



Original Article



Trends in the Incidence Rates of Breast and Gynecological Cancers in Asia from 1998–2012: An Ecological Study

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Abstract

Background: There is limited evidence on the epidemiology and time trend analysis of incidence rates of gynecological cancer in Asia as a whole. We conducted this study to demonstrate breast and gynecological cancers incidence and trends in selected Asian populations.

Method: We conducted this ecological study using cancer and population data from cancer incidence in five continents (CI5). We extracted the data of breast, uterine, cervix and ovary cancers in selected Asian populations from 1998 to 2012 from CI5plus. We used Joinpoint regression model (version 4.8.0.1) to evaluate the annual percentage change (APC), which characterizes trends in cancer rates over time, and the average annual percent changes (AAPCs), which describes the average APCs over a period of multiple years. Results were considered statistically significant at $P < 0.05$.

Results: Between breast and gynecological cancers, breast cancer has the highest incidence rates among women in Asia. The time trend of the incidence rates showed a constant growth in breast, ovary and corpus uteri cancers. This rising trend was obviously sharper for uterine cancer (AAPC 95% CI = 3.4 [3.0, 3.7]) followed by breast [AAPC 95% CI = 2.1 (2.0, 2.2)] and ovarian cancers (AAPC 95% CI = 0.5 [-0.4, 1.3]). The age-adjusted incidence rate (ASR) of cervical cancer displayed a declining trend from 1998 to 2012 (AAPC 95% CI = -1.4 [-2.4, -0.5]).

Conclusion: Incidence rates of breast and gynecological cancers have a rising trend in Asian countries. However, breast and gynecological cancers have different patterns of time trend.

Keywords: Asian populations, Breast cancer, Gynecological cancers, Incidence

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Introduction

Breast and gynecological cancers are a significant global public health problem and one of the most common causes of cancer-related mortality worldwide.^{1,2} Gynecologic cancers have profound effects on the various physical functions of women.³ According to Globocan 2020, the highest number of new cases and deaths of breast and gynecological cancers was in Asia with 47.5% and 52.3% of all new cases, respectively.⁴ By 2040, it is predicted that new cases of breast cancer will increase by 33.8%, cervical cancer by 40.3%, corpus uteri by 30.3%, ovary by 36.6%, vulva by 48.2%, and vaginal cancer by 53.1% compared to 2020.⁴ Deaths from these cancers will also increase significantly by 2040 compared to 2020. Deaths due to breast, cervix uteri, vulva, and vaginal cancers will more than double by 2040 compared to 2020. The mortality of ovary and corpus uteri cancers will increase by 47.6% and 49.8%, respectively, in the same time.⁴

Worldwide, breast cancer was the most common cancer in terms of new cases with nearly 2.26 million in 2020. It was the fifth most common cause of cancer-induced mortality in 2020 with 685 000 deaths worldwide.⁵ Breast cancer is the most common cancer in women according to incidence and mortality rates worldwide.⁶ Cervical cancer

ranks third for both incidence and mortality in women.⁷ Among gynecologic cancers, cervix uteri cancer is the most common in terms of incidence, but vagina cancer is the deadliest.⁸ Currently, Asia accounts for 60% of the global population, so any change in Asia will have a global impact. Over the past five decades, Asian countries have achieved remarkable economic success. However, cancer burden in Asia remains a growing “global health threat”.⁹

Investigations of the changing temporal patterns of incidence and mortality of particular diseases are standard tools in epidemiological science and public health surveillance. Long-term data from vital sources enables a quantification of the evolution of population-based rates over time and may provide clues to the underlying determinants. Trend analyses may establish novel hypotheses or provide confirmatory evidence of existing ones. Time trend studies at the population level are an essential component in the implementation and evaluation of preventative strategies aimed at the primary, secondary and tertiary levels.¹⁰ Several studies have investigated the incidence of and mortality from gynecological cancers in some Asian countries. However, to the best of our knowledge, there is scarce evidence on the epidemiology and time trend analysis of incidence

rates of breast and gynecological cancers in Asia as a whole. We conducted this study to demonstrate breast and gynecological cancers incidence and trend in Asia.

Materials and Methods

Asia is the largest continent of the world with an area of 31,033,131 km². It contains 51 countries and has approximately 60% of world population share (<https://www.worldometers.info/geography/7-continent/>).

We conducted an ecological study based on the most recent cancer data from the International Agency for Research on Cancer (IARC) database (<https://ci5.iarc.fr/CI5plus/Pages/download.aspx>).⁹ The database includes incidence data as well as population denominators for 122 selected populations from 106 cancer registries worldwide for which histological data were available for a minimum of 15 consecutive years (up to 2012). CI5plus has provided cancer cases and population data files covered by selected cancer registry centers across the 5 continents of Africa, Americas, Asia, Europe and Oceania in separate files. We obtained cancer cases and population data files for selected cancer registries from Asia. The names of Asian cancer registries for which cancer data are available in the CI5plus are presented in a supplementary file.

The cancer case data file included information on the codes of registry centers, year, sex, type of cancer, counts of cancer in total population and each age group (0–4, 5–9, 10–14, ..., and ≥85 years) covered by each cancer registry. The population data file included information on codes of registry centers, year, sex, the population covered by each cancer registry in total and in each age group (0–4, 5–9, 10–14, ..., and ≥85 years). We extracted the incidence data for breast, cervix, uterine and ovary cancers, as well

as women's population in selected Asian populations from 1998 to 2012 from the CI5 database. According to the International Classification of Diseases for Oncology (ICD-O-3), the breast, cervix, uterine and ovary cancers were identified by topography codes C50, C53, C54-55 and C56, respectively. We calculated the age-standardized incidence rate (ASR) of breast and gynecological cancers for 18 age groups (0–4, 5–9 ... and ≥85 years) using the direct standardization method and the world population in 2000 as the standard population.¹¹ We used Joinpoint version 4.8.0.1 to conduct the Joinpoint regression model to evaluate the annual percentage change (APC), which characterizes trends in cancer rates over time, and the average annual percent changes (AAPCs), which describes the average APCs over a period of multiple years. The corresponding 95% confidence intervals (CIs) were calculated. P values less than 0.05 were considered statistically significant.

Results

There were 387 709 new cases of breast cancer, 56 645 new cases of ovarian cancer, 79 006 new cases of cervix cancer and 63 169 new cases of uterine cancer recorded in the selected Asian cancer registries included in the CI5 database between 1998 and 2012.

The ASR of breast cancer was between 39.58 per 100 000 and 53.08 per 100 000 in 1998 and 2012, respectively. Breast cancer incidence rates had an upward trend during the period 1998–2012. The time trend of the incidence rate showed a constant growth for breast cancer (AAPC 95% CI = 2.1 [2.0, 2.2]) (Tables 1 and 2, Figure 1A).

The ASR of ovarian cancer was between 6.12 per 100 000 and 6.55 per 100 000 in 1998 and 2012, respectively. The

Table 1. Annual Number of New Cases, Crude Rate and ASR of Breast and Gynecological Cancers in Selected Asian Population Included in the CI5 Plus in the Period 1998–2012

Year	Breast			Ovary			Cervix			Corpus Uteri		
	Number of New Cases	Crude	ASR	Number of New Cases	Crude	ASR	Number of New Cases	Crude	ASR	Number of New Cases	Crude	ASR
1998	18533	13.51	39.60	2970	2.27	6.41	5054	3.21	10.77	2600	1.95	5.63
1999	19609	13.52	40.51	3034	2.14	6.36	5267	3.20	10.87	2883	2.04	6.09
2000	20589	13.96	41.76	3011	2.12	6.2	5161	3.06	10.47	2907	2.06	5.96
2001	21307	14.08	42.29	3471	2.36	7	5409	3.14	10.76	3278	2.26	6.55
2002	22349	14.45	43.51	3552	2.35	6.97	5289	3.06	10.32	3498	2.32	6.85
2003	23064	14.25	43.51	3622	2.30	6.94	5194	2.87	9.89	3601	2.37	6.79
2004	24576	14.54	45.40	3731	2.37	6.96	5181	2.78	9.70	4076	2.55	7.49
2005	25673	14.89	46.44	3758	2.28	6.85	5092	2.67	9.31	4124	2.56	7.36
2006	26727	14.96	47.09	4078	2.35	7.07	5175	2.68	9.22	4353	2.52	7.59
2007	28137	15.46	48.48	4249	2.44	7.38	5141	2.54	9	4760	2.70	8.11
2008	29239	15.38	49.01	4290	2.34	7.31	5487	2.62	9.40	4938	2.69	8.15
2009	30283	15.67	49.51	4177	2.21	6.92	5439	2.64	9.04	5234	2.77	8.40
2010	32085	16.27	51.34	4224	2.18	6.85	5507	2.55	9.04	5495	2.88	8.58
2011	32255	16.48	52.52	4162	2.20	6.84	5288	2.50	8.78	5501	2.85	8.78
2012	33283	16.65	53.09	4316	2.16	6.96	5322	2.50	8.73	5921	3.05	9.13

Table 2. Annual Percentage Change (APC) and Average Annual Percentage Change (AAPC) in Incidence Rates of Breast and Gynecological Cancers in Selected Asian Population Included in the CI5 Plus between 1998 and 2012

Cancer	Period	Annual Percentage Change (APC)	95% CI	Average annual percentage change (AAPC) (1998-2012)	95% CI
Breast	1998–2012	2.1	2.0, 2.2	2.1	2.0, 2.2
Ovary	1998–2007	1.5	0.6, 2.4	0.5	-0.4, 1.3
Ovary	2007–2012	-1.3	-3.5, 0.9		
Cervix	1998–2001	-0.4	-3.3, 2.5	-1.4	-2.4, -0.5
Cervix	2001–2005	-3.2	-6.0, -0.3		
Cervix	2005–2012	-0.9	-1.6, -0.1		
Corpus Uteri	1998–2012	3.4	3.0, 3.7	3.4	3.0, 3.7

incidence of ovarian cancer showed an upward trend until 2007 [APC 95% CI = 1.5 (0.6, 2.4)], then it declined up to the end of study (APC 95% CI = -1.3 [-3.5, 0.9]). The average annual percentage change for ovarian cancer was (AAPC 95% CI = 0.5 [-0.4, 1.3]) (Tables 1 and 2, Figure 1B).

The ASR of cervical cancer was between 10.77 per 100 000 and 8.73 per 100 000 in 1998 and 2012, respectively. The ASR of cervical cancer displayed a declining trend [AAPC 95% CI = -1.4 (-2.4, -0.5)] (Figure 1). The results of Joinpoint analysis showed a declining trend for the incidence rates of cervical cancer. This decline was sharper during 2001–2005 (APC = -3.2 [-6.0, -0.3]) compared to 2005–2012 (APC = -0.9 [-1.6, -0.1]) (Tables 1 and 2, Figure 1C).

The ASR of uterine cancer was between 5.63 per 100 000 and 9.13 per 100 000, with a rising trend in the period 1998–2012. The results of Joinpoint analysis showed a constant growth for corpus uteri during the period 1998–2012 (AAPC 95% CI = 3.4 [3.0, 3.7]) (Tables 1 and 2, Figure 1D).

Discussion

Our study showed that the incidence rates of breast, corpus uteri and ovary cancers in Asia had an upward trend, while incidence rates of cervical cancer had a declining trend between 1998 and 2012. Several studies on the epidemiology of breast and gynecological cancers worldwide have shown increasing incidence trends as follows.

In line with our study, a meta-analysis in the period 2005–2019 revealed that the ASR of breast cancer had been increasing in the Eastern Mediterranean Region (EMRO).¹² The Breast cancer ASR for Asia in the present study was higher than that for EMRO. An increasing trend of breast cancer incidence rates was also noted in Hong Kong in the period 1983–2008¹³ and in China during 2000–2015.¹⁴ According to Takiar and Srivastav, several registries in India reported an upward trend for breast cancer, while some others reported no change in the upward trend for breast cancer from 1990 to 2003.¹⁵ Krishnamoorthy et al showed increasing worldwide trends in breast cancer incidence during 1993–2012.¹⁶ Also, an overall increasing trend in the incidence of breast cancer was shown in Zurich, Switzerland between 1981 and 2017.¹⁷ A trend analysis of the global incidence of

breast cancer showed a rapidly rising incidence in a large number of countries including Asian countries, especially those with rapid economic development in the past several decades.¹⁸ However, between 1971 and 2015 in Canada, breast cancer incidence had an increasing trend among women under the age of 40 since 2000, and a stable trend for women under 50 years.¹⁹

Several studies have investigated the time trend of gynecological cancer incidence around the world. In line with our study, an international study on the trends of ovarian cancer incidence showed an increase in the ASRs of ovarian cancer in non-Asian populations during 2008–2012.²⁰ Similar to our results, Eftekhazadeh et al depicted a rising trend in the incidence of gynecological cancers in Iran in the period 1990–2016.²¹ A time trend study in Iran showed that the incidence rates of ovarian cancers had an upward trend in the period from 2003 to 2009.²² Xie et al studied the trends in the incidence of common cancers in Hong Kong and reported an upward trend for ovarian cancer in the period 1983–2008.¹³ In contrast to the findings of our study, Bekmukhambetov et al stated that ovarian cancer showed no noticeable change in the Aktobe Region of Kazakhstan in the period between 2004 and 2013.²³ Another study in Poland during 1980–2013 revealed a decrease in ovarian cancer incidence after 1994.²⁴

Similarly, several studies have displayed this upward trend for cervical cancer. A time trend study showed rising trends of cervical cancer incidence in Lithuania, Bulgaria and Romania.²⁵ Another study on the cancer incidence trends among Asian-American populations in the United States revealed a decreasing trend for cervical cancer among Laotians and the Vietnamese and an increasing trend of uterine cancer in Asian Indians, the Chinese, Filipina, and Japanese during 1990–2008.²⁶ Similar to our findings, Boo et al in South Korea showed a reducing trend in the cervical cancer ASR during 1997 to 2008.²⁷ A declining trend of cervical cancer was also observed in Hong Kong in the period 1983–2008¹³ and in several registries in India between 1990 and 2003, while some other registries in India reported no considerable change in cervical cancer incidence rates.¹⁵ In contrast, an increasing trend of cervical cancer was reported in Japan since the late 1990s, especially among young women.²⁸ Cervical cancer incidence rate was also increasing in South

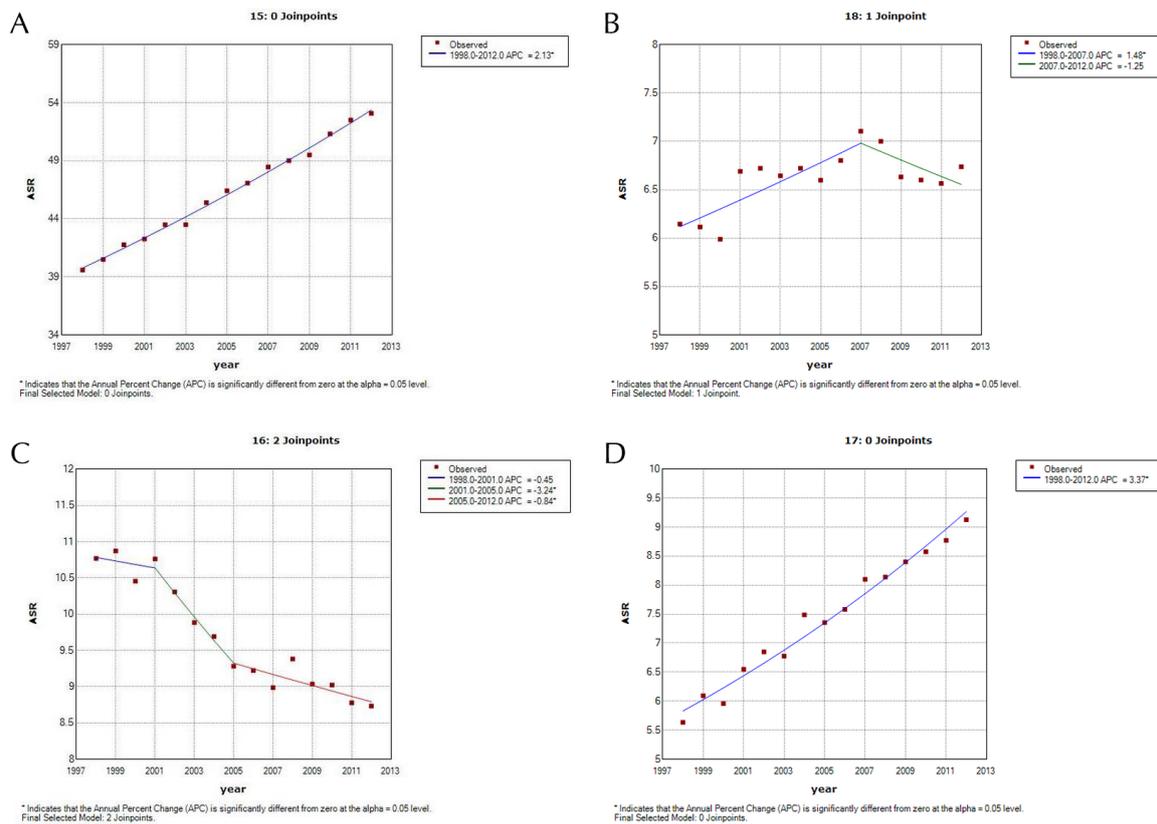


Figure 1. Time Trends of Breast and Gynecological Cancers Incidence for Age-Standardized Rates (ASR) in Selected Asian Population Included in the CI5 Plus in the Period 1998–2012. **A)** for breast cancer, **B)** for ovarian cancer, **C)** for cervical cancer, **D)** for corpus uteri cancer

Korea from 1997 to 2008²⁷ and in the Aktobe Region of Kazakhstan in the period between 2004 and 2013.²³

Our study revealed an increasing trend for uterine cancer in Asia. Similarly, a 30-year nationwide surveillance for uterine cancer in Taiwan revealed an increasing trend of this cancer from 1979 to 2008.²⁹ An increasing trend in the incidence rates of uterine cancer was also observed in the Songkhla Province, Thailand during 1989–2016³⁰ and in Hong Kong in the period 1983–2008.¹³ A time trend analysis of the incidence of gynecological cancers in Iran displayed a consistent increasing pattern for incidence rates of corpus uteri cancer at the national level during 1990–2016.

Social disparities contribute substantially to the incidence rates of the breast and ovarian cancers. Moreover, social disparities are more profound for breast cancer.²² The high incidence rate of breast cancer may be partially associated with genetic factors. However, the incidence of breast cancer is strongly correlated with HDI.¹⁸ A tendency towards the Western lifestyle, changes in reproductive behaviors, increased age of marriage and age at first birth, dietary habits, obesity, reduced physical activity, and smoking might partially explain these uptrends in breast and gynecological cancers.²⁰ On the other hand, improved diagnostic and therapeutic services might cause such upward trends. In addition, improved cancer registration systems that have expanded from confirmed histological cases to a population-based registry might explain the increasing trends.²² Lifestyle

changes in the past three decades,²¹ increased prevalence of obesity, increased age at first childbirth, high body mass index,³¹ diabetes mellitus³² and hypertension³³ have been presented as risk factors for endometrial cancer. Urgent prevention measures including the development of a healthy diet, giving birth at a younger age, increased breastfeeding, limiting menopause estrogen therapy, and control of alcohol consumption are important for interrupting uptrends.¹⁴

Limitations

Given the ecological nature of the study, the results of the present study are vulnerable to ecological fallacy. Trends are presented for the Asian continent and cannot be interpreted at the national level. In addition, the CI5plus database is useful for time trend analyses, but trends should be interpreted with caution due to differences over time in registration practices and coding. Differences in quality of data over time and across different Asian registries should be considered as a limitation of this study and the findings should thus be interpreted with caution.

Conclusion

In conclusion, there is a rising trend in the incidence rates of breast and gynecological cancers in Asia, except for cervical cancer which shows a declining trend. Reducing the burden of cancer requires extensive community-wide measures by governments. For instance, healthy lifestyles, screening programs, and HPV vaccination may

lead to reduction in the incidence rates of breast and gynecological cancers.

Authors' Contribution

ME and GR conceived the study and contributed to study design, analysis and wrote the first draft of the manuscript. ST contributed to wrote the first draft the manuscript and data preparation. All authors read and approved the final manuscript.

Conflict of Interest Disclosures

The authors declare that they have no conflict of interest.

Ethical Statement

Not applicable.

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