Iran J Public Health, Vol. 53, No.8, Aug 2024, pp.1890-1897

Original Article

Mortality Rate and Years of Life Lost Due to Breast and Gynecologic Cancers in Southern Iran 2004-2019: A Population-Based Study

Habibollah Azarbakhsh [1], Alireza Heiran [2], Amir Askarinejad [1], Jafar Hassanzadeh [3], Maryam Janfada [4], *Alireza Mirahmadizadeh [2]

1. *Department of Epidemiology, Faculty of Health, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran*
2. *Non-Communicable Diseases Research Center, Shiraz University of Medical Sciences, Shiraz, Iran*
3. *Research Center for Health Sciences, Institute of Health, Department of Epidemiology, Shiraz University of Medical Sciences, Shiraz, Iran*
4. *Medical Records, Health Vice-chancellor, Shiraz University of Medical Sciences, Shiraz, Iran*

***Corresponding Author:** Email: mirahmadia@sums.ac.ir

(Received 07 May 2023; accepted 15 Jul 2023)

Abstract

Background: There is an increase in the incidence of breast and gynecologic cancers in Iran during the last three decades. Literature is inadequate about the Years of Life Lost (YLL) attributed to these cancers in Iran.

Methods: Mortality data due to these cancers amongst females aged >20 yr from 2004 to 2019 was acquired from "Electronic Death Registry System", Fars Province, Iran. Using local health centers' databases and national census reports from 1996 to 2016, the age-standardized incidence rate (ASR) per 100,000 people were estimated. YLLs were calculated using the WHO's 2015 "YLL template".

Results: During 2004–2019, 1886 and 829 deaths occurred due to breast and gynecologic cancers, respectively. The ASR due to breast and gynecologic cancers showed a significant increasing trend (P<0.001 for each). The total YLL due to breast, cervical/uterine/vaginal/vulvar, and ovary cancers' deaths in the 16-year period were 33,077, 7,172 and 6,584 yr, respectively. The highest YLLs were observed in 50-59-year-old females, followed by 40-49- and 60-69-year-old females. The 16- year trend of YLL rate due to premature mortality in breast cancer, ovary cancer and cervix cancer was increasing: annual percent change (APC) was 7.6% (95% CI: 5.5-9.7, P<0.001), 19.0% (95% CI: 12.2-26.1, P<0.001) and 9.2% (95% CI: -9.2 to 31.3, P>0.05, respectively.

Conclusion: Mortality rate and YLLs due to breast and gynecologic cancers have been increased in southern Iran during the last twenty years. Early detection programs and allocating treatments at early stages should be prioritized.

Keywords: Years of life lost; Mortality; Breast cancer; Gynecologic cancer; Cervical cancer; Ovarian cancer; Iran.

Introduction

Breast cancer is the most common cancer in women worldwide (1, 2) with approximately 1.7 million cases diagnosed and more than 7 billion USD medical costs annually (3, 4). The annual rate of breast cancer had 3.1% increase from 1980 to 2010 (5). Based on reports from WHO in 2020, half a million women in low- and middle-income

countries pass away because of breast cancer, accounting for almost 75% of worldwide deaths from the disease (6). In Iranian populations, breast cancer is one of the most common cancers, with the incidence of ranging 22-120 per 100,000 women (7). Age-standardized Years of Life Lost rate (ASYR) had an increase from 85.1 (65.6 to 110.4) per 100,000 people in 1990 to 196.1 (156.5 to 245.7) per 100,000 people in 2010, followed by an insignificant decline of 20%, which reached to 151.1 (119.7 to 190.6) per 100,000 people in 2015 (8).

The annual economic burden of gynecological cancers in Iran was estimated at 51 million USD, consisting the direct costs of 32 million USD and the indirect costs of 19 million USD (9). About 240,000 women diagnose with ovarian cancer every year in the world to make it the seventh most common women cancers (2). Almost 70% of ovarian cancers are detected at the advanced stage; that is, the 5-year survival of women with such cancers is estimated as only 30% (10). Its' incidence and mortality have been increased in Iran in the last decade (11).

Cervical cancer is the second most common cancer amongst women (12). The estimated age-standardized incidence rate (ASR) of cervical neoplasm is about 13.1 per 100,000 women globally (13). The mean cervical cancer ASR is reported as 2.5 per 100,000 women in Iran, with a mortality-to-incidence ratio of 42% (9).

Previous studies have been only focused on mortality, incidence or prevalence of breast, ovary, or cervical cancers in Iran. Few researches have addressed the issue of Years of Life Lost (YLL) attributed to the breast, ovary and cervical cancers in Iran.

We aimed to evaluate and track the trends of the mortality rate and YLLs of breast, ovary and cervical cancer in Southern Iran women from 2004 to 2019.

Materials and Methods

Data

In this population-based study, mortality rate and YLL due to the breast and gynecologic (i.e., uterine, vaginal and vulvar) cancers were assessed in the Fars Province, southern Iran, during 2004-2019. This data was collected from "Electronic Death Registry System (EDRS)", Fars Province. We included all deaths due to the just-mentioned cancers amongst females aged >20 yr, stratified by the age groups (i.e., 20-29, 30-39, 40-49, 50-59, 60-69, 70-79, and >80 yr). The corresponding ICD-10 codes were C50 and C53-56. Duplicated events were excluded by any similarities in national identification ID as well as the date of death.

Statistical analysis

The population of the Fars Province was estimated using local health centers' databases and national census reports from 1996 to 2016, which was adjusted with respect to the estimated annual population growth as well as the standard population for low-and middle-income countries in 2013 (14).

The crude mortality rate (CMR) and ASR per 100,000 people were estimated using the Statistical Package for Social Sciences (SPSS) (Ver. 22.0 for Windows, Released 2013. Armonk, NY: IBM Corp.). The trends of CMR and ASR for each studied cancer during 2004-2019 were assessed by χ^2 test. The significance level of p value was set at .05.

To estimate YLL, the WHO's 2015 "YLL template", which ran in Microsoft Excel spreadsheet (2016), was used. YLLs were calculated by the method represented in the WHO's second edition of "National burden of disease studies: a practical guide" booklet in 2001 (15).

$$YLL = N\,Ce^{(ra)} / (\beta+r)^2\,[e^{-(\beta+r)(L+a)}[-(\beta+r)(L+a)-1] - e^{-(\beta+r)a}[-(\beta+r)a-1]]$$

N= the number of deaths is at a certain age and gender.

L= the standard of living of the deceased is the same age and gender.

r = Discounting Rate is equal to 0.03.

β = the contract rate in calculating the age value is equal to 0.04.
C is a modified constant value equal to 0.1658 and β is equal to 0.04 and these two numbers estimate the value of different ages (x).
a = the age at which death occurred
e = constant; equivalent to 2.71.
Moreover, to assess the trend of YLL rates per 1,000 people during the studied period, joinpoint regression based on the log-linear model was applied. Joinpoint regression analysis describes changing trends over successive segments of time as well as the levels of increase or decrease within each segment. The resulting line segment between join points is described by the annual percent change (APC) that is based on the slope of the line segment and the average annual percent change (AAPC). The analysis for the trend was carried out by Joinpoint Regression Program 4.9.0.0.

Ethics approval

This study was approved by the local Ethics Committee of Shiraz University of Medical Sciences (code: IR.SUMS.REC.1399.772).

Results

During 2004–2019 in the Fars Province, 1886 and 829 deaths occurred due to breast and gynecologic cancers, respectively. Generally, ASR due to breast and gynecologic cancers showed a significant increasing trend from 2004 to 2019 in the Fars Province, with 5.3 per 100,000 people (95% CI: 4.6, 6.0) in 2004 to 16.5 per 100,000 people (95% CI: 15.4, 17.7) in 2019 for breast cancer (P <0.001), 1.2 per 100,000 people (95% CI: 0.9, 1.5) in 2004 to 3.8 per 100,000 people (95% CI: 3.3, 4.3) in 2019 for cervical/uterine/vaginal/vulvar cancers (P <0.001), and 0.2 per 100,000 people (95% CI: 0.1, 0.3) in 2004 to 3.2 per 100,000 people (95% CI: 2.7, 3.7) in 2019 for ovary cancer (P <0.001) (Table 1).

Table 1: Absolute mortality, CMR (per 100,000 people), ASR (per 100,000 people), and YLL due to breast and gynecologic cancers in southern Iran, 2004–2019 ["cervical cancer" is also included uterine/vaginal/vulvar cancers]

Year	*Death, n*			*CMR*			*ASR (95% CI)*			*YLL, n*		
	Breast	Cervical +	Ovary	Breast	Cervical +	Ovary	Breast	Cervical +	Ovary	Breast	Cervical +	Ovary
2004	41	9	2	3.8	0.8	0.2	5.3 (4.6, 6.0)	1.2 (0.9, 1.5)	0.2 (0.1, 0.3)	814	125	35
2005	49	18	3	4.4	1.6	0.3	6.0 (5.2, 6.7)	2.4 (2.0, 2.8)	0.4 (0.2, 0.6)	933	319	64
2006	62	30	8	5.4	2.6	0.7	7.4 (6.6, 8.2)	3.7 (3.2, 4.3)	1.1 (0.8, 1.4)	1,177	509	143
2007	82	32	11	6.9	2.7	0.9	9.4 (8.5, 10.3)	3.7 (3.2, 4.3)	1.4 (1.1, 1.7)	1,570	597	174
2008	98	23	24	8.0	1.9	2.0	10.4 (9.4, 11.3)	2.7 (2.3, 3.2)	2.6 (2.1, 3.1)	1,829	350	462
2009	74	15	20	5.9	1.2	1.6	7.2 (6.4, 8.0)	1.5 (1.1, 1.8)	2.1 (1.6, 2.6)	1,342	259	377
2010	85	19	19	6.5	1.5	1.5	8.2 (7.4, 9.1)	1.9 (1.5, 2.3)	1.8 (1.4, 2.2)	1,503	304	334
2011	106	26	29	7.9	1.9	2.2	9.9 (9.0, 10.8)	2.6 (2.1, 3.0)	3.0 (2.5, 3.5)	1,807	448	525
2012	111	24	23	8.1	1.8	1.7	9.6 (8.6, 10.5)	2.1 (1.6, 2.5)	1.9 (1.5, 2.3)	1,401	293	288
2013	115	24	29	8.3	1.7	2.1	10.3 (9.4, 11.2)	2.3 (1.8, 2.8)	2.5 (2.1, 2.9)	2,126	407	510

Table 1: Continued…

2014	122	42	25	8.7	3.0	1.8	10.4 (9.5, 11.3)	3.7 (3.1, 4.2)	2.3 (1.9, 2.7)	2,118	703	393
2015	166	22	40	11.7	1.5	2.8	13.8 (12.8, 14.8)	1.8 (1.4, 2.2)	3.4 (2.9, 3.9)	2,787	308	654
2016	154	33	41	10.7	2.3	2.8	12.2 (11.2, 13.2)	2.8 (2.4, 3.3)	3.5 (3.0, 4.0)	2,795	562	683
2017	195	31	42	13.5	2.1	2.9	15.5 (14.4, 16.6)	2.6 (2.2, 3.0)	3.5 (3.0, 4.0)	3,537	507	721
2018	213	45	33	14.7	3.1	2.3	16.7 (15.5, 17.8)	3.6 (3.1, 4.2)	2.7 (2.2, 3.2)	3,624	778	564
2019	213	46	41	14.6	3.1	2.8	16.5 (15.4, 17.7)	3.8 (3.3, 4.3)	3.2 (2.7, 3.7)	3,714	703	657
Total	1,886	439	390	9.0	2.1	1.9	11.1 (10.9, 11.3)	2.7 (2.6, 2.8)	2.4 (2.3, 2.5)	33,077	7,172	6,584
P	-	-	-	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	-	-	-

Abbreviations: CMR, crude mortality rate; ASR, age-standardized rate; YLL, years of life lost; CI, confidence interval.
† "Cervical cancer" is also included uterine/vaginal/vulvar cancers.

The total YLL due to breast, cervical/uterine/vaginal/vulvar, and ovary cancers' deaths in the 16-year period were 33,077, 7,172 and 6,584 yr, respectively. The highest YLLs were observed in 50-59-year-old females, followed by 40-49- and 60-69-year-old females for deaths due to breast and gynecologic cancers. In addition, extreme age groups (20-29- and >80-year-old females) comprised the lowest YLL (Fig. 1).

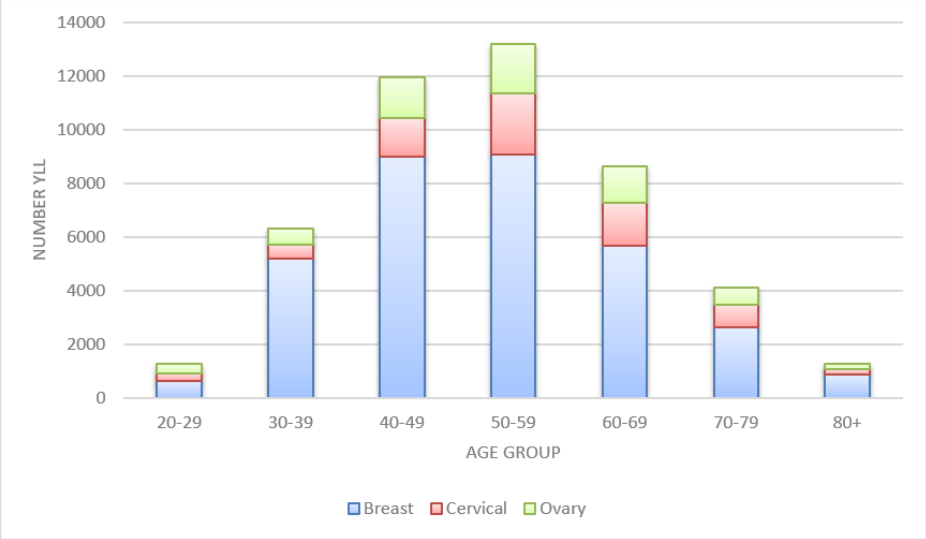

Fig. 1: YLL due to breast and gynecologic cancers in different age groups, southern Iran, 2004–2019 ["cervical cancer" is also included uterine/vaginal/vulvar cancers]

According to the join point regression, the 16-year trend of YLL rate due to premature mortality in breast cancer was increasing: annual percent change (APC) was 7.6% (95% CI 5.5-9.7, *P*<0.001). The model did not show any joinpoint, and hence, the AAPC (average annual percent change) is the same as APC (Fig. 2).

In addition, the trend of YLL rate due to premature mortality in ovary cancer was increasing: average annual percent change (AAPC) was 19.0%

(95% CI 12.2-26.1, *P*<0.001). The model shows one join point in 2008 when the APC was 71.6% (95% CI 38.8- 112.0, *P*<0.001) (Fig. 2).
Moreover, the trend of YLL rate due to premature mortality in cervix cancer was increasing: Average annual percent change (AAPC) was 9.2% (95% CI -9.2 to 31.3, *P*>0.05). The model shows two join point in 2006 and 2009, when the APC was 105.5% (95% CI -15.1 to 397.5, *P*=0.097) and -25.4% (95% CI -69.2 to 80.7, *P*= 0.467) (Fig. 2).

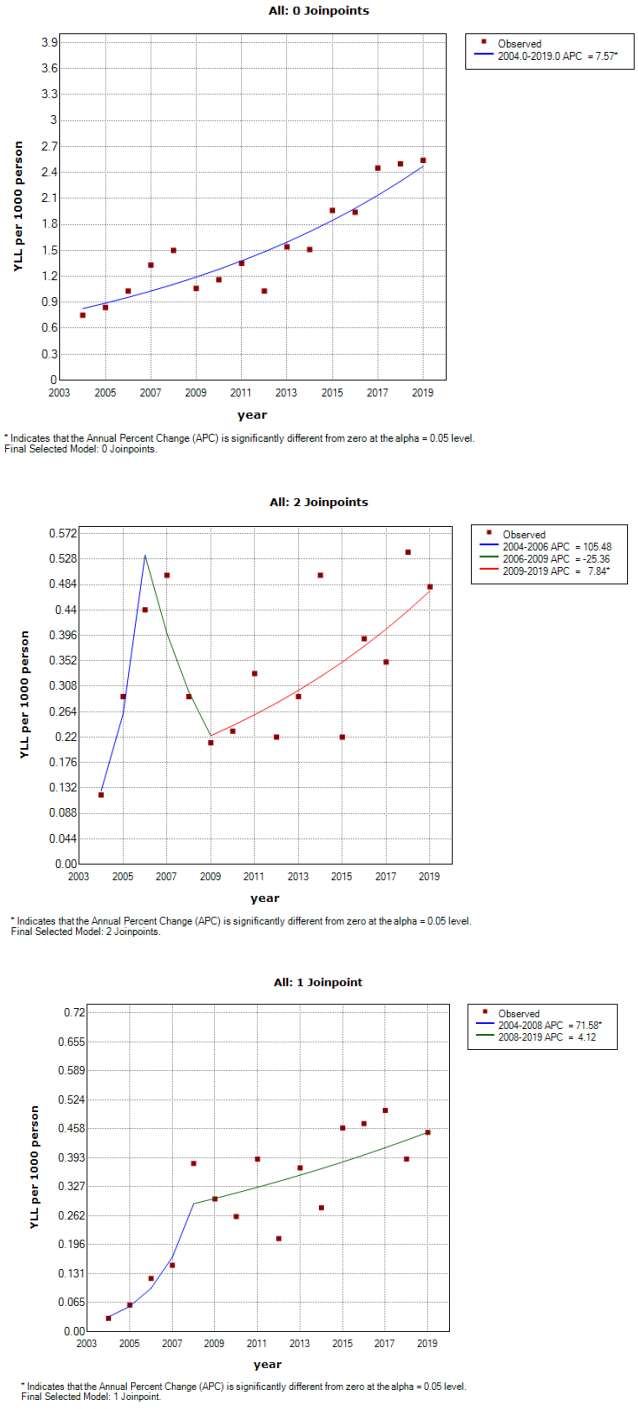

Fig. 2: 16-year trend of YLL (per 1,000 people) due to breast (A), cervical (B) and ovary (C) cancers in southern Iran, 2004–2019 ["cervical cancer" is also included uterine/vaginal/vulvar cancers]

Discussion

During 2004-2019 in the southern Iran, the highest YLLs were observed in 50-59-year-old females, followed by 40-49- and 60-69-year-old females due to breast and gynecologic cancers, respectively. Notably, the lowest YLLs were observed in extreme age groups (20-29- and >80-year-old females). The 16-year trend of YLLs due to breast cancer premature death was constantly increasing. This trend showed a significant increasing pattern from 2009 to 2019 for cervical/uterine/vaginal/vulvar cancers premature death. Moreover, the 16-year trend of YLLs due to ovary cancer premature death was significantly increasing with one join point in 2008.

In our study, mortality rate of breast cancer had an increase from 5.3 per 100,000 people in 2004 to 16.5 per 100,000 people in 2019 in south of Iran. Similarly, the mean breast cancer mortality rate in middle east and north Africa region (MENA) is shown an increase from 8.70 per 100,000 people in 2005 to 9.72 per 100,000 people in 2015 (7). In another study, Sharifian et al. (16), reported an increase in YLLs due to breast cancer in Iran, which was 152.8 yr per 100,000 people in 1990 to 175.64 yr per 100,000 people in 2010. Furthermore, during 2004-2019, we found that the APC of YLLs due to breast cancer premature death was 7.6%. The APC estimated by Ataeinia et al. (8), was 4.8% during 1990-2015. In contrast, it was decreased from 24.5 per 100,000 people in 2004 to 19.4 per 100.000 people in 2019 in United States (US) (17). This decrease postulated the role of generalized use of mammography and improvement of breast cancer treatment in US. (2). in this respect, in Iran, only 18% of breast cancer patients are estimated to detect in stage 1 (7). More than 80% of these patients initially diagnose with stage II in Iran (18). Moreover, in a multi-center study in Iran, a significant percentage of cases (96%) were diagnosed at stage II or III (19). Up-trend of YLLs due to breast cancer is observed in south of Iran, which this might be because of progress in diagnosis, as well as the Iranian population changes such as increase in life expectancy and urbanization (20,21). Therefore, screening programs should be prioritized to detect patients at early stages, coupled with early treatment's allocation (8, 22).

Another finding of this study was 0.2 death per 100,000 women due to ovarian cancer in 2004 that was increased to 3.2 per 100,000 women in 2019. In-line with or finding, Sharifian et al. (11), showed an increase in ASR and crude rate of ovarian cancer mortality in Iran from 2004 to 2013. Life style changes (e.g., low fiber intake, overweight and obesity, etc.), which are the risk factors of ovarian cancer, might be led to such increase (11, 23, 24). Eastern Mediterranean Region had an increase in disability adjusted life years (DALYs) due to cervical cancers from 2000 to 2017 (25). In our study, the aggregated mortality rate in cervical, uterine, vaginal, and vulvar cancers had an upsurge from 1.2 in 2004 to 3.8 in 2019 with a corresponding APC of 7.8%. Worth noting, a significant increasing trend was just observed after 2009. According to the 2019 Global Burdon of disease (GBD) report, the mortality and YLLs of cervical, uterine and ovarian cancers in south of Iran showed an increase (44.81 to 351.78% and 145.69 to 668.03%, respectively) from 1990 to 2019 (26). Another study from Iran represented a decreasing trend in mortality due to cervical cancer and corpus uterine cancer during 1990-2016 (27). This difference might be because of population diversities, as our population is accounted for as the geographical area with the highest incidence of cervical cancer in Iran as well as the second highest ASR of mortality due to cervical cancer (28).

Last by not least, the highest YLLs were observed in 50-59-year-old females, followed by 40-49- and 60-69-year-old females for deaths due to breast and gynecologic cancers. In Western world, breast cancer occurs at older ages, while the average age of 50 is the peak age of breast cancer in Asian counties (29, 30). In Iran, during 2005-2006, the age group of 50-54 had the highest mortality rate of breast cancer (31). While in another Iranian study, 49% of patients were diagnosed during 35-49 yr of age and 27% during 50-64 yr of age (32). By and large, our result in consistent with in-line

studies; that is, highest incidence and mortality in the fifth and sixth decades in Iran, in addition to the diagnosis tendency toward stages II and III, might be led to a high YLLs.
Some limitations of this study include the possibility of undercounting the cases of death due to cancer, whereas some of the strengths of the study are the wide range of time and the appropriate sample size. This study is one of the few studies which analyses the trend of the years of life lost due to women's cancer.

Conclusion

Mortality rate and YLLs due to breast and gynecologic cancers have been increased in southern Iran during the last twenty years. Early detection programs and allocating treatments at early stages should be prioritized.

Journalism Ethics considerations

Ethical issues (Including plagiarism, informed consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc.) have been completely observed by the authors.

Acknowledgements

We would like to acknowledge the Health Vice-chancellor, Shiraz University of medical sciences.

Funding

This research received no external funding.

Conflict of interests

The authors declare no competing interests.

References

1. Ferlay J, Soerjomataram I, Dikshit R, et al (2015). Cancer incidence and mortality worldwide: sources, methods and major patterns in GLOBOCAN 2012. *Int J Cancer*, 136(5): E359-86.
2. Global Cancer Observatory. Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 11 (2013). Lyon, France: International Agency for Research on Cancer.
3. Winters S, Martin C, Murphy D, et al (2017). Breast Cancer Epidemiology, Prevention, and Screening. *Prog Mol Biol Transl Sci*, 151: 1-32.
4. Forbes JF (1997). The incidence of breast cancer: the global burden, public health considerations. *Semin Oncol,* 24 (1 Suppl 1): S1-20-S1-35.
5. Bray F, Ferlay J, Laversanne M, et al (2015). Cancer Incidence in Five Continents: Inclusion criteria, highlights from Volume X and the global status of cancer registration. *Int J Cancer,* 137(9): 2060-71.
6. World health Organization. Breast Cancer Awareness Month 2021 (2021). International Agency for Research on Cancer. 2021. Available from: https://www.iarc.who.int/featured-news/breast-cancer-awareness-month-2021/
7. Mousavi SM, Montazeri A, Mohagheghi MA, et al (2007). Breast cancer in Iran: an epidemiological review. *Breast J*, 13(4): 383-91.
8. Ataeinia B, Saeedi Moghaddam S, Shabani M, et al (2021). National and Subnational Incidence, Mortality, and Years of Life Lost Due to Breast Cancer in Iran: Trends and Age-Period-Cohort Analysis Since 1990. *Front Oncol*, 11: 561376.
9. Sargazi N, Daroudi R, Zendehdel K, et al (2022). Economic Burden of Gynecological Cancers in Iran. *Value Health Reg Issues*, 28: 1-6.
10. Cho KR, Shih IeM (2009). Ovarian cancer. *Annu Rev Pathol*, 4: 287-313.
11. Sharifian A, Pourhoseingholi MA, Norouzinia M, et al (2014). Ovarian cancer in Iranian women, a trend analysis of mortality and incidence. *Asian Pac J Cancer Prev*, 15 (24): 10787-90.
12. Waggoner SE (2003). Cervical cancer. *Lancet*, 361 (9376): 2217-25.
13. Arbyn M, Weiderpass E, Bruni L, et al (2020). Estimates of incidence and mortality of cervical cancer in 2018: a worldwide analysis. *Lancet Glob Health,* 8 (2): e191-e203.
14. Sankoh O, Sharrow D, Herbst K, et al (2014). The INDEPTH standard population for low-and middle-income countries, 2013. *Glob Health Action*, 7: 23286.

15. World Health Organization (2001). National Burden of Disease Studies: A Practical Guide. 2nd ed. WHO, Geneva.
16. S Sharifian A, Pourhoseingholi MA, Emadedin M, et al (2015). Burden of Breast Cancer in Iranian Women is Increasing. *Asian Pac J Cancer Prev*, 16 (12): 5049-52.
17. National Institutes of Health: SEER*Explorer Application (2022). Available from: https://seer.cancer.gov/statistics-network/explorer/application.html
18. Mobarakeh ZS, Mirzaei K, Hatmi N, et al (2014). Dietary habits contributing to breast cancer risk among Iranian women. *Asian Pac J Cancer Prev*, 15 (21): 9543-7.
19. Harirchi I, Karbakhsh M, Kashefi A, et al (2004). Breast cancer in Iran: results of a multi-center study. *Asian Pac J Cancer Prev*, 5 (1): 24-27.
20. Abedi G, Janbabai G, Moosazadeh M, et al (2016). Survival Rate of Breast Cancer in Iran: A Meta-Analysis. *Asian Pac J Cancer Prev*, 17 (10): 4615-21.
21. Movahedi M, Haghighat S, Khayamzadeh M, et al (2012). Survival rate of breast cancer based on geographical variation in Iran, a national study. *Iran Red Crescent Med J*, 14 (12): 798-804.
22. Baghestani AR, Zayeri F, Akbari ME, et al (2015). Fitting Cure Rate Model to Breast Cancer Data of Cancer Research Center. *Asian Pac J Cancer Prev*, 16 (17): 7923-7.
23. Stewart C, Ralyea C, Lockwood S (2019). Ovarian Cancer: An Integrated Review. Semin Oncol Nurs, 35 (2): 151-156.
24. Financial Tribune. Daily and Contributors (2016). Available from: https://financialtribune.com/articles/people/53113/dietary-fiber-intake-low
25. Safaeian F, Ghaemimood S, El-Khatib Z, et al (2021). Burden of Cervical Cancer in the Eastern Mediterranean Region During the Years 2000 and 2017: Retrospective Data Analysis of the Global Burden of Disease Study. *JMIR Public Health Surveill*, 7 (5): e22160.
26. IHME GHDx. GBD results (2019). Available from: https://vizhub.healthdata.org/gbd-results/
27. Eftekharzadeh S, Ebrahimi N, Samaei M, et al (2020). National and Subnational Trends of Incidence and Mortality of Female Genital Cancers in Iran; 1990-2016. *Arch Iran Med*, 23 (7): 434-44.
28. Khorasanizadeh F, Hassanloo J, Khaksar N, et al (2013). Epidemiology of cervical cancer and human papilloma virus infection among Iranian women - analyses of national data and systematic review of the literature. *Gynecol Oncol,* 128 (2): 277-81.
29. Yip CH, Taib NA, Mohamed I (2006). Epidemiology of breast cancer in Malaysia. *Asian Pac J Cancer Prev*, 7 (3): 369-74.
30. Remennick L (2006). The challenge of early breast cancer detection among immigrant and minority women in multicultural societies. *Breast J*, 12 Suppl 1: S103-10.
31. Nafissi N, Khayamzadeh M, Zeinali Z, et al (2018). Epidemiology and histopathology of breast cancer in Iran versus other Middle Eastern countries. *Middle East J Cancer*, 9(3): 243-51.
32. Vostakolaei FA, Broeders MJ, Rostami N, et al (2012). Age at Diagnosis and Breast Cancer Survival in Iran. *Int J Breast Cancer*, 2012:517976.