Frequency of Malignant Ovarian Germ Cell Tumor and Distribution of Demographic Features in a Main Tertiary Hospital in Iran

**ABSTRACT**

**Aims** Ovarian cancer is the 4th cause of women's mortality occurring due to cancer. Malignant germ cell tumors (GCTs) account for 5% of malignant ovarian tumors and 70% of ovarian tumors in women between the ages of 10-30 years old. The aim of the present study was to detect the frequency of malignant ovarian germ cell tumor and distribution of demographic features in the most crowded gynecology oncology clinic.

**Materials and Methods** This cohort descriptive-analytical study was conducted on cases with malignant ovarian tumor managed in Vali-Asr hospital, Tehran, Iran, from 2001 to 2018 (n=1540). The malignant germ cell tumors cases were extracted (n=128) and evaluated in point of epidemiologic and demographic data via the software SPSS 24.

**Findings** 128 patients (8.3%) had GCTs. The average age was 23.88±7.85 years. 79.7% lived in the city. 76.6% had medium economic status and 53.6% had normal body mass index. Premature puberty was revealed in one person. Karyotype XY was detected in 5 persons. About 70.3% of the patients had no parity. In parous women, the highest percentage was related to a childbirth (55.0%). A history of infertility was detected at 6.1%. In 10 patients, the tumor was detected during pregnancy.

**Conclusion** The highest frequency is related to the early young women with no considerable association with socioeconomic and weight status. It is possible that parity would be a protective factor for this tumor. In the case of adnexal mass during pregnancy, Malignant germ cell tumors should be rolled out.

**Keywords** Infertility; Ovarian Neoplasms; Germ Cell Tumor; Pregnancy

**CITATION LINKS**

[1] Endogenous hormones and ovarian cancer ... [2] Clinicopathological analysis of ovarian tumours at birendra military ... [3] Histological pattern of ovarian tumors and their ... [4] Cancer ... [5] Estimates of worldwide burden of cancer ... [6] Cancer incidence and mortality worldwide: Sources, methods and major ... [7] A quick guide to cancer ... [8] Ovarian cancer: Epidemiology ... [9] Morules with optically clear nuclei in ovarian borderline ... [10] Misdiagnosis of a giant uterine leiomyosarcoma ... [11] Mismanagement of ... [12] Malignant germ cell tumors of ... [13] Incidence and survival rates for female ... [14] Anti-NMDA-receptor encephalitis: Case series ... [15] Pattern recognition using transabdominal ultrasound ... [16] Update on malignant ovarian ... [17] Non-epithelial ovarian cancer: ESMO clinical practice ... [18] Identification of 19 new risk loci and potential ... [19] The significance of spermatoc orchid involvement by testicular germ cell tumors: Should we be staging discontinuous invasion from involved ... [20] Repair shielding of platinum-DNA lesions in testicular germ cell tumors by high-mobility group box protein ... [21] Germ cell tumors of the ... [22] Management of ovarian germ ... [23] Crude and age-specific incidence rate ... [24] Incidence rate of ovarian cancer in Iran ... [25] Malignant struma ovarii: An analysis of 88 cases, including ... [26] Natural history of biologically malignant struma ... [27] Ovary: Germ cell ... [28] Age-specific ovarian cancer incidence rate ... [29] Body mass index and ... [30] Evaluation of risk factors and prognostic factors of ... [31] Malignant germ cell tumors of the ovary ... [32] Papillary serous cystadenoma of ovary: A huge ovarian cyst complicating the ... [33] Risk of high-grade serous ovarian cancer associated ... [34] Ovarian cancer complicated by pregnancy ... [35] Williams Obstetrics 22nd Edition Study ... [36] Epidemiology and etiology of infertility in Iran, systematic ... [37] Epidemiology of ovarian cancer ... [38] Ovarian and fallopian tube ... [39] Epithelial ovarian ... [40] Epidemiology of epithelial ovarian ...
Introduction

Studies on the causes of women’s mortality have shown that cancer is the second cause in rank [1]. Among the cancers of female, ovarian cancer is the 4th cause of women’s mortality [2]. The vast variety of ovarian tissue makes it prone to various types of tumors [3]. In fact, ovarian cancer is the most fatal type among genital cancers in women [4]. In 2008, 225,000 women were reported to have ovarian cancer, and 145,000 of women died due to the mentioned cancer [5-8].

Due to the position of the ovaries, which is deep down the pelvis, the diagnosis of this cancer may be missed in its early stages [9]. Also, it may mimic symptoms of other disorders such as gastrointestinal or uterine abnormalities which may delay its diagnosis [10, 11]. Ovarian germ cell tumors result from primordial cells and may be malignant or benign. These tumors account for 20-25% of ovarian neoplasms and 5% of malignant tumors. They also account for 70% of ovarian tumors in women aged 10-30 years old [12, 13].

No clear risk factors have been reported for it [14, 15]. There are a few papers which do relate to family background. Malignant germ cell tumors (GCTs) are categorized as the following pathological groups: Dysgerminoma (the most common type), Yolk sac, Endodermal sinus tumor (EST), Embryonal carcinoma, Polyembryoma, Choriocarcinoma, Teratomas, and Mixed GCTs [16]. Most GCTs are diagnosed in the beginning stages. Generally, in these stages, the patients have an acceptable survival rate (Above 90%) [17].

Studies concerning malignant GCTs in women are fewer than men [18-20]. Also, there seems to be no comprehensive study in this field in Iran. Therefore, it was decided to conduct a research project on this issue, to determine the frequency and demographic features of the patients suffering from malignant GCTs in Iran.

The aim of the present study was to detect the frequency of malignant ovarian germ cell tumor and distribution of demographic features in the most crowded gynecology oncology clinic in Iran.

Materials and Methods

This cohort study is a descriptive-analytical type of study. It was conducted in the gynecology oncology clinic of Vali-Asr Hospital, Tehran, Iran, which is the major referral center of gynecology oncology in Iran in a 17-year period of time from 2001 to 2018. 1540 patients with ovarian tumors were as population study.

After taking approval of the ethics committee (IR.TUMS JKHC.Rec.1396.4819), the subjects with malignant ovarian tumor were evaluated and the cases of malignant GCTs were detected and investigated.

All the information about demographic features and risk factors was completed using a questionnaire containing personal information such as age, date of marriage, place of residence, economic status, education, and body mass index. It also contained such medical records as the age of menstruation, amenorrhea, dysmenorrhea, hirsutism, premature puberty, pregnancy, number of children, infertility, abortion, type of childbirth, family history of tumor, history of diseases, history of ovarian cyst or mass. The data, including qualitative and quantitative variables, were numbered and analyzed via SPSS 24 software. Frequency tables and statistical indexes were used to interpret the data.

Findings

The frequency of the malignant GCTs was 128 (8.3%) patients, out of 1540 ovarian tumors. Their average age was 23.88±7.85 years old. About 57.0% of the subjects were under 25 and 43.0% of them were over 25 years old. 72.6% were high school and university students. 51.6%, were married, and they had been married for 3.50±2.73 years on average. About 70.3% parous of the patients had no parity. About 29.7% who had childbirth, the highest percentage was related to a child with 54.7% (Table 1).

In 10 patients the tumor was detected during pregnancy. 24 patients (18.7%) had not completed their puberty and therefore had not experienced their first menstruation. Five of these patients had XY karyotype and 2 patients did not have any manifestation of secondary traits. Among these patients, there was the history of menstruation disorders including amenorrhea (5.76%), dysmenorrhea (14.42%), menorrhagia (10.57%), menstrual irregularities (15.38%) and hirsutism (7.69%). The average age of menstruation was 12.63±1.43 years old. One patient had shown premature puberty (Table 2). Seven patients had a family history of cancer (2 uterine cancers, 4 breast cancers, and 1 blood cancer). Moreover, some other patients had a history of other diseases (7 thyroid disorders, 1 diabetes, and 6 other diseases including 1 deafness, 1 hypertension, 1 breast cancer, 1 Swyer syndrome, and 2 mentally retarded people). Seven percent of the subjects stated history of benign ovarian cysts. The diagram of the frequency of malignant ovarian germ cell tumor during 2001-2018 shows that this frequency has been just descending after 2014 (Diagram 1). The youngest patient was 11 years old and the oldest one was 50 years old. The highest frequency was for 15-19 age group and the lowest one was for 45-50 age group (Diagram 2).
Table 1) Distribution of relative frequency of qualitative demographic variables (n=128)

| Variables          | Percentage |
|--------------------|------------|
| Marital Status     |            |
| Single             | 48.4       |
| Married            | 51.6       |
| Place of Residence |            |
| Urban              | 79.7       |
| Rural              | 20.3       |
| Socio-economic Condition |       |
| Well-off           | 15.6       |
| Medium             | 76.6       |
| Poor               | 7.8        |
| Body Mass Index    |            |
| Thin               | 25.0       |
| Normal             | 53.6       |
| Fat                | 21.4       |

Table 2) Distribution of relative frequency of medical history (n=128)

| Medical history            | Percentage |
|----------------------------|------------|
| Menstrual irregularities   | 15.38      |
| Amenorrhea                 | 5.76       |
| Dysmenorrhea               | 14.42      |
| Menorrhagia                | 10.57      |
| Disfunction                | 7.06       |
| Premature puberty          | 0.8        |
| Lack of secondary traits   | 1.5        |
| Infertility                | 6.1        |
| Abortion                   | 9.2        |
| Infertility treatment      | 6.15       |
| Uteral contraceptive pill  | 7.7        |
| (OCP)                      |            |
| Pregnancy                  | 7.8        |
| Karyotype XY               | 3.9        |

Discussion

The aim of the present study was to detect the frequency of malignant ovarian germ cell tumor and distribution of demographic features in the most crowded gynecology oncology clinic in Iran. Germ cell tumors have been declined in developed countries due to an aging population but they still consist of a considerable number of tumors in developing countries and importantly, they involve children and young women, frequently [21, 22].

In the present study, the frequency of malignant GCTs was ascending but it was descending from 2014. The clear reduction after 2014 might have been due to the presence of specialized oncology fellowships in different cities who have been trained in recent years, which decreases the number of patients who referred to the Hospitals in Tehran. In this study, the frequency of the malignant GCTs was 8.3% of whole malignant ovarian tumors. This number was reported at 13.8% in Iran [21] and 2.6% for the USA [24]. It has also been reported that the frequency of germ cell among black-skinned people and Asians has been three times as much as others, and its prognosis has been worse than the white-skinned people. There are various opinions on this issue though [25, 26], there seems to be no racial aptitude for GCTs, compared to epithelial ovarian cancers. In over 60% of cases, GCTs happen in children and adults, one-third of which is malignant [27].

The average age of the patients in this study was 23.88±7.85 years old, the most frequent age group was 15-19 and in the second place was 20-24 (Fertility age). Previous studies also show that it mostly affects young and middle-aged women and its peak comes at the age of 20 years old [28].

Similarly, Arab et al. declared the average age of the patients in Iran was 23 years old [24]. In total, 57.0% of the subjects were under 25 and 43.0% of them were over 25 years old. Therefore, this range of ages is risky and worthy of attention, and maintaining fertility during surgical procedures might be a solution. 53.6% were of normal body mass index, which showed this index was not an important variable in having this tumor. In the previous studies, it was mentioned that obesity is associated with some types of ovarian cancer [29], but in another study, the average weight of patients in germ cell tumors was the lowest [30]. The highest frequency was related to residents of urban areas with 79.7%. About 76.6% of the patients had medium economic status, which showed that socio-economic status was not an important variable, although more studies are needed to prove this point firmly.

24 patients had not had their first menstruation by the time of the study, 20.8% of which had XY karyotype. This accounts for 3.9% of the patients who had malignant germ cell mass. This shows the importance of checking the karyotype in these
The average infertility rate reported for Iran is 10.9%. High risk of ovarian cancer [37]. According to this with refractory infertility may harbor a particularly development of ovarian cancer. Nulliparous women Infertility alone is an independent risk factor for the rate is accounted in whole fertility age (12-50 years population was young while the public infertility and the impact may be due to this fact that the studied women with no considerable association with socio-economic and weight status. It is possible that parity would be a protective factor for this tumor. In the case of adnexal mass during pregnancy, Malignant Germ cell tumors should be rolled out.

Conclusion

The highest frequency is related to the early young women with no considerable association with socio-economic and weight status. It is possible that parity would be a protective factor for this tumor. In the case of adnexal mass during pregnancy, Malignant Germ cell tumors should be rolled out.

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Ethical permissions: After taking approval of the ethics committee (IR.TUMS JHCR.REC.1396.4819), the subjects with malignant ovarian tumor were evaluated and the cases of malignant GCTs were detected and investigated.

Conflict of interests: The author declares that they have no conflict of interest.

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patients, especially those who have not menstruated yet. In the study of Lee-Jones in 2003, 95% of the patients had normal karyotype, but 5% of them showed chromosome Y in their karyotype [27], 81.25% had menstruation. According to the result of this study, among these patients, 15.38% had a history of menstrual irregularities, it showed that hormonal disorders do not have an important role in occurrence of this tumor. The average age of menstruation was 12.63±1.43. One patient had experienced premature puberty which confirms the secretion of hormones from the tumor.

Malignant GCT is the most common type of malignant tumor in pregnancy [31]. In ten (7.8%) cases of the population study, it was revealed, 40% of that showed it in first trimester, 50% in second and 10% in the third trimester. In 40% of them, the tumor was detected incidentally during ultrasonography. Previous studies showed that physiological symptoms during pregnancy may mimic manifestation of the disease in pregnancy. The majority of ovarian masses in early pregnancy are physiological and resolve spontaneously, but some persist and the management of such tumors is variable. Masses persisting after the first trimester are generally excised to prevent torsion or rupture during pregnancy and to exclude malignancy. The risk of ovarian malignancy is rare in pregnancy [32]. Consequently, underdiagnosis of any abdominal complaint may lead to life-threatening situations such as overgrowth or torsion of ovarian masses [32]. About 70% of the patients had no parity which confirms the other studies that have been claimed low parity is related to ovarian cancer [33]. From about 30% who had childbirth, the highest percentage was related to a child with 55%. However, since the age of first childbearing has been increased, the incidence of cancer is also likely to rise [34]. A history of infertility was detected at 6.1% which is higher than general population, and abortion at 9.3%. Infertility is common and affects 10% to 15% of reproductive-aged couples [35]. The average infertility rate reported for Iran is 10.9% [36]. That is higher than the findings of this study (6.1%). It may be due to this fact that the studied population was young while the public infertility rate is accounted in whole fertility age (12-50 years old). Therefore this study cannot exclude the impact of infertility on the occurrence of ovarian cancer. Infertility alone is an independent risk factor for the development of ovarian cancer. Nulliparous women with refractory infertility may harbor a particularly high risk of ovarian cancer [37]. According to this study, 7.7% of patients had used contraceptives. The use of contraceptives is a protection factor [38, 39], but this study cannot have clear proof in that respect since that percentage was not enough to draw a conclusion. Seven patients had a history of cancer in their relatives. In the case of epithelial cancer, the role of family history has been proved [40]. But in present study, it is not yet proved as a risk factor and more research is needed. Seven percent had a history of benign ovarian cyst which is not considered as a risk factor.

Having in mind that the highest frequency was related to the average age of 23, maintaining the function of ovaries at young ages is highly important. There was no relationship between body mass index and socioeconomic status with GCTs. Low parity can be a risk factor for this tumor. The patients who have not experienced menstruation should be checked for karyotype and gonad diseases. Further studies with wider sampling and more investigation time are recommended. This study had some limitations such as the lack of further investigation of the patient’s cases and the lack of recording the data in their files. A study without these limitations can give us better results.
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