Crude and Age-Specific Incidence Rate Patterns for Histopathologic Subtypes of Ovarian Cancer in Iran

Maliheh Arab MD^{•1,2}, Maryam Khayamzadeh MD^{1,3}, Mohammad Hashemi MD⁴, Maryam Hosseini MD², Morteza Tabatabaeefar MD⁵, Robab Anbiaee MD^{1,5}, Nahid Anvari MD⁶, Mojgan Ebrahimi MD⁶, Mohammad E. Akbari MD^{1,7}

Abstract:

Background: The purpose of this study was to report age-specific incidence rates of histopathological subtypes of ovarian cancer in Iran.

Methods: Data published by the pathology-based Cancer Registry, Iranian Ministry of Health and Medical Education for the year 2004, was utilized. This study included 793 new ovarian cancer cases which were analyzed by SPSS software (version 13).

Results: There were 45 different histologies reported in 793 new cases which were categorized into ten major groups. Epithelial tumors displayed the highest age specific incidence rate, followed by germ cell tumors. Serous epithelial tumors were the most common in the epithelial group.

Conclusion: The age-specific incidence rate of ovarian cancer varies based on histology.

Keywords: Age at diagnosis - histology - incidence - Iran - ovarian cancer

Introduction

Ovarian cancer is the 8th most frequent for incidence, the 12th most frequent for mortality and 16th for cancer burden in Iran.¹

Ovarian cancer is a family of malignancies that displays a great histopathological diversity.^{2–6} From 2000 – 2004, ovarian cancer survival in Iran, was 61% with better survival seen in younger women and certain histologic subtypes. The five year survival for germ cell tumor and epithelial groups were 85% and 59%, respectively (P<0.05).⁷

Ovarian tumors, although often inappropriately considered as a single entity, consist of many types, which each are further classi fied into subtypes.⁸⁻⁹ The common epithelial tumors are by far the most frequently encountered forms of ovarian tumors, accounting for three-fifths of all ovarian neoplasms.⁸

Epithelial ovarian neoplasms are derived from tissues that arise from the coelomic epithelium or mesothelium.^{3,6}

Germ cell tumors are the second group of ovarian tumors which embrace the total neoplasms that have been derived from primitive germ cells of the embry-onic gonad.¹⁰

Sex cord-stromal tumors, the third main group of ovarian neoplasms, are derived from the sex cord and the ovarian stroma or mesenchyme.^{4,11}

A comparison of the respective age-specific incidences shows that various histological groups may either share similar, or have different incidence patterns.¹²⁻¹³

The purpose of this study was to present, at first, the frequency of ovarian cancer histologic subtypes according to age distribution. Secondly, the study presented age-specific annual incidence rates of ovarian cancer histologic subtypes. It is expected to assist with future public health planning according to age groups exposed to specific risk or protective factors for ovarian cancer.

Authors' affiliations: ¹Cancer Research Center, ²Department of Gynecology-Oncology, ³Department of Community Medicine, ⁴Department of Pathology, ⁵Department of Radiation-Oncology, Shaheed Beheshti University of Medical Sciences, Tehran, Iran. ⁶Department of Pathology, Hamadan University of Medical Sciences, Hamadan, Iran. ⁷Department of Surgical Oncology, Shaheed Beheshti University of Medical Sciences, Tehran, Iran.

[•]Corresponding author and reprints: Maliheh Arab MD, Department of Gynecology-Oncology, Shaheed Beheshti University of Medical Sciences, Imam Hossein Teaching Hospital and Cancer Research Center, Tehran, Iran.

E-mail: drmarab@yahoo.com

Accepted for publication: 2 December 2009

Patients and Methods

According to the 2005 - 2006 Cancer Registry Data published by the Ministry of Health and Medical Education of the Islamic Republic of Iran (MOH&ME), there were 793 new ovarian cancer cases diagnosed in 2004 - 2005.¹⁴

Data was actively collected from all pathology centers in Iran. Hospital and death certificate based data were not included. A total of 45 different histopathologic reports of ovarian malignancies were reported in the 793 cases. In the present study, we classified them into ten main clusters6,^{15,16} which included: all ovarian, all epithelial, serous, mucinous, endometrioid, clear cell, other epithelial, germ cell, sex cord-stromal, and other ovarian cancers.

For the initial stepa, the frequency of the ten pathologic clusters was reported in nine age groups.

Secondly, the age-specific annual incidence rate of various histopathologic subtypes per 100,000 women was estimated. The age distribution of exposed women, or the general female Iranian population, was extracted from the 2004 - 2005 MOH&ME Report. The number of each histologic subtype cases in ten year interval groups of the female population was cal-

culated.

Data analysis was done by SPSS software (version 13).

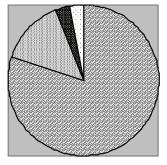
Results

There were 11 out of 793 (14%) malignant ovarian cancers which were excluded due to unknown age. Among the remaining 782 cases, epithelial ovarian tumor (630 cases) was the most frequent followed by germ cell tumor with 108 cases (Figure 1).

Among epithelial ovarian tumors, serous (N=372) and mucinous (N=72) were the most common (Figure 2).

The age distribution of all ovarian cancer patients is shown in Figure 3. There were 42% of ovarian cancers diagnosed in the 40 - 59 age group. During 2004 - 2005, the median age of ovarian cancer diagnosed in Iran was 49 years of age or less.

Histopathologic subtypes of ovarian cancer according to age are presented in Table 1. Epithelial ovarian cancer was most common in the 30 - 59 age groups with endometrioid being the most frequent subtype (77%). In contrast, 78% of germ cell tumors were found in patients younger than 30 years of age. Clear cell (40%) and other epithelial tumors (36%) were the



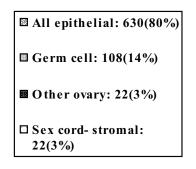


Figure 1. Frequency of ovarian cancer subtypes in Iran, 2004

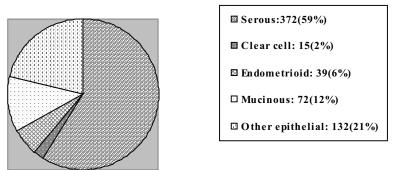


Figure 2. Frequency of epithelial ovarian cancer subtypes in Iran, 2004

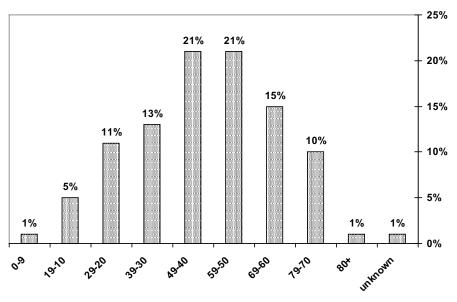


Figure 3. Age distribution of ovarian cancer in Iran, 2004

	Ν	%	Age (median)	Age Distribution						
Classification										
Classification				<30	30 - 59	<u>≥</u> 60				
All ovarian cancer	782	100.0	49	17.0%))133	56.3%))440	26.7%))209				
All epithelial	630	80.6	52	5.9%))37	63.7%))401	30.5%))192				
Serous	372	47.6	52	5.1%))19	65.3%))243	29.6%))110				
Mucinous	72	9.2	51	15.3%))11	54.2%))39	30.6%))22				
Endometrioid	39	5.0	48	7.7%))3	76.9%))30	15.4%))6				
Clear cell	15	1.9	57	0.0%))0	60.0%))9	40.0%))6				
Other epithelial	132	16.9	54	3.0%))4	60.0%))80	36.4%))48				
Germ cell	108	13.8	23	77.8%))84	17.6%))19	4.6%))5				
Sex cord-stromal	22	2.8	40	18.2%))4	54.5%))12	27.3%))6				
Other ovary	22	2.8	38	36.4%))8	36.4%))8	27.3%))6				
* Percentage of 782 ovarian cancer cases										

 Table 2. Age specific annual incidence rates (per 100,000 women)

 of epithelial ovarian tumors according to subtype, Iran, 2004

Age group	All ovarian cancer	All epithelial	Serous	Mucinous	Endometrioid	Clear cell	Other epithelial	Germ cell	Sex cord- stromal	Other ovary
0-9	0.06	0.00	0.00	0.00	0.00	0.00	0.00	0.06	0.00	0.00
10-19	0.44	0.02	0.02	0.00	0.00	0.00	0.00	0.40	0.00	0.02
20-29	1.43	0.57	0.28	0.18	0.05	0.00	0.06	0.70	0.06	0.10
30-39	2.36	1.82	1.06	0.22	0.16	0.04	0.34	0.31	0.13	0.09
40-49	5.26	5.04	2.95	0.44	0.40	0.09	1.15	0.09	0.03	0.09
50-59	8.21	7.81	5.00	0.74	0.49	0.20	1.38	0.10	0.25	0.05
60-69	9.74	9.33	4.79	1.22	0.32	0.32	2.68	0.08	0.08	0.24
70-79	9.66	8.17	5.33	0.74	0.12	0.25	1.73	0.50	0.62	0.37
80+	5.33	5.33	3.88	0.48	0.48	0.00	0.48	0.00	0.00	0.00

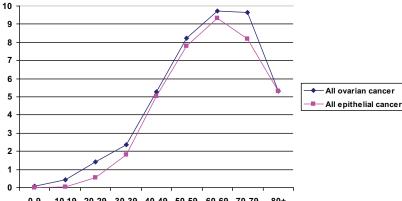
most frequent types in patients who were 60 or older. Age specific incidence rate calculations revealed that ovarian cancer incidence increased with age (Table 2). The highest incidence rate belonged to the age group of 60 - 69 (9.74 per 100000). The second highest incidence rate was seen in the 70 - 79 age group (9.66 per 100000), followed by 5.33 per 100,000 (Figure 4). Epithelial ovarian and its subtypes exhibited the same trend (Figures 4 - 5).

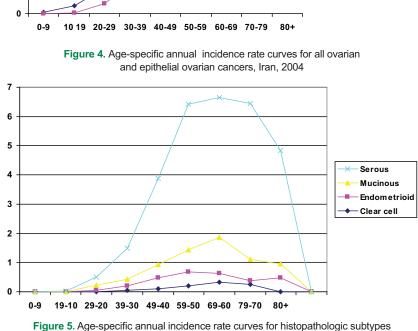
Germ cell tumors had two peaks, first in the 20 -29 age group (0.7 per 100,000) and second in the 70 - 79 age group (0.5 per 100,000) (Figure 6).

Discussion

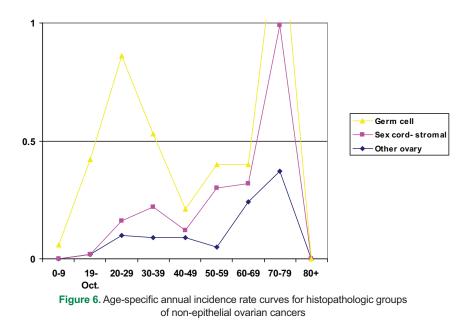
Ovarian cancer is an important health problem throughout the world and in Iran. A population-based cancer registry in Kolkata (eastern India), 1998 – 1999, showed the ovaries as the fourth site for cancer in women.¹⁷ In a study in Tehran, the fourth most frequent site of cancer in females were the ovaries, as well.¹⁸ The median age of ovarian cancer patients in the present study was 49 years of age. In a study in Sweden, 1960 – 2005, the median age of ovarian cancer patients was 61.6 years which did not change over the 30-year period of the study.¹⁹ An older, stable population in Sweden and younger population in Iran might explain the 12-year difference in median age.

However, it is important to mention that the age distribution of the Iranian population is changing. As a result, all health agencies have to use a standard population for the calculation of age- adjusted rates. Otherwise, comparing the rates of previously published studies would not be valid because different population standards have been used. For this reason, in the present study, an age distribution of the same year was





of epithelial ovarian cancers, Iran, 2004.



used for age adjustment. A comparison of the respective age-specific incidence rates showed that various histologic subtypes might either share similar, or have different incidence patterns.¹²

In the present study, the age-specific incidence rate of ovarian cancer increased with age. The highest incidence rate belonged to the age group of 60 - 69. Epithelial ovarian and its subtypes including serous, mucinous, and endometrioid exhibited the same trend (Figures 4 – 5). In a Japanese study, serous carcinoma showed higher rates than mucinous carcinoma in those aged 35 years and over, and vice versa in those aged younger than 35.⁵

In our study, the germ cell tumor incidence rate showed two peaks; first in the 20 - 29 age group (0.7 per 100,000) and second in the 70 - 79 age group (0.5 per 100,000) (Figure 6). In Japan, however, as an Asian country, the incidence rate of germ cell tumors peaked in the age group of 15 - 24 and leveled off after middle age.⁵

The proportion of germ cell tumors in Japan was more than those in the US.⁵

The Center for Adult Disease in Japan reported that germ cell tumors appeared more frequently at younger ages and in low-incidence areas, while epithelial ovarian cancers were more apparent amongst older age groups and in high-incidence areas.²⁰

The epidemiologic pattern of cancers in developing countries differs in many aspects from that of industrialized nations.^{21,22}

Many factors may influence the proportion and in-

cidence rate of ovarian cancer subtypes in different areas. Overall distribution of population, as old or young, oral contraceptive (OC) use, family size, diet, and access to diagnostic techniques are the main parameters affecting the proportion and incidence of subtypes. It is worth mentioning that OC has a strong effect only on epithelial ovarian cancers, and mainly on serous tumors. The incidence of mucinous tumors is rarely affected by OC.²³

Some limitations of this study should be noted. At first, histological diagnoses of these cases were made in numerous labs by various pathologists without the supervision of a reference lab. Therefore, the possibility of incorrect diagnosis in some cases must be considered.

Secondly, data of the Cancer Registry Program of MOH&ME in Iran, as reported in 2005 - 2006, is estimated to cover nearly 80% of all ovarian cancer cases of the country. Third, continuous annual cancer registry data of more than one year intervals may increase accuracy of the results and comparative points, and would reveal true trends of the incidence rates.

In conclusion, we hope that the age-specific incidence rates of ovarian cancer and its subtypes presented in this report will serve as a useful point of reference for future studies of ovarian cancer subtype incidences in Iran. Determination and approval of a standard Iranian population for standardizing the incidence rates for all health problems, particularly cancers, would help to specify their trend in the future and highlight our status worldwide. They would undoubtedly empower community health programs to solve health problems including in the field of cancer.

Acknowledgment

The authors wish to thank all the histopathology diagnostic laboratories in Iran which indirectly supported our study.

References

- 1. Akbari ME, Abachizadeh K, Khayamzadeh M, Tabatabaee M, Esnaashari F, Motlagh AG, et al. *Iran Cancer Report*. Tehran, Iran: CRC. SBMU; 2008.
- Russell P. Farnsworth A. Surgical Pathology of the Ovaries. 2nd ed. New York, NY: Churchill Livingstone; 1997.
- Berek JS, Natarajan S. Ovarian and fallopian tube cancer. In: Berek JS, ed. *Berek and Novaks Gynecology*. 14th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2007.
- van Nagell JR Jr, Gershenson DM. Ovarian cancer: etiology, screening, and surgery. In: Rock JA, Jones HW, eds. *Telindes Operative Gynecology*. 10th ed. Philadelphia, PA: Wolters Kluwer; 2008.
- Loka A, Tsukuma H, Ajiki W, Oshima A. Ovarian cancer incidence and survival by histologic type in Osaka, Japan. *Cancer Sci.* 2003; 94: 292 – 296.
- Scully RE, Young RH, Clement PB. Atlas of tumor pathology. Third series. *Fascicle 23: Tumors of the Ovary, Maldeveloped Gonads, Fallopian Tube, and broad ligament.* Washington, DC. Armed Forces Institute of Pathology; 1998.
- Arab M, Khayamzadeh M, Mohit M, Hosseini M, Anbiaee R, Tabatabaeefar M, et al. Survival of ovarian cancer in Iran 2000 – 2004. *Asian Pac J Cancer Prev.* 2009; 10: 555 – 558.
- Hoskins WJ, Perez CA, Young RC, Barakat RR, Markman M, Randall ME. *Principles and Practice* of Gynecologic Oncology. 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2005.
- Robboy SJ, Anderson MC, Russell P. Pathology of the Female Reproductive Tract. London: Churchill Livingstone; 2002.
- Bidus MA, Zahn CM, Rose GS. Germ cell, stromal, and other ovarian tumors. In: Disaia PJ, Creasman WT, eds. *Clinical Gynecologic Oncology*. 7th ed. Philadelphia, PA: Mosby Elsevier; 2007.
- 11. Berek JS, Hacker NF. Nonepithelial ovarian and

fallopian tube cancers. In: Berek JS, Hacker NF. *Practical Gynecologic Oncology*. 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2005.

- Quirk JT, Natarajan N. Age-specific ovarian cancer incidence rate patterns in the United States [letter]. *Gyn Oncol.* 2005; **99:** 248 – 250.
- Guirck JT, Natarajan N. Ovarian cancer incidence in the United States, 1992 – 1999. *Gyn Oncol.* 2005; 97: 519 – 523.
- Islamic Republic of Iran, Ministry of Health and Medical Education, Health Deputy, Center for Disease Control & Prevention, Noncommunicable Deputy, Cancer Office. Iranian Annual of National Cancer Registration Report; 2005 – 2006.
- 15. Scully RE. *Histological Classification of Ovarian Tumors*. 2nd ed. Berlin: Springer-Verlog; 1999.
- Berg JW. Morphologic classification of human cancer. In: Schottenfeld D, Fraumcri JJ, eds. *Cancer Epidemiology and Prevention*. 2nd ed. New York, NY: Oxford; 1996.
- Sen U, Sankaranarayanan R, Mandal S, Ramanakumar A, Parkin DM, Sliddiqi M. Cancer patterns in eastern India: the first report of the Kolkata cancer registry. *Int J Cancer*. 2002; 100: 86 – 91.
- Mohagheghi MA, Mosavi-Jarrahi A, Malekzadeh R, Parkin M. Cancer incidence in Tehran metropolis: The first report from the Tehran populationbased cancer registry, 1998 – 2001. *Arch Iran Med*. 2009; 12: 15 – 23.
- Skirnisdottir I, Garmo H, Wilander E, Holmberg L. Borderline ovarian tumors in Sweden 1960 – 2005: Trends in incidence and age at diagnosis compared to ovarian cancer. *Int J Cancer*. 2008; **123**: 1897 – 1901.
- Hanai A. Trends and differentials in ovarian cancer: incidence, mortality and survival experience. *AP-MIS Suppl.* 1990; 12: 1 – 20.
- Basile S, Angioli R, Manci N. Gynecological cancers in developing countries: The challenge of chemotherapy in low-resources setting. *Int J Gynecol Cancer*. 2006; 16: 1491 1497.
- Liu MC, Hai A, Huang AT. Cancer epidemiology in the Far East – contrast with the United States. Oncology. 1993; 7: 99 – 110.
- Beral V, Doll R, Hermon C, Peto R, Reeves G, Brimton L. et al. Ovarian cancer and oral contraceptives: collaborative reanalysis of data from 45 epidemiological studies including 23257 women with ovarian cancer and 87303 controls. *Lancet*. 2008; **371:** 303 – 314.