World Cancer Research Journal WCRJ 2023; 10: e2555

CLINICO-PATHOLOGICAL AND EPIDEMIOLOGICAL SPECTRUM OF OVARIAN CANCER IN KASHMIR: A RETROSPECTIVE CASE CONTROL STUDY

S. SHABIR[1], A. ASIAF[2]

[1]Centre for Interdisciplinary Biomedical Research, Adesh University, Bathinda, India
[2]Department of Clinical Biochemistry, GCW, Cluster University of Srinagar, Srinagar, India

Abstract – *Objective:* *Ovarian cancer is the most dreadful gynecological malignancy among females worldwide, with worst prognosis and non-effectiveness of its screening markers yielding false negative cases. The aim of the present study was to investigate the clinicopathological and epidemiological profile of ovarian cancer patients in Kashmir ethnicity.*

Patients and Methods: *The present observational cross-sectional study was conducted on 50 ovarian cancer patients who reported to the Department of General Surgery and Medical Oncology, SKIMS, Srinagar, from 2017 to 2019 and on 50 healthy female volunteers as age-matched controls. The clinicopathological and epidemiological profiles of the ovarian cancer patients were compared with those of normal controls. A detailed description of clinico-pathological, epidemiological, and etiological data was obtained from the in-patient record and questionnaire method and analyzed by Student's t-test to estimate statistically significant differences between cases and controls. The blood samples were assessed for CA-125 levels.* $p \geq 0.05$ *differences were considered statistically significant.*

Results: *Of the 50 ovarian cancer patients, the most affected (48%) age group was 44–59 years. The majority (64%) of the patients belonged to stages III and IV of the disease. Abdominal distension and pelvic pain were the most frequent symptoms observed in 46% and 44% of cases, respectively. Using Pearson's correlation coefficient, we observed a significant negative correlation of risk of ovarian cancer with menarcheal age and a highly significant positive correlation with menopausal age, age at marriage, BMI, and CA125 in ovarian cancer patients.*

Conclusions: *Most of the patients presented in an advanced stage of the disease and had CA125 levels of 500 U/ml. Awareness must be raised among women regarding the symptoms, warning signs, and risk factors of ovarian cancer because doing so will facilitate the early diagnosis of the disease.*

KEYWORDS: *Ovarian cancer, Clinicopathological, Kashmir, Epidemiology, CA-125.*

INTRODUCTION

Among different gynaecological cancers, ovarian cancer (OC) is one of the most mysterious malignancy and the second leading cause of mortality in females all over the world [1]. According to global research published by the International Federation of Gynaecology and Obstetrics (FIGO), the prevalence of OC is increasing in younger women, although various investigations have outlined menopausal women as being the most affected group [2,3]. The reasons for the increased incidence of OC in younger women are controversial. Its uniqueness in enclosing unclear signs and symptoms in early as well as advanced stages, a non-reliable screening tool, and no known premalignant

DOI: 10.32113/wcrj_20235_2555

Corresponding Author: Asia Asiaf, MD; e-mail: asiaf29@gmail.com

stage underscores the importance of identifying risk factors for early diagnosis, prevention, and perhaps a step towards illustrating its aetiology [4].

Worldwide, OC is the 8th most common cancer, constituting 3.4% of all female cancers, and the eighth leading cause of cancer death, constituting 4.7% of all cancer-related deaths across all sites [5]. In India, OC is estimated to be the third most common cancer among women, constituting 6.6% of all cancer cases among females [6]. In Kashmir, data collected from population-based cancer registries between 2010 and 2018 registered 1,019 (2.94%) incident cases of OC with a mean age of 50 ± 12.85 years [7].

The risk factors for OC are ambiguous, and the proper understanding of the aetiology has remained elusive [8]. The increase in the OC risk is attained by the repeated exposure to the acute pro-inflammatory environment over the reproductive years of females, radiation and asbestos exposure, familial predisposition to ovarian and/or breast cancer, red meat consumption, hormone replacement therapy, an increase in the Body Mass Index (BMI), increasing age, and nulliparity [9, 10]. These risk factors act as 'increasing mediators' for OC.

The OC is considered the "silent killer" due to its asymptomatic nature. It is a prerequisite to have an efficient screening technique for the early detection of this deadly asymptomatic neoplasm, which must be of high sensitivity and specificity [11]. Transvaginal sonography (TVS) and the Cancer Antigen 125 (CA125) marker are the tools that are widely used for the detection of this fatal disease [12].

In Kashmir, only a handful of published studies have evaluated the clinicopathological characteristics of OC patients [7,13]. Therefore, the aim of the present study was to evaluate the clinico-pathological and demographic profiles of OC patients in Kashmir. The study might help a large subset of young females to understand the complexity and early detection of this dreadful disease, which may eventually lead to proper management and a good outcome, therefore preserving their fertility.

PATIENTS AND METHODS

Study design and setting

This observational cross-sectional study was conducted on 50 OC patients , admitted and treated in the Department of General Surgery and Medical Oncology, SKIMS, Soura, Srinagar, from 2017 to 2019, and 50 controls. The control group consisted of 50 healthy female volunteers. Controls were age-matched to samples from patients with Stage 1- 4 OCs.

Study Participants and Eligibility Criteria

An informed written consent was obtained from all the enrolled participants in their local language before their enrollment in the present study. Inclusion criteria for cases were as follows: (a) patients with complete histological documentation; (b) known surgery information; (c) both operated and non-operated patients; (d) patients without any cardiac complications; (e) patients eligible for neoadjuvant treatment or inoperable; (f) patients metastatic at presentation; and (g) patients mentally fit to give informed consent. Exclusion criteria were (a) patients identified with tubo-ovarian masses, pelvic inflammatory disease (PID), and ectopic pregnancies on ultrasound; (b) Patients whose specimen turned out to be benign on histopathological examination.

Assessment measures and data recording

After proper counseling and using the questionnaire method, socio-demographic parameters like age (in years), area of residence, educational status, occupation, age at marriage, and number of marriages were taken from participants, along with risk factors like familial history, contraception, parity, menarcheal age, weekly aerobic physical activity, sleeping pattern, menopausal age, diet pattern, smoking history, parity, and BMI.

Assays

Peripheral blood samples were obtained from all controls and all the cases for the measurement of CA125 concentrations. The concentrations of CA125 were measured and confirmed by a one-step Sandwich Immunoassay (Biogenix Cancer Antigen-125 Kit). A CA125 concentration of 35 U/ml was defined as abnormal.

Statistical analysis

The results of the present study were reported as a mean standard deviation. The Student's *t*-test was used to estimate statistically significant differences between groups. $p \geq 0.05$ differences will be considered statistically significant. When the test yielded $p \geq 0.05$, the relevant data was considered to be statistically significant.

RESULTS

Demographic characteristics

The present study included 50 OC patients and 50 healthy female volunteers from Kashmir, India. The distribution of OC patients and controls according to age is given in Table 1. The most affected age group of women with OC was 44-59 years, with a mean age of 47.56 ± 15.07. The least affected age groups were 75+ years and 15-29 years, accounting for 4% and 12% of all patients, respectively. There was a non-significant difference in mean age in OC patients (47.56 ± 15.07) as compared to the control group (48.02 ± 16.21). Most of the patients were from rural backgrounds, and the majorities had lower educational attainment and were housewives. Most of the patients were married (Table 2). As far as dwelling, marital status, educational attainment, and occupation are concerned; there was no statistically significant difference at $p \geq 0.05$ between the cases and controls.

Risk factors

All the cases and controls in the present study were non-vegetarians, and the differences in eating habits between the two groups were not significant. The results also showed that the majority of cases (52%) were overweight, followed by twenty-one cases (42%), which had normal weight, two cases (4%) were obese, and the least number of cases (2%) were underweight (18.5 kg/m^2). On the contrary, the majority of controls (78%) had normal weight, followed by six controls (12%) as overweight; four controls (8%) were underweight, and only one control (2%) was obese. The difference in the mean value of BMI (at the time of diagnosis) in cases as compared to controls was statistically significant (Table 3).

The present study also found only two cases and a control with a smoking habit, as smoking is uncommon among Kashmiri women, and there was no significant difference between the two groups. This finding is consistent with previous

TABLE 1. Distribution of ovarian cancer patients and controls according to age interval.

Age Interval (years)	Cases			Control			p- value
	Frequency		Mean	Frequency		Mean	
	Number	Percentage		Number	Percentage		
15-29	6	12%	47.56 ±	7	14%	48.02 ±	0.102
30-44	1	22%	15.07	10	20%	16.21	
45-59	24	48%		21	42%		
60-74	7	14%		9	18%		
75+	2	4%		3	6%		
Total	**50**	**100%**	-	**50**	**100**	-	-

TABLE 2. Distribution of ovarian cancer patients and controls according to demographic parameters.

Variables	Characteristics	Cases		Controls		χ^2	p-value
		Frequency		Frequency			
		Number	Percentage	Number	Percentage		
Area	Rural	34	68%	32	64%	0.06	**0.80**
	Urban	16	32%	18	36%	0.12	**0.73**
Marital status	Married	46	98%	46	98%	0	**1**
	Single	4	2%	4	2%	0	**1**
Education	Illiterate	34	68%	30	60%	0.25	**0.61**
	≤ High school	5	10%	6	12%	0.90	**0.34**
	≥Higher secondary school	11	22%	14	28%	0.36	**0.54**
Occupation	Student	3	6%	5	10%	0.50	**0.47**
	Govt. employee	2	4%	1	2%	0.33	**0.56**
	Working	14	28%	16	32%	0.13	**0.71**
	Housewife	31	62%	28	56%	0.15	**0.69**
Total		50	100%	50	100%	-	-

TABLE 3. Distribution of ovarian cancer patients and controls according to the risk factors.

Variables	Characteristics	Cases		Controls		χ^2	p-value
		Frequency		Frequency			
		Number	Percentage	Number	Percentage		
Diet pattern	Non-vegetarian	50	100%	50	100%	0	**1**
BMI (kgm^{-2}) at the time of diagnoses	Underweight (<18.5) kgm^{-2}	1	2%	4	8	1.8	**0.179**
	Normal (18.5-24.9) kgm^{-2}	21	42%	39	78	5.4	**0.02**
	Overweight (25-29.5) kgm^{-2}	26	52%	6	12	12.5	**0.00**
	Obese (≥30) kgm^{-2}	2	4%	1	2	0.33	**0.56**
Mean		**27.60 ± 3.68**		**22.64 ± 3.27**		-	
Smoking habit		2	4%	1	2%	0.34	**0.55**
Familial predisposition		14	28	3	6	7.12	**0.00**
Parity	Nullparity	5	10.9%	3	6.5%	0.50	**0.47**
	Uniparity	10	21.7%	9	19.6%	0.05	**0.82**
	Multiparity	31	67.4%	34	73.9%	0.14	**0.70**
Contraception		8	16%	11	22%	0.47	**0.49**
Age at menarche (years)	<10 years	7	14%	5	10%	0.32	**0.57**
	10-15 years	33	66%	34	68%	0.01	**0.92**
	>15 years	10	20%	11	22%	0.04	**0.84**
Age at menopause	40-45 years	7	28%	11	44%	0.89	**0.34**
	46-50 years	18	72%	14	56%	0.50	**0.47**
	>51 years	0	0%	0	0%	-	
Total	50	100%	50	100%	-		

studies that have reported low rates of smoking among women in the Kashmir Valley [14]. However, future studies with larger sample sizes may be needed to confirm these results and explore potential differences in smoking behavior among subgroups of Kashmiri women. In the present investigation, the familial history of cases and controls up to third degree (3°) was taken into consideration. Of the 50 cases included in the present study, fourteen cases (28%) and of the 50 controls, three (6%) had a family predisposition to cancer. The differences between cases and controls were highly significant ($p \geq 0.05$). While elucidating the role of parity with OC, the present study found no significant difference in parity between the two groups. Also, non-significant differences in cases and controls were found while establishing the use of contraceptives between the two groups. In the present study, thirty-three cases (66%) and thirty-four controls (68%) had menarcheal ages between 10 and 15 years, followed by ten cases (20%) and eleven controls (22%), with menarcheal ages >15 years, and seven cases (14%), and five controls (10%), with menarcheal ages 10 years. A non-significant difference was reported in cases and controls with respect to menarcheal age.

Eighteen cases (72%) and fourteen controls (56%) in the present study had their age of menopause between 46 and 50 years, followed by seven cases (28%), and eleven controls (44%), having menopause at 40 to 45 years. The differences in the age of menopause between the cases and controls were also not significant.

Symptoms

The OC subjects differed significantly from the control group for all six symptoms except for the urinary complaints, which were similar in both groups (Table 4).

CA-125 tumour marker

All the cases and controls used for the present study were assessed for the CA125 U/ml marker. In the present investigation, 78% of the cases

TABLE 4. Distribution of ovarian cancer subjects and controls according to the symptoms.

Symptoms	Cases		Controls		p-value
	Frequency		Frequency		
	Number	Percentage	Number	Percentage	
Pelvic pain	22	44%	11	22%	**0.02**
Abdominal distention	23	46%	04	08%	**0.00**
Vaginal bleeding	07	14%	03	06%	**0.18**
Urinary symptoms	03	6%	02	04%	**0.65**
GI symptoms	10	20%	06	12%	**0.27**
Ascities	17	34%	02	04%	**0.000**
Leg edema	12	24%	01	02%	**0.00**
Total	50	100%	50	100%	-

TABLE 5. Distribution of ovarian cancer patients and controls according to CA125 (U/ml) value.

CA125 Value	Cases			Control			p- value
	Frequency		Mean 2599.33 ± 1909.85	Frequency		Mean 11.18 ± 5.44	
	Number	Percentage		Number	Percentage		
60 to >35 U/ml	4	8%		50	100%		
35-100 U/ml	6	12%		-	-		
101-299 U/ml	1	2%		-	-		
300-499 U/ml	4	8%		-	-		
≥500 U/ml	35	70%		-	-		
Total	**50**	**100%**	-	**50**	**100**	-	-

had a CA125 tumour marker value of ≥ 500 U/ml, and all controls reported a CA125 value between 0 and 35 U/ml, thus reporting a significant difference in the mean value of the CA125 tumour marker between the cases and controls (Table 5).

Diagnosed stage

The distribution of OC patients according to their diagnosed stage is shown in Table 6. The majority of cases (64%) belonged to stages III and IV of the disease at the time of presentation.

TABLE 6. Distribution of ovarian cancer patients according to their diagnosed stage.

Stage	Frequency	
	Number	Percentage
Stage I	8	16%
Stage II	10	20%
Stage III	14	28%
Stage IV	18	36%
Total V	**50**	**100%**

Distribution of OC patients according to their diagnosed stage and histological subtype

In the present study, the majority of cases had malignant pathologies at the time of presentation, as shown in Table 7. The distribution of OC patients according to their diagnosed stages and histolog-

TABLE 7. Classification of ovarian cancer patients based on the type's tumors.

Type of ovarian cancer	Frequency	
	Number	Percentage
Benign	3	6%
Malignant	36	72%
Borderline	1	2%
Granulosa	1	2%
Sertoli leydig cell tumor	2	4%
Fibroma	2	4%
Dysgerminoma	2	4%
Endometroid carcinoma	2	4%
Ovarian clear cell carcinoma	1	2%
Total	50	100%

TABLE 8. Distribution of ovarian cancer patients according to their diagnosed stage and histological subtype.

Stage	Benign	Malignant	Borderline	Granulosa	Sertoli ley dig cell tumor	Fibroma	Dysgerminoma	Endometroid cancer	Clear cell cancer
Stage I	3	3	0	1	1	0	0	0	0
Stage II	0	5	1	0	1	0	1	1	1
Stage III	0	13	0	0	0	0	0	1	0
Stage IV	0	15	0	0	0	2	1	0	0
Total	**3**	**36**	**1**	**1**	**2**	**2**	**2**	**2**	**1**

ical subtypes is shown in Table 8. Of the stage I cases, three cases each had benign and malignant tumours, one had granulosa, and one had a Sertoli-Leydig cell tumour. Of the stage II cases, five cases had malignancy; one was a borderline case, followed by a Sertoli-Leydig cell tumour (1 case), dysgerminoma (1 case), endometrial cancer (1 case), and clear cell cancer (1 case). Of the stage III cases, thirteen cases had malignant pathologies, and one was endometrial cancer. Of the stage IV cases, fifteen were malignant pathologies, followed by fibroma (2 cases) and dysgerminoma (1 case).

Aerobic activity and sleep pattern

An attempt to examine the weekly aerobic (physical) activity and sleeping pattern of OC patients prior to diagnosis and control was also done. The majority of cases (70%) and one control group (2%) had 1 hour of physical activity, with a highly significant difference between the two groups. The least number of cases (2%) and forty-three controls (86%) were observed with > 3 h of physical activity prior to diagnosis, with highly significant differences at $p \geq 0.05$ between the two groups, as shown in Table 10.

The sleeping pattern of OC patients was disturbed in forty cases (80% cases) and three controls (6%), and the differences between the two groups were significant. The normal circadian rhythm was reported in only ten cases (20%), as compared to forty-seven controls (94%). The differences between the two groups were significant, as shown in Table 10.

Correlation between the onset of OC and risk factors

The interrelationship of age, menarcheal age, menopausal age, BMI, and CA125 in OC patients as well as controls was worked out using Pearson's correlation coefficient (r). In OC patients, there was a significant negative correlation of age at diagnosis of OC with menarcheal age and a highly significant positive correlation with menopausal age, age at marriage, BMI, and CA125. There was a significant negative correlation between menarcheal age and BMI and CA125. Moreover, in OC patients, there was a significant positive correlation of age at marriage with BMI and CA125. There was a highly significant positive correlation between BMI and CA125 levels. In control group, there was a negative and non-significant correlation of age with menarcheal age and CA125, non-significant positive correlation with menopausal age and BMI. There was a non-significant negative correlation of menarcheal age with menopausal age, BMI and CA125 levels in a control group. In control group, there was a non-significant positive correlation of menopausal age with BMI and CA125. There was a non- significant negative correlation of BMI and CA125 in control group. The interrelationship among the above parameters is shown in Table 11.

TABLE 9. Distribution of ovarian cancer patients according to their diagnosed stage.

Treatment regime	Frequency	
	Number	Percentage
Total hysterectomy/ with bilateral salpingo-oophorectomy with Chemotherapy and/ or Radiotherapy	36	72%
Only operated	11	22%
Non-operated and non-treated (at the time of sample collection)	3	6%
Total	**50**	**100%**

TABLE 10. The aerobic activity and sleep pattern of ovarian cancer patients and control group.

Variables	*Characteristics*	*Cases*		*Controls*		χ^2	*p-value*
		Frequency		*Frequency*			
		Number	*Percentage*	*Number*	*Percentage*		
Weekly hours of (physical activity) prior to diagnosis	≤1 hour	35	70%	1	2%	32.10	0.00
	>1hr to ≤2 hr	12	24%	2	4%	7.14	0.00
	>2 hr to ≤3 hr	2	4%	5	10%	1.38	0.24
	>3 hr	1	2%	43	86%	40.08	0.00
Circadian rhythm	Good	10	20%	47	94%	20.12	0.00
	Poor	40	80%	3	6%	31.85	0.00
Total		**50**	**100%**	**50**	**100%**	-	

TABLE 11. Correlation between age, menarcheal age, age at marriage, menopausal age, BMI and CA125 in ovarian cancer patients and controls.

Ovarian cancer Controls	*Age (years)*	*Menarcheal age in years*	*Age at marriage in years*	*Menopausal age in yrs*	*BMI Kg/m²*	*CA125 U/ml*
Age (years)	-	**-0.274***	**0.598****	**0.270****	**0.285****	**0.301****
Menarcheal age	-0.124	-	-0.136	0.036	-0.114	-0.287*
Age at marriage	0.204	-0.136	-	0.049	**0.241***	**0.283***
Menopausal age	0.070	-0.116	0.078	-	0.066	0.146
BMI	0.092	-0.114	0.115	0.130	-	**0.321****
CA125	-0.030	-0.087	0.083	0.126	-0.024	-

DISCUSSION

In the present study, the most affected age group of women was 44–59 years, with a mean of 47.56 ± 15.07. There was a non-significant difference in mean age in OC patients (47.56 ± 15.07) as compared to the control group (48.02 ± 16.21). Our study is in concurrence with many other studies that also found that the risk of OC increases with ageing and peaks between 50 and 80 years of age [15,16].

In the present study, there were non-significant differences in the number of cases and controls hailing from rural and urban areas; however, the majority of OC patients were from rural backgrounds. Our findings are in line with a study by Li et al[17] who have shown that rural residents are at a higher risk of developing cancer as compared to urban ones, as urban residents get more privileges on healthcare benefits, medical services, and health education. The unaffordable and expensive medical expenditure results in a difference in healthcare utilization between the two groups. On the contrary, a study on the Utah population from the USA carried out by Park et al[18] reported 1,661 patients as a total number of women diagnosed with OC, among whom only 11.8% were from rural regions and had diverse characteristics as compared with metropolitan residents.

A plethora of studies has found the impact of marital status on cancer prognosis. In this study, we didn't find a significant impact of marital status on the incidence of OC. The results of the present study are in agreement with the study by Kvikstad et al[19] which reported that there was no statistically significant difference between 12,237 married and 14,667 unmarried OC cases when compared to 26,075 married and 27,688 unmarried controls. Wang et al[20] found that unmarried OC patients had a substantially higher risk of death after being diagnosed with OC.

While establishing the association of education and occupation with OC in the present study, the majority of cases and controls were illiterate and housewives, with non-significant differences between cases and controls. This outcome could be illustrated by the fact that housewives lack a longer duration of weekly aerobic activity (busy with house chores) and are less likely to have a high level of cancer awareness as compared to working and educated females. A study led by Khan et al[21] on 75 OC patients from Karachi reported 52% of patients as uneducated and 25.3% as above the higher secondary level, and concluded that uneducated women are at higher risk of getting OC due to their lack of understanding of the enormity of this disease. The results of the present study are in

concurrence with other studies also that reported that women with low education or who are uneducated are at higher risk of getting OC in their lifetimes [21,22].

All the cases and controls in the present study were non-vegetarians, and the differences in eating habits between the two groups were not significant. Many studies have found a decline in the risk of OC with an increase in the consumption of vegetables and fruits and an increase in OC risk in high meat eaters [23-25]. Therefore, it would be interesting to conduct further research with a larger sample size that includes vegetarians to better understand the relationship between dietary habits and OC risk. Additionally, it may be useful to investigate other lifestyle factors that could contribute to the development of OC. Moreover, the results of the present study are in discordance with studies reported above because the majority of the population of Jammu and Kashmir is non-vegetarian and the sample size of the study was too small to draw any conclusions.

In the present study, a statistically significant difference in the BMI was found between the cases and controls, indicating that increased BMI or obesity is a risk factor for OC. The results of the present study are in agreement with other studies [26,27]. According to the systematic analysis and review by Tzenios et al[28] and Del Pup et al[29] there is an indispensable role for effective management of BMI in decreasing the incidence and mortality rates in OC patients.

In the present investigation, the familial history of cases and controls up to third degree (3°) was taken into consideration. We found that the family history of OC is associated with increased OC risk, as there were significant differences between cases and controls. Similar findings were also observed in other studies [30-32].

While elucidating the role of parity in OC, the present study found no significant difference in parity between the two groups. On the contrary, a US-based epidemiological study conducted by Vachon et al[32] concluded that the increased risk of OC is seen in women with nulliparity as compared to parous women.

Also, non-significant differences in cases and controls were found while establishing the use of contraceptives between the two groups. Only 16% of the cases and 22% of the controls had taken oral contraceptives. The results of the present study are in disagreement with most of the studies, which concluded that the use of contraceptives reduces the risk of OC [33-35].

The majority of cases in the current study had their menarche between the ages of 10-15 years; however, no significant difference in menarcheal age was found between cases and controls. Our findings are inconsistent with many studies suggesting early menarche to be the high risk factor for OC [36,37].

The differences in the age of menopause between the cases and controls were not significant in our study. Our results are in line with the study conducted by Schildkraut et al[38] which reported a non-significant difference between the age at natural menopause and the risk of OC. However, another study conducted by Moorman et al[39] reported a significant association between the OC risk and early menopause (premenopause). As per incessant ovulation theory, an increase in the number of ovulatory cycles increases the chances of OC [40]. However, our study reported weak evidence regarding the association between OC risk and women with early menopause. Several reports have concluded that the natural menopause occurs in women between the ages of 40 and 46 in India, which can vary according to ethnicity [41,42].

The OC subjects differed significantly from the control group for all six symptoms except for the urinary complaints, which were similar in both groups. Abdominal distension and pelvic pain were the most frequent symptoms observed in 46% and 44% of cases, respectively. The results are in accordance with the study by Gajjar et al[10] in which abdominal swelling, followed by abdominal bloating, and pelvic pain were the highest scored symptoms. Another study by Olson et al[43] reported bloating, fullness, and abdominal pressure in 70% of cases and 9% of controls; abdominal pain in 52% of cases and 15% of controls; and a lack of energy (fatigue) in 43% of cases and in 16% of controls. The study investigated by Khan et al[21] included 75 OC patients, who reported abdominal pain (57.3%) to be the most common symptom, followed by abdominal distension (22.6%), urinary symptoms (5.3%), and vaginal bleeding (12%).

All the cases and controls used for the present study were assessed for the CA125 U/ml marker. Our present investigation reported a significant difference in the mean value of the CA125 tumour marker between the cases and controls. Our findings are consistent with many earlier studies[7,44,45].

The majority (64%) of cases belonged to stages III and IV of the disease and had malignant pathologies at the time of presentation, similar to the findings reported in other Indian studies[7,46,47]. Lack of proper screening tests, delayed referral by the primary care physician, and chronic symptoms mimicking other common ailments are reasons for the late stage of presentation in these patients.

An attempt to examine the weekly aerobic (physical) activity and sleeping patterns of OC patients and controls was also done. The duration of physical activity prior to diagnosis was significantly higher in controls compared with cases, indicating its effect on reducing the risk of OC, similar to the results reported by other studies[48,49].

Wang et al[50] observed a direct association between poor sleeping quality or disturbance and an increase in the risk of getting cancer. In this study, we observed that normal circadian rhythm (sleeping pattern) prior to diagnosis was reported in only ten cases (20%) as compared to forty-seven controls (94%), and the differences between the two groups were statistically significant.

Using Pearson's correlation coefficient, we observed a significant negative correlation of risk of OC with menarcheal age and a highly significant positive correlation with menopausal age, age at marriage, BMI, and CA125 in OC patients. Gong et al[51] found a statistically significant inverse association between menarcheal age and the risk of OC. Data from our study confirmed the same: patients with early menarche and early menopause have an increased risk of OC. We also found a significant negative correlation of menarcheal age with BMI, similar to observations made by Leidy[52], who also found a significantly negative correlation between age at menarche and BMI. In addition, we found a highly significant positive correlation between the BMI of OC patients and CA-125 levels. CA 125 is also a marker of obesity that is related to an increased risk of OC[53]. Moreover, we found a significant negative correlation of menarcheal age with CA125; however, we didn't find a significant relationship between menopausal age and CA125 levels. We found a non-significant positive correlation of menopausal age with BMI, and the results are in agreement with other studies that also found that underweight women are more likely to have early menopause compared with women with normal BMI[54,55]. Skrzypczak et al[56] found a positive correlation between overweight and underweight and menopausal age and reported that being overweight or underweight has a direct impact on menopausal age.

CONCLUSIONS

The majority of the clinical, demographical, and pathological features of OC patients in our population were similar to those reported in other parts of India and worldwide. The foremost problem associated with OC is its late-stage diagnosis and high metastatic potential. Greater awareness is necessitated to understand the complexity and encourage early detection among our population to decrease the morbidity and mortality associated with this dreadful disease. This may also help young females by preserving their fertility. The findings of this study can be used to evaluate and design OC prevention programs.

Acknowledgment:
The authors are grateful to Prof. Ram Gopal Saini, Chairperson, Centre for Interdisciplinary Biomedical Research and Dean, Postgraduate Studies and Research, Adesh University, Bathinda, for his expertise, supervision, and useful comments in this study.

Author Contributions:
Conception and design: [SS], [AA]; Collection and assembly of data: [SS], [AA]; Data analysis and interpretation: [SS], [AA]; Manuscript writing: [SS], [AA]; Final approval of manuscript: [SS], [AA]; Accountable for all aspects of the work: [SS], [AA].

Funding:
The authors have received no funding for this article.

Institutional Review Board Statement:
This study was approved by the Doctoral Advisory Committee, Institutional Research Committee, and Ethics Committee of Adesh University, Bathinda (Ref. No. AU/EC/FM/156/2018) from 2017 to 2020.

Informed Consent:
All study participants, or their legal guardian, provided informed written consent prior to study enrollment.

Data availability statement:
The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available.

Conflict of interest:
The authors declare they have no conflict of interest.

REFERENCES

1. Qin T, Fan J, Lu F, Zhang L, Liu C, Xiong Q, et al. Harnessing preclinical models for the interrogation of ovarian cancer. J Exp Clin Cancer Res. 2022; 41: 1-27.
2. Lukanović D, Kobal B, Černe K. Ovarian Cancer: Treatment and Resistance to Pharmacotherapy. Reproductive Medicine 2022; 3: 127-40.
3. Achimaș-Cadariu PA, Păun DL, Pașca A. Impact of Hormone Replacement Therapy on the Overall Survival and Progression Free Survival of Ovarian Cancer Patients: A Systematic Review and Meta-Analysis. Cancers (Basel). 2023; 15: 356.
4. López-Árias E, Aguilar-Lemarroy A, Felipe Jave-Suárez L, Morgan-Villela G, Mariscal-Ramírez I, Martínez-Velázquez M, Alvarez AH, Gutiérrez-Ortega A, Hernández-Gutiérrez R. Alpha 1-antitrypsin: A novel tumor-associated antigen identified in patients with early-stage breast cancer. Electrophoresis 2012; 33: 2130-7.

5. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, Bray F. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. CA Cancer J Clin 2021; 71: 209-249.
6. WHO. India Fact Sheet IARC 2022. Available from: https://gco.iarc.fr/today/data/factsheets/populations/356-india-fact-sheets.pdf.
7. Meena RK, Syed NA, Sheikh ZA, Guru FR, Mir MH, Banday SZ, Mp AK, Parveen S, Dar NA, Bhat GM. Patterns of Treatment and Outcomes in Epithelial Ovarian Cancer: A Retrospective North Indian Single-Institution Experience. JCO Global Oncol 2022; 8: e2200032.
8. Tymon-Rosario JR, Chui MH, Santin AD. Ovarian carcinosarcoma. Diagnosis and Treatment of Rare Gynecologic Cancers: Elsevier 2023; pp. 41-54.
9. Trabert B, Tworoger SS, O'Brien KM, Townsend MK, Fortner RT, Iversen ES. The risk of ovarian cancer increases with an increase in the lifetime number of ovulatory cycles: an analysis from the Ovarian Cancer Cohort Consortium (OC3). Cancer Res 2020; 80: 1210-8.
10. Gajjar K, Ogden G, Mujahid M, Razvi K. Symptoms and risk factors of ovarian cancer: a survey in primary care. Int Scholarly Res Notices 2012; 2012: 754197.
11. Manasa G, Mascarenhas RJ, Shetti NP, Malode SJ, Aminabhavi TM. Biomarkers for early diagnosis of ovarian carcinoma. ACS Biomat Sci Eng 2022; 8: 2726-46.
12. Levine M, Naumann RW. Ovarian Cancer Screening and Early Detection. Advances in Diagnosis and Management Ovarian Cancer: Springe 2022; pp. 9-25.
13. Jamwal G, Charak A, Kaul I, Sharma P, Goel M, Sharma S. Clinicopathological findings and sociodemographic variables of malignant ovarian tumors: A hospital based study. Int Med J 2016; 3: 1051-4
14. Asiaf A, Ahmad ST, Zargar MA, Mufti SM, Mir SH. Prevalence of human papillomavirus infection in a Kashmiri ethnic female population. Genet Test Mol Biomarkers 2012; 16: 904-9.
15. McBride CM, Pathak S, Johnson CE, Alberg AJ, Bandera EV, Barnholtz-Sloan JS. Psychosocial factors associated with genetic testing status among African American women with ovarian cancer: Results from the African American Cancer Epidemiology Study. Cancer 2022; 128: 1252-9.
16. Murthy NS, Shalini S, Suman G, Pruthvish S, Mathew A. Changing trends in incidence of ovarian cancer-the Indian scenario. Asian Pac J Cancer Prev 2009; 10: 1025-30.
17. Li X, Deng Y, Tang W, Sun Q, Chen Y, Yang C, et al. Urban-rural disparity in cancer incidence, mortality, and survivals in Shanghai, China, during 2002 and 2015. Front Oncol 2018; 8: 579.
18. Park J, Blackburn BE, Rowe K, Snyder J, Wan Y, Deshmukh V. Rural-metropolitan disparities in ovarian cancer survival: a statewide population-based study. Ann Epidemiol 2018; 28: 377-84.
19. Kvikstad A, Vatten LJ. Cancer risk and prognosis in Norway: comparing women in their first marriage with women who have never married. J Epidemiol Community Health 1996; 50: 51-5.
20. Wang X, Li X, Su S, Liu M. Marital status and survival in epithelial ovarian cancer patients: a SEER-based study. Oncotarget 2017; 8: 89040.
21. Khan A, Sultana K. Presenting signs and symptoms of ovarian cancer at a tertiary care hospital. J Pakistan Med Ass 2010; 60: 260.
22. Elshami M, Tuffaha A, Yaseen A, Alser M, Al-Slaibi I, Jabr H. Awareness of ovarian cancer risk and protective factors: A national cross-sectional study from Palestine. PLoS One 2022; 17: e0265452.
23. Zhang M, Yang Z, Binns C, Lee A. Diet and ovarian cancer risk: a case–control study in China. Br J Cancer 2002; 86: 712-7.
24. Kolahdooz F, van der Pols JC, Bain CJ, Marks GC, Hughes MC, Whiteman DC. Meat, fish, and ovarian cancer risk: results from 2 Australian case-control studies, a systematic review, and meta-analysis. The Am J Clin Nutr 2010; 91: 1752-63.
25. Zhong GC, Zhu Q, Cai D, Hu JJ, Dai X, Gong JP. Ultra-processed food consumption and the risk of pancreatic cancer in the Prostate, Lung, Colorectal and Ovarian Cancer Screening Trial. Int J Cancer 2023; 152: 835-44.
26. Poorolajal J, Jenabi E, Masoumi SZ. Body mass index effects on risk of ovarian cancer: a meta-analysis. Asian Pac J Cancer Prev 2014; 15: 7665-71.
27. Delort L, Kwiatkowski F, Chalabi N, Satih S, Bignon YJ, Bernard-Gallon DJ. Central adiposity as a major risk factor of ovarian cancer. Anticancer Res 2009; 29: 5229-34.
28. Tzenios N, Tazanios M, Chahine M. The impact of BMI on Ovarian Cancer-An Updated Systematic Review and Metanalysis. 2022.
29. Del Pup L, Driul L, Peccatori F. Lifestyle advice to reduce Ovarian Cancer risk. WCRJ 2020; 7: e1466.
30. Mangone L, Marinelli F, Bisceglia I, Braghiroli MB, Mastrofilippo V, Cerullo L, et al. Ovarian Cancer in a Northern Italian Province and the Multidisciplinary Team. Cancers (Basel) 2023; 15: 299.
31. Doubeni CA, Doubeni AR, Myers AE. Diagnosis and management of ovarian cancer. Am Fam Physician 2016; 93: 937-44.
32. Vachon CM, Mink PJ, Janney CA, Sellers TA, Cerhan JR, Hartmann L. Association of parity and ovarian cancer risk by family history of breast or ovarian cancer in a population-based study of postmenopausal women. Epidemiology 20022; 3: 66-71.
33. Ferris J, Daly M, Buys S, Genkinger J, Liao Y, Terry M. Oral contraceptive and reproductive risk factors for ovarian cancer within sisters in the breast cancer family registry. Br J Cancer 2014; 110: 1074-80.
34. Huang Z, Gao Y, Wen W, Li H, Zheng W, Shu XO. Contraceptive methods and ovarian cancer risk among Chinese women: A report from the Shanghai Women's Health Study. Int J Cancer 2015; 137: 607-14.
35. Fu Z, Brooks MM, Irvin S, Jordan S, Aben KK, Anton-Culver H, et al. Lifetime ovulatory years and risk of epithelial ovarian cancer: a multinational pooled analysis. J Natl Cancer Inst. 2023 Jan 23: djad011.
36. Yang H, Dai H, Li L, Wang X, Wang P, Song F, Zhang B, Chen K. Age at menarche and epithelial ovarian cancer risk: A meta-analysis and Mendelian randomization study. Cancer Med 2019; 8: 4012-4022.
37. Titus-Ernstoff L, Perez K, Cramer D, Harlow B, Baron J, Greenberg E. Menstrual and reproductive factors in relation to ovarian cancer risk. Br J Cancer 2001; 84: 714-21.
38. Schildkraut JM, Cooper GS, Halabi S, Calingaert B, Hartge P, Whittemore AS. Age at natural menopause and the risk of epithelial ovarian cancer. Obstet Gynecol 2001; 98: 85-90.
39. Moorman PG, Calingaert B, Palmieri RT, Iversen ES, Bentley RC, Halabi S, Berchuck A, Schildkraut JM. Hormonal risk factors for ovarian cancer in premenopausal and postmenopausal women. Am J Epidemiol 2008; 167: 1059-69.

40. Vercellini P, Crosignani P, Somigliana E, Viganò P, Buggio L, Bolis G, Fedele L. The 'incessant menstruation' hypothesis: a mechanistic ovarian cancer model with implications for prevention. Hum Reprod 2011; 26: 2262-73.
41. Ahuja M. Age of menopause and determinants of menopause age: A PAN India survey by IMS. J Midlife Health 2016; 7: 126-131.
42. Dasgupta D, Pal B, Ray S. Factors that discriminate age at menopause: A study of Bengali Hindu women of West Bengal. Am J Hum Biol 2015; 27: 710-5.
43. Olson SH, Mignone L, Nakraseive C, Caputo T, Barakat R, Harlap S. Symptoms of ovarian cancer. Obstet Gynecol 2001; 98: 212-7.
44. Deeba F, Alam AM, Banu J. Clinlcopathological study of ovarian cancer: a multi centered study. J Shaheed Suhrawardy Med College 2013; 5: 3-6.
45. Ahmad DS, Banday SZ, Ajaz S, Ahmad DI, Kaneez S. Clinico-demographic Profile of Ovarian Cancer in Kashmir. Int J Sci Study 2019; 6: 232-5.
46. Saini SK, Srivastava S, Singh Y, Dixit AK, Prasad SN. Epidemiology of epithelial ovarian cancer, a single institution-based study in India. Clin Cancer Investig J 2016; 5: 20-4.
47. Georgeena P, Rajanbabu A, Vijaykumar D, Pavithran K, Sundaram K, Deepak K, et al. Surgical treatment pattern and outcomes in epithelial ovarian cancer patients from a cancer institute in Kerala, India. Ecancermedicalscience 2016; 10: 619.
48. Zhang M, Lee AH, Binns CW. Physical activity and epithelial ovarian cancer risk: A case-control study in China. Int J Cancer 2003; 105: 838-43.
49. Lee J. Physical activity, sitting time, and the risk of ovarian cancer: a brief research report employing a meta-analysis of existing. Health Care Women Int 2019; 40: 433-58.
50. Wang Z, Du W, Jin S, Zhu Y, Quan C, Zhang X, Feng Y, Mo Y, Wang J. Analysis of preoperative sleep quality and related influencing factors in cancer patients. Support Care Cancer 2022; 31: 4.
51. Gong TT, Wu QJ, Vogtmann E, Lin B, Wang YL. Age at menarche and risk of ovarian cancer: a meta-analysis of epidemiological studies. Int J Cancer 2013; 132: 2894-900.
52. Leidy LE. Timing of menopause in relation to body size and weight change. Hum Biol 1996: 967-82.
53. Joo NS, Kim KN, Kim KS. Serum CA125 concentration has inverse correlation with metabolic syndrome. J Korean Med Sci 2011; 26: 1328-32.
54. Wang M, Gong WW, Hu RY, Wang H, Guo Y, Bian Z. Age at natural menopause and associated factors in adult women: findings from the China Kadoorie Biobank study in Zhejiang rural area. PLoS One 2018; 13: e0195658.
55. Hardy R, Mishra GD, Kuh D. Body mass index trajectories and age at menopause in a British birth cohort. Maturitas 2008; 59: 304-14.
56. Skrzypczak M, Szwed A, Pawlińska-Chmara R, Skrzypulec V. Assessment of the BMI, WHR and W/Ht in pre-and postmenopausal women. Anthropological Review 2007; 70: 3-13.