Incidence Trend of Breast Cancer and its Risk Factors in Women of Eastern Mediterranean Region Countries between 1998 and 2018: A Systematic Review and Meta-Analysis

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Abstract

Abstract Background This study was conducted to provide evidence on the current status of breast cancer (BC) and its incidence trend in EMR during 1998-2018. Also, this study aimed to investigate the association between the incidence of BC and HDI and some factors related to this index, including total fertility rate (TFR), and obesity, using a meta-analysis. Method Data on incidence of BC were collected from various sources, including PubMed, Embase, Web of Science, and WHO, from 1998 to 2018 using systematic review and meta-analysis. Pooled ASR (age standardized rate) was calculated based on study duration and quality of data using a subgroup analysis and random effect meta-analysis. Results A total of 76 studies (499 data points) were analyzed. Pooled ASR of BC for EMR was 39.8 per 100 000 person-year (95% confidence interval [CI], 36.01, 43.9) during 2011-2018. ASR of BC had an upward trend in EMR from 2005 to 2018. However, the increasing trend was found to be slightly different in various regions based on quality of data. Moreover, pooled ASR had a significant association with Human Development Index (HDI) [-6.6 (95% CI, -8.9, -4.3)] and obesity [0.1 (95% CI, 0.07, 0.1)]. Conclusion Pooled ASR of BC in EMR was lower than the global average. Also, the ASR value and its incremental trend have been higher in countries with low-quality data than in other countries of this region in recent years. Data quality or physiological factors, such as increase in obesity rates, could be the reasons for this incremental trend.

Introduction

Breast cancer (BC) is the most prevalent cancer among women worldwide and has also been the fifth leading cause of death among cancers in both sexes globally between 2005 and 2015 [1]. According to previous studies, BC will be one of the most important causes of death in women in reproductive age in developing countries in the future [2].The age standardized rate (ASR) of BC in women increased from 58 to 65.5 per 100 000 person-year worldwide during 2005-2015. A more incremental trend of ASR in BC has been observed in countries with low socioeconomic index than in countries with a high socioeconomic index. In 2015, the lowest ASR of BC belonged to Southeast Asian countries, with 35.8 (95% CI, 27.5-45.4), followed by South Asian countries, with 44.4 per 100 000 person-year (95% CI, 37.1-52.3) [1].

According to World Health Organization (WHO), Eastern Mediterranean Region (EMR) comprises of 21 countries, with the population of about 583 million. The countries in this region have diverse economic, social, health indexes, and life expectancy [3].

In some studies, socioeconomic factors have been mentioned as possible factors influencing BC incidence [1, 4]. Human Development Index (HDI), a composite index comprised of life expectancy at birth, salary, and education, is one of the indicators used to study the level of welfare in human societies [5]. Considering the lack of proper cancer registration systems and surveillance structure in most of developing countries, particularly in EMR countries [6], and given that EMR includes countries with diverse socioeconomic and health status [3], similar patterns may be found in this region and in other similar countries in the present and future. This study was conducted to provide evidence on the current status of BC and its incidence trend in the EMR during1998-2018. Moreover, this study investigated the association between the incidence of BC and HDI and some factors related to this index, including total fertility rate (TFR) and obesity, using a meta-analysis.

Materials & Methods

2.1. Search Strategy

Studies were selected using a systematic and comprehensive search of the literature, review of references, government publications, and recommendations by active researchers in the field. Electronic databases were searched using the following keywords: "breast neoplasms", "breast cancer", "breast tumor", "incidence", "frequency", "distribution", and "epidemiology" by adding the names of all the 21 EMR countries separately (Web table1). Relevant studies were identified

by searching the WHO Global Index Medicus Database, Medline, PubMed, Embase, and Web of Science. The *grey literature* was found on the websites of WHO, IARC, IRCT, Pecos, Google, and Google Scholar. The papers and reports published up to November 2018 were searched.

2.2. Inclusion and Exclusion Criteria

All national and international studies and reports on the incidence of BC in EMR countries (Iran, Afghanistan, Pakistan, Qatar, Kuwait, Egypt, Lebanon, Oman, Jordan, Yemen, Iraq, Bahrain, Libya, Morocco, Saudi Arabia, Sudan, Syria, Tunisia, Djibouti, United Arab Emirates (UAE), and Somalia; based on WHO classification) during 1998-2018 were included in this study.

Review studies and abstract papers of conferences and congresses that did not have full-texts and studies conducted on specific age groups or on a specific histology of BC were excluded. When studies with similar data were found, the one with higher quality was selected. Quality assessment of studies was done using JBI (The Joanna Brigge Institute) checklist [7] and risk assessment checklist [8]; each checklist has 10 items, with the scores ranging from 0 to 10. The average scores were calculated using the checklists, and studies with a score below 5 were excluded from the study, based on the average score of both checklists.

2.3. Extracted Data

Extracted data included title of the study, DOI (digital object identifier) of the paper, writer's name, year of the study, location of the study, name of the journal, year of publication, and writer's address. Specific information included study period, sampling method, sample size, number of BC cases, data collection source, and study results. Also, crude incidence rate and ASR of BC were standardized based on WHO population and standard error (SE), standard deviation (SD), or confidence interval (CI) of these indexes.

2.4. Data Manipulation

Crude incidence rate and sample size were used to calculate the number of BC cases when their number was not reported. However, when the number was reported but no information was provided on dispersion index (SD, SE, or CI), Keyfitz formula was used to estimate SE [9]. When neither the dispersion index (such as SE) nor the number of BC cases was reported, SE was obtained using MICE (Multiple Imputation via Chained Equations) [10]. SE was calculated using this method in approximately 13% of the cases.

In cases where a study was conducted during several years and the annual ASR was not reported, but the average of ASR was reported for that period, the mid-point year of the study was considered as a data point. Quality assessment of the studies and data extraction were done by 2 investigators (ZR & TF) independently. Disagreement between the investigators was resolved by discussion and review or by referring to the third author (ZF).

2.5. Final Data Used in the Analysis

In addition to the data extracted from the systematic review of the literature, other information, such as TFR, was extracted from HDI of United Nations Development Program during 1998-2016 (UNDP) [5] and from Index Mundi website, from which data on the prevalence of obesity in every EMR country were extracted [11].

2.6. Data Analysis

All ASR index analyses were run based on SQRT (square root) and according to Poisson distribution due to the positive skewness of the studied variables [12]. Considering the high values of I square index (68.4%, p value < 0.001) and Tau^2= 2.2(Tau^2 is the estimated standard deviation of underlying effects across studies), and according to the results of the

initial meta-regression analyses, the variables of time, location, and quality of cancer registry system were significant. Therefore, subgroup analysis was done to reduce heterogeneity based on 4 separate time periods (1998-2000; 2000-2005; 2006-2010; and 2011-2018) and also based on 3 categories of the quality of cancer registry system. As the major part of data were reported based on the data of the cancer registry system, the extracted data were categorized according to the quality of cancer registry system in each country. of data , Group 1 had high-quality data and included countries in which the coverage of population-based registry of cancer was over 50% (Qatar, Kuwait, Bahrain, and Oman); group 2 had medium-quality data and included countries in which the coverage of population-based registry of cancer was lower than 50% (Iran, Morocco, Saudi Arabia, Libya, Tunisia, Egypt, and Jordan); and group 3 had low-quality data based on pathology, treatment centers, or survey (Afghanistan, Pakistan, Iraq, Yemen, Djibouti, Somalia, Syria, Sudan, UAE, Lebanon).

In this study, a meta-analysis was done in 3 parts:

2.6.1. Determining the Current Status of Breast Cancer

The data on the ASR of BC during 2011-2018 were used to determine the current status of BC. The pooled ASR of BC was calculated separately for each country in EMR using random-effect meta-analysis method.

2.6.2. Studying the ASR Trend of Breast Cancer

To find the trend of BC, data were analyzed based on the data of the whole region from 1998 to 2018 and then based on the quality of data in the corresponding period. Data were analyzed using metan command in random-effects meta-analysis and fractional polynomial regression method for the subgroups based on quality of data.

2.6.3. Studying the Association between Related Factors influencing the ASR of Breast Cancer

The association between the ASR of BC and HDI, TFR, and obesity were investigated using unadjusted (univariate) and adjusted (multivariate) meta-regression method. In addition, meta-regression method was used to investigate the effect of time, location, and quality of cancer registry system on the heterogeneity of the extracted ASR of BC.

As about 60% of data points were related to Iran, sensitivity analysis was used to estimate the pooled ASR of BC in EMR. In the sensitivity analysis, the results were reported by including the studies related to Iran and then by excluding them. All the analyses were done using STATA 12.0 software (StataCorp, College Station, TX, USA). All p values were 2-sided, and significance level was set at less than 0.05.

Results

In the initial search, 3980 papers, international, and national reports were identified, among which 76 studies met the criteria to be included in the analysis [1, 6, 13-86]. The search processes are illustrated in flowchart 1, and the summarized characteristics of the included studies are presented in Appendix1 (Web table 2). The average agreement between the 2 researchers (ZR&TF) to select the studies, conduct quality assessment, and data extraction was good (Cohen's unweighted $\kappa = 0.87$). A total of 499 data points of BC incidence were extracted from 76 studies, among which 57% (285 data points) belonged to Iran. In this study, most of the data (82%) belonged to the national cancer registry system and 43% to the third period of the study (2006-2010). Also, 66% of the data belonged to those EMR countries that had medium-quality of data (group 2) (Table 1).

3.1. The Current Status of ASR of Breast Cancer in Countries in EMR from 2011 to 2018

Pooled ASR of BC in EMR was about 39.8 per 100 000 person-year (95% CI, 36, 43.9) during 2011-2018. However, after removing the data from Iran, the estimated number was 45.1 per 100 000 person-year (95% CI, 39.9, 50.6); this difference

was statistically significant (p value < 0.001) (Table 2).

According to the meta-analysis of the existing reports on the ASR of BC, Lebanon had the highest rate of BC incidence, with 81.8 (95% CI, 56.1, 112.4), and Syria the lowest rate, with 23.6 (95% CI, 15.8, 32.9) per 100 000 person-year, among the 21 countries of the EMR from 2011 to 2018 (Table 2). Among EMR countries, Lebanon had the highest ASR of BC during the fourth period of the study (Appendix1, Fig.1).

3.2. Trend Changes of Breast Cancer Incidence in EMR from 1998 to 2018

The pooled ASR of BC in EMR had a constant trend, followed by an increasing trend [23.7 (95% CI, 17.9, 30.2) to 23.7 (95% CI, 20.7, 26.9)] from 1998 to 2005. However, later on, it showed an upward trend to 39.8 (95% CI, 36, 43.9) per 100 000 person-year in the fourth period of the study (Table 3, Appendix1, Graph1).

3.3. Trend Changes of Breast Cancer Incidence in EMR according to Subgroups of the Quality of the Data Registration from 1998 to 2018

3.3.1. Countries with High Quality Data (Group 1)

Pooled ASR of BC in the group with high data registration quality had an upward trend in the first 2 time periods [19.6 (95% CI, 13.1, 27.4) to 40.1 (95% CI, 31.5, 49.8)]. However, later on, it showed a decline to 37.7 (95% CI, 28.3, 48.4) per 100 000 person-year in the fourth period of the study (Table 3, Appendix 1, Graph 2).

3.3.2. Countries with Medium Quality of Data (Group 2)

Unlike the group with high data quality, a downward trend, followed by an increasing trend was observed in the group with medium data quality; the corresponding figures were 21.3 (95% CI, 17.1, 26) to 17.1 (95% CI, 14.6, 19.8) and to 33.2 (95% CI, 29.9, 36.6) per 100 000 person-year, respectively (Table 3, appendix 1, Graph 2). A similar trend was observed after exclusion of Iran, after which the pooled ASR showed an increase in 4 periods [from 35.4 (95% CI, 25.5, 46.9) in the first period to 40.6 (95% CI, 40.6 (34.4, 47.4) in the last period] (Table 3, Appendix1, Graph2).

3.2.2.3. Countries with Low Quality of Data (Group 3)

The trend of BC incidence in countries with low quality of data registration in EMR experienced a significant increase in the second period [29.9 (95% CI, 14.4, 50.9) to 41.8 (95% CI, 32.2, 52.7)]. However, in the third period, the incidence of BC decreased considerably and increased again to 48.3 (95% CI, 41.01, 56.3) per 100 000 person-year in the fourth period of the study (Table 3, Appendix1, Graph 2).

3.3. The Association between the ASR of Breast Cancer and Developmental risk Factors in EMR

The results of the initial analysis showed that location of the study, year of study, and quality of data had significant effects on the heterogeneity of data. The results also revealed that tau 2 [from 2.2 to 1.01] was decreased significantly after insertion of these variables in the meta-regression model (Table 4).

In the univariate and multivariate tests, HDI [univariate: -1.2 (95% CI, -3.2, 0.7); multivariate:

-6.6 (95% CI, -8.9, -4.3)] and obesity [univariate: 0.05 (95% CI, 0.03, 0.07); multivariate: 0.1 (95% CI, 0.07, 0.1)] had a significant association with BC incidence (Table 4).

Discussion

4.1. The current status of the ASR of Breast cancer

The pooled ASR of BC occurrence was estimated to be about 40 per 100 000 person-year in EMR during 2011-2018. However, after excluding Iran, the results of sensitivity analysis showed that ASR of BC had a significant increase. The global average of BC in women was 65.5 in 2015 according to Global Burden of Disease [41] and it was 41.9 in EMR in 2012 according to GLOBOCAN [5]. The results of the present study were more consistent with GLOBOCAN 2012.

In Lebanon, the ASR of BC was almost 4 times more than that of Syria during 2011-2018. This was confirmed by another study conducted in 2004, in which the ASR of BC was higher than other Arab countries and Iran [85].

4.2 Trend of Breast Cancer Incidence

There was an upward trend for the ASR of BC in EMR from 1998 to 2018. However, based on the quality of data during 1998-2018, the pattern of BC incidence has been somewhat different in EMR countries. The studies performed on Asian and EMR countries in recent years have shown an increasing trend in the occurrence of BC in these countries [42, 53, 79, 81-83, 87]. Also, WHO has predicted that the increasing trend of BC will continue in EMR countries in the next decade [78].

The highest value of BC ASR in the last period and the highest increase in the incidence of BC for the last 2 periods of the study belonged to countries with low-quality data. In fact, only 4 countries (Kuwait, Oman, Jordan, and Tunisia) have had a population-based cancer registry prior to 1998 (11). Cancer registration systems were changed from pathological data collection to a population-based registration system during 1998-2005 in Bahrain, Qatar, Morocco, Egypt, Iran, and Libya. Therefore, cancer registry has improved overtime among countries in the region, which can be explained by the fluctuation in the trend of ASR of BC, with a noticeable increase in the last period [40]. Moreover, the diversity in the increasing patterns of BC in various EMR countries may be due to the difference in the time of upgrading the cancer registry systems in these countries.

4.3. Effects of Developmental Factors on Breast Cancer Incidence

HDI showed a negative association with the incidence of BC in the adjusted and unadjusted models, which was significant in the adjusted model; the negative association of HDI with BC incidence contradicted the findings of other studies [1, 42, 79, 88]. HDI cannot cause an increase in the incidence of BC directly; however, increased longevity, decreased fertility, increased obesity, or changes in lifestyle can increase the incidence of BC [79, 89].The highest HDI in EMR belonged to Arab countries, such as Saudi Arabia, Oman, Kuwait, Qatar, UAE, and Bahrain. The ASR of BC in these countries was lower than that of some other countries in EMR and European countries. The lower ASR of BC reported by Arab countries, compared to the Western countries, may be due to women's higher fertility and breast-feeding. Therefore, the reverse association between HDI and ASR of BC in this study, compared to other studies, may be due to the reproductive pattern and lifestyle variety in highest HDI countries in EMR than the Western countries. [90].Lebanon, Pakistan, and Iraq, which had the highest ASR of BC during the recent years belonged to the middle, low, and middle HDI countries, respectively [5]. Several studies suggested that the higher incidence of BC in Pakistan and Iraq may be less affected by hormonal- and parity-related factors and more affected by genetic and environmental factors [91-92]. The ASR of BC showed a positive association with obesity, as this association was confirmed by other studies [1, 42, 79, 89]. The association between ASR of BC and TFR was positive in the unadjusted and negative in the adjusted models, but it was not significant, indicating that the positive association in the unadjusted model may be due to the confounder effect of other variables, such as quality of data, location, time of the study, HDI, and obesity. Other studies have reported a significant negative association between TFR and ASR of BC [93-94]. The difference between the findings of this study and those of others may be due to the decline in TFR in all EMR countries [11].

Limitations of the Study

Considering that no comprehensive study has been conducted on the incidence rate of BC and its trend in EMR, the results of this study can help policymakers of these countries to develop and implement programs to reduce BC incidence and improve the data registry system. However, this study had some limitations that should be taken into consideration when interpreting the results: the small number of studies; lack of availability of adequate data in some counties, especially in recent years; and the mere use of English papers. Nevertheless, in this study, it was not possible to investigate some other risk factors of BC, such as breastfeeding, diet, hormone therapy, and physical activity, which could justify the incremental trend of BC incidence. Thus, when interpreting the results of studies that have used ecological methods to investigate the association between BC incidence and risk factors, their limitations should also be taken into account.

Conclusion

Based on the results of the study, pooled ASR of BC in EMR was lower than its global average. Also, the highest and lowest value of ASR belonged to countries with low-quality data during 2011-2018. Furthermore, there was an increasing trend in the ASR of BC in EMR in recent years, especially in the low-quality data group. The possible reasons for the incremental trend of BC incidence may be data availability and quality, or physiological factors, such as increase in the rate of obesity. Although the quality of data in cancer registry systems has improved, the published data on the incidence of BC in EMR countries have been limited in recent years. Some EMR countries still lack a national registry system or a population-based system. Thus, after development and improvements in the registry systems of EMR countries, an upward trend of BC is highly expected in this region in the future.

Declarations

Ethics approval and consent to participate

The research was approved by ethical committee of Kerman University of Medical Sciences. The Ethic approval Cod is IR.KMU.REC.1396.1617.

Consent for publication

Not applicable.

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare no conflict of interest.

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Authorship contributions

Concept and design of the study: FZ and RZ& HMV; search strategy: RES&RZ; Literature search RZ and FT; Screening of literature and data extraction: RZ and FT; analyzed the data: AAH, MRB& RZ; Manuscript writing: RZ (draft) and FZ & HMV (revision). All authors approved the final version of the manuscript.

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List Of Abbreviations

- **EMR:** Eastern Mediterranean Region
- **WHO: world health organization**
- **ASR:** Age Standardized Rate
- **Human Development Index (HDI):** A metric to assess the social and economic development levels of countries. Four principal areas of examination are used to rank countries: mean years of schooling, expected years of schooling, life expectancy at birth and gross national income per capita.
- **Total fertility rate (TFR):** This entry gives a figure for the average number of children that would be born per woman if all women lived to the end of their childbearing years and bore children according to a given fertility rate at each age.
- **Obesity - adult prevalence rate:** Obesity is defined as an adult having a Body Mass Index (BMI) greater to or equal to 30.0.

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Tables

Table1: Characteristics of 499 data points on Adjusted Incidence Rate of breast cancer in Eastern Mediterranean countries, published between 1998 and 2018

Source of Data point	Number of Data point (%)
International report(GLOBOCAN , IARC, Global burden)	68 (13.6)
Cancer registry report(National)	409 (81.9)
Survey , pathology or hospital report	22 (4.4)
Period of study	
1998-2000	42 (8.4)
2001-2005	140 (28.1)
2006-2010	214 (42.9)
2011-2018	103 (20.6)
Quality of Data	
Group1: High Quality (population base coverage over 50%)	59 (11.8)
Group2: Medium Quality (population base coverage lower 10%)	328 (65.7)
Group3: Low Quality of National data (Survey , pathology or hospital report)	112 (22.4)

Table2: The ASR of Breast Cancer in Eastern Mediterranean Countries in 2011-2018

Country	Rank for ASR of female breast cancer	HDI index	Quality of Data[a]	N Data point	ASR of breast cancer (95%CI)	Number of breast cancer cases (% of total cases)	Total of sample size (%of total sample size)
Lebanon	1	0.763	3	3	81.8 (56.1,112.4)	5908 (1.5)	7717060 (0.6)
Pakistan	2	0.55	3	5	68.7 (59.3,78.9)	173768 (43.9)	281000438 (21.9)
Iraq	3	0.649	3	3	62.2 (47.4,78.9)	22766 (5.7)	51396093 (4.0)
Bahrain	4	0.824	1	3	55.1 (27.5,92.2)	695 (0.2)	1537277 (0.1)
Jordan	5	0.742	2	5	54.5 (39.2,72.2)	5461 (1.4)	16901905 (1.3)
Kuwait	6	0.8	1	3	54.05 (29.9,85.2)	1396 (0.4)	4010811 (0.3)
Qatar	7	0.856	1	3	54.02 (25.7,92.8)	9813 (2.5)	26686518 (2.1)
UAE	8	0.84	3	3	51.5 (31.4,76.5)	2616 (0.7)	7357716 (0.6)
Morocco	9	0.647	2	3	48.1 (36.9,60.7)	25575 (6.5)	50864911 (3.9)
Djibouti	10	0.473	3	4	45.5 (19.8,81.7)	598 (0.1)	1621024 (0.1)
Egypt	11	0.691	2	3	44.7 (36.1,54.4)	50002 (12.6)	93279217 (7.3)
Tunisia	12	0.725	2	3	40.6 (28.3,55.1)	7772 (1.9)	16625705 (1.3)
Afghanistan	13	0.479	3	3	38.6 (26.3,53.2)	6746 (1.7)	48588869 (3.8)
Somalia	14	___	3	3	38.5 (24.5,55.6)	3689 (0.9)	18502099 (1.4)
Yemen	15	0.482	3	3	37.1 (26.03,50.2)	448 (0.1)	1383852 (0.1)
Sudan	16	0.49	3	3	36.8 (27.03,48.1)	14788 (3.7)	56335878 (4.4)
Iran	17	0.774	2	35	31.7 (27.6, 36)	45641 (11.5)	484392544 (37.7)
Libya	18	0.716	2	4	30.8 (19.7,44.4)	2714 (0.7)	12806644 (0.9)
Oman	19	0.796	1	6	25.9 (15.8,38.5)	1191 (0.3)	30466497 (2.4)
Saudi Arabia	20	0.847	2	3	25.7 (17.8,35.05)	6915 (1.7)	39440443 (3.1)
Syrian Arab republic	21	0.536	3	3	23.6 (15.8,32.9)	7196 (1.8)	32237054 (2.5)
Total of EMR**	.....	....	....	104	39.8 (36.01, 43.9)	382367 (100)	1283152555 (100)
Total of EMR** without Iran	.....	....	....	68	45.1 (39.9, 50.6)	350057 (90.6)	798760011 (62.2)

a:Group1(High quality data), Group2(Medium quality of data), Group3(Low quality of data)

*UAE: United Arab Emirate, ** Eastern Mediterranean Region

Table3: Comparison the ASR of Breast Cancer by Quality of Data Registration and period of the study in Eastern Mediterranean Region

Year	1998-2000			2001-2005			2006-2010			2011-2018		
Data	N Data point	ASR of breast cancer	I^2 Index	N Data point	ASR of breast cancer	I^2 Index	N Data point	ASR of breast cancer	I^2 Index	N Data point	ASR of breast cancer	I^2 Index
Total EMR	42	23.7 (17.9,30.2)	82.9	140	23.7 (20.7,26.9)	68.7	214	25.4 (23.5,27.4)	38.8	103	39.8 (36, 43.9)	56.6
Group1: High Quality of Data	8	19.6 (13.1,27.4)	24.3	19	40.1 (31.5,49.8)	0	17	35.1 (28.3,42.6)	0	15	37.7 (28.3,48.4)	0
Group2: Medium Quality of Data	23	21.3 (17.1, 26)	32.7	90	17.1 (14.6, 19.8)	54	170	22.7 (19.9, 24.9)	35.9	45	33.2 (29.9, 36.6)	0.8
Group2:Medium Quality of Data without Iran	6	35.4 (25.5, 46.9)	0	21	31.03 (26.4, 35.9)	0	6	34.8 (27.4, 43.1)	14.6	10	40.6 (34.4, 47.4)	0
Group2:Iran	17	18.4 (14.3, 23.01)	26	69	13.7 (11.3, 16.4)	50.7	164	22.1 (20, 24.2)	33	35	29.9 (26.2, 33.9)	0
Group3: Low Quality of Data	11	29.9 (14.4, 50.9)	92.8	31	41.8 (32.2, 52.7)	80.5	27	34.9 (30.3, 39.9)	34.4	43	48.3 (41.01, 56.03)	73.3

Table4: The Association between ASR[a] of Breast Cancer and Risk Factors

Risk Factors	Unadjusted B(95%CI)	Pvalue	Tau2	Adjusted[b] B(95% CI)	P value	Tau2
HDI[c]	-1.2 (-3.2,0.7)	0.2	1.802	-6.6 (-8.9, -4.3)	<0.001	1.15
TFR[d]	0.2 (0.1,0.3)	0.001	1.778	-0.05 (-0.2,0.1)	0.538	_____
Obesity[e]	0.05 (0.03,0.07)	<0.001	1.735	0.1 (0.07,0.1)	<0.001	_____
Country of study	0.13 (0.1,0.15)	<0.001	1.432	_____	_____	_____
Year of study	0.16 (0.1,0.2)	<0.001	1.411	_____	_____	_____
Quality of Data	0.6 (0.3,0.9)	<0.001	1.68	_____	_____	_____

a:Ajusted Standard Rate of breast cancer, b: adjusted on Country of study , Year of study , Quality of Data , HDI, TFR and obesity variables, c: Human Index Development, d:Total Fertility Rate, e:Obesity= if Body Mass Index≥30,

Figures

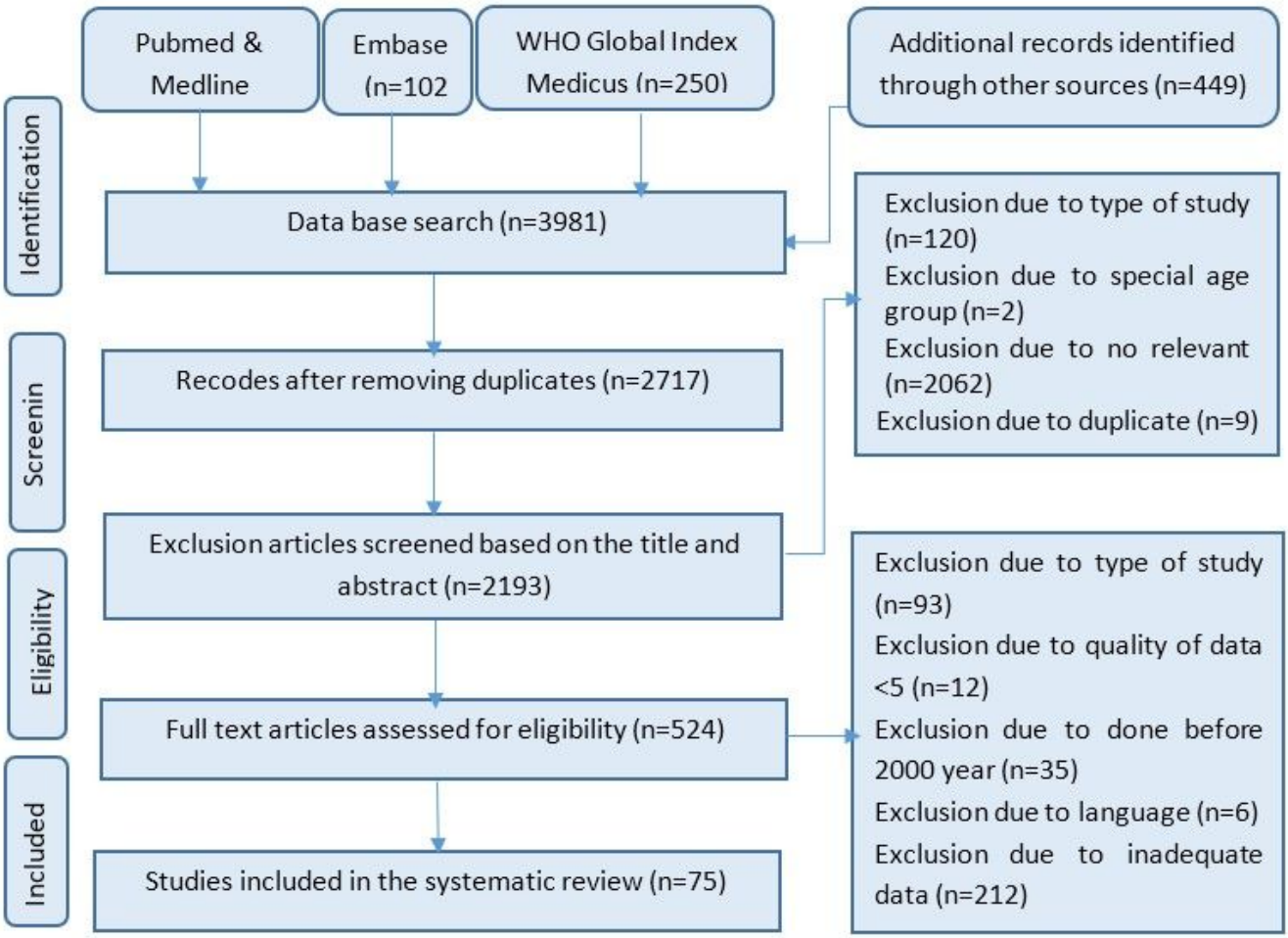

Figure 1

Flow chart1:The selection process of papers relevent to the systematic review

Supplementary Files

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