A prospective study of risk factors and histopathological spectrum of patients with ovarian tumors admitted in a tertiary care hospital

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Abstract:

Objectives: This prospective study was conducted to evaluate risk factors and histopathological spectrum of patients with ovarian tumors. **Methods**: This study was conducted in NSCB Medical College, Jabalpur from February 2019 to July 2020 on 120 subjects with ultrasonographically diagnosed ovarian tumors. Relevant history was obtained and all the risk factors for ovarian tumors were recorded. Gynecological examination was done and investigations were recorded. Subjects followed upto collection of histopathological report and correlation of various risk factors with histopathology done. **Results**: Out of 120 subjects, malignant and benign ovarian tumors were 39.16% and 60.83% respectively. The mean age of patients with benign ovarian tumor was 40.5 years and for malignant tumor was 45.5 years. The risk factors that were found associated with ovarian malignancy were early menarche (55.31%), late menopause (66.66%), history of infertility (55.31%), history of laparotomy for ovarian tumors (25.53%), family history of ovarian (46.80%) and breast cancer (4.25%). Majority of patients with benign (82.19%) as well as malignant ovarian tumors (52.57%) were not having history of tubal ligation. Benign serous cystadenoma was the commonest histopathological pattern in the present study contributing to 27.5% (33 cases). Among malignant tumors serous cystadenocarcinoma was the most common type accounting for 20% (24 cases), followed by mucinous carcinoma 13.3% (16 cases). **Conclusion**: Identification of risk factors for ovarian cancer is essential for prevention, early diagnosis and treatment of ovarian tumors because this cancer is predominantly detected at late stages when treatment is difficult. Determination of various histopathologic patterns of ovarian tumors helps in diagnosis, management as well as prognosis of ovarian tumors.

Keywords: Ovarian tumor, risk factors, histopathological types.

Ovarian malignancy is the most common gynecological cancer in females after breast and cervical carcinoma in India as well as worldwide.[1] It is second most common cancer of the female reproductive system and the leading cause of the death from gynaecologic malignancy.[2]

There are various risk factors associated with ovarian cancer. It mostly affects postmenopausal women, where increasing age is associated with an increased incidence, advanced stage of this disease, and lower reported survival

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rates. Parity poses a protective role according to a few case-control studies.[3] The strongest risk factor of ovarian cancer is a positive family history of breast or ovarian cancer, whereas personal history of breast cancer also augments the risk.[4] Increasing parity, lactation, oral contraceptive use, tubal ligation, and hysterectomy seem protective, while infertility may be associated with higher risk.[5] The identification of risk factors for patients with ovarian tumors enable us to supplement patient follow-up with various screening methods. Identification of modifiable risk factors for ovarian cancer is essential for prevention because this cancer is predominantly detected at late stages when treatment is difficult.

Most of these cancers (>80%) are epithelial in nature and among epithelial tumors, most common variety is serous cystadenoma.[6] Broadly the ovarian tumors are classified into primary and secondary tumors. Surface epithelial stromal tumors, germ cell tumors and sex cord stromal tumors are more common among the primary tumors of the ovary. The peak incidence of invasive epithelial ovarian cancer is at about 60 years of age and for borderline tumors, it is approximately 46 years. In the first two decades of life, almost 70% of ovarian tumors are of germ cell origin, and one-third of these are malignant. These are rapidly growing tumors.[7] Aggressive debulking surgery, followed by platinum-based chemotherapy, usually results in clinical remission. But, up to 80 percent of these women will develop a relapse that leads to disease progression and death.[8] To analyse the risk factor for different histopathologic types of ovarian cancer we have conducted prospective study on 120 subjects diagnosed to be ovarian tumor in ultrasound.

Materials and methods

This prospective observational study was conducted in Netaji Subhash Chandra Bose Medical College, Jabalpur (MP) from February 2019 to July 2020. Approval from institutional ethics committee was obtained. Total 120 subjects were included in study.

Inclusion criteria: All subjects with ultrasonographical diagnosis of ovarian tumors included.

Exclusion criteria: Pelvic masses other than ovarian tumours, functional, inflammatory and metaplastic ovarian cyst excluded.

Verbal consent was obtained from study subjects and were evaluated according to relevant history, high risk factors for ovarian tumors and demographic characteristics. Clinical evaluation, gynecological examination, ultrasonography, biochemical profile and other relevant investigations were done for the subjects. Out of 120 cases, 118 underwent laparotomy and 2 patients were not fit for laparotomy so they were subjected to fine needle aspiration cytology which turned out to be malignant. Surgical staging was done in cases with operable malignant ovarian tumors. Subjects followed up upto collection of histopathological report and high risk factors were correlated.

Statistical analysis: Compiled data was statistically analysed using Chi Square test and /or Fischers exact test to compare 2×2 contingency distribution as appropriate and ROC analysis was performed to predict benign and malignant ovarian tumors. $P<0.05$ was considered statistically significant. All statistical calculations were done with SPSS Statistics version 20.0.

Results

Total 120 cases of sonographically confirmed ovarian tumors were studied. 39.16% were malignant and 60.83% were benign neoplasms. The mean age of patient with benign ovarian tumor was 40.5years and for malignant tumor was 45.5 yr. This study shows no correlation of ovarian malignancy with parity of female and residence. Majority of the patients with malignant ovarian tumors were in postmenopausal age group (75%) and only 25% of patients with benign ovarian tumors were in postmenopausal age group ($p<0.0001$). Early menarche i.e. menarche at less than 12 years was found in 55.31% of malignant ovarian tumor cases and 73.97% of benign ovarian tumors ($p=0.034$) (table 1).

Table 1: Correlation of high risk factors with histopathological report of ovarian tumors			
Parameters	**Benign (n=73)**	**Malignant (n=47)**	**P value**
Age of menarche (years)	<12 - 54 (73.97%) >12 - 19 (26.02%)	<12 - 26 (55.31%) >12 - 21(44.68%)	0.034
Regularity of menstrual cycle	Regular - 67 (91.78%) Irregular - 6 (8.21%)	Regular - 40 (85.10%) Irregular - 7 (14.89%)	0.251
Age of menopause (years) n=40	<50 - 9 (90%) >50 - 1(10%)	<50 - 10 (33.33%) >50 - 20 (66.66%)	0.003
Parity	Nulliparous - 21(28.76) Primiparous - 9(12.32) Multiparous - 43(58.90)	Nulliparous - 11(23.40) Primiparous - 5(10.63) Multiparous - 31(65.95)	0.737
History of infertility	Yes - 5 (6.84%) No - 68 (93.15%)	Yes - 26 (55.31%) No - 21 (44.68%)	<0.0001
History of laparotomy for ovarian tumors	Yes - 5 (6.84%) No - 68 (93.15%)	Yes - 12 (25.53%) No - 35 (74.46%)	0.004
Family history of breast or ovarian cancer	Family history of ovarian cancer - 4 (5.47%); Family history of breast cancer - 1 (1.36%); No family history of breast or ovarian cancer - 68 (93.15%)	Family history of ovarian cancer - 22 (46.80%); Family history of breast cancer - 2 (4.25%); No family history of breast or ovarian cancer – 23 (48.93%)	<0.0001
Tubal ligation	Yes - 13 (17.80%) No - 60 (82.19 %)	Yes - 19 (40.42%) No - 28 (59.57%)	0.006

Late menopause i.e. menopause after 50 years of age was present in 66.66% of postmenopausal patients with malignant and 10% of postmenopausal patients with benign ovarian tumors (p=0.003). History of infertility was present in 55.31% of patients with malignant and 6.84% of patients with benign ovarian tumors (p=0.0001). Total 25.53% of patients with malignant and 6.84% of patients with benign ovarian tumors have history of laparotomy for ovarian tumors (p=0.004). Family history of ovarian cancer was seen in 46.80% of patients with malignant and 5.47% of patients with benign ovarian tumors (p=0.0001). Total 4.25% of patients with malignant and 1.36% of patients with benign ovarian tumors had family history of breast cancer (p=0.0001). Personal history of breast cancer was not seen in any study subjects. It is seen in our study that 8.19% of patients with benign ovarian tumors and 59.57% of malignant ovarian tumors were not having history of tubal ligation (p=0.006).

Figure 1: Histological distribution of ovarian tumors

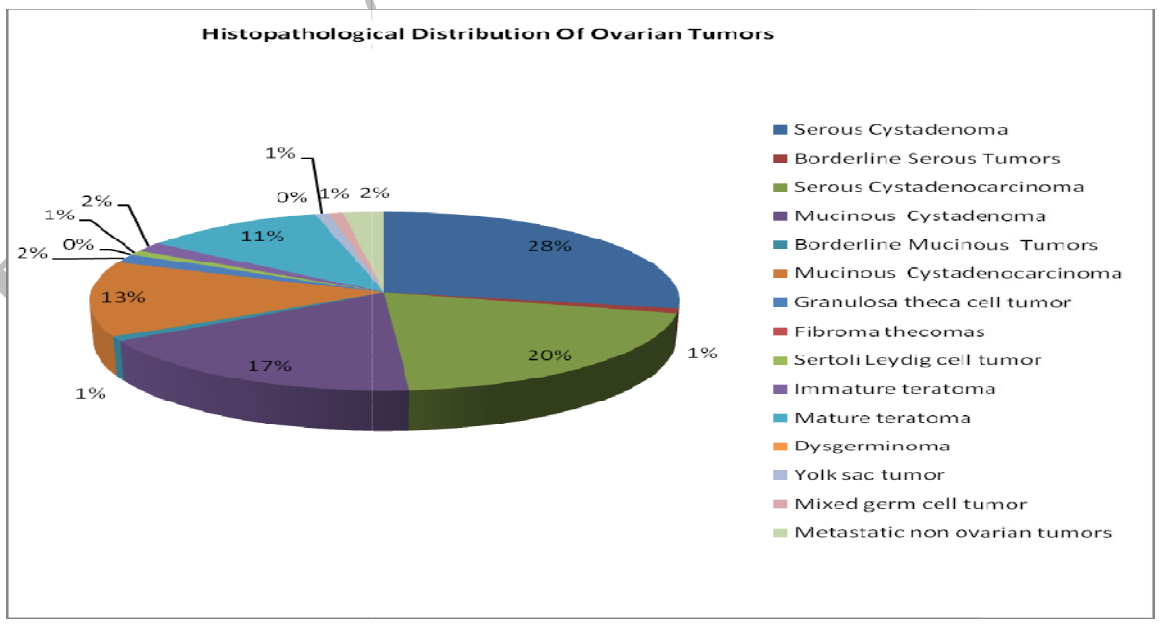

Table 2: Histopathological spectrum of ovarian tumors			
Histopathological Diagnosis	**Nature of tumor**	**Types**	**No (%)**
Surface epithelial stromal tumors	Serous	Benign	33(27.5)
		Borderline	1 (0.83)
		Malignant	24(20)
	Mucinous	Benign	21 (17.5)
		Borderline	1 (0.83)
		Malignant	16(13.33)
	Endometriod		0
	Transitional cell tumors (Brenner tumor)		0
	Epithelial stromal (Adenosarcoma)		0
Sex cord stromal tumor	Granulosa theca cell tumor		2 (1.66)
	Fibroma thecomas		1 (0.83)
	Sertoli Leydig cell tumor		1 (0.83)
	Other sex cord stromal tumors		0
Germ cell tumor	Immature teratoma		2 (1.66)
	Mature teratoma		13 (10.83)
	Dysgerminoma		0
	Yolk sac tumor		1 (0.83)
	Mixed germ cell tumor		1 (0.83)
Metastatic non ovarian tumors			3(2.5)
Total			120

Benign serous cystadenoma was the commonest histopathological pattern in the present study contributing to 27.5% (33 cases). Mucinous cystadenoma was the second most common contributing to 17.5% (21 cases) (table 2). Among malignant tumors serous cystadenocarcinoma was the most common type accounting for 20% (24 cases), followed by mucinous carcinoma 13.3% (16 cases) (figure 1).

Discussion

Ovarian cancer is one of the most common gynecological cancer that rank third after cervical and breast cancer. It has worst prognosis and highest mortality rate. It is predicted that, by the year 2040 the mortality rate of this cancer will rise significantly. It is a silent killer as it is diagnosed late. The statistics show that between one third to two fifth of total cancer cases can be prevented by eliminating and reducing risk factors.[9] This study was conducted with aim of studying high risk factors present in patients with ovarian tumors and correlate with histopathology report.

In the present study, out of 120 cases of ovarian tumors, 39.16% were malignant and 60.83% were benign neoplasms. The mean age of patient with benign ovarian tumor was 40.5 years and for malignant tumor was 45.5 yr. These findings were comparable with the study done by Radhamani S et al [10] in which mean age for benign ovarian tumors was 40.80 years but mean age for malignant ovarian tumors was 55.1 years indicating that malignant ovarian tumors are more prevalent in older age group as compared to benign ovarian tumors.

Present study shows no correlation of ovarian malignancy with low parity of females which was consistent with the study conducted by Dweep Jindal et al[11] which showed increasing parity did not have decreased incidence of ovarian cancer. Although nulliparity or low parity is a known high risk factors for ovarian tumors.

Out of 120 cases, total postmenopausal patients were 40, in which 10 patients had benign ovarian tumors and 30 patients had malignant ovarian tumors respectively. Majority of malignant ovarian tumors were in the postmenopausal females. The findings in our study are consistent with Mojgan Karimi Zarchi et al[12] who found that in pre-menopausal patients 12% had malignant tumors and 61% had benign tumors, while out of 54 post-menopausal patients, 33 had malignant tumors and 21 had benign tumors. It concludes that postmenopausal women are more likely to have ovarian cancer.

No significant association was found between residence and risk of ovarian tumor. This finding in our study is consistent with Jihye Park MSPH et al.[13]

Cut off value of menarche taken as 12 years. In the present study there were 80 cases (66.66%) of ovarian tumors who have menarche <12 years and amongst the malignant ovarian tumor cases, 55.31% attained menarche at less than 12 years. Findings in our study were comparable to the study by Ting-Ting Gong et al[14] who reported inverse associations between age at menarche and ovarian cancer risk.

53.84% of malignant ovarian tumors were presented with irregular menstrual cycles though it was not found statistically significance whereas Piera M Cirillo et al found higher risk for women with irregular cycles and increase in mortality over the 50-year follow-up.[15] These findings are not consistent with our study.

Majority of patients with malignant ovarian tumors (66.66%) have their menopause after 50 years of age. Majority of patients with benign ovarian tumors (90%) have their menopause before 50 years of age. Findings of our study are similar to Hankinson et al and Danforth et al (2006).[16] This shows that late menopause is a high risk factor for malignant ovarian tumors.

Out of 31 cases that presented with history of infertility and ovarian masses, 83.87% patients had malignant ovarian disease; rest 16.1% patients had benign ovarian mass. There is increased risk of malignancy associated with history of infertility according to the present study. The findings of our study are consistent with Yu-Ting Jiang et al [17] who suggested that infertility in women is associated with a 51% increased risk of ovarian cancer.

In our study, 17 cases had history of surgery for removal of ovarian tumor, out of which 70.58% cases developed ovarian malignancy and 29.41% developed benign ovarian tumor. It was to be highly significant in our study (p <0.0001). It is also seen in study done by Chen-Yu Huang et al.[18]

Out of 26 cases of ovarian cancer who had family history of ovarian cancer 84.61% cases (n=22) developed malignant ovarian tumor. This finding is also proved to be significant in study of Hsiao-Mei Lu et al and La Vecchia et al in which there is a strong association with a family history of ovarian cancer.[19, 20]

Out of 3 patients who had family history of breast cancer 66.66% cases developed ovarian malignancy. It is similar to findings of Neely Kazerouni et al [21] who found that breast cancer in a first- or second-degree relative was associated with increased risk of ovarian cancer (RR = 1.4; 95% confidence interval; CI = 1.1–1.7).

Tubal ligation decreases the risk of ovarian malignancy. It is seen in our study also as most of benign ovarian tumors (82.19%) as well as malignant ovarian tumors (59.57%) not having history of tubal ligation. The study by MS Poornima et al also showed that previous tubal ligation/salpingectomy reduces the risk of developing epithelial ovarian carcinoma which is consistent with our study.[22]

The ovarian tumors were classified according to WHO classification. In our study, surface epithelial- stromal tumors comprised the largest group of tumors constituting 96 cases. Germ cell tumors were the second largest group and comprised 17 cases. There were 4 cases of sex cord stromal tumors and 3 cases of metastatic tumor. Benign serous cystadenoma was the commonest histopathological pattern in the present study contributing to 27.5% (33 cases). Mucinous cystadenoma was the second most common contributing to 17.5% (21 cases). Similar findings were observed by Mukut Jyoti Das et al, Kanthikar SN et al, Sharma I et al and Prakash A et al where serous cyst adenoma was found in 41.89%, 35.71% , 34% and 64.5% respectively [23-26].

Among malignant tumors serous cystadenocarcinoma was the most common type accounting for 24% (20 cases), followed by mucinous Carcinoma 13.33% (16 cases which is similar to Kanthikar SN et al (8.57%) and Sharma I et al (12.74%) [24, 25] in which serous cystadenocarcinoma was the most common among malignant ovarian tumors.

Among the germ cell tumors, maximum number of cases were of mature cystic teratoma 10.83% (13 cases) followed by immature cystic teratoma 1.66 % (2 cases). There was 1 case of yolk sac tumor and 1 case of mixed germ cell tumor (dysgerminoma + yolk sac tumor). Among the sex cord stromal tumors there are 2 cases of

granulosa cell tumor 1.66%, 1 case of fibroma (0.83%), 1 case of sertoli leydig cell tumor. Among the metastatic tumors there are 3 cases of Krukenberg tumor reported in our study.

Limitations of study: Follow up could not be done of these patients because of limited time duration of study. In further studies, we will include the follow up.

Conclusion

This study provides significance evidence about increased risk of ovarian malignancy in females with early menarche, late menopause, history of infertility, history of laparotomy for ovarian tumors, family history of ovarian and breast cancer and decreased risk of ovarian malignancy was seen in patients with history of tubal ligation. Our present study concludes that identification of risk factors for ovarian cancer is essential for prevention, early diagnosis and treatment of ovarian tumors because this cancer is predominantly detected at late stages when treatment is difficult. Determination of various histopathologic patterns of ovarian tumors helps in diagnosis, management as well as prognosis of ovarian tumors. Considering the heavy burden and the fatal outcome of ovarian malignancies, preventive measures, health education and early detection in high risk group is recommended.

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