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## Facts about ovarian cancer in Maysanian women

### Dane dotyczące raka jajnika u kobiet z irackiej prowincji Majsan

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#### Abstract

**Background:** Ovarian cancer is one of the commonest gynecologic malignancy. It is the most common cause of death due to gynecologic tumors, and accounts for 50% of deaths due to all gynecologic cancer types. **Objectives:** The aim was to discuss and assess ovarian cancer in Misan province and to underline its impact for increased awareness and interest in screening and early diagnosis by the determination of the prevalence rates among Maysanian women. **Methods:** The study lasted six months. During this period, we obtained a lot of data from records of the Al-Shifaa Oncology Center in Misan province, Iraq. Between September 2016 and February 2017, 50 cases of ovarian cancer from 282 gynecologic cancers were recorded. Complete history was obtained for every case. **Results:** The study showed that ovarian cancer constituted 17.73% of all types of cancer. It usually occurred in patients aged 60–70 years (30%). Women lived in urban areas 1.5 times more frequently than in rural areas. The most common histopathological type of ovarian cancer was ovarian serous carcinoma (46%). The most common stages were stage III and IV, accounting for 76%. **Conclusion:** Ovarian cancer is the third most common gynecologic cancer type. It was more common in women aged 60–70 years. Regarding the family history, the results were insignificant. The most common histopathological type of ovarian cancer in this study was ovarian serous carcinoma. The most common stages of the disease were advanced stages III and IV.

**Keywords:** gynecologic malignancy, ovarian cancer, Misan province, serous carcinoma

#### Streszczenie

**Wstęp:** Rak jajnika jest jednym z najczęstszych nowotworów złośliwych żeńskich narządów płciowych oraz główną przyczyną umieralności z powodu tych nowotworów – odpowiada za 50% zgonów wśród chorych z nowotworami kobiecego układu płciowego. **Cele:** Omówienie i ocena występowania raka jajnika w irackiej prowincji Majsan w celu zwiększenia świadomości i zainteresowania badaniami przesiewowymi i wczesnym rozpoznaniem choroby poprzez określenie częstości występowania omawianego nowotworu wśród kobiet zamieszkujących region Majsan. **Metody:** Badanie trwało sześć miesięcy. Uzyskano liczne dane z Centrum Onkologii Al-Shifaa w prowincji Majsan w Iraku. W okresie od września 2016 do lutego 2017 roku odnotowano 50 przypadków raka jajnika wśród ogółem 282 przypadków nowotworów narządów płciowych. Od każdej pacjentki zebrano pełny wywiad. **Wyniki:** Badanie wykazało, że rak jajnika stanowił 17,73% nowotworów. Rozpoznawano go zwykle u kobiet w wieku 60–70 lat (30%). Pacjentki częściej (o 1,5 razy) zamieszkiwały rejony wiejskie. Najczęstszym typem histopatologicznym był surowiczy rak jajnika (46%). Chorobę zwykle rozpoznawano w stadium III i IV, co stanowiło 76% przypadków. **Wnioski:** Rak jajnika to trzeci co do częstości nowotwór żeńskich narządów płciowych. Występował częściej u kobiet w wieku 60–70 lat. Wyniki dotyczące wywiadu rodzinnego nie były istotne. Najczęstszy typ histopatologiczny stanowił surowiczy rak jajnika. Chorobę rozpoznawano przeważnie w zaawansowanym stadium – III i IV.

**Słowa kluczowe:** nowotwory złośliwe żeńskich narządów płciowych, rak jajnika, prowincja Majsan, rak surowiczy

## INTRODUCTION

Ovarian cancer is one of the three most common gynecologic malignancy and is the major cause of death from gynecologic cancer. It constitutes about 15–20% of genital malignancies. It is more prevalent in the United States and Scandinavian countries but much less common in Oriental or Latin American and Asian countries<sup>(1,2)</sup>. The most common type of ovarian cancer, with more than 95% of cases, is ovarian epithelial carcinoma. Less common types include germ cell tumors and sex cord stromal tumors<sup>(3)</sup>. The diagnosis is confirmed through a biopsy of tissue, usually removed during surgery. If detected and treated in an early stage, it may be curable. Treatment usually includes some combination of surgery, chemotherapy, and radiation therapy<sup>(4)</sup>. The overall five-year survival rate in the United States is 45%<sup>(5)</sup>. Globally, as of 2010, about 160,000 people died of ovarian cancer, up from 113,000 in 1990<sup>(6)</sup>. As of 2014, more than 220,000 diagnoses of epithelial ovarian cancer were made yearly<sup>(7)</sup>. In 2010, in the United States, an estimated 21,880 new cases were diagnosed and 13,850 women died of ovarian cancer. In the United Kingdom, as of 2014, approximately 7,000–7,100 yearly diagnoses were made and 4,200 deaths occurred<sup>(7,8)</sup>. It is the 5<sup>th</sup> most common

cancer in United Kingdom women<sup>(9)</sup>. Ovarian cancer is most commonly diagnosed after menopause, between the age of 60 and 64. Ninety per cent of ovarian cancer cases are women over the age of 45 and 80% are women over the age of 50<sup>(8)</sup>. Ovarian cancer represents approximately 4% of cancers diagnosed in women<sup>(9)</sup>. It occurs more commonly in developed countries. Ovarian cancer is the most deadly gynecologic cancer<sup>(10)</sup>. The overall incidence in Europe is approximately 5–15 per 100,000 women<sup>(9)</sup>. In general, a family history of ovarian cancer can indicate a predisposition to developing it. The major genetic risk factor for ovarian cancer is a mutation in *BRCA1* or *BRCA2* DNA mismatch repair genes, which is present in 10% of ovarian cancer cases. Generally, 5–10% of ovarian cancer cases have a genetic cause. A significant family history of endometrial cancer, colon cancer, or other gastrointestinal cancers may indicate the presence of a syndrome known as hereditary non-polyposis colorectal cancer (also known as Lynch syndrome), which confers a higher risk for developing a number of cancers, including ovarian cancer<sup>(10,11)</sup>. Ovarian cancers are classified according to the microscopic appearance (histology or histopathology)<sup>(12)</sup>. Their gross pathology is very similar regardless of histologic type: tumors have solid and cystic masses<sup>(7,10)</sup>. Ovarian cancer is staged using the FIGO staging system (Tab. 1)<sup>(13)</sup>.

Stage	Description	T N M
I	Tumor confined to ovaries or fallopian tube(s)	T1
IA	Tumor limited to one ovary (capsule intact) or fallopian tube; no tumor on ovarian or fallopian tube surface; no malignant cells in the ascites or peritoneal washings	T1a
IB	Tumor limited to both ovaries (capsules intact) or fallopian tubes; no tumor on ovarian or fallopian tube surface; no malignant cells in the ascites or peritoneal washings	T1b
IC	Tumor limited to one or both ovaries or fallopian tubes, with any of the following: <ul style="list-style-type: none"> <li>• IC1: Surgical spill intra-operatively</li> <li>• IC2: Capsule ruptured before surgery or tumor on ovarian or fallopian tube surface</li> <li>• IC3: Malignant cells present in the ascites or peritoneal washings</li> </ul>	T1c
II	Tumor involves one or both ovaries or fallopian tubes with pelvic extension (below pelvic brim) or peritoneal cancer (Tp)	T2
IIA	Extension and/or implants on the uterus and/or fallopian tubes and/or ovaries	T2a
IIB	Extension to other pelvic intraperitoneal tissues	T2b
III	Tumor involves one or both ovaries or fallopian tubes, or primary peritoneal cancer, with cytologically or histologically confirmed spread to the peritoneum outside the pelvis and/or metastasis to the retroperitoneal lymph nodes	T3
IIIA	Metastasis to the retroperitoneal lymph nodes with or without microscopic peritoneal involvement beyond the pelvis	T1,T2,T3aN1
IIIA1	Positive retroperitoneal lymph nodes only (cytologically or histologically proven)	T3a/T3aN1
IIIA1	(i) Metastasis ≤10 mm in greatest dimension (note this is tumor dimension and not lymph node dimension)	
IIIA1	(ii) Metastasis >10 mm in greatest dimension	
IIIA2	Microscopic extrapelvic (above the pelvic brim) peritoneal involvement with or without positive retroperitoneal lymph nodes	T3a/T3aN1
IIIB	Macroscopic peritoneal metastases beyond the pelvic brim ≤2 cm in greatest dimension, with or without metastasis to the retroperitoneal lymph nodes	T3b/T3bN1
IIIC	Macroscopic peritoneal metastases beyond the pelvic brim >2 cm in greatest dimension, with or without metastases to the retroperitoneal nodes*	T3c/T3cN1
IV	Distant metastasis excluding peritoneal metastases: <ul style="list-style-type: none"> <li>• IVA: Pleural effusion with positive cytology</li> <li>• IVB: Metastases to extra-abdominal organs (including inguinal lymph nodes and lymph nodes outside of abdominal cavity)**</li> </ul>	Any T, any N, M1 T3c/T3cN1

\* Includes extension of tumor to capsule of liver and spleen without parenchymal involvement of either organ.

\*\* Parenchymal metastases are stage IVB.

The histologic grade of a tumor measures how abnormal or malignant its cells look under the microscope. The four grades indicate the likelihood of the cancer to spread and the higher the grade, the more likely it is for this to occur.

- i. **Grade I** tumors have well differentiated cells (look very similar to the normal tissue) and are the ones with the best prognosis.
- ii. **Grade II** tumors are also called moderately well-differentiated and they are made up of cells that resemble the normal tissue.
- iii. **Grade III** tumors have the worst prognosis and their cells are abnormal, referred to as poorly differentiated.
- iv. **Grade IV** – metastasis in ovarian cancer is very common in the abdomen, and occurs via exfoliation, where cancer cells burst through the ovarian capsule and are able to move freely throughout the peritoneal cavity. Cancer cells can also travel through the lymphatic system and metastasize to lymph nodes connected to the ovaries via blood vessels<sup>(10,14)</sup>.

Chemotherapy with variable protocols is a general standard of care for ovarian cancer. Chemotherapy is used after surgery to treat any residual disease, if appropriate. In some cases, there may be a reason to perform chemotherapy first, followed by surgery. Chemotherapy is curative in approximately 20% of cases; it is more often curative with malignant germ cell tumors than epithelial tumors<sup>(15)</sup>. Chemotherapy in ovarian cancer typically consists of platins, a group of platinum-based drugs, combined with non-platins. Common therapies can include paclitaxel, cisplatin, topotecan, doxorubicin, epirubicin, and gemcitabine. Carboplatin is typically given in combination with either paclitaxel or docetaxel; the typical combination is carboplatin with paclitaxel<sup>(7,9,10,13,15)</sup>. Specific follow-up depends on the type and stage of ovarian cancer, the treatment, and the presence of any symptoms. Usually, a check-up appointment is made every 2 to 3 months initially, followed by twice per year for up to 5 years. For epithelial ovarian cancers, the most common follow-up test is CA-125 level<sup>(16)</sup>. Ovarian cancer usually has a relatively poor prognosis. However, in some cases, its recurrences are chronically treatable<sup>(7)</sup>. Outcomes are worse in the developing world. In 2012, ovarian cancer occurred in 239,000 women and resulted in 152,000 deaths worldwide. This makes it, among women, the seventh most common cancer and the eighth most common cause of death from cancer<sup>(4)</sup>.

## MATERIAL AND METHODS

### Study design and setting

The cross sectional study was based on records from the Al-Shifaa Oncology Center in Misan province, Iraq, evaluated between September 2016 and February 2017.

## Participants and data collection

One thousand seven hundred and sixty-four cancerous women, who were treated in the Al-Shifaa Oncology Center and Misan Radiotherapy Center, were analyzed. Fifty cases of ovarian cancer from 282 gynecologic cancers were referred for chemotherapy and radiotherapy.

## Clinical parameters

Clinical and pathological data were collected and analyzed. Full past history was taken for every case including age, address, occupation, marital status, pregnancy history, parity, contraceptive history, family history, histopathology and staging of the disease.

## Statistical analysis

The statistical analysis was performed using the Chi-square test. The lowest level of statistically significant differences is equal or below 0.05<sup>(17)</sup>.

## RESULTS

### The overall prevalence of ovarian cancer

Of 1,064 female cancer patients, only 282 women had gynecologic cancer. Cancer affected five reproductive organs: cervix, ovary, uterus, vagina, and vulva. The results revealed that ovarian cancer constituted 17.73% of gynecologic cancer types, which is of statistical significance ( $p < 0.05$ ) (Tab. 2).

### Ovarian cancer in relation to socio-demographic variables

The study showed that ovarian cancer usually occurred in patients aged 60–70 years (30%) while the percentage was zero in extreme age groups, namely 1–10 years and 80–90 years, with statistical significance of  $p < 0.01$ . Ovarian cancer patients typically lived in urban areas: 1.5 times more frequently than in rural areas, with a significant difference ( $p < 0.05$ ). Pregnancy and parity in this study showed relative ratios. As for educational level, 60% had low,

Gynecologic cancer	Cases	%
Ovarian	50	17.73%
Cervical	83	29.43%
Uterine	134	47.52%
Vaginal	11	3.90%
Vulvar	4	1.42%
Total	282	100.00%

Tab. 2. The overall prevalence of ovarian cancer among all gynecologic cancer types

Age (years)	Cases	%
1–10	0	0%
10–20	2	4%
20–30	3	6%
30–40	9	18%
40–50	11	22%
50–60	8	16%
60–70	15	30%
70–80	2	4%
80–90	0	0%
<i>Total</i>	<i>50</i>	<i>100%</i>
Place of residence	Cases	%
Rural	19	38%
Urban	31	62%
<i>Total</i>	<i>50</i>	<i>100%</i>
Pregnancy history	Cases	%
Nulliparous	16	32%
1–5	17	34%
6–10	17	34%
<i>Total</i>	<i>50</i>	<i>100%</i>
Education level	Cases	%
Illiterate	10	20%
Primary school	20	40%
Secondary school	13	26%
University	6	12%
Postgraduate	1	2%
<i>Total</i>	<i>50</i>	<i>100%</i>
Marital status	Cases	%
Single	11	22%
Married	27	54%
Divorced	3	6%
Widow	9	18%
<i>Total</i>	<i>50</i>	<i>100%</i>
Contraception	Cases	%
Yes	12	24%
No	38	76%
<i>Total</i>	<i>50</i>	<i>100%</i>
Occupation	Cases	%
Government employee	7	14%
Housewife	43	86%
<i>Total</i>	<i>50</i>	<i>100%</i>
Family history	Cases	%
Positive	9	18%
Negative	20	40%
Unknown	21	42%
<i>Total</i>	<i>50</i>	<i>100%</i>

Tab. 3. The percentage of ovarian cancer in relation to socio-demographic variables

26% intermediate and 14% high education. Ovarian cancer was more common among married women: 39 (78%), compared with single women: 11 (22%), which is a significant difference ( $p < 0.01$ ). There was a significant difference ( $p < 0.05$ ) between the percentage of ovarian cancer women who used and did not use contraception. Also, there was a significant difference in the rate of ovarian cancer between housewives (86%) and employed women (14%). The family history is a risk factor in the predisposition to ovarian cancer, but in this study, the results were insignificant because most of the women were uncertain about cancer history in their families (Tab. 3).

### Ovarian cancer in histopathology

The most common histopathological type of ovarian cancer in this study was ovarian serous carcinoma: 24 (48%), with presence of other types in different proportions (Tab. 4).

### Ovarian cancer and staging

The most common stage of the disease was stage IV, found in 42% of cases (Tab. 5).

Histopathology pattern	Cases	%
Serous	24	48%
Mucinous	9	18%
Yolk sac	1	2%
Lipid cell tumor	1	2%
Dysgerminoma	1	2%
Borderline	1	2%
Atypical epithelial	3	6%
Brenner	0	0%
Cystic follicle	1	2%
Cystic teratoma	1	2%
Undifferentiated	1	2%
Metastasis from colon	5	10%
Metastasis from breast	2	4%
<i>Total</i>	<i>50</i>	<i>100%</i>

Tab. 4. Ovarian cancer percentages and histopathological pattern of cancer

Stage	Cases	%
I	6	12%
II	6	12%
III	17	34%
IV	21	42%
<i>Total</i>	<i>50</i>	<i>100%</i>

Tab. 5. Ovarian cancer percentages and stages

## DISCUSSION

Ovarian cancer is one of the most common gynecologic cancer types and is the third type after uterine and cervical cancers. It constituted 17.73% of all gynecologic cancer types. These percentages were obtained due to improved ovarian cancer diagnosis, mainly thanks to sonography, which is now more widely available in Misan province. This result is similar to the results in other studies in Egypt and Jordan<sup>(18,19)</sup>. However, it is lower than the percentage reported in studies done in Iran<sup>(20)</sup>. Other obtained data showed that ovarian cancer was most common in women between 60 and 70 years of age, with the percentage of 30%, but it was rare in age groups 1–10 years and 80–90 years, with the percentage of 0%; this result is the same in other countries, such as Egypt, Iran, Canada, Japan, Brazil and the USA<sup>(18,20,21)</sup>. In the year 2007, the Middle East Cancer Consortium (MECC) evaluated the incidence of ovarian cancer in its four member countries, namely Egypt, Cyprus, Jordan, and USA and compared it to the incidence in the USA based on the SEER data base. This study revealed that in Cypriots and US SEER data, most patients with ovarian cancer were in the age group from 50 to 69, while in Egypt and Jordan, most patients were below the age of 50 years<sup>(20)</sup>. Ovarian cancer distribution by age in Saudi Arabia in 2008 was 32% in patients aged 45–59 years, 31% in patients aged 60–74 years, and 3.7% in patients aged 0–14 years<sup>(22)</sup>, while in the United Kingdom it was 70.6% in women aged 75–79 years<sup>(23)</sup>.

Regarding the place of residence, the majority of patients were from urban areas (about 62%) and fewer patients came from rural areas. In Iran, the rates of female reproductive cancers were significantly higher among residents of cities than villages<sup>(24)</sup>. Differences in the prevalence of risk factors, including reproductive behavior, between the two populations may partly explain this diversity. Regarding parity, 32% of women were nulliparous, 34% had between 1 and 5 children and 34% had between 6 and 10 children. The percentage of women that were single was 22%, married 54%, divorced 6% and widows 18%. Seventy-six per cent of women in this study did not use contraception and 24% used contraception. The majority of patients were housewives (about 86%) while the remaining women were employed. There was no significant difference in the relationship between family history and ovarian cancer due to the low educational level of most patients and social phobia. It has been estimated that ovarian cancer is familial hereditary in about 5–10% of cases. The most important risk factor of ovarian cancer is the presence of this disease in first-degree relatives (mother, daughter, sister). The risk increases considerably with significant family history, meaning two first-degree relatives with ovarian cancer. Familial hereditary ovarian cancer falls into three categories: site-specific familial ovarian cancer, breast-ovarian cancer syndrome, and

Lynch syndrome type II. The true familial ovarian cancer and/or breast cancer develop mainly due to mutation of *BRCA1* which is located on the long arm of chromosome 17q21. The mutation of *BRCA2* gene (location on chromosome 13q21) is also responsible for ovarian and breast cancer syndrome<sup>(25)</sup>.

The most common histopathological type was serous type (48%) followed by mucinous type (about 18%), while the following types were the least common: yolk sac, dysgerminoma, lipid cell tumor, borderline, cystic teratoma and undifferentiated epithelial cell (about 2%). As in the Middle East consortium study, serous carcinomas predominated, ranging between 27.2% and 49.9%, followed by adenocarcinomas in Jordanians (28.7%) and Egyptians (27.2%). The proportion of mucinous carcinomas among Egyptians was 16.1% and among Jordanians 11.7%, whereas the percentages were low in Cypriot registries (ranging from 6 to 8.7%<sup>(19)</sup>), Australia (3.4%), and Japan (5.4%)<sup>(26)</sup>. In a Turkish study, 69% of ovarian cancers were epithelial stromal tumors, 9% were sex-cord stromal tumors, 5% germ cell tumors, and 15% were metastatic<sup>(27)</sup>. In Iran, serous adenocarcinoma (57.6%) was the most common pathology found in patients with epithelial ovarian cancer<sup>(28)</sup>. In Alexandria, serous carcinoma constituted 58%, and mucinous carcinoma 17.2%<sup>(18)</sup>. The incidence of the serous type in all ovarian cancer cases in our study was higher than that of some studies, whereas the incidence of the mucinous type was nearly the same, and this could be explained by the predominance of the molecular phenotype and genotype that expresses the serous histology more in our country.

The largest percentage of our patients presented in a late stage: stage III was noted in 34% and stage IV in 42% of patients. For all patients in this study, the typical presentation was late; stages III and IV were seen in 76% of the cases. Similar results, with 78% of stage III or IV cases, have also been reported<sup>(22)</sup>. Another study found that stages III and IV accounted for only 56.2% of their cases<sup>(21)</sup>. In Alexandria, typical presentation was late; stage III was the initial presentation in 48 patients (41.3%) and stage IV in 44 patients (37.9%), which adds up to the total of 79.2% of cases<sup>(18)</sup>. Most of the patients in Egypt (84.3%) presented with advanced stage III and IV, whereas only 15.7% of patients presented with stage I and II<sup>(28)</sup>. While in England, the percentage of stage III was 31.1% and stage IV was 18.1% whereas stage I was noted in 30.6% and stage II in 5% of cases<sup>(23)</sup>. In Iran, most patients had a stage I (36.7%) or stage II (35%) disease<sup>(28)</sup>. This could be explained by low education standards in Misan, resulting in late presentation after the disease has advanced and low interest in early detection with regular screening tests, such as ultrasound examination, as well as overlooked cancer risk factors, such as obesity, immobility and poor diet in this province. Ovarian cancer metastasizes early in its development, often before it has been diagnosed. More than 60% of women presented

with a stage III or stage IV disease, with cancer already spreading beyond the ovaries. Complications of ovarian cancer can include its spread to other organs, progressive function loss of various organs, ascites, and intestinal obstructions, which can be fatal. Intestinal obstructions in multiple sites are the most common proximate cause of death. Intestinal obstruction in ovarian cancer can either be a true obstruction, where tumor blocks the intestinal lumen, or a pseudo-obstruction when tumor prevents normal peristalsis. It is disproportionately deadly because it lacks any clear early detection or screening, meaning that most cases are not diagnosed until they have reached advanced stages<sup>(11)</sup>.

## CONCLUSION

Ovarian cancer represents the third most common gynecologic cancer type. It was more common in women aged 60–70 years. It occurred more frequently in women living in urban areas than rural areas while housewives developed it more frequently than employed women. Pregnancy and parity in this study showed relative ratios. A high percentage of cancer was noted among married women. Ovarian cancer was less common in women who used contraception compared with those with no history of contraception. Regarding the family history, the results were insignificant. The most common histopathological type of ovarian cancer in this study was ovarian serous carcinoma. The most common stages of the disease were stage III and IV (advanced stages). Tumor marker tests play important roles in screening and prognosis of cancer.

## RECOMMENDATIONS

Increasing awareness of ovarian cancer. Engaging in cancer screening tests for pre-detection and early diagnosis. Organizing workshops and conferences with a multidisciplinary team of surgeons, gynecologists, pathologists, physicians, oncologists and radiotherapists. Conducting further studies to investigate other gynecological cancer types, other than ovarian cancer.

### Limitations of the study

*In this study, the collected data reflect the percentage in our province and not in all cities in our country.*

### Conflict of interest

*There is no conflict of interest and this research has not been funded by any organization.*

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