

Gynecologic Cancers Estimates in the I.R. Iran, 2012-2040

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ABSTRACT

Background: Gynecologic cancers (GCs) are among the leading causes of morbidity and mortality in females worldwide. Estimating the cancer burden is invaluable to set up priorities for research funding allocations, cancer control policies, and prevention strategies. The International Agency for Research on Cancer (IARC) has recently released the latest estimates on the prevalence, incidence, and mortality for 36 types of cancer and all cancer sites combined in 185 countries in 2020. We aimed to report GCs estimates in the I.R. Iran from 2012 to 2040 based on the GLOBOCAN 2020.

Methods: We obtained data on the incidence, mortality, and prevalence of GCs in the Iranian female population from the GLOBOCAN 2020 database presented by the IARC, compared the burden with the previous reports presented in 2012 and 2018, and provided the estimates for 2040. In addition, we compared the burden to that of the WHO Eastern Mediterranean Region (EMRO) and the world.

Results: The top 3 incident GCs were ovarian, uterine, and cervical cancer, respectively. In 2020, approximately 2,000 new cases of ovarian cancer (ASR: 4.4), 1,535 new patients with uterine cancer (ASR: 3.5), and 1,056 incident cervical cancer cases (ASR: 2.3) were diagnosed in the I.R. Iran. With 1,269 cancer deaths and an age-standardized mortality rate (ASMR) of 3.0, ovarian cancer is considered to be the leading cause of death from GCs, followed by cervical cancer (644 deaths; ASMR: 1.5) and uterine cancer (537 deaths; ASMR: 1.3). Among 157,930 prevalent female cases reported in the GLOBOCAN 2020 database, 13,663 cases were categorized as GC. With a 5-year prevalence of 5,539, ovarian cancer was the most prevalent type, while uterine cancer (with 4,904 prevalent cases) and cervical cancer (with 2,948 prevalent cases) were less prevalent types.

Conclusion: There has been a slight increase in the incidence of GCs in recent years after stable rates for a couple of decades. Therefore, primary and secondary prevention measures such as lifestyle modifications and screening programs must be prioritized.

Keywords: Gynecologic Cancers, Uterine Cancer, Ovarian Cancer, Cervical Cancer, Cancer Burden

INTRODUCTION:

With 3.9 billion people, women represent almost half of the global population (1). Due to their unique biological traits, central role in childbearing, crucial contribution to providing health care, and numerous other critical functions within family and society, research on the burden of gynecologic diseases deserves a high priority (2). Numerous conditions affect women's health during their lifespan. Gynecologic cancers (GCs) are among the leading causes of morbidity and mortality in females worldwide (3). According to the National Cancer Institute's (NCI) dictionary of cancer terms (4), any cancer that arises from the female reproductive system is classified as GC. The most common types are cervical, ovarian, uterine, vaginal, and vulvar cancers, followed by a sixth type, the very rare fallopian tube cancer. Despite being often classified together, predisposing factors, signs and symptoms, prognosis, and cancer burden vary across GC types (5). Therefore, estimating cancer burden, including 5-year prevalent cancer cases, incident cases, and mortality rates, is invaluable to set up priorities for research, funding allocations, cancer control policies, and prevention strategies (6).

The International Agency for Research on Cancer (IARC) (7) has recently released the latest estimates on the prevalence, incidence, and mortality for 36 cancer types and all cancer sites combined in 185 countries or territories worldwide in 2020. The data can be accessed via the Global Cancer Observatory (GCO) homepage (<https://gco.iarc.fr>) (8). GCO is an interactive web-based platform that provides global cancer burden data, and the data is the most comprehensive for each country worldwide. These estimates are derived from the latest data available to IARC through collaborations with population-based cancer registries (PBCRs) and with the World Health Organization (WHO) or are based on information publicly accessible online. The quality and availability of the data sources are constantly improving due to developing PBCRs. Thus, the latest worldwide cancer statistics from the IARC appear to be more accurate than the previous ones for 2018 and 2012 (9). In this

recent report, GCs present 7.25% of 19.3 million estimated incident cases, accounting for about 972,000 cancer deaths, and over 3.9 million 5-year prevalent cancer cases among women worldwide in 2020.

The easternmost country in the Middle East, Iran, formerly known as Persia and officially known as the Islamic Republic of Iran (the I.R. Iran), is a member of the WHO Eastern Mediterranean Region (EMRO). The total population is 83,992,953, of whom 41,584,547 are females (8). We aimed to provide the latest estimates on the 5-year prevalence, incidence, and mortality for GCs, compared them with the previous global cancer data in 2012 and 2018, as well as the EMRO and global stats, discussed the most concerning trends, and in the end, provided estimates for the future of GC burden up until 2040 in the I.R. Iran.

Data Sources and Methods

We obtained data on the incidence, mortality, and prevalence of GCs in the Iranian female population from the GLOBOCAN 2020 database presented by the IARC, compared the burden with the previous reports presented in 2012 (10) and 2018 (11), and provided the estimates for 2040. In addition, we compared the burden to that of the EMRO and the world.

GLOBOCAN presents estimates of cancer burden in 185 countries or territories of the world, which can be listed in alphabetical or geographical order within the application. The latter follows the geographical definition of the United Nations (World Population Prospects, the 2019 revision <https://population.un.org/wpp/>), except Cyprus, located in Southern Europe. In addition to the countries and regions defined by the United Nations, GLOBOCAN also provides build-in estimates for country groups. International Classification of Disease (ICD, 10th revision, version 2010) codes are also used. ICD-10 codes for malignant neoplasms of female genital organs are C51: malignant neoplasm of vulva; C52: malignant neoplasm of vagina; C53: malignant neoplasm of cervix uteri; C54: malignant neoplasm of corpus uteri; C55: malignant neoplasm of uterus, part unspecified; and C56: malignant neoplasm of ovary.

The estimation methods are country-specific, and the quality of the national estimates depends on the coverage, accuracy, and timeliness of the recorded incidence and mortality data in a given country. A summary of the steps used in the GCO to generate the current set of cancer burden estimates is provided below:

Incidence and mortality

The methods used to estimate the sex- and age-standardized incidence and mortality rates (ASR and ASMR) of cancer in a specific country fall into the following broad categories, ordered by priority:

1. Projecting national mortality rates for 2020 based on the observed mortality rates
2. Applying the most recently observed mortality rates to the 2020 population
3. Modeling the national incidence estimates (mortality to incidence ratios) to estimate the rates
4. Estimating the age- and sex-specific national incidence rates for all cancers by averaging overall rates from neighboring countries
5. Estimating the rates from an average of those from selected neighboring countries

Prevalence

Using sex-, site-, and age-specific ratios of incidence to 1-, 3-, and 5-year prevalence from Nordic countries for the period 2006–2015, the prevalence estimates were calculated for 2020. Human Development Index (HDI) ratios were used to scale these ratios. Details of methods are available in <https://gco.iarc.fr/today/data-sources-methods>.

Selected Findings

GC burden in 2020 in Iran

Based on the GLOBOCAN 2020 database, 60,487 new cancer cases with an ASR of 139 per 100,000 person-years were diagnosed among Iranian women, of which 4,644 were classified GCs. The top 3 incident GCs were ovarian, uterine, and cervical cancer. In 2020, there were approximately 2,000 new cases of ovarian cancer (ASR: 4.4), 1,535 new patients with uterine cancer (ASR: 3.5), and 1,056 incident cervical cancer cases (ASR: 2.3) diagnosed in the I.R. Iran. The least common types of GCs were vulvar cancer with 46 new cases (ASR: 0.10) and vaginal cancer with 41 new cases (ASR: 0.09), respectively. With 1,269 cancer deaths and an ASMR of 3.0, ovarian cancer is considered the leading cause of death from

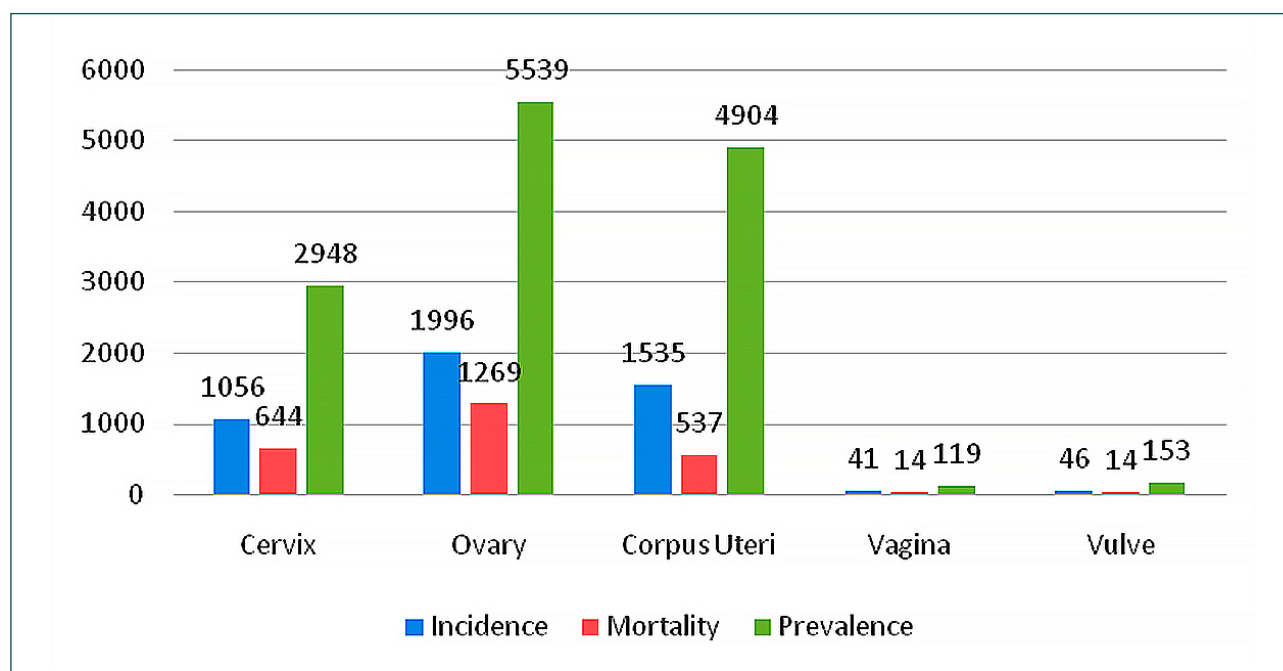


Figure.1. Comparison of the prevalence, mortality, and incidence of GCs

GCs, followed by cervical cancer (644 deaths; ASMR: 1.5) and uterine cancer (537 deaths; ASMR: 1.3). Finally, 28 deaths are attributed to vaginal and vulvar cancers (14 deaths to each; ASMR: 0.03).

Among 157,930 prevalent female cases reported in the GLOBOCAN 2020 database, 13,663 cases were categorized as GCs. With a 5-year prevalence of 5,539, ovarian cancer was the most prevalent type. Uterine cancer (with 4,904 prevalent cases) and cervical cancer (with 2,948 prevalent cases) were less prevalent types. Finally, vulvar and vaginal cancers, with 5-year prevalence rates of 153 and 119, respectively, were the rarest GCs in the I.R. Iran (Figure 1).

Comparison with 2012 and 2018 statistics

Coping with the cancer burden requires a thorough understanding of the trends in cancer incidence and mortality rates. A notable observation in 2020 is an increase in the incidence and mortality rates of uterine cancer in Iran (Table 1). The ASRs of uterine cancer have changed from 2.5 per 100,000 in 2012 to 1.8 per 100,000 in 2018 and 3.5 per 100,000 in 2020.

ASRs for ovarian cancer have decreased from 4.8 per 100,000 in 2012 to 4.3 and 4.4 per 100,000 in 2018 and 2020, respectively. However, while ASMR dropped from 3.4 per 100,000 in 2012 to 2.3 per 100,000 in 2018, it climbed to 3 per 100,000 in 2020.

Estimated projection of incidence and mortality to 2040

The GLOBOCAN report has provided predictions for

the future cancer incidence and mortality burden worldwide from the current estimates in 2020 until 2040. The incidence/ mortality rates of GCs are estimated to increase slightly within the next two decades. In particular, uterine cancer will experience the highest growth, with an increase of 89.4% in incidence rate (Figure 2). There will also be an estimated 76.1% increase in ovarian cancer cases.

Nevertheless, the estimated top 3 incident GCs in 2040 will be unchanged from 2020: ovarian (3,460 new cases), uterine (2,90 new cases), and cervical cancer (1,860 new cases), with vaginal and vulvar cancers as the fourth and fifth cancers.

When it comes to mortality, with a 114.7% increase, uterine cancer (1,150 deaths) accounts for the most notable increase in the mortality rate. However, with a 104.3% increase, ovarian cancer (2,590 deaths) will remain the leading cause of death from GCs. An estimated 3,460 women will be diagnosed with ovarian cancer, and approximately 2,590 will die from it in 2040. Cervical cancer (1,350 deaths) will also meet a 110.2% increase in cancer deaths by 2040 (Figure 3).

DISCUSSION

There has been a slight increase in the incidence of GCs in recent years after stable rates for a couple of decades. One of the underlying reasons for the ascending trend

	2012			2018			2020		
	Incidence (ASR)	Mortality (ASMR)	5-year prevalence	Incidence (ASR)	Mortality (ASMR)	5-year prevalence	Incidence (ASR)	Mortality (ASMR)	5-year prevalence
Ovary	1,637 (4.8)	1,76 (3.4)	4,074	1,773 (4.3)	863 (2.3)	4,928	1,966 (4.4)	1,269 (3.0)	5,539
Corpus Uteri	1,637 (4.8)	196 (0.6)	2,929	1,370 (1.8)	329 (0.9)	4,271	1,535 (3.5)	537 (1.3)	4,904
Cervix Uteri	947 (2.8)	370 (1.2)	2,647	917 (2.2)	467 (1.2)	2,613	1,056 (2.3)	644 (1.5)	2,948
Vagina	NA	NA	NA	54 (0.13)	7 (0.02)	156	41 (0.1)	14 (0.03)	119
Vulva	NA	NA	NA	51 (0.13)	2 (0.01)	166	46 (0.09)	14 (0.03)	153

Table 1. The prevalence, incidence, and mortality of GCs in 2012, 2018, and 2020 (10-12)

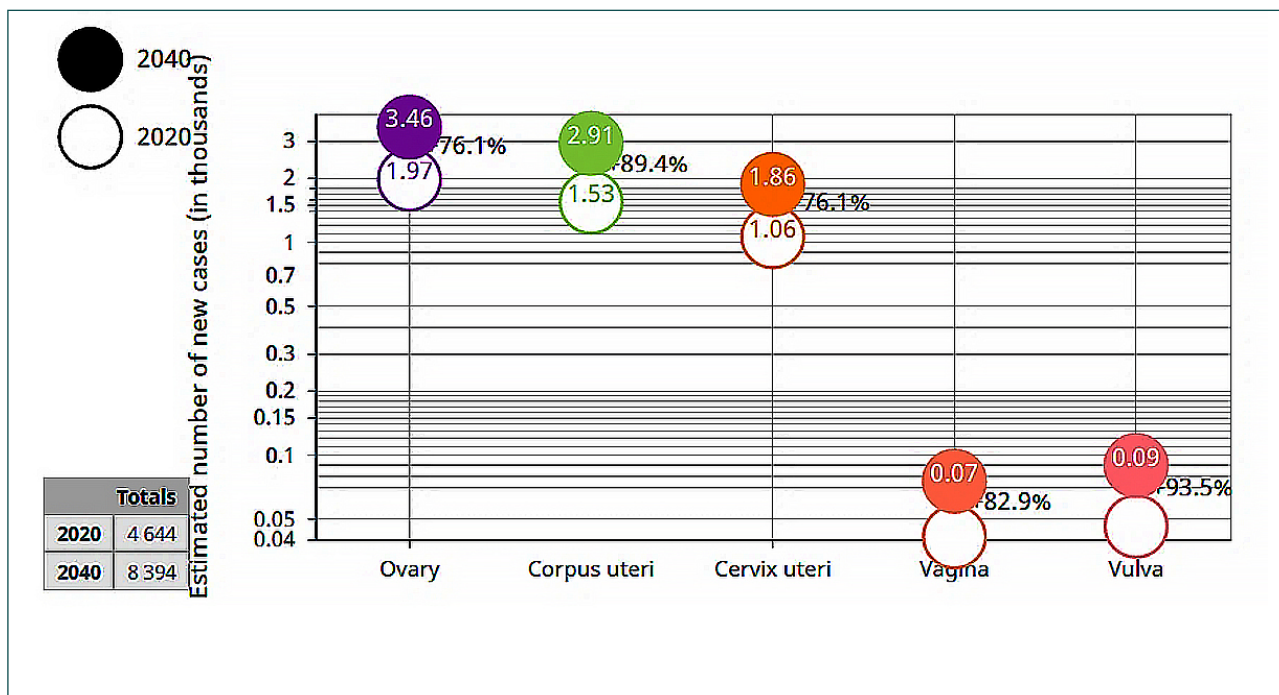


Figure.2. Estimated number of GC cases in 2040 in the I.R. Iran. Numbers in circles are the ASRs, and the percentages are the rate of increase in the corresponding values in 2040

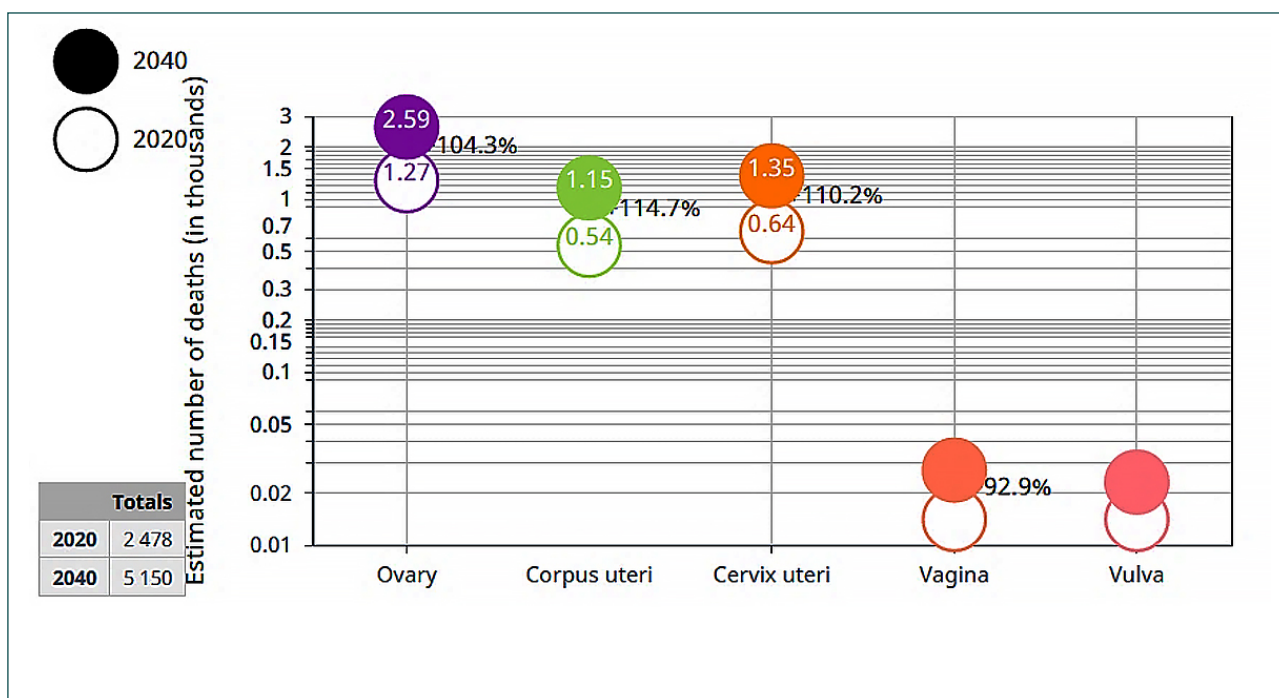


Figure.3. Estimated number of deaths from GCs in 2040 in the I.R. Iran. Numbers in circles are the ASMRs, and the percentages are the rate of increase in the corresponding values in 2040

in the ASRs of uterine cancer may be the ongoing changes in key risk factors, including a trend toward Western dietary patterns, obesity/ overweight, physical inactivity, type 2 diabetes, hormonal imbalance, polycystic ovarian syndrome (PCOS), estrogen therapy, infertility, and low parity (13). While, the ascending trend in ASMRs of uterine cancer from 0.6 in 2012 to 1.3 in 2020 may reflect the rise in non-endometrioid carcinoma, an aggressive, poorly prognosed subtype (14). The growing availability of incidence rates from PBCRs and mortality rates from vital statistics offices in Iran may also account for the increasing trend.

Although low- and middle-income countries (LMICs) such as Iran lack an organized screening program, with an ASR less than 3 and an ASMR under 2 for over 8 years, cervical cancer incidence and mortality rates have remained low in the I.R. Iran. Low prevalence of persistent HPV infection (9%), the leading predisposing factor for cervical cancer, due to improvements in genital hygiene, reduced parity, the religious culture of the Iranian population, and a diminishing prevalence of other sexually transmittable infections (HIV and Chlamydia trachomatis), smoking, long-term use of oral contraceptive pills (OCPs), and exposure to diethylstilbestrol (DES) and immunosuppressants might account for the trend (15-17). An increasing average socioeconomic level may also account for the decline. Cervical cancer is considered relatively preventable due to the remarkably effective primary (HPV vaccine) and secondary (screening) prevention measures (12). In Iran, despite the lack of organized cervical cancer screening, opportunistic screening is available, and women may have access to Pap smear through health care centers or independent clinics. HPV testing starting at age 35 and repeated every 10 years is also available as the most cost-effective cervical cancer screening method (18). However, HPV vaccination to prevent HPV-related cervical, vaginal, and vulvar cancers has not been deemed cost-effective among low-risk populations such as Iran (12, 19, 20).

We have witnessed changes in the ASRs and ASMRs for ovarian cancer in the new data presented in 2020. The increase in ASR may be due to the changes in key risk

factors, including obesity/ overweight, low physical activity, hormone replacement therapy after menopause, infertility, low parity, and pregnancy after the age of 30 due to Western lifestyle (21). Ovarian cancer is also the leading cause of death among GCs. Unfortunately, there are no specific early symptoms and effective early detection strategies to diagnose ovarian cancer early in women with median risk. Thus, diagnosis in the advanced stages and the aggressive nature of the predominant high-grade serous carcinoma, the most common subtype of epithelial ovarian cancer, results in higher mortality rates than other GCs (14). Further studies are warranted to better understand the disease, identify modifiable risk factors, develop effective early detection methods, and optimize treatment (21).

Vulvar and vaginal cancers were not estimated in GLOBOCAN 2012. These two HPV-related malignancies were added in the cancer dictionary started in 2018. Compared to 2018, a notable observation in 2020 is a of vulvar cancer, which seems to require further investigation. However, due to the low incidence of these HPV-associated cancers, their trend is difficult to discuss. Besides, as the IARC emphasizes, due to the growing availability of incidence rates from PBCRs and mortality rates from vital statistics offices, and the ongoing revision of the GLOBOCAN estimation methods, the latest estimates of cancer burden must be interpreted and compared with those of previous versions with extreme caution.

Among the EMRO countries, Iran ranks third regarding the incidence and mortality of GCs after Pakistan and Egypt (15). Figure 4 presents a comparison between the burden of GCs in Iran, the EMRO, and the world. While the ASRs of ovarian (4) and uterine cancer (3.3) in Iran are similar to those of the EMRO (4.9 and 3.8, respectively), the ASR of cervical cancer is far less (Iran: 2.1 vs. EMRO: 5). Uterine and cervical cancers are much less incident in the I.R. Iran compared to the world (8.1 and 13, respectively). Although cervical cancer was the leading cause of death in 36 countries of the world in 2020 (12), the ASMR of cervical cancer in Iran (1.2) appears to be far less than the global stat (6.8).

According to the estimated projections of incidence and mortality of GCs to 2040, uterine cancer will experience an 89.4% increase in the incidence rate. There will also be an estimated 76.1% increase in ovarian cancer incident cases. The rise in the incidence of these closely entwined hormone-related cancers may be attributed to obesity, a rise in age at marriage leading to continued declines in the fertility rate, taking menopausal hormones, increased infertility incidence and using fertility treatments, and PCOS. Cervical cancer, the one with more available but not fully implemented prevention and early detection methods, will also continue to increase by 76.1%. Concerning the increasing trend of cervical cancer in Iran, more HPV infection rates are considered than are officially reported (13).

Research suggests that non-governmental organizations (NGOs) can improve cancer awareness by developing evidence-based campaigns and implementing high-quality prevention programs (22). Similar campaigns may help reduce the burden of GC in Iran.

This report faces some limitations. Vulvar and vaginal cancers were not estimated in GLOBOCAN 2012. These

two cancers were added to the cancer dictionary starting from 2018. Moreover, the increasing availability of incidence data from cancer registries and mortality data from vital statistics offices, coupled with a continued reassessment of the GLOBOCAN estimation methods, means that the current incidence and mortality estimates (for 2020) cannot be directly compared with estimates from previous versions. To avoid potential confusion among users, only the latest and most reliable statistics are provided on the current global cancer incidence and mortality burden (for 2020). Thus, extreme caution is warranted when interpreting and comparing these estimates because the sources of information and the methods of estimation have changed during the different GLOBOCAN exercises, particularly in low- and middle-income countries.

CONCLUSION

In 2020, about 4,700 women were estimated to develop GCs, and about 2,500 women were estimated to die from GCs in the I.R. Iran. The slight increase in the incidence of GCs in recent years might be attributed to

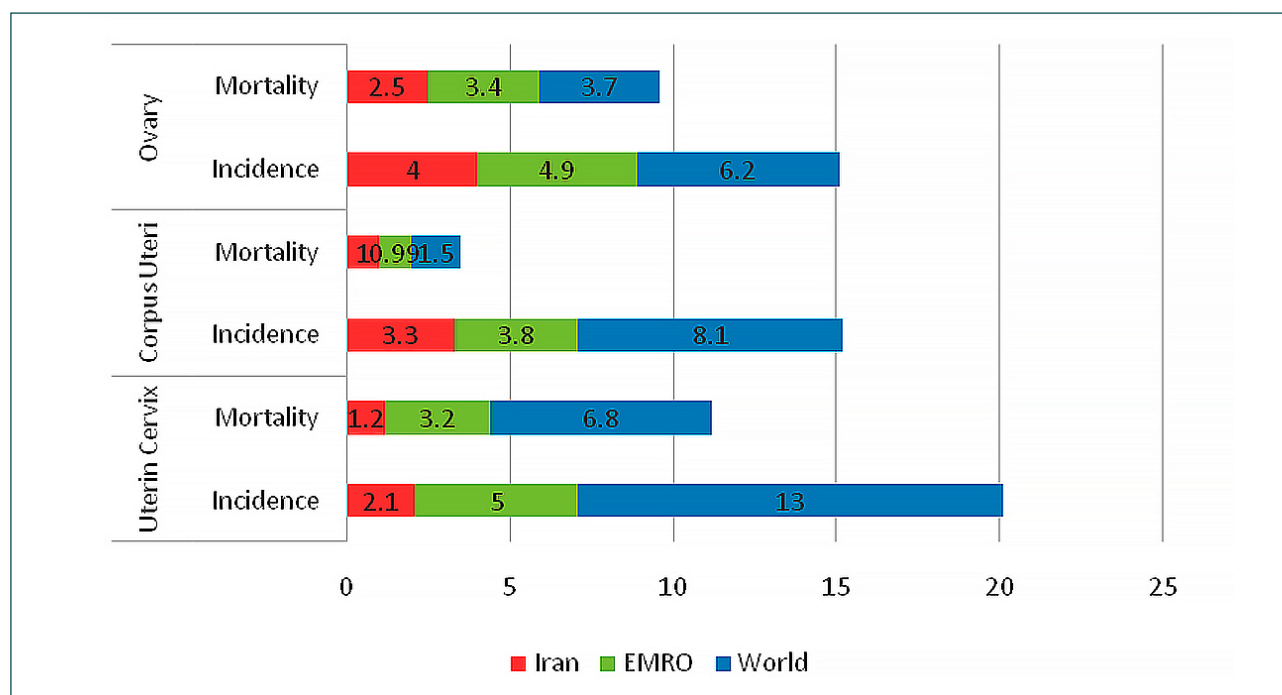


Figure.4. Comparison of the incidence (ASR) and mortality (ASMRs) of the most common GCs in the I.R. Iran with those of the EMRO and the world

the growing availability of incidence and mortality data from PBCRs and vital statistics offices. Lack of organized screening strategies for early detection of GCs and low cancer awareness in the general population leads to a late diagnosis and lower success rate in treatment, which may explain the ongoing rise in mortality rates. The rising trend is greatly influenced by risk and protective factors and/or screening preventive modalities. Preventative measures such as lifestyle modifications and avoiding exogenous hormone use reduce the risk of developing ovarian and uterine cancer. Meanwhile, cervical cancer screening by HPV testing starting at age 35 and repeated every 10 years would effectively reduce cervical cancer incident cases. Cancer awareness campaigns and high-quality prevention programs may result in better cancer prevention among women.

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