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Variations in the Incidence and Mortality of Ovarian Cancer and Their Relationship with the Human Development Index in European Countries in 2012

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Abstract

Background: Ovarian cancer (OC) has high incidence and mortality rates among the reproductive system cancers. This study investigated the relationship between the age-standardized incidence rate (ASIR) and age-standardized mortality rate (ASMR) of OC and Human Development Index (HDI) in European countries in 2012. **Material and methods:** This ecological study assessed the correlation between the ASIR and ASMR of OC and HDI and its components including life expectancy at birth, average years of schooling, and gross national income (GNI) per capita. Bivariate correlation analysis was used for assessing the correlation between the ASIR and ASMR of OC and HDI and its components. All reported P values were two-sided. Statistical analyses were performed using SPSS (Version 15.0, SPSS Inc.). **Results:** The maximum ASIR of OC was observed in Latvia, Bulgaria, and Poland. The highest ASMR of OC was observed in Latvia, Lithuania, and Poland. The incidence and mortality rates of OC are expected to increase between 2012 and 2035. This increase will be more pronounced in women ≥ 65 years. HDI had a weak negative correlation with the ASIR of OC (r=- 0.213; P=0.186) and a weak positive correlation with the ASMR of OC (r=0.072; P=0.659). **Conclusion:** According to the results of this study, health policy makers must make appropriate decisions to deal with the increasing morbidity and mortality of OC, especially in women over 65 years of age, in regions with lower access to prevention and treatment services.

Keywords

Europe, HDI, Incidence, Mortality, Ovarian Cancer

Introduction

Ovarian cancer (OC) is the seventh leading cancer diagnosis and the fifth leading cause of cancer-related mortalities (Coburn et al., 2017). OC has high incidence and mortality rates among the reproductive system cancers (Ferlay et al., 2010). Based on the global estimates, about 225,000 new cases of OC are diagnosed every year and 140,000 women annually die from this disease worldwide (Ferlay et al., 2010). In 2014, the lifetime risk of OC among women in the United States was ranging from 4% to 9%, 73% of women had no family history of ovarian cancer (Pearce et al., 2015).

The incidence and mortality rates of OC vary in different areas of the world (Coburn et al., 2017). Although the incidence and mortality rates of OC are globally high, the cause and etiology of the disease are not completely understood (Razi et al., 2015). However, several factors associated with OC have been identified and classified into three categories of protective factors, e.g. parity and contraceptive use, risk factors, e.g. no history of a full-term pregnancy, a positive family history of OC, and age, and other factors, e.g. such as lactation, age at menopause, and age at menarche, whose relations with OC are not clearly determined (Poorolajal et al., 2014). One of the significant factors related with OC is the Human Development Index (HDI) which reflects the socioeconomic position of individuals living in different countries (Mahdavifar et al., 2016; Mohammadian et al., 2015; Shuja et al., 2017).

Socioeconomic factors affect cancer incidence and mortality through complex and changeable mechanisms. In a study in Asian countries in 2012, Razi et al. found a positive correlation between age-standardized incidence rate (ASIR) of OC and HDI and its components including life expectancy at birth, average years of schooling, and gross national income (GNI) per capita. However, no significant correlation was observed between age-standardized mortality rate (ASMR) of OC and HDI and its components (Razi et al., 2016). While several

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other studies have evaluated the relationship between HDI and various cancers, especially in Asian countries (Ghoncheh et al., 2015; Hassanipour-Azgomi et al., 2016; Mohammadian et al., 2015; Pakzad et al., 2015a, b; Pakzad et al., 2016; Rafiemanesh et al., 2015), the relationships between the incidence and mortality of OC and HDI have not been assessed in European countries. Therefore, this study aimed to investigate the relationship between the ASIR and ASMR of OC with HDI and its components, i.e. life expectancy at birth, the average years of schooling, and the country's GNI per capita in 2012. We used HDI as an indicator of socioeconomic development (Bray et al., 2012).

Materials-Methods

This ecological study examined the relationship between ASIR and ASMR of OC and HDI and its components including life expectancy at birth, average years of schooling, and GNI per capita. The 2012 ASIR and ASMR data for each European country were collected from the GLOBOCAN project (available at http://globocan.iarc.fr/Default.aspx) (Ferlay et al., 2015). Data about the HDI were extracted from the Human Development Report 2013 (Malik, 2013). The details of the methods to estimate the ASIR and ASMR in GLOBOCAN project have been provided in previous reports (Ferlay et al., 2010; Ferlay et al., 2015; Foulkes and Cooney, 2010; Pakzad et al., 2015b; Pakzad et al., 2016).

Statistical analysis: Pearson's correlation analysis was used to assess the correlations between the ASIR and ASMR of OC and HDI and its components. All reported ASIR and ASMR were per 100,000. Statistical significance was considered at $P \leq 0.05$. All P values reported in this study are two-sided. All statistical analyses were performed using SPSS 15.0 (SPSS Inc., Chicago, IL, USA).

Results

A total of 65584 cases of OC were recorded in European countries in 2012. Five countries, including the Russian Federation (13,373 cases), the United Kingdom (6,692 cases), Germany (6,673 cases), Italy (5,911 cases) and France (metropolitan; 4,592 cases), had the highest numbers of OC. Overall, 37,241 cases (56.78%) of OC were reported in these five countries.

The highest ASIRs of OC were seen in Latvia (14.2 per 100,000), Bulgaria (14 per 100,000), Poland (13.6 per 100,000), Serbia (12.8 per 100,000), and Lithuania (12.2 per 100,000). The lowest ASIRs of the OC belonged to Albania (3.2 per 100,000), Ireland (6 per 100,000), Portugal (6.2 per 100,000), the Netherlands (6.5 per 100,000), and Cyprus (7 per 100,000). The number, crude incidence rate, and ASIR of the OC based on sex are presented in **Table 1**. The countries with the highest and lowest ASIR in both sexes are shown in **Table 1**, **Fig. 1**, and **3**.

Table 1. Number, crude incidence rate, and age-standardized incidence rate (ASIR) of ovarian cancer

Estimated incidence, all ages				Estimated mortality, all ages			
Population	**Numbers**	**Crude Rate**	**ASIR (W)**	**Population**	**Numbers**	**Crude Rate**	**ASMR (W)**
Latvia	304	25.2	14.2	Latvia	223	18.5	8.8
Bulgaria	899	23.5	14.0	Lithuania	301	17.1	8.4
Poland	4456	22.5	13.6	Poland	2692	13.6	7.3
Serbia	935	18.8	12.8	Ireland	264	11.5	6.9
Lithuania	369	20.9	12.2	Malta	32	15.2	6.8
Montenegro	51	15.8	12.0	Croatia	321	14.1	6.6
Malta	46	21.8	11.8	Denmark	401	14.2	6.5
Estonia	156	21.6	11.8	Slovenia	150	14.4	6.4
United Kingdom	6692	21.0	11.7	Norway	326	13.2	6.4
Slovakia	518	18.4	11.6	Czech Republic	708	13.2	6.3
FYR Macedonia	169	16.4	11.3	Serbia	530	10.7	6.2
Russian Federation	13373	17.4	11.3	Russian Federation	7971	10.4	5.9
Ireland	380	16.6	11.2	Ukraine	2454	10.1	5.9
Czech Republic	1092	20.3	11.1	Bulgaria	440	11.5	5.9
Belarus	844	16.5	10.9	Estonia	97	13.4	5.8
Ukraine	4032	16.6	10.7	Montenegro	28	8.7	5.8
Hungary	999	19.1	10.6	United Kingdom	4040	12.7	5.7
Slovenia	192	18.4	10.4	Hungary	644	12.3	5.6
Denmark	544	19.3	10.3	Slovakia	280	9.9	5.6
Croatia	428	18.8	10.3	Sweden	609	12.8	5.6
Romania	1850	16.8	10.3	The Netherlands	1019	12.1	5.5

Italy	5911	19.0	10.2	Belarus	484	9.5	5.5
Norway	418	16.9	9.5	Belgium	731	13.3	5.5
Finland	457	16.6	8.4	FYR Macedonia	91	8.8	5.4
Greece	915	15.9	8.4	Luxembourg	27	10.3	5.1
Bosnia Herzegovina	245	12.6	8.1	Romania	1020	9.3	5.0
Belgium	840	15.3	8.1	Finland	329	12.0	4.9
France (metropolitan)	4592	14.1	7.9	Switzerland	436	11.1	4.8
Switzerland	621	15.8	7.9	Italy	3617	11.6	4.7
Spain	3236	13.7	7.7	Germany	5379	12.9	4.7
Sweden	659	13.8	7.5	Austria	504	11.7	4.6
Republic of Moldova	196	10.6	7.5	France (metropolitan)	3389	10.4	4.3
Germany	6673	16.0	7.4	Greece	578	10.0	4.2
Austria	636	14.8	7.3	Republic of Moldova	117	6.3	4.2
Luxembourg	36	13.7	7.3	Bosnia Herzegovina	148	7.6	4.1
Cyprus	56	10.1	7.0	Cyprus	37	6.7	3.9
The Netherlands	1025	12.2	6.8	Spain	1878	7.9	3.7
Portugal	616	11.2	6.2	Iceland	10	6.1	3.5
Iceland	15	9.2	6.0	Portugal	381	6.9	3.1
Albania	62	3.8	3.2	Albania	30	1.9	1.5

A total of 42,749 deaths due to OC were recorded in 2012. The Russian Federation (7,971 cases), Germany (5,379 cases), the United Kingdom (4,040 cases), Italy (3,617 cases) and France (metropolitan; 3,389 cases) were the five countries with the highest numbers of deaths. Overall, 57.06% of deaths due to OC occurred in these five countries.

Latvia (8.8 per 100,000), Lithuania (8.4 per 100,000), Poland (7.3 per 100,000), Ireland (6.9 per 100,000), and Malta (6.8 per 100,000) had the highest ASMRs of OC. Albania (1.5 per 100,000), Portugal (3.1 per 100,000), Iceland (3.5 per 100,000), Spain (3.7 per 100,000), and Cyprus (3.9 per 100,000) had the lowest ASMRs of OC (**Table 2**, **Fig. 2** and **3**).

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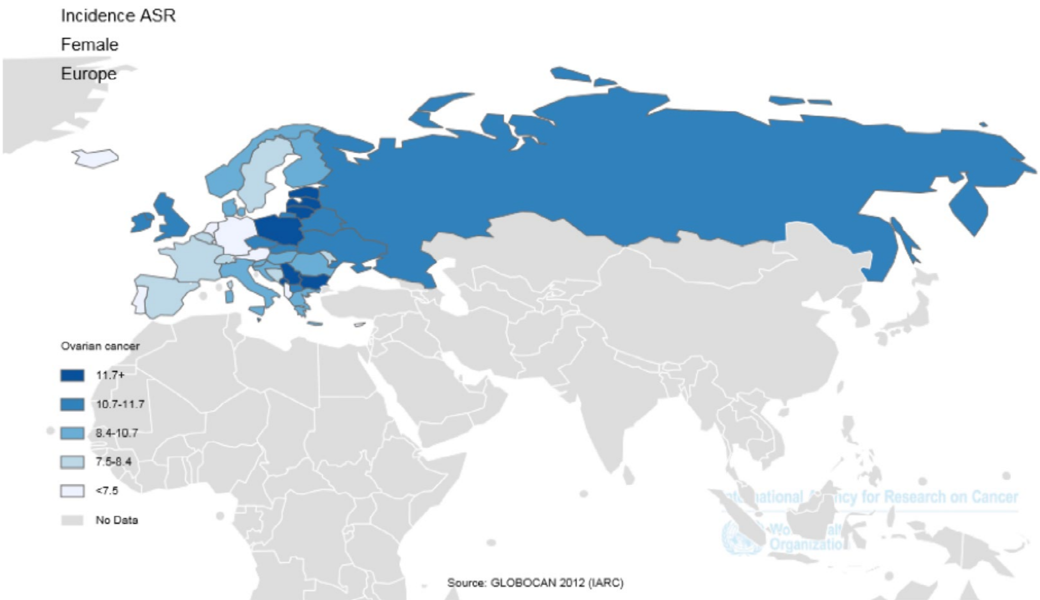

Figure 1. Distribution of the age-standardized incidence rate (ASIR) of ovarian cancer.

Of the 65,584 new cases of OC reported in 2012, 36,175 cases (55.15%) were in women below 65 years old and 29,409 cases (44.85%) were in those 65 years old or older. The numbers of new cases of OC in 2015, 2020, 2025, 2030, and 2035 are predicted to be 67,397, 69,663, 71,821, 73,730 and 74,982, respectively. These numbers are respectively 1,813 (2.76%), 4,079 (6.21%), 6,237 (9.50%), 8,146 (12.42%), and 9,398 (14.32%) higher than the new cases in 2012. While the number of new cases of OC is expected to increase in women ≥ 65 years old during 2012-2035, it is predicted to decrease in the age group below 65 years.

Of the 42,749 deaths due to OC in 2012, 16,547 (38.70%) and 26,202 deaths (61.30%) belonged to the age groups < 65 years and ≥ 65 years, respectively. The numbers of deaths due to OC are expected to reach 44,235, 46,217, 48,420, 50,622, and 52419 in 2015, 2020, 2025, 2030, and 2035, respectively. These numbers are 1,486 (3.47%), 3,468 (8.11%), 5,671 (13.26%), 7,873 (18.41%), and 9,670 (22.62%) higher than the rate reported in 2012. Apparently, the number of deaths due to OC is expected to increase between 2012 and 2035 and this increase is predicted to be more pronounced in women ≥ 65 years old.

Table 3 shows the HDI and its components in 2012. Accordingly, the European countries were classified to have very high HDI (n = 29), high HDI (n = 9), and moderate HDI (n = 2).

Figure 2. Distribution of the age-standardized mortality rate (ASMR) of ovarian cancer.

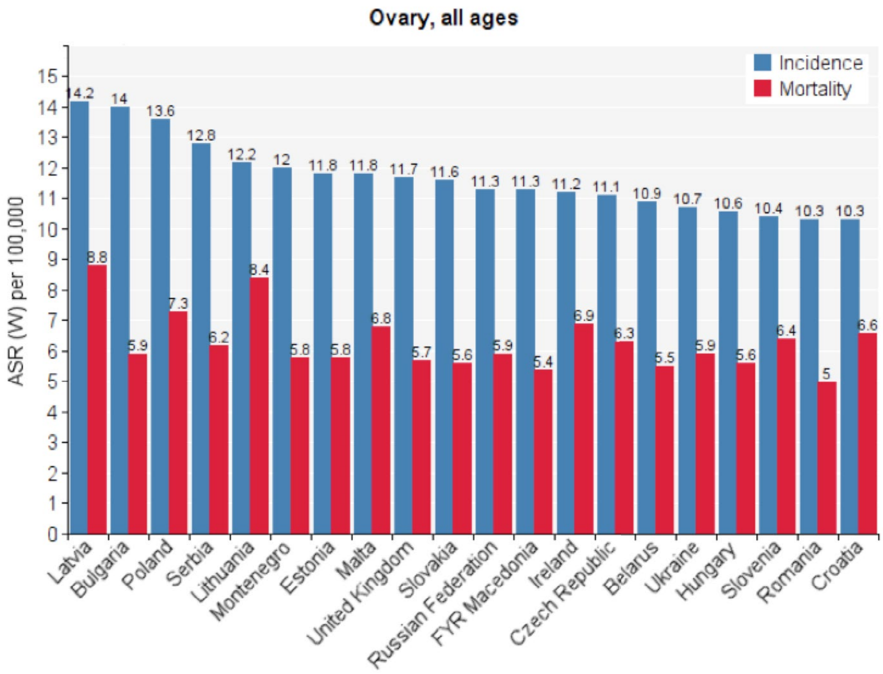

Figure 3. The age-standardized incidence rate (ASIR) and age-standardized mortality rate (ASMR) of ovarian cancer.

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Table 2. Estimated morbidity and mortality rates from ovarian cancer in 2012-2035

Year	Age group	Estimated number of new cancers	Age group	Estimated number of cancer deaths
2012		65584		42749
	ages < 65	36175	ages < 65	16547
	ages >= 65	29409	ages >= 65	26202
2015		67397		44235
	ages < 65	36730	ages < 65	16961
	ages >= 65	30667	ages >= 65	27274
	Demographic change	1813		1486
	ages < 65	555	ages < 65	414
	ages >= 65	1258	ages >= 65	1072
2020		69663		46217
	ages < 65	36472	ages < 65	16969
	ages >= 65	33191	ages >= 65	29248
	Demographic change	4079		3468
	ages < 65	297	ages < 65	422
	ages >= 65	3782	ages >= 65	3046
2025		71821		48420
	ages < 65	35920	ages < 65	16759
	ages >= 65	35901	ages >= 65	31661
	Demographic change	6237		5671
	ages < 65	-255	ages < 65	212
	ages >= 65	6492	ages >= 65	5459
2030		73730		50622
	ages < 65	35100	ages < 65	16351
	ages >= 65	38630	ages >= 65	34271
	Demographic change	8146		7873
	ages < 65	-1075	ages < 65	-196
	ages >= 65	9221	ages >= 65	8069
2035		74982		52419
	ages < 65	34437	ages < 65	16125

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	ages >= 65	40545	ages >= 65	36294
	Demographic change	9398		9670
	ages < 65	-1738	ages < 65	-422
	ages >= 65	11136	ages >= 65	10092

Population forecasts were extracted from the *United Nations, World Population prospects, the 2012 revision. Numbers are computed using age-specific rates and corresponding populations for 10 age-groups. GLOBOCAN 2012 (IARC) - 15.3.2016*

ASIR and HDI

A weak negative correlation was seen between the HDI and the ASIR of OC (r = -0.213; P = 0.186). There was a strong negative correlation between life expectancy at birth and the ASIR of OC (r = -0.480; P = 0.002). The mean years of schooling and the ASIR of OC had a weak positive correlation (r = 0.115; P = 0.481). Moreover, the GNI per capita and the ASIR of OC had a strong negative correlation (r = -0.348; P = 0.028) (**Fig. 4**).

ASMR and HDI

There was a weak positive correlation between the HDI and the ASMR of OC (r = 0.072; P = 0.659). Meanwhile, life expectancy at birth and the ASMR of OC were negatively correlated (r = -0.275; P = 0.086). A strong positive correlation was seen between the mean years of schooling and the ASMR of OC (r = 0.325; P = 0.041). The GNI per capita and the ASMR of OC had a weak negative correlation (r = -0.088; P = 0.591) (**Fig. 5**).

ASIR and ASMR

There was a strong positive correlation between the ASIR and ASMR of OC (r = 0.824; P ≤ 0.001) (**Fig. 6**).

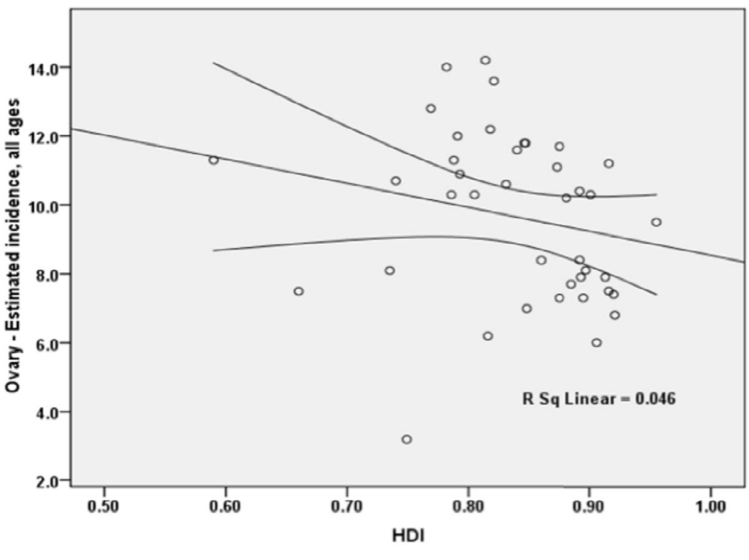

Figure 4. The correlation between the Human Development Index (HDI) and age-standardized incidence rate (ASIR) of ovarian cancer.

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Table 3. The Human Development Index (HDI) in 2012

HDI status	POPULATION	Human Development Index(HDI)	Life expectancy at birth	Average Year of schooling	Gross national income (GNI) per capita
Very high human development	Norway	0.955	81.3	12.6	48688
	The Netherlands	0.921	80.8	11.6	37282
	Germany	0.92	80.6	12.2	35431
	Ireland	0.916	80.7	11.6	28671
	Sweden	0.916	81.6	11.7	36143
	Switzerland	0.913	82.5	11	40527
	Iceland	0.906	81.9	10.4	29176
	Denmark	0.901	79	11.4	33518
	Belgium	0.897	80	10.9	33429
	Austria	0.895	81	10.8	36438
	France (metropolitan	0.893	81.7	10.6	30277
	Finland	0.892	80.1	10.3	32510
	Slovenia	0.892	79.5	11.7	23999
	Spain	0.885	81.6	10.4	25947
	Italy	0.881	82	10.1	26158
	Luxembourg	0.875	80.1	10.1	48285
	United Kingdom	0.875	80.1	9.4	32538
	Czech Republic	0.873	77.8	12.3	22067
	Greece	0.86	80	10.1	20511
	Cyprus	0.848	79.8	9.8	23825
	Malta	0.847	79.8	9.9	21184
	Estonia	0.846	75	12	17402
	Slovakia	0.84	75.6	11.6	19696
	Hungary	0.831	74.6	11.7	16088
	Poland	0.821	76.3	10	17776
	Lithuania	0.818	72.5	10.9	16858
	Portugal	0.816	79.7	7.7	19907

	Latvia	0.814	73.6	11.5	14724
	Croatia	0.805	76.8	9.8	15419
High human development	Belarus	0.793	70.6	11.51	13385
	Montenegro	0.791	74.8	10.5	10471
	Russian Federation	0.788	69.1	11.7	14461
	Romania	0.786	74.2	10.4	11011
	Bulgaria	0.782	73.6	10.6	11474
	Serbia	0.769	74.7	10.2	9533
	Albania	0.749	77.1	10.4	7822
	Ukraine	0.74	68.8	11.3	6428
	Bosnia Herzegovina	0.735	75.8	8.3	7713
Medium human development	Republic of Moldova	0.66	69.6	9.7	3319
	FYR Macedonia	0.59	69.6	5.6	3557

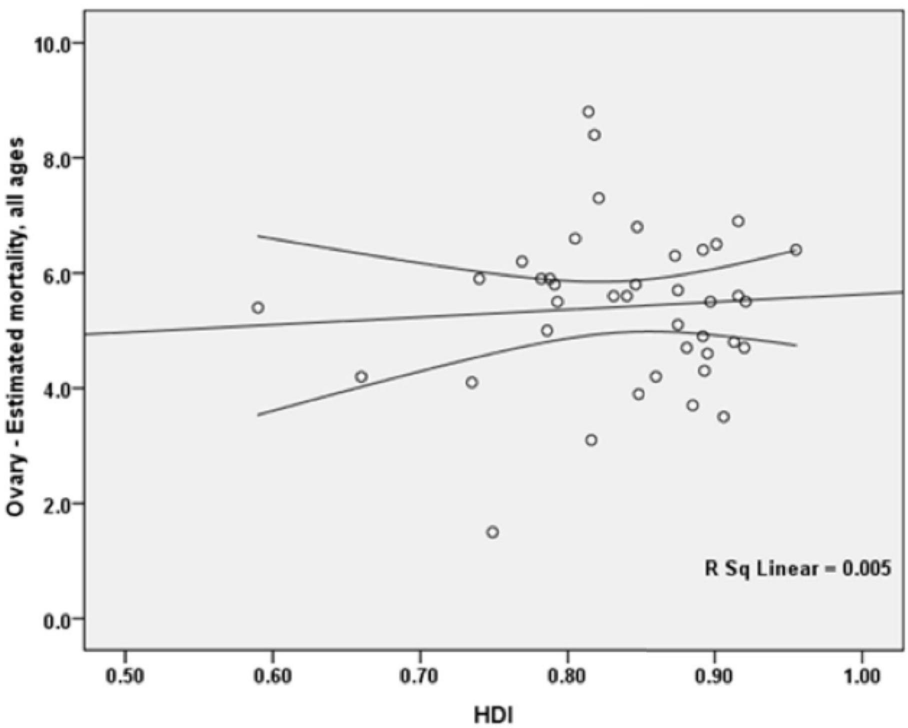

Figure 5. The correlation between the Human Development Index (HDI) and age-standardized mortality rate (ASMR) of ovarian cancer.

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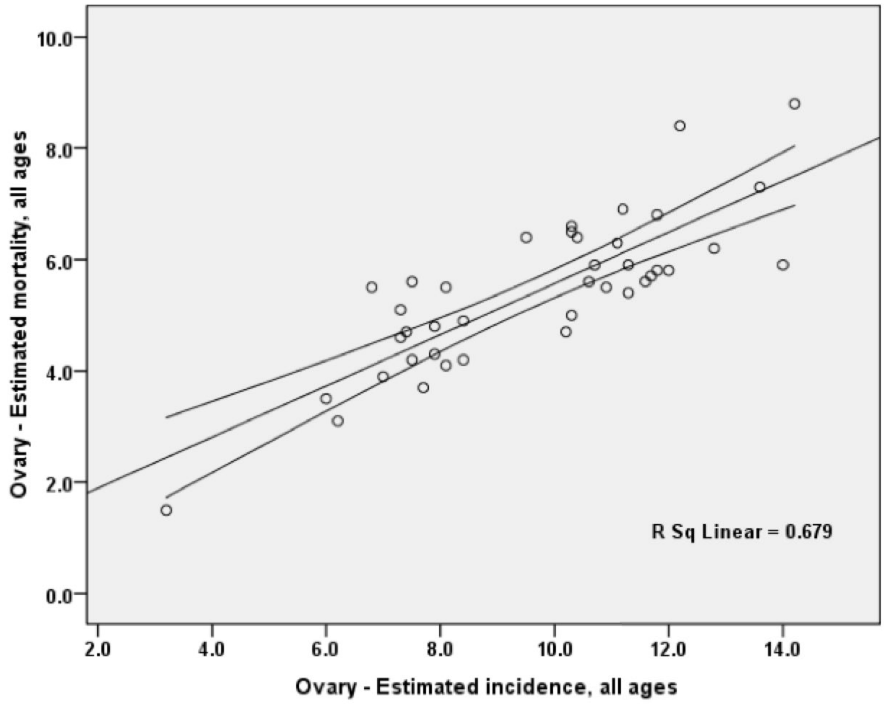

Figure 6. The correlation between age-standardized incidence rate (ASIR) and age-standardized mortality rate (ASMR) of ovarian cancer.

Discussion

According to the results of this study, among the European countries, Latvia, Bulgaria, Poland, Serbia, and Lithuania had the highest ASIR of OC and Latvia, Lithuania, Poland, Ireland, and Malta had the highest ASMR of OC. The incidence and mortality rates of OC are expected to increase between 2012 and 2035 and this increase is predicted to be more pronounced in women over 65 years of age. Moreover, our findings showed that increased HDI was associated with decreased ASIR and increased ASMR, but these relationships were not statistically significant.

According to the results of this study, European countries will have an increasing trend in OC morbidity and mortality. The morbidity and mortality caused by OC are expected to increase between 2012 and 2035 and this increase will be more significant in women over 65 years of age. In the past, the world's population used to consist mainly of teenagers and children. However, due to the aging phenomenon (following improved life expectancy) and decreased birth rate in recent decades, older adults currently constitute a high proportion of the world's population. With the aging of the population, an increase in the occurrence of non-communicable diseases, such as cancers, is predictable. Based on the World Health Organization (WHO) report in 2012, the aging of the population can increase the number of new cancer cases to

19.3 million in 2025. The largest rates of new cancer cases (56.8%) and deaths (64.9%) will be seen in developing countries (Ferlay et al., 2013). Cancer is estimated to be responsible for 12.6% of all deaths. While cancer is now the second cause of death, after cardiovascular diseases, worldwide, its mortality rate is expected to exceed that of cardiovascular diseases in the coming years (Arab et al., 2014).

The incidence of cancer in diverse geographic areas can partly be attributed to variances in the lifestyle of their residents (Rohani-Rasaf et al., 2013). The incidence of cancer can be affected by numerous factors including work-related factors, alcohol and tobacco use, food and nutrition, pollution, water pollution, infectious agents, obesity, physical activity, and ultraviolet (UV) radiation (Jemal et al., 2010). Risk factors of cancer include type of nutrition, smoking, and reproductive behaviors in developed countries and infectious causes in developing countries (Rohani-Rasaf et al., 2013).

One of the significant factors in decreasing cancer morbidity and mortality might be HDI, which assesses long-term advancement in three areas of human development. It is a merged index of three rudimentary dimensions of human development including life expectancy at birth, access to education (according to a combination of adult literacy rate and primary to tertiary education enrollment rates), and income (based on per capita gross domestic product adjusted for purchasing power equality in US$).

According to the results of this study, among European countries, Latvia, Bulgaria, Poland, Serbia, and Lithuania had the highest ASIR of OC. Moreover, Latvia, Lithuania, Poland, Ireland, and Malta had the highest ASMR of OC. All these countries, except for Bulgaria and Serbia, are considered to have very high human development. Evaluating the associations between HDI and the ASIR and ASMR of OC revealed that an increase in HDI decreased the ASIR and increased the ASMR of OC. Likewise, in a study on Asian countries, the relationship between HDI and the ASMR of OC was negative and not significant. However, in contrast to our findings, the results of this study showed a significant positive correlation between HDI and the ASIR of OC (Razi et al., 2016).

Socioeconomic factors affect the incidence of cancer through complex and variable mechanisms. Fidler et al. reported positive correlations between HDI and the ASIR of leukemia, multiple myeloma, and lung, pancreas, gallbladder, brain/nervous system, colorectal, kidney, and thyroid cancer. Moreover, positive relations were detected between HDI and the ASIR of melanoma of the skin, Hodgkin lymphoma, and bladder, testicular, and lip/oral cavity cancers in males. HDI was also positively related with non-Hodgkin lymphoma, and breast, corpus uteri, and ovarian cancers in females. A negative correlation was detected between HDI and the ASIR of Kaposi sarcoma, and cervical and other pharyngeal cancers in females (Fidler et al., 2016). Moreover, Præstegaard et al.

indicated a relationship between lower level of education and an increased risk of progressive tumor stage at diagnosis of OC (Præstegaard et al., 2016).

Limitations

Since this was an ecological study, its results are significant and interpretable at the population level and ecological fallacy will happen if the results are interpreted at the individual level. Some factors such as gynecological surgeries, tubal ligation, number of deliveries, gravidity, oral contraception and breastfeeding may reduce the risk of OC. On the other hand, some medical conditions and environmental factors such as endometriosis, hyperthyroidism, ovarian cysts, medical history and occupation hazards increase the risk of OC. However, in this study, we did not have access to adequate data on these factors to discuss their effects on the incidence and mortality of OC. Therefore, in addition to ecological research in each of the European countries, studies at an individual level with case-control or cohort designs are required to detect the role of factors associated with the incidence and mortality of OC at an individual level.

Conclusion

According to the results of this study, among European countries, Latvia, Bulgaria, Poland, Serbia, and Lithuania had the highest ASIR and Latvia, Lithuania, Poland, Ireland, and Malta had the highest ASMR of OC. Moreover, an increase in in HDI was associated with decreased ASIR and increased ASMR of OC. However, these relationships were not statistically significant. The morbidity and mortality of OC had an increasing trend in European countries. Therefore, it seems that health policy makers in these countries should make appropriate decisions to deal with the growth in the morbidity and mortality of OC, especially in women older than 65 years of age, in regions which may have lower access to prevention and treatment services.

Abbreviations

ASIR: Age-specific incidence rate
ASMR: Age-specific mortality rate
HDI: Human Development Index
OC: Ovarian Cancer

Acknowledgment

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Author Contribution

All authors contributed to the design of the research. MM, MG, BK and HS collected the data. HS, BK and AMH conducted analysis and interpretation of data. All authors drafted the first version. MM, MA, FAB, MG, AMH edited the first draft. All authors reviewed and commented on final draft.

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