



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

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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

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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 with age 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).

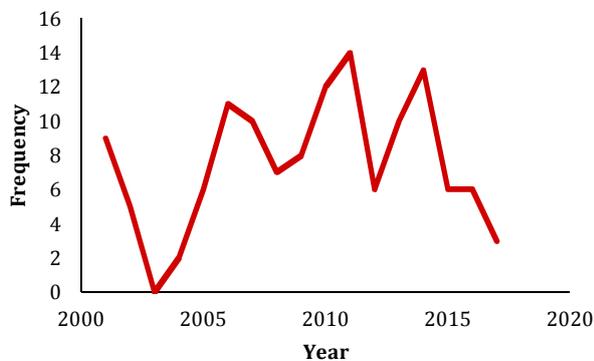
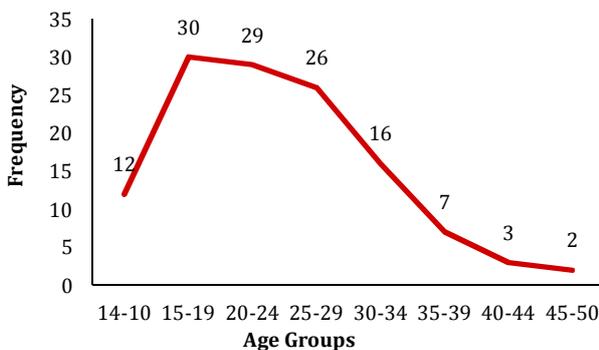
The youngest patient was 11 years old and the oldest one was 50 years old. The highest frequency was for 15-19 age group and the lowest one was for 45-50 age group (Diagram 2).

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	
Amenorrhea	5.76
Dysmenorrhea	14.42
Menorrhagia	10.57
Hirsutism	7.69
Premature puberty	0.8
Lack of secondary traits	1.6
Infertility	6.1
Abortion	9.2
Infertility treatment	6.15
Oral contraceptive pill (OCP)	7.7
Pregnancy	7.8
Karyotype XY	3.9

**Diagram 1)** Germ cell tumor frequency during 2001-2018**Diagram 2)** Frequency of tumor patients over various age groups

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 [23] 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

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.

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.

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Ethical permissions: 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.

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

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References

- 1- Lukanova A, Kaaks R. Endogenous hormones and ovarian cancer: Epidemiology and current hypotheses. *Cancer Epidemiol Biomarkers Prev.* 2005;14(1):98-107.
- 2- Khatri R. Clinicopathological analysis of ovarian tumours at birendra military hospital. *Med J Shree Birendra Hosp.* 2011;10(1):26-31.
- 3- Jha R, Karki S. Histological pattern of ovarian tumors and their age distribution. *Nepal Med Coll J.* 2008;10(2):81-5.
- 4- Jemal A, Thomas A, Murray T, Thun M. Cancer statistics, 2002. *CA Cancer J Clin.* 2002;52(1):23-47.

- 5- Ferlay J, Shin HR, Bray F, Forman D, Mathers C, Parkin DM. Estimates of worldwide burden of cancer in 2008: GLOBOCAN 2008. *Int J Cancer*. 2010;127(12):2893-917.
- 6- Ferlay J, Soerjomataram I, Dikshit R, Eser S, Mathers C, Rebelo M, et al. Cancer incidence and mortality worldwide: Sources, methods and major patterns in GLOBOCAN 2012. *Int J Cancer*. 2015;136(5):E359-86.
- 7- Boffetta P, Boccia S, La Vecchia C. A quick guide to cancer epidemiology. Heidelberg: Springer Science & Business Media; 2014.
- 8- La Vecchia C. Ovarian cancer: Epidemiology and risk factors. *Eur J Cancer Prev*. 2017;26(1):55-62.
- 9- Li CC, Hirokawa M, Qian Z, Fujii Y, Ino H, Wakatsuki S, et al. Morules with optically clear nuclei in ovarian borderline endometrioid tumor. *Apmis*. 2002;110(11):783-8.
- 10- Agah J, Karimzadeh S, Moharrer Ahmadi F. Misdiagnosis of a giant uterine leiomyosarcoma: Clinic and image challenges. *Case Rep Oncol Med*. 2017;2017:3568328.
- 11- Agah J, Jafarzadeh Esfehiani R, Kamalimanesh B, Fattahi Abdizadeh M, Jalilian AR. Mismanagement of a huge ovarian serous cystadenoma in a young girl, a case report. *J Midwifery Reprod Health*. 2015;3(1):315-7.
- 12- Tewari K, Cappuccini F, Disaia PJ, Berman ML, Manetta A, Kohler MF. Malignant germ cell tumors of the ovary. *Obstet Gynecol*. 2000;95(1):128-33.
- 13- Smith HO, Berwick M, Verschraegen CF, Wiggins C, Lansing L, Muller CY, et al. Incidence and survival rates for female malignant germ cell tumors. *Obstet Gynecol*. 2006;107(5):1075-85.
- 14- Dalmau J, Gleichman AJ, Hughes EG, Rossi JE, Peng X, Lai M, et al. Anti-NMDA-receptor encephalitis: Case series and analysis of the effects of antibodies. *Lancet Neurol*. 2008;7(12):1091-8.
- 15- Tongsong T, Luewan S, Phadungkiatwattana P, Neeyalavira V, Wanapirak C, Khunamornpong S, et al. Pattern recognition using transabdominal ultrasound to diagnose ovarian mature cystic teratoma. *Int J Gynaecol Obstet*. 2008;103(2):99-104.
- 16- Gershenson DM. Update on malignant ovarian germ cell tumors. *Cancer*. 1993;71(S4):1581-90.
- 17- Colombo N, Peiretti M, Garbi A, Carinelli S, Marini C, Sessa C, et al. Non-epithelial ovarian cancer: ESMO clinical practice guidelines for diagnosis, treatment and follow-up. *Ann Oncol*. 2012;23 Suppl 7:vii20-6.
- 18- Litchfield K, Levy M, Orlando G, Loveday C, Law PJ, Migliorini G, et al. Identification of 19 new risk loci and potential regulatory mechanisms influencing susceptibility to testicular germ cell tumor. *Nat Genet*. 2017;49(7):1133-40.
- 19- Sanfrancesco JM, Trevino KE, Xu H, Ulbright TM, Idrees MT. The significance of spermatic cord involvement by testicular germ cell tumors: Should we be staging discontinuous invasion from involved lymphovascular spaces differently from direct extension?. *Am J Surg Pathol*. 2018;42(3):306-11.
- 20- Awuah SG, Riddell IA, Lippard SJ. Repair shielding of platinum-DNA lesions in testicular germ cell tumors by high-mobility group box protein 4 imparts cisplatin hypersensitivity. *Proc Natl Acad Sci U S A*. 2017;114(5):950-5.
- 21- Pectasides D, Pectasides E, Kassanos D. Germ cell tumors of the ovary. *Cancer Treat Rev*. 2008;34(5):427-41.
- 22- Gershenson DM. Management of ovarian germ cell tumors. *J Clin Oncol*. 2007;25(20):2938-43.
- 23- Arab M, Khayamzadeh M, Hashemi M, Hosseini M, Tabatabaefar M, Anbiaee R, et al. Crude and age-specific incidence rate patterns for histopathologic subtypes of ovarian cancer in Iran. *Arch Iran Med*. 2010;13(3):203-8.
- 24- Arab M, Khayamzadeh M, Tehranian A, Tabatabaefar M, Hosseini M, Anbiaee R, et al. Incidence rate of ovarian cancer in Iran in comparison with developed countries. *Indian J Cancer*. 2010;47(3):322-7.
- 25- Robboy SJ, Shaco-Levy R, Peng RY, Snyder MJ, Donahue J, Bentley RC, et al. Malignant struma ovarii: An analysis of 88 cases, including 27 with extraovarian spread. *Int J Gynecol Pathol*. 2009;28(5):405-22.
- 26- Shaco-Levy R, Bean SM, Bentley RC, Robboy SJ. Natural history of biologically malignant struma ovarii: Analysis of 27 cases with extraovarian spread. *Int J Gynecol Pathol*. 2010;29(3):212-27.
- 27- Lee-Jones L. Ovary: Germ cell tumors. *Atlas Genet Cytogenet Oncol Haematol*. 2003;7(4):278-84.
- 28- Quirk JT, Natarajan N, Mettlin CJ. Age-specific ovarian cancer incidence rate patterns in the United States. *Gynecol Oncol*. 2005;99(1):248-50.
- 29- Leitzmann MF, Koebnick C, Danforth KN, Brinton LA, Moore SC, Hollenbeck AR, et al. Body mass index and risk of ovarian cancer. *Cancer*. 2009;115(4):812-22.
- 30- Yosefi Z, Homaei F. Evaluation of risk factors and prognostic factors of ovarian cancer. *J Med Counc Iran*. 2006;24(3):279-88. [Persian]
- 31- Bakri YN, Ezzat A, Akhtar M, Dohami H, Zahrani A. Malignant germ cell tumors of the ovary: Pregnancy considerations. *Eur J Obstet Gynecol Reprod Biol*. 2000;90(1):87-91.
- 32- Kamalimanesh B, Jafarzadeh Esfehiani R, Agah J. Papillary serous cystadenoma of ovary: A huge ovarian cyst complicating the pregnancy. *J Cases Obstet Gynecol*. 2016;3(4):121-4.
- 33- Stewart LM, Spilsbury K, Jordan S, Stewart C, Holman CDJ, Powell A, et al. Risk of high-grade serous ovarian cancer associated with pelvic inflammatory disease, parity and breast cancer. *Cancer Epidemiol*. 2018;55:110-6.
- 34- Dobashi M, Isonishi S, Morikawa A, Takahashi K, Ueda K, Umezawa S, et al. Ovarian cancer complicated by pregnancy: Analysis of 10 cases. *Oncol Lett*. 2012;3(3):577-80.
- 35- Cox S, Werner C, Hoffman B, Cunningham F. Williams Obstetrics 22nd Edition Study Guide. New York City: McGraw-Hill Professional; 2005.
- 36- Parsanezhad ME, Jahromi BN, Zare N, Keramati P, Khalili A, Parsa Nezhad M. Epidemiology and etiology of infertility in Iran, systematic review and meta-analysis. *J Womens Health Issues Care*. 2013;2(6).
- 37- Reid BM, Permeth JB, Sellers TA. Epidemiology of ovarian cancer: A review. *Cancer Biol Med*. 2017;14(1):9-32.
- 38- Berek JS, Natarajan S. Ovarian and fallopian tube cancer. In: Berek JS, editor. *Berek & Novak's gynecology*. 14th Edition. Philadelphia: Lippincott Williams & Wilkins; 2007. pp. 1457-549.
- 39- Copeland LJ. Epithelial ovarian cancer. In: Di Saia P, Creasman W. *Clinical gynecologic oncology*. 7th Edition. Maryland Heights: Mosby; 2007. pp. 313-67.
- 40- Webb PM, Jordan SJ. Epidemiology of epithelial ovarian cancer. *Best Pract Res Clin Obstet Gynaecol*. 2017;41:3-14.