

Risk Factors and Symptoms of Ovarian Cancer in Patients Attending Hiwa Oncology/Hematology Hospital in Sulaimaniyah City

عوامل الخطر واعراض الاصابة بسرطان المبيض لدى المريضات اللواتي يترددن على مستشفى هيو للأورام/ امراض الدم في مدينة السليمانية

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الخلاصة:

خلفية البحث: ان سرطان المبيض مسؤول عن معدل وفيات أعلى من أي سرطان آخر في الجهاز التناسلي للمرأة. **الاهداف:** تهدف هذه الدراسة إلى معرفة جوانب الخطر وأعراض سرطان المبيض لدى المرضى الذين يزورون مستشفى هيو للأورام / أمراض الدم في مدينة السليمانية.

المنهجية: دراسة استرجاعية وصفية أجريت في مستشفى هيو للأورام / امراض الدم للفترة من 1 / تموز / 2019 الى 1 / آذار / 2020، قائمة على المستشفى تم إنجازها في أكثر من 6 سنوات (2013-2019)، وشملت 100 مريضة تم تشخيصهم و 200 امرأة سليمة كسيطرة تم جمع المعلومات الشخصية مثل العمر، التعليم، الوضع الاقتصادي، تدخين السجائر، الطول، الوزن، النظام الغذائي، عادات الأكل، وحجوب منع الحمل المستخدمة عن طريق الفم.

النتائج: بلغت نسبة الإصابة بسرطان المبيض 13 حالة في عام 2013 وارتفعت إلى 83 حالة في عام 2019. وكانت أعلى نسبة (30%) للمرضى من الفئة العمرية 40-49 سنة ($p = 0.004$). وكانت معظم الحالات (60%) كان لديهم حالة اقتصادية غير كافية، بالإضافة إلى (33%) من المريضات اميات. ويبدو أن النساء اللاتي لديهن تدخين سلبي أكثر عرضة للإصابة بسرطان المبيض، خاصة النساء اللواتي مارسن التدخين مدة تزيد عن 5 سنوات. بالإضافة إلى ذلك، (68%) من المرضى استخدمن حجوب منع الحمل بمدى 1-5 سنوات. كما تم العثور على علاقة ارتباط ذات دلالة إحصائية بين النظام الغذائي وسرطان المبيض في المرضى. واشتكت غالبية المرضى (76%) من آلام في البطن وانتفاخ في البطن كأول ظهور لأعراض سرطان المبيض.

الاستنتاج: تستنتج هذه الدراسة إلى أن العمر، الحالة الاقتصادية، المستوى التعليمي، الطول، الوزن، التدخين السلبي، النظام الغذائي، واستخدام حجوب منع الحمل كانت مصحوبة بشكل مباشر باحتمالية الإصابة بسرطان المبيض.

التوصيات: يوصي الباحث ان على جميع النساء خاصة بعد عمر الأربعين، الاهتمام بالتعليم والوعي الصحي يشمل اعراض واسباب الإصابة بمرض سرطان المبيض وخاصة الاهتمام بتقليل الوزن والتدخين السلبي و اتباع النظام الصحي للطعام بتقليل الحلويات، منتجات الألبان والدهون وزيادة استهلاك البقوليات، لحم الأسماك، الفواكه والخضار.

الكلمات المفتاحية: سرطان المبيض، عوامل الخطر، الأعراض، دراسة بأثر رجعي، قاتل صامت.

Abstract:

Background: Ovarian cancer is responsible for higher mortality rate than any other cancer of the woman genital system.

Aims of the study: this study aims to find the risk aspects and symptoms of ovarian cancer in patients visiting Hiwa Oncology/Hematology hospital in Sulaimaniyah City.

Methodology: This study was a retrospective case-control study conducted in Hiwa Oncology / Hematology Hospital in Sulaimaniyah city, Northern Iraq, from 1 / July / 2019 to 1 / march / 2020, based on the recorded database system of Hiwa Oncology / Hematology Hospital from 2013 - 2019, involving 100 diagnosed patients and 200 healthy women as control. Personal information such as age, education, economic status, cigarette smoking, height, weight, diet and eating habits, and used oral contraceptive pills were collected.

Results: The incidence of ovarian cancer in 2013 was 13 cases which increased to 83 cases in 2019. The highest percentage (30%) of patients' age range were 40- 49 years ($p = 0.004$). Most cases 60% had an insufficient economic state and 33 % of cases were illiterate women. Passive smoking appeared to be more prone to ovarian cancer: especially those with a smoking duration of > 5 years. Additionally, 68% of patients used oral contraceptive pills with a duration range of 1-5 years. Also, a highly significant correlation between diet and ovarian cancer was found in patients. The majority of the patients (76%) complained of abdominal pain and abdominal distension as the first presenting symptoms of ovarian cancer.

Conclusion: This study concluded that age, economic status, educational level, height, passive smoking, weight, diet, and oral contraceptive pill usage were directly accompanied by the possibility of ovarian cancer.

Recommendations: All women especially those after age of 40 years old, should pay attention to education and health awareness including symptoms and causes of ovarian cancer, especially attention to decrease weight and passive smoking and using a healthy diet through decrease consumption the sweets, dairy products, and animal fat and increase consumption of legumes, fish meat, vegetable and fruits.

Keywords: Ovarian cancer, Risk factors, Symptoms, Retrospective study, Silent killer.

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INTRODUCTION

Ovarian cancer is one of the most prominent reproductive system cancers, and accounts for 2.5% of all distortions with the highest mortality rate compared to other types of cancers in females. The incidence of ovarian cancers is ranking 3rd globally after cervical and uterine cancers. A female's risk for ovarian cancer during her life is about 1/78 cases, while their lifetime risk of mortality from ovarian cancer is about 1/108 cases ⁽¹⁾.

The great death rate of ovarian cancer is produced by asymptomatic and silent growth of the tumor, late onset of symptoms, and improper screening results in its diagnosis in the progressed stages. Thus, the nickname: "silent killer" has been given to ovarian cancer ⁽²⁾.

In 2018, about 295,414 newly diagnosed cases and 184,799 deaths by ovarian cancer were recorded globally, and the data varies from one country to another depending on many factors. The socioeconomic status is one of the predictors of incidence and survival for ovarian cancer, while the exact etiology of ovarian cancer is complex and only partially understood ⁽³⁾.

Many factors can increase the risk of ovarian cancer, including older age, inherited gene mutations, family history, and estrogen hormone replacement therapy ⁽⁴⁾.

The statistic shows that between 1/3 to 2/5 of all cancers can be prohibited by eradicating and decreasing risk factors by promoting healthcare awareness, cancer education, patient attentiveness about the clinical signs of ovarian cancer, timely response to symptoms, changing lifestyles (especially physical activities), diet, and treating original disorders ⁽⁵⁾.

Because data on the incidence, mortality of ovarian cancer, the onset of symptoms, and its risk factors are very essential for managing and averting its complication, we aimed to find the risk factors and symptoms of ovarian cancer in patients attending Hiwa Oncology / Hematology Hospital in Sulaimaniyah city, Northern Iraq.

AIMS OF THE STUDY

This study aims to find the risk aspects and symptoms of ovarian cancer in patients visiting Hiwa Oncology/Hematology hospital in Sulaimaniyah City.

METHODOLOGY

- Study Design

This study was a retrospective case-control study conducted in Hiwa Oncology / Hematology Hospital in Sulaimaniyah city, Northern Iraq, from 1 / July / 2019 to 1 / march / 2020, based on the recorded database system of Hiwa Oncology / Hematology Hospital from 2013 - 2019.

- Study Setting

The total recorded patients with ovarian cancer from 3rd of January 2013 to 30th of December 2019 at Hiwa Oncology/Hematology Hospital were 331 patients, of which 49 of them died due to the severity of the disease. Among the remaining number, only 100 patients participated in this study as some of them refused to participate in this study due to their unstable psychological and health conditions. However, we could not reach some of the remaining patients because their saved cell phone numbers at Hiwa Oncology / Hematology database system were closed.

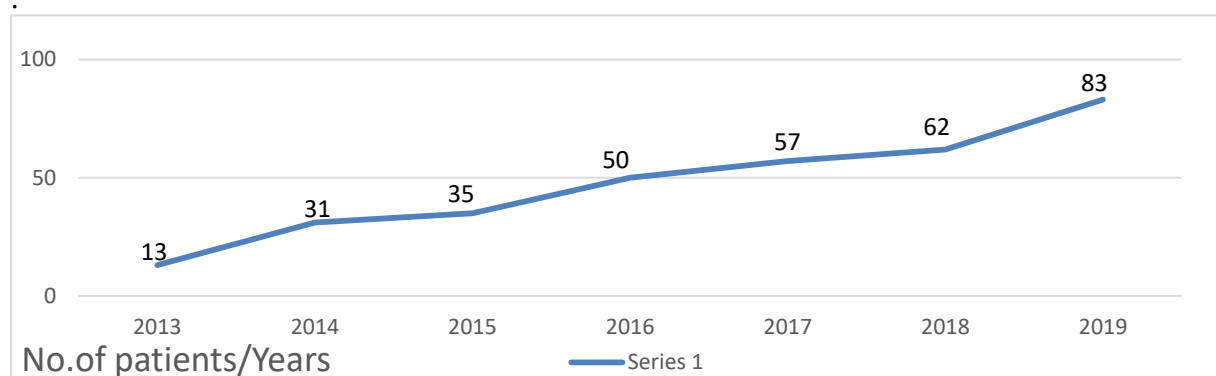
Also, 200 healthy subjects without ovarian cancer (depending on normal ovaries by ultrasound) were accounted for as control participants, then, personal information such as age, education status, and economic status, history of cigarette smoking, height, weight, diet, eating habits, and use of oral contraceptive pills were collected. All participants provided informed written consent to contribute to this research before the commencement of the study.

- Statistical Analysis

The collected data were compiled and analyzed using percentages, mean, median, ANOVA and Chi-square tests using SPSS version 24. P values of 0.05 were used as a cut-off point for the significance of the statistical test.

RESULTS:

Figure (1): Demonstrates the incidence of ovarian cancer in Hiwa Oncology/Hematology Hospital from 3rd of January 2013 to 30th of December 2019



The findings in Figure (1) shows that the incidence of ovarian cancer in 2013 was 13 cases which increased gradually to reached 83 cases in 2019.

Table (1): Shows distribution of study samples according to demographic characteristics.

Characteristic		Cases group (Total No.=200) No. (%)	Control group (Total No.=200) No. (%)	P value
Age (Year)	< 20	4 (4)	14 (7)	0.004
	20 – 29	11 (11)	38 (19)	
	30 – 39	21 (21)	54 (27)	
	40 – 49	30 (30)**	36 (18)	
	50 – 59	18 (18)	28 (14)	
	≥ 60	16 (16)	30 (15)	
	Mean ± S.D	44.9 ±13.9	43.9 ±13.6	>0.05
Age of menarche/years	Mean ± S.D	13.43 ± 1.36	13.11 ± 1.11	0.1
Age of marriage/years	Mean ± S.D	24.23 ± 9.48	23.30 ± 11.01	0.2
Occupation	House wife	67 (67)**	74 (37)	< 0.001
	Employee	26 (26)	104 (52)	
	Student	4 (4)	18 (9)	
	Retired	3 (3)	4 (2)	
Economic status	Sufficient	40 (40)	138 (69)	< 0.001
	Insufficient	60 (60)**	62 (31)	
Educational level	Illiterate	33 (33)**	12 (6)	< 0.001
	Primary	23 (23)	44 (22)	
	Secondary	22 (22)	36 (18)	
	High education	22 (22)	108 (54)	
Residency	Urban	87 (87)	154 (77)	>0.05
	Rural	13 (13)	46 (23)	

* Highly significant from control group (p< 0.01).

Table (1) indicate that the mean age of the participants 15 - 72 years was (44.9 ± 13.9 and 43.9 ± 13.6 for patients and controls, respectively ($p > 0.05$). Also, age of menarche and age of marriage for both groups were comparable ($p > 0.05$). Whereas the higher percentage (30%) of patients' age range was 40- 49 years ($p = 0.004$). Most of the patients were housewife (67%) and 33% were illiterate ($p < 0.001$). About 60% of patients were in an insufficient economic state compared to controls ($p < 0.001$), and 87% of patients were from urban areas, with no significant difference compared to the control group ($p > 0.05$).

Table (2): Shows distribution of study samples according to some life style characteristics and reproductive history

Characteristic		Cancer group (Total No.=100) No. (%)	Control group (Total No.=200) No. (%)	P value
Smoking	Never smoker	64 (64)	170 (85)	0.02
	Passive smoker	31 (31)**	22 (11)	
	Active smoker	3 (3)	6 (3)	
	Quit smoking	2 (2)	2 (1)	
Passive Smoking / Year	< 1	2 (6.5%)	6 (27.3%)	< 0.001
	1 – 5	2 (6.5%)	4 (18.2%)	
	> 5	27 (87%) **	12 (54.5%)	
Total		31 (31)	64 (32)	
BMI	Underweight	2 (2)	10 (5)	0.04
	Normal	31 (31)	74 (37)	
	Overweight	40 (40)	74 (37)	
	Obese	27 (27)	42 (21)	
	Mean $\pm$ S.D	27.73 $\pm$ 5.42	26.21 $\pm$ 4.96	
Oral contraceptive pills	Yes	68 (68) **	48 (24)	< 0.001
	No	32 (32)	152 (76)	
Duration(Year) of oral Contraceptive pills usage	< 1	8 (12%)	0 (0%)	0.04
	1 – 5	48 (70%) *	26 (54%)	
	> 5	12 (18%)	22 (46%)	
Total		68 (100%)	48 (100%)	

*Statistical significant from control group ($p < 0.05$).

** Highly significant from control group ($p < 0.01$).

Table (2) indicates that passive smokers were more in the patient's group (31%) than the control group (11%) ($p = 0.02$). Passive smokers were more prone to ovarian cancer, especially with a smoking duration of > 5 years ($p < 0.001$). Moreover, a significant difference ($p = 0.04$) was demonstrated in body mass index (BMI) for both patients and control groups (27.73 ± 5.42 and 26.21 ± 4.96 , respectively). In addition to most of the patients, 68% of the patients used oral contraceptive pills with a duration of 1-5 years, ($p < 0.001$).

Table (3): Shows distribution of study samples according to diet and eating habits

Type of Food Consumption		Cancer Group (Total No.100) No. (%)	Control Group (Total No.200) No. (%)	P value
Grains consumption	Refined White cereals	69 (69)	122 (61)	0.13
	Whole White cereals	29 (29)	62 (31)	
	Refined Brown cereals	2 (2)	16 (8)	
Legumes	None	5 (5)	4 (2)	0.002

	Once – twice monthly	59 (59)**	48 (24)	
	One-three times weekly	15 (15)	18 (9)	
	Three or more weekly	21 (21)**	130 (65)	
Animal fat	Always	52 (52)**	46 (23)	< 0.001
	Sometimes	12 (12)	74 (37)	
	Never	33 (33)	80 (40)	
Meat consumption	1 to 2 monthly	24 (24)	40 (20)	0.21
	1 to 2 weekly	23 (23)	46 (23)	
	3 or more weekly	18 (18)	30 (15)	
	3 to 4 monthly	25 (25)	76 (38)	
	never or less than once weekly	10 (10)	(4) 8	
Chicken consumption	None	2 (2)	(2) 4	0.06
	One - Four per month	20 (20)	56 (28)	
	Once - twice weekly	34 (34)	70 (35)	
	Three - four weekly	38 (38)	(30) 60	
	Five times a week	6 (6)	5 (10)	
Fish consumption	None	49 (49)**	20 (10)	< 0.001
	1 to 2 per month	33 (33)	30 (60)	
	3 to 4 monthly	14 (14)	10 (20)	
	8 per month	4 (4)	50 (100)	
Dairy product (week)	None	6 (6)	10 (20)	0.003
	1 - 3 times	20 (20)	26 (52)	
	4 - 5 times	9 (9)	(24) 48	
	6 - 7 times	65 (65)**	40 (80)	
Vegetables (Week)	None	1 (1)	(4) 8	< 0.001
	1 - 2 times	58 (58)**	(23) 46	
	3 - 4 times	17 (17)	(25) 50	
	5 - 7 times	24 (24)**	96 (48)	
Fruit (Day)	None	3 (3)	(2) 4	< 0.001
	Once – twice	90 (90)	60 (120)	
	Three – four	7 (7)	(38) 76	
Sweets consumption	Yes	85 (85)**	(45) 90	< 0.001
	No	15 (15)	110 (55)	

** Highly significant from control group ($p < 0.01$).

Table (3) represents no correlations were demonstrated between ovarian cancer and the consumption of Grains, red meat, and chicken meat ($p > 0.05$). On the other hand, low consumption of legumes, fish meat, vegetables, and fruits had highly significant correlations to risk of ovarian cancer ($p < 0.01$), while high consumption of animal fat, dairy products, and sweets lead to an increased risk of ovarian cancer ($p < 0.01$).

Figure (2): Demonstrates the signs and symptoms of ovarian cancer in patients.

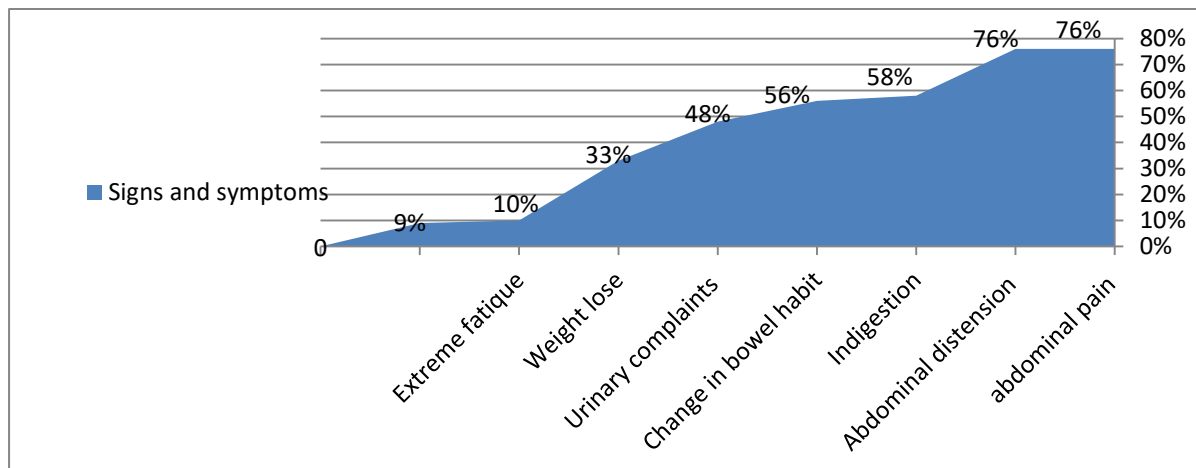


Figure (2) demonstrates the majority of the patients complained from abdominal pain and abdominal distension (76%) as the first 2 presenting symptoms followed by indigestion (58%), change in bowel habit (56%), urinary complaints (dysuria, retention, and frequency of micturition) (48%), weight loss (33%), extreme fatigue (10%), and postmenopausal bleeding (9%).

DISCUSSION

The result of the present study shows that the incidence of ovarian cancer in Sulaimaniyah city has been increasing over the years and this result is in line with other researches ^(6, 7) which found that the global ovarian cancer frequency / incidence has increased gradually. As the world becomes more industrialized and areas become more urbanized, the risk of young individuals with the growth of ovarian cancer is on the rise. Thus, ovarian cancers are more reported in developed / developing countries because of increasing population, increased longevity, and increased risk due to environmental factors ⁽⁸⁾.

In the present study, the age of the patients was ranged between 40-49 years which is close to a study conducted by Bjørge et al. ⁽⁹⁾. Generally, most studies concluded that the risk of developing ovarian cancer gets higher with age and indicated that ovarian cancer rarely occurs in women aged <40 years, but is common after menopause in which 1/2 ovarian cancer cases are found in women ≥ 63 years ⁽¹⁰⁾.

Approximately, 60% of patients had an insufficient economic status, and this result is in agreement with other studies conducted on African-American women in which it is apparent that ovarian cancer risk may be inversely associated with socioeconomic status ⁽¹¹⁾.

Regarding the patient's residency, the majority of the patients were from urban areas but without significant correlation, which are inconsistent with the observations of other researchers which suggested that these findings might be due to environmental pollution, presence of large factories, and car fumes within cities ⁽¹²⁾. In addition, another study reported that there is no correlation between getting ovarian cancer and variation in residency areas of patients ⁽¹³⁾.

The side stream smoke is a major source of secondhand smoke as toxicants from cigarette smoke can produce DNA adducts which is believed to represent the first step of carcinogenesis, and if not repaired correctly; it might lead to mutations and cancer ⁽¹⁴⁾. In this respect, we also revealed that there is a high correlation between passive smoking and ovarian cancer. Similarly, Mohammed, 2017 displayed that passive smoking is associated with an increased risk of ovarian cancer, in which he concluded that the premenopausal women who undertook passive smoking developed ovarian cancer 17.9 times more than those without passive smoking. Additionally, he confirmed that postmenopausal women exposed to passive

smoking developed ovarian cancer 3.5 times more than those that are not exposed to passive smoking ⁽¹⁵⁾.

Furthermore, in this study, the majority of patients were overweight, with a significant increase in their mean BMI compared to the control group. This finding is similar to a study conducted by Beehler et al. as they mentioned that numerous concepts have been anticipated to correlate the link between obesity and cancer development such as insulin resistance, estrogen level, adiposity, and low-grade chronic inflammation ⁽¹⁶⁾.

The majority of studied patients used oral contraceptive pills for about 1-5 years, which is a finding that is different from all previous studies that concluded oral contraceptive pills as a protective agent against ovarian cancer. In this regard, it was demonstrated that oral contraceptives protect against the development of ovarian cancer ⁽¹⁷⁾. It was also confirmed that increasing duration of oral contraceptive use was associated with a progressive reduction in risk; those who used oral contraceptives for 10 or more years had a 45% lower risk compared with users of 1 year or less (13% lower risk/5 years of use) ⁽¹⁸⁾.

Regarding the correlation of nutritional consumption and the possibility of ovarian cancer; we found that there is no significant difference between grain consumption and ovarian cancer, which is supported by data from a systematic review ⁽¹⁹⁾, but it is not in agreement with a study that suggested whole-grain food consumption may be associated with mild risk of ovarian cancer due to its high dietary fiber content which results in low serum estrogen levels that stimulate ovarian epithelial cell proliferation and the promotion of ovarian tumor progression ⁽²⁰⁾. On the other hand, a highly significant association between consumption of legumes and reduced risk of ovarian cancer was found, which is consistent with the results of other studies conducted earlier ⁽²¹⁾, which suggested that dietary fiber intake including legumes is associated with a reduced risk of ovarian cancer. Long-term consumption of a diet high in carbohydrates can lead to chronic hyperinsulinemia and it has been hypothesized that hyperinsulinemia may increase risk of ovarian cancer by lowering insulin-like growth factor binding protein (IGFBP) concentrations, thereby increasing the bioavailability of insulin-like growth factor 1 (IGF-1) which reduces apoptosis, stimulates cellular proliferation and sex steroid synthesis, and decreases the concentration of sex hormone-binding globulin (SHBG), all of which have been implicated in the development of ovarian cancer ⁽²²⁾.

Additionally, we found that patients consumed animal fat more than the controls which are in line with outcomes of Rice et al. ⁽²³⁾. Generally, it was confirmed that the high consumed fats and animal yields might be related to ovarian cancer as the recurrent rupture of the follicle accompanying ovulation is thought to expose the ovarian epithelium to hormones in the surrounding fluid; then, increased estrogen levels may raise the opportunity of cancer development ⁽²⁴⁾.

Regarding red meat consumption and ovarian cancer, we did not find any significant difference, and this observation is supported by another study conducted by Wallin et al. ⁽²⁵⁾, while it is inconsistent with another study that recommended a potential link between meat intake and ovarian cancer risk ⁽²⁶⁾. Besides, no significant correlation between chicken consumption and ovarian cancer was demonstrated, which is not in agreement with a study that concluded that higher intake of poultry may decrease the risk of ovarian cancer ⁽²⁷⁾. Moreover, we showed that a high significant correlation between no fish consumption and ovarian cancer is present which is supported by other researches that found that there is a risk reduction in ovarian cancer with consuming more fish ⁽²⁷⁾, this may refer to the polyunsaturated omega-3 fatty acids in fish are thought to be able to reduce the risk of some types of cancers.

Consequently, we agreed that an increase in dairy product consumption was directly correlated with ovarian cancer which is in line with research that hypothesizes the galactose

and lactose components of dairy products might have a toxic effect on oocytes and prematurely raises gonadotropins to that observed in mouse/rat models where high lactose diets led to ovulatory dysfunction and hypogonadism ⁽²⁸⁾. In the same manner, Liao et al. showed that whole milk intake might contribute to a higher ovarian cancer risk, whereas low-fat milk, dietary calcium, and dietary vitamin D might reduce the risk ⁽²⁹⁾.

Virtually, vegetables and fruits containing various vitamins, minerals, fiber, carotenoids, flavonoids, and other bioactive substances, (such as sterols, in doles, and phenols) may help avoid cancer. Many vegetables and fruits are low in energy, high in fiber, and have a high-water content, which may increase satiety and decrease overall energy intake, and thus should contribute to weight loss and maintenance of that loss ⁽³⁰⁾. Hence, we found that most of the patients consumed fewer amounts of vegetables and fruits than the control group which is in agreement with other researches that found that the ovarian cancer risk is inversely associated with higher intakes of dietary fiber available in fruits and vegetables ⁽³¹⁾.

The association between sugar consumption and cancer is largely unknown since it has been suggested that diets high in sugars may promote carcinogenesis by stimulating the synthesis of insulin and insulin-like growth factor-I (IGF-I), promoting oxidative stress and weight gain that might increase the risks for certain cancers ⁽³²⁾. In the present study, we found that women with ovarian cancer significantly consumed more sweets than those of the control group, which is consistent to the work of Qin et al. who found that the dietary glycemic index and glycemic load associated with ovarian cancer ⁽²⁸⁾.

We also revealed that the majority of the patients complained of abdominal pain and abdominal distension as the first presenting symptom followed by indigestion, change in bowel habit, urinary complaints (such as dysuria), retention, and frequency of micturition, weight loss, extreme fatigue, and postmenopausal bleeding. These findings are consistent with the findings of other studies ^(33, 34). On the contrary, it was stated that ovarian cancer showed no symptoms at the early stage, and it is generally advanced when diagnosed ⁽³⁵⁾. Also, it was stated that ovarian cancer is a “silent killer” as it is an asymptomatic disease that results from the secret growth of a tumor ⁽³⁶⁾.

CONCLUSION

In conclusion, we found that many factors increased the risk of ovarian cancer, such as socioeconomic status, cigarette smoking, contraceptives pill usage, weight, and consumption of certain products (sweets, dairy products, and animal fat) while some other factors reduced the possibility and chances of ovarian cancer, such as younger age (before 40 years old), and diet (including the consumption of legumes, fish meat, vegetable and fruits).

RECOMMENDATIONS

All women especially those after age of 40 years old, should pay attention to education and health awareness including symptoms and causes of ovarian cancer, especially attention to decrease weight and passive smoking and using a healthy diet through decrease consumption the sweets, dairy products, and animal fat and increase consumption of legumes, fish meat, vegetable and fruits.

- Ethical Approval

This study was completed following the Declaration of Helsinki and approved by the College of Nursing, University of Sulaimani, Sulaimaniyah, Iraq, with the approval number of NUR-UoS-53-2021.

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