

Breast Cancer Incidence Trends in Isfahan Province Compared with those in England over the Period 2001–2013

Abstract

Background: Figures from Iranian cancer registries indicate that Isfahan ranks first in female breast cancer incidence. Although few previous studies have examined whether the breast cancer incidence trend in Isfahan province has increased over a given period of time, this study employed a joint point regression analysis to answer the same question. Moreover, it compared the data of Isfahan province, from a developing country, with those of England, as a representative of developed countries, and tried to explain the causes of the differences observed between the trends. **Methods:** This repeated cross-sectional study was conducted on the data of 6057 women in Isfahan province and of 141,011 women in England with breast cancer over the years 2001–2013. The incidence rates were calculated using direct standardization method and based on the 2013 standard European population. For an analysis of the trends in breast cancer incidence rates, Joint Point Regression program, version 4.3.1.0, released in April 2016, was employed. **Results:** The mean age-standardized incidence rate (ASR) was calculated to be 34.7 per 100,000 population over the years 2001 to 2013, which indicated an increase from 22 to 68 in Isfahan province. The corresponding mean ASR for England has also risen from 147.5 to 170.1 per 100,000 women during the same time period. The average annual percentage changes (AAPCs) for Isfahan and England were also calculated to be 9.6 and 1.1, respectively. This indicated an increasing trend in breast cancer incidence rates for Isfahan province over the period in question. **Conclusions:** The drastic discrepancy in breast cancer incidence rates between these two regions may be attributed to differences in an improved cancer registry system in Iran and women's developing awareness of the cancer over time.

Keywords: Breast cancer, England, incidence, Iran, trend

Introduction

Today, cancer is known as the second leading cause of death across all age ranges in the world.^[1] According to the World Health Organization (WHO) reports, over 13 million new cases of cancer have occurred in 2008. It has been predicted that they will increase by 75%, reaching 22 million cases by the year 2030.^[2] Breast cancer is the most prevalent type of cancers in women, and it accounts for 23% of new cases of cancer among women alone. In 2008, the incidence rate and the age-standardized mortality rate (ASMR) have been 38.9 and 12.4 per 100,000 population, respectively.^[3]

Breast cancer incidence is related to various risk factors including age, geographical variation, menarche and menopause ages, family history, previous breast diseases, ray

contacts, lifestyle (including diet, weight, alcohol consumption, and smoking), consumption of contraceptive pills, and alternative hormone therapy. Global discrepancies in breast cancer incidence rates are predominantly related to differences in the risk factors for post-menopause breast cancer and to changes in handling of issues such as pregnancy and lifestyle.^[4-7]

In the Eastern Mediterranean Region, including Iran, breast cancer ranks the highest among all types of cancers. According to the Iran National Cancer Registry (INCR) report, breast cancer in women is the most prevalent type of cancer with an age standardized incidence rate (ASR) of 28.25 per 100,000 population and has accounted for 22% of cancer cases among Iranian women. Moreover, it ranks twelfth among the main causes of death in women, with a rate of 4.92 per 100,000 population.^[8,9] The incidence rate

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Access this article online

Website:
www.ijpvmjournal.net/www.ijpvm.net

DOI:
10.4103/ijpvm.IJPVM_360_19

Quick Response Code:



How to cite this article: Ainvand MH, Shakibaei N, Ravankhah Z, Yadegarfar G. Breast cancer incidence trends in Isfahan province compared with those in England over the period 2001–2013. *Int J Prev Med* 2021;12:54.

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of cancers, notably breast cancer, in Isfahan province has grown, and, as the figures for 2005 reveals,^[10-12] 10% of the breast cancer cases in Iran have occurred in this province. Isfahan province is geographically located in central Iran [Figure 1], with an overall area of 107027 square kilometers and a population of 4,879,312. Nearly 83.3% of the population of this province are urban residents, and 16.7% live in rural areas. The province consists of 18 sub-provinces (or counties), 38 bakhsh (or districts), 67 cities, and 2470 villages. In addition, 88.6% of the people have been reported as literate.

Analyzing age-specific standardized incidence trends over time can serve as a useful and simple instrument for assessing the effectiveness of health and preventive measures for this cancer in screening programs. Such studies also provide a chance for assessing cancer registry data.

This study in Isfahan province is significant in that this province ranks first in breast cancer incidence rate among women across Iran.^[13] Moreover, Isfahan is among the five metropolises of Iran, and there is the possibility of accessing breast cancer data as well. In this study, England as a representative of developed countries with a high breast cancer incidence rate (125 cases per 100,000 female population^[14]) has been chosen for comparison. In addition, England enjoys an accurate and strong system of registering cancer data. As the country's cancer registry reports reveal, the difference in breast cancer incidence age for England is remarkable compared with that for Iran.^[15] Accordingly, the present study was intended to explore age trends in female breast cancer incidence in Isfahan province over the time span 2001–2013, and to compare them with those found in England.



Figure 1: Location of Isfahan province in Iran

Methods

This repeated cross-sectional study was conducted using data recorded in the Cancer Registry of the Ministry of Health and Medical Education (MOHME) and in the Noncommunicable Unit of the Health Deputy of Isfahan University of Medical Sciences (IUMS). The data, in accordance with the third edition of the International Classification of Diseases for Oncology (ICD-O-3), were provided to the research team by the National Cancer Registry (NCR) of the MOHME, having been de-duplicated and purified. The data in question include all new cases of female breast cancer in Isfahan province recorded in the NCR during the years 2000–2007 as well as those recorded in the Cancer Registry of Isfahan province during the years 2007–2013, which were accordingly analyzed. To access the data for England, the researchers visited the Website ONS (www.ons.gov.uk) and requested the necessary data by contacting the country's cancer registry via email. Accordingly, the research team was provided with the data for the time period 2001–2013.

In this study, using direct standardization and based on the 2013 standard European population, the crude incidence rate (CIR) and age-standardized rate (ASR) were calculated through STATAL14 program. As the data from England were standardized based on the 2013 standard European population, the incidence rates for Isfahan data were accordingly standardized. To determine breast cancer incidence rate for the period 2001–2013, an estimation of the population of Isfahan was required. To do so, the annual population growth rate for the two censuses in 1996 and 2006 were calculated, and based on the average annual growth rate, the denominator of the rates was calculated. In determining and analyzing variations of the trend in breast cancer incidence rate in Isfahan province and its comparison with those in England, joint point regression analysis was performed using Joint Point Regression program version 4.3.1.0 released in April 2016.

Results

The study was conducted on data of 6057 women infected with breast cancer already registered both in the NCR and the Cancer Registry of Isfahan Province during the years 2001–2013. For the same period of time, the number of women infected with breast cancer in England has been 141,011. According to the findings, the CIR and the ASR in Isfahan for the period in question have increased from 13.0 to 40.4 and from 22.0 to 68 per 100,000 population, respectively. During the same years, this rate for England has risen from 147.5 to 170.1 per 100,000 population. Based on the findings of the study, the ASR for the period 2001–2013 was calculated to be 34.7 on average per 100,000 population [Table 1].

In the joint point regression analysis for Isfahan province, two statistically significant joint points (2004 and 2007)

along with three trends in breast cancer incidence rates can be observed [Table 2]. The first trend of variations in breast cancer incidence rates can be observed during the years 2001–2004 with an APC of -31.0. That is, a 31% reduction has occurred each year compared with the previous year. The next trend of variations in breast cancer incidence rates can be observed during the years 2004–2007. In the calculated model for this trend, the value for APC is as high as 77.0, which means a 77% increase in the incidence rate for each year over the same period of time, and this value was found statistically significant. The next trend of variations in breast cancer rates in Isfahan province has occurred during the years 2007–2013, with an APC of 9.0%. This indicates a 9% increase in breast cancer rates for each year during the period in question, and this trend has been found statistically significant [Figure 2].

In examining the breast cancer incidence trend for England, the final model obtained on the basis of joint point regression analysis was one with one significant joint point and two trends. APCs of 2.3 and 0.67 were obtained for the time periods 2000–2004 and 2004–2013, respectively [Table 3]. The APC for the first trend shows an increasing flow with a faster slope and a 2.3% increase in the breast cancer incidence rate in women in England, which was not statistically significant. It was followed by an increasing flow with a more gentle slope, compared with the previous period, in breast cancer incidence with an APC of 0.67% in the incidence rate. This means that annually a

value approximately as much as 0.67% incidence rate for the period 2001–2005 is added to the incidence rate for the period 2004–2013, a trend which was found statistically significant [Figure 3].

The AAPCs for the period in question were calculated to be 9.6 and 1.1 for Isfahan and England, respectively, implying that the AAPC for breast cancer incidence in Isfahan is nine times as high as that for England [Table 4]. In other words, annually an amount approximately as much as 10% on average has been added to the breast cancer incidence rate in Isfahan province during the period in question while it is 1.1% for England per year. The difference between the AAPCs for Isfahan and England was calculated to be -9.8, and this difference is statistically significant. In addition,

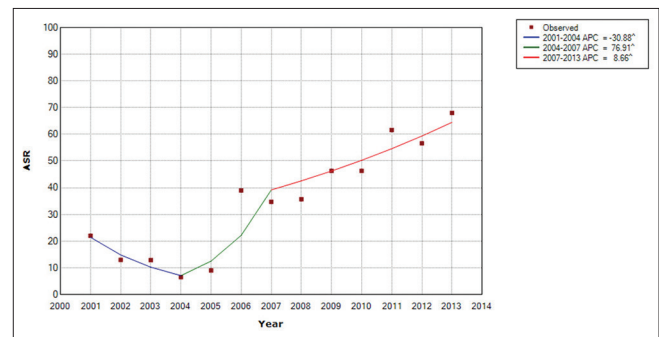


Figure 2: Joint point regression analysis: breast cancer trends in women in Isfahan province for the period 2001–2013

Table 1: Distribution of the population, number of breast cancer cases, breast cancer crude incidence rate (CIR), and breast cancer age-standardized rate (ASR) between Isfahan province and England for the period 2001–2013 (per 100,000 population)

Year	Population		Breast number		CIR		ASR		ASR 95% CI	
	Isfahan	England	Isfahan	England	Isfahan	England	Isfahan	England	Isfahan	England
2001	2049466	25284159	267	34312	13	135.7	22	147.5	0.000190, 0.000249	0.001459, 0.001491
2002	2070018	25386508	163	34319	7.9	135.2	13	146.8	0.000107, 0.000150	0.001453, 0.001484
2003	2117519	25497812	164	36509	7.7	143.2	12.9	155.2	0.000107, 0.000150	0.001536, 0.001568
2004	2152387	25549100	81	36939	3.8	144.1	6.5	156	0.000049, 0.000081	0.001544, 0.001576
2005	2187830	25987496	114	38212	5.2	148	9	160.3	0.000072, 0.000108	0.001587, 0.001619
2006	2223857	26180560	486	38004	21.9	146.2	39	158.1	0.000352, 0.000429	0.001565, 0.001597
2007	2335399	26380927	275	38048	11.8	145.3	34.7	156.5	0.000303, 0.000391	0.001549, 0.001581
2008	2367393	26562549	506	39681	21.4	150.4	35.7	161.3	0.000323, 0.000392	0.001597, 0.001629
2009	2399819	26562549	542	40260	21.8	151.6	46.3	161.5	0.000338, 0.000409	0.001599, 0.001630
2010	2432698	26765208	646	45259	26.6	154.2	46.3	163.5	0.000424, 0.000503	0.001619, 0.001651
2011	2466024	26974007	914	41523	37.1	153.9	61.6	162.7	0.000572, 0.000660	0.001611, 0.001643
2012	2499808	27160281	843	42489	33.7	156.4	56.6	164.1	0.000524, 0.000609	0.001625, 0.001657
2013	2534056	27331848	1024	44540	40.4	163	68	170.1	0.000634, 0.000726	0.001685, 0.001717

Table 2: The final model in the joint point regression analysis: breast cancer trends among women in Isfahan province for the period 2001–2013

Test number	Null hypothesis	Alternate hypothesis	Numerator degrees of freedom	Denominator degrees of freedom	Number of permutations	P	Significance level~
1	0 Jointpoint(s)	2 Jointpoint(s)*	4	7	4500	0.0008889	0.0250000
2	1 Jointpoint(s)	2 Jointpoint(s)*	2	7	4500	0.0008889	0.0500000

Final Selected Model 2 Jointpoint(s)

as the findings of the study reveal, the hypothesis that the breast cancer incidence trends in women in Isfahan province and England are parallel and are coincident was rejected at the significance level of 0.05 ($P = 0.00022$) [Table 5 and Figure 4].

Discussion

The findings of this study indicate an increasing trend in the rates or an increase in registration of cases in Isfahan, which is in line with those from similar studies conducted in Iran.^[16-21]

However, the ASR for breast cancer in Isfahan province and Iran, compared with Western countries including England and Asian countries, is lower.^[22] This remarkable difference in incidence rate between these two regions can be attributed to differences in established risk factors across different ethnic groups for breast cancer in women including certain reproductive factors, including earlier menarche, later age at first pregnancy, less breastfeeding, lower parity, and longer interval between births, older age, postmenopausal hormone use and other risk factors including a family history of breast cancer, greater height,

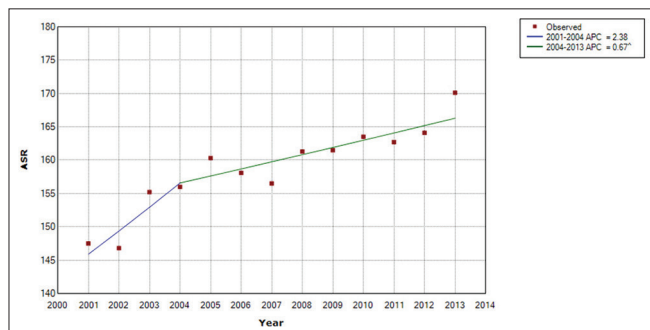


Figure 3: Joint point regression analysis: breast cancer trends in women in England for the period 2001–2013

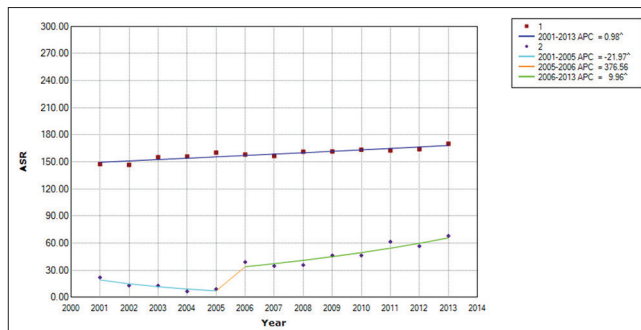


Figure 4: Joint point regression analysis: breast cancer trends in women in Isfahan province and England for the period 2001–2013

Table 3: Final model in the joint point regression analysis: breast cancer trends among women in England for the period 2001-2013

Test number	Null hypothesis	Alternate hypothesis	Numerator degrees of freedom	Denominator degrees of freedom	Number of permutations	P	Significance level~
1	0 Jointpoint(s)	2 Jointpoint(s)*	4	7	4500	0.0175556	0.0250000
2	1 Jointpoint(s)	2 Jointpoint(s)*	2	7	4500	0.1853333	0.0500000

Final Selected Model 1 Jointpoint(s)

Table 4: APCs for incidence rates, confidence interval, and mean scores for breast cancer trends in women in Isfahan province compared with those for England during the years 2001-2013

	Full range (2001-2013)		Trend 1 (2001-2004)		Trend 2 (2004-2007)		Trend 3 (2007-2013)	
	**AAPC	95% CI	*APC	95% CI	APC	95% CI	APC	95% CI
Isfahan	9.6^	1.1-18.9	-30.9^	-46.7-20.8	76.9^	20.4-160.0	8.7^	4.0 to 13.6
England	1.1^	0.6-1.6	2.4	-0.0-4.8	0.7^	0.4-1.0		
Comparison	-9.8^	-14.9-4.7						

*APC (annual percent change) and **.AAPC (Average Annual Percent Change). ^APC or AAPC is significantly different from zero at alpha=0.05

Table 5: Result of testing parallelism and coincidence of breast cancer incidence trends in women in Isfahan province and England for the period 2001-2013

Test for parallelism					
Number of jointpoints	Numerator degrees of freedom	Denominator degrees of freedom	Number of permutations	P	Significance level~
2 Jointpoint(s)	5	14	4500	0.0002222	0.0500000

Final Selected Model: Rejected Parallelism

Test for coincidence					
Number of jointpoints	Numerator degrees of freedom	Denominator degrees of freedom	Number of permutations	P	Significance level~
2 Jointpoint(s)	5	14	4500	0.0002222	0.0500000

Final Selected Model: Rejected Coincidence

adult weight gain, high birth weight, alcohol intake, and high mammographic density.^[23] For example, the beneficial effects of earlier first birth, higher parity, later age at menarche, and breastfeeding have been confirmed for Asian women including Iran.^[24,25] Cultural and socioeconomic factors such as access to healthcare services, execution of screening programs, and effectiveness of patient care and cancer registry system may also be considered as other factors indicating a difference in the incidence rate of breast cancer in two countries.

The results from joint point regression analysis in this study indicate, on the whole, an increasing trend in breast cancer incidence in women in both Isfahan province and England within the time span of 2001–2013. Although the ASRs for breast cancer in women in the province have undergone changes over the years, they have preserved their increasing trend with an AAPC of 9.6%, and this increasing trend of changes in incidence rates was found statistically significant.

Given the analysis performed in this study, it is observed that cancer registry in Iran, as the findings reveal, has had a decreasing and significant trend from 2001 to 2004, which implies a serious problem in registry system for this type of cancer during the time span in question. As of 2004 onwards, an increasing trend is observed in breast cancer incidence, which indicates an improvement in the registration of this cancer in the country. In addition, it is worth mentioning that the third trend of changes in cancer incidence (2007 to 2013) is coincided with a change in the cancer registry system from pathology-based to population-based, indicating an improvement in the status of registry systems both in the province and in Iran, though for the beginning years of the study period (2001 to 2004) the breast cancer incidence registry is unreasonably different than expected.

According to the results from joint point regression analysis, the trend of breast cancer incidence rate in women in England also indicates an increase in breast cancer incidence with an AAPC of 1.1%. The results from joint point regression analysis of joint points of the breast cancer incidence trend for England showed that only one significant joint point has occurred in the trend of breast cancer incidence rates (the year 2004) over the period in question. Generally, in the joint point regression analysis, the breast cancer incidence trend for England has seen slight changes in the APCs compared to Isfahan province. The existence of slight changes in the APC for England implies an effective and strong cancer registry system.

Comparing the overall female breast cancer incidence trends between Isfahan province and England indicates a drastic difference in incidence in these regions. The findings of this study show a significant increase in breast cancer incidence trend in Isfahan province, which is in agreement with similar studies conducted in Iran.^[26-28] In

other parts of the world, an increasing trend for variations of breast cancer incidence rate was observed as well.^[29-32]

In brief, the discrepancy observed between the incidence rates in this study and those in England can stem from the following:

1. A weak cancer registry system

There has been a weak cancer registry system in force in Iran, though it has been improved particularly over the past few years. Cancer registry in Iran began in 1968. However, the first national statistics for cancer was published in 1986, two years after the act of compulsory cancer registry was legislated by the Iranian Parliament. In contrast, in England an integrated cancer registry system has been in force since 1960 by employing regional centers. Presently, the registered data in the National Registry System are incomplete and are more limited to patients' individual characteristics and tumor diagnosis.^[33-35]

2. Cultural issues

A critical issue seen among a high majority of educated women in the Iranian society is their noncompliance with academic prescriptions. The denial of the possibility of being infected to disease by justifying that there is no history in family or next of kin is mostly cited. The most methods used to handle breast cancer in newly diagnosed women rely on fighting against and not surrendering the disease, and in so doing, religious inspirations and teachings play a vital role.^[36]

3. Diagnosis of cancer at later stages

In Iran, a main cause of death and other unwelcome repercussions of the disease stem from women's late visits to doctors. No study has yet examined this behavior.

4. The culture of breastfeeding in Iran

Breastfeeding reduces the possibility of getting breast cancer. The longer the time of breastfeeding, the lower the possibility of getting breast cancer. It is interesting that the effectiveness of breastfeeding in protecting against getting breast cancer is observed predominantly among women with two to three years of experience in breastfeeding. Moreover, Iran is an Islamic state, and Islamic teachings encourage breastfeeding, and that this may act as a protective factor against breast cancer.^[24,37]

One of the strengths of this study is the use of data from the Cancer Registry of Isfahan province as well as data from the MOHME over a time span of nearly ten years, paving the way for an assessment of the data. As is the case with any study involving second-hand data, this study has weaknesses such as lack of coverage of all cases of cancers occurred, lack of handling of missing data and conducting a qualitative control of the data, and a limitation on the number of registered variables in the cancer registry database.

Conclusions

It is concluded that the cancer registry data in Iran and Isfahan are more dependable and have more complete coverage from 2004 onwards. According to the findings of the study, the ASR in Isfahan for the time period 2001–2013 was estimated to be 34.7 per 100,000 populations. On average, the AAPC for Isfahan was calculated to be nine times as high as that for England. In other words, this index was 9.6% in Isfahan province and 1.1 in England.

Abbreviations

ANOVA: Analysis of Variance; WHO: World Health Organization; ASR: Age-Standardized Incidence Rate; NCR: National Cancer Registry; MOHME: Ministry of Health and Medical Education; ONS: Office for National Statistics; APC: Annual Percentage Change; AAPC: Average Annual Percentage Change; IUMS: Isfahan University of Medical Sciences; CI: Confidence Interval; CIR: Crude Incidence Rate; ASMR: Age-Standardized Mortality Rate

Declarations

Ethics approval and consent to participate

Ethics approval for this study was given by the Ethics Committee of Isfahan University of Medical Sciences on 14th January 2016 under the Reference Number 394940. The secondary data were given to the research team by the Cancer Registry Office (MUI-CRO) without any individual identification. The researchers guaranteed that the data provided by MUI-CRO will remain confidential, and will be used for research purposes only.

Availability of data and materials

The data that support the findings of this study are available from the corresponding author upon request. However, restrictions apply to the availability of data, which were used under license for the current study, so they are not publicly available.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

Received: 26 Sep 19 **Accepted:** 17 Jan 20

Published: 27 May 21

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