
	Serous borderline tumor	10(2.9%)
	Clear cell carcinoma	9(2.6%)
	Endometroid high grade	30(8.6%)
	Endometroid low grade	4(1.14%)
	Mucinous high grade	30(8.6%)
	Borderline mucinous tumor	13(3.7%)
	Mucinous low grade	3(0.9%)
	Small cell carcinoma	1(0.3%)
	Squamous cell carcinoma	2(0.6%)
	Seromucinous	5(1.4%)
	Serous papillary carcinoma high grade	1(0.3%)
	Invasive papillary carcinoma	1(0.3%)
Germ Cell Tumours	Yolk sac tumor	4(1.14%)
	Mixed germ cell tumor	5(1.4%)
	Dysgerminoma	9(2.6%)
	Malignant mixed mullerian tumor	1(0.3%)
Sex Cord-stromal Tumours	Adult granulosa cell tumor	15(4.3%)
	Juvenile granulosa cell tumor	2(0.6%)
	Sertoli-leydig cell	2(0.6%)
	Neuroendocrine tumor of ovary	1(0.3%)
Others	Sarcoma low grade	1(0.3%)
	Sarcoma high grade	1(0.3%)
	Mixed carcinosarcoma	2(0.6%)

Table-III: Relationship Between Age and Histological Types (n=350)

Age groups	Surface Epithelial Tumours	Germ Cell Tumours	Sex Cord-stromal Tumours	Others	*p*-value
0-18 years (Childhood to adolescence)	3(1%)	2(10%)	2(10%)	0	0.0001
18-40 years (Adult age)	78(25.5%)	15(75%)	9(45%)	1(25%)	
40-60 years (Middle age)	179(58.5%)	2(10%)	8(40%)	1(25%)	
>60 years (Old age)	46(15%)	1(5%)	1(5%)	2(50%)	

Table-IV: Relationship Between Age and Histological Subtypes (n=350)

Histological Types	Subtype	0-18 years (Childhood-adolescence)	18-40 years (Adults)	40-60 years (Middle age)	>60 years (Old age)	*p*-value
Surface Epithelial Tumours	Serous high grade	0	27(15.5%)	120(69%)	27(15.5%)	0.001
	Serous low grade	0	8(33.3%)	12(50%)	4(16.7%)	
	Serous borderline tumor	1(10%)	7(70%)	2(20%)	0	
	Clear cell carcinoma	0	2(22.2%)	7(77.8%)	0	
	Endometroid high grade	0	8(26.7%)	13(43.3%)	9(30%)	
	Endometroid low grade	0	2(50%)	2(50%)	0	
	Mucinous high grade	2(6.7%)	13(43.3%)	11 (36.7%)	4(13.3%)	
	Borderline mucinous tumor	0	6(46.2%)	6(46.2%)	1(7.7%)	
	Mucinous low grade	0	2(66.7%)	1(33.3%)	0	
	Small cell carcinoma	0	1(100%)	0	0	
	Squamous cell carcinoma	0	1(50%)	1(50%)	0	
	Seromucinous	0	1(20%)	3(60%)	1(20%)	
	Serous papillary carcinoma high grade	0	0	1(100%)	0	
	Invasive papillary carcinoma	0	0	0	1(100%)	
Germ Cell Tumours	Yolk sac tumor	0	3(75%)	1(25%)	0	0.001
	Mixed germ cell tumor	1(20%)	3 (60%)	1(20%)	0	
	Dysgerminoma	1(11.1%)	8(88.9%)	0	0	
	Malignant mixed mullerian tumor	0	0	0	1(100%)	
Sex Cord-stromal Tumours	Adult granulosa cell tumor	0	8(53.3%)	6(40%)	1(6.7%)	0.028
	Juvenile granulosa cell tumor	1(50%)	1(50%)	0	0	
	Sertoli-leydig cell	1(50%)	0	1 (50%)	0	
	Neuroendocrine tumor of ovary	0	0	1(100%)	0	
Others	Sarcoma low grade	0	1(100%)	0	0	0.999
	Sarcoma high grade	0	0	0	1(100%)	0.999
	Mixed carcinosarcoma	0	1(50%)	1(50%)	0	0.999

DISCUSSION

With the unfortunate reality of increasing incidence of ovarian cancer globally, it is imperative to conduct in-depth research in this context. The clinic pathological findings in the current study regarding ovarian cancer reports that only 48 cases out of 348 had a positive family history of cancer including breast cancer, ovarian cancer and other cancers. Despite of the fact that family history is an important risk factor,[11] one more study reported similar findings in Sudanese.[12] The mean age of patients at presentation was 44.27±12.7 years. The results are contradictory to other study by Wentzensen in 2016, where in ovarian cancers are presented in ≥63 years of age.[13] However, in an Indian.[14] and Pakistani study.[15] the results are in agreement with present findings with regards to mean age. Hence, it can be said that western population has higher risk of developing cancer at older age as compare to Asian population.

In the present study of 348 ovarian tumours, surface epithelial tumours comprised of the bulk (87.7%, 308 cases) in the pie chart followed by germ cell tumours consisting of 19 cases (5.43%). The results are in concurrence with numerous studies conducted in different parts of the world 16-20. However, the results followed same sequence of histological whereas the percentages were different due to different sample size. The most common tumour originating from surface epithelium was high grade serous tumour consisting of 49.71% cases. A study conducted by Hala M *et al*.[21] Reported cases similar results in terms of epithelial tumours 41 cases (62%). However, it showed slight disagreement between ranking of sex cord stro-mal cells (17 cases (25.7%) and germ cells tumours 8(12%) which is similar to one Pakistani study.[22] Overall, in comparison with United states, a higher incidence of epithelial tumours has been reported.[23]

Overall, ovarian tumours were found in the age range between 14-92 years in the present study. Between childhood to adolescent i.e. until 18 years, 2 cases were reported having germ cell (mixed germ cell & dysgerminoma) and sex cord stromal tumour (juvenile granulosa cell tumour & sertolileydig cell tumour) whereas 3 cases was reported to have epithelial tumour having serous borderline and mucinous high grade tumour. However, the other study reported teratoma 2 years 24 and germ cell tumour was found common among children.[12] Similarly, in a Pakistani study, mature cystic teratoma, serous cystic adenoma and mucinous cyst adenoma was reported in cases having upto 20 years of age 22. The present study showed that most of the tumours occurred in between 10-60 years of age and surface epithelial tumours were at peak in between these ages. However germ cell tumour mostly occurred in between 18-40 years. The findings are in concurrence with three studies conducted in 2015 and 2018.[12,22,25]

CONCLUSION

It is concluded that age is an important factor in determining risk of developing various different types of ovarian cancers. The result showed that most commonly presenting ovarian cancer is originate from surface epithelium and is serous in nature which is a common finding in between 18-60 years of age. By knowing the histopathology of ovarian cancer, the management becomes more specific according to individual. Therefore, screening and histological analysis is of utmost importance.

Conflict of Interest: None.

Author's Contribution

Following authors have made substantial contributions to the manuscript as under:

PK & GH & HP: Data acquisition, data analysis, concept, drafting the manuscript, critical review, approval of the final version to be published.

MH & RK & AH: Study design, drafting the manuscript, data interpretation, critical review, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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