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

Razieh Zahedi
Kerman University of Medical Sciences
Hossein Molavi Vardanjani
Shiraz University of Medical Sciences
Mohammad Reza Baneshi
Kerman University of Medical Sciences
Ali Akbar Haghdoost
Kerman University of Medical Sciences
Reza Malekpour Afshar
Kerman University of Medical Sciences
Roghayeh Ershad Sarabi
Kerman University of Medical Sciences
Ftemeh Tavakoli
Kerman University of Medical Sciences
Farzaneh Zolala (zolalafarzaneh@gmail.com)
Kerman University of Medical Sciences https://orcid.org/0000-0002-1848-183X

Research article

Keywords: Breast cancer, meta-analysis, Eastern Mediterranean region, Incidence

Posted Date: August 31st, 2019

DOI: https://doi.org/10.21203/rs.2.13816/v1

Version of Record: A version of this preprint was published at BMC Women's Health on March 17th, 2020. See the published version at https://doi.org/10.1186/s12905-020-00903-z.

Abstract

Background This study was conducted to determine the current Age Standardized Rate (ASR) of breast cancer and its trend from 1998 to 2018, and relational factors of countries' development as risk factors in breast cancer occurrence in Eastern Mediterranean Region (EMR). Methods Using systematic review and meta-analysis method, data on incidence of breast cancer was collected from various sources including Pubmed, Embase, Web of Science, WHO from 1998 to 2018. Pooled ASR was calculated using subgroup analysis according to period of study and quality of data, by applying random effect meta-analysis method. Results 499 data points (76 studies) were analyzed. Pooled ASR of breast cancer for EMR during 2011-2018 was 39.8 per 100,000 person-years (95% confidence interval [CI], 36.01, 43.9). ASR of Breast cancer had an upward trend in EMR from 2005 to 2018; however, the increasing pattern had been somewhat different in various regions based on data quality groups 1998-2018. Pooled ASR had a significant association with Human Development Index [-6.6 (95%CI, -8.9, -4.3)] and obesity [0.1 (95% CI, 0.07, 0.1)]. Conclusion Pooled ASR of breast cancer in EMR is lower than the global average. The ASR value and incremental trend in low-quality data group is higher than others in recent years. The possible reasons for the incremental trend are data quality or physiological ones such as increasing obesity.

Introduction

Breast Cancer is the most prevalent cancer among women worldwide and was the fifth leading cause of death among cancers in both sexes globally between 2005 and 2015[1]. According to the studies BC will be one of the most important cause of death for female in reproductive age in the future in developing countries [2].The Age Standardized Rate (ASR) of breast cancer in women had an increase from 58 to 65.5 per 100,000 person-years worldwide between2005 and 2015. The incremental trend of this cancer regarding ASR in countries with low socioeconomic index has been more than the countries with a high socioeconomic index. In 2015, the lowest rates regarding ASR of breast cancer belonged to Southeast Asian countries with 35.8 (95% CI, 27.5–45.4), and after that, South Asian countries with 44.4 per 100,000 person-years (95% CI, 37.1–52.3)[1].

Eastern Mediterranean region (EMR) is one of the six regions according to World Health Organization (WHO), in which 21 countries exists with a population about 583 million people. This region is comprised of countries with diverse economic, social, health indexes and life expectancy [3].

In some studies, socioeconomic factors have been mentioned as possible factors influencing breast cancer incidence [1, 4]. Human Development Index (HDI) is one of the indicators used to study the level of welfare in human societies, which is a composite index comprised of life expectancy at birth, salary, and education[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 various levels of socioeconomic and health status[3], thus there is the probability of a similar pattern in the present and the future in this region and other analogous countries globally. However, this study was conducted to provide evidence regarding the current state of breast cancer and the incidence trend in this region between 1998 and 2018. On the other hand, this study investigated the association between the incidence of breast cancer and HDI, as well as some factors related to this index including Total Fertility Rate (TFR) and Obesity using the meta-analysis method.

Materials & Methods

2.1. Search Strategy

Studies were identified through a systematic and comprehensive search on 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 (webtable1). Relevant studies were identified by searching on: 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. Search was done for papers and reports up to the November, 2018.

2.2. Inclusion and Exclusion Criteria

All the national and international studies and reports that had published the incidence data on breast cancer in EMR (including countries such as 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 World Health Organization’s classification) between 1998 and to 2018, were included in the study.

Review studies and abstract papers of conferences and congresses that did not have full text and studies conducted on specific age groups or on a specific histology of breast cancer were excluded from the study. In cases where there were similar studies regarding data, the higher quality studies were selected. Quality assessment of studies was done using two checklists: JBI (The Joanna Brigge Institute) checklist which is a critical appraisal tool [7] and risk assessment checklist,[8] which both has 10 items and the range score is between 0 to 10. The average scores were calculated from the two checklists and studies that had scored below 5 were excluded from the study based on the average score of both checklists.

2.3. Extracted Data

Extracted data included general information: Title of study, DOI (Digital Object Identifier) of paper, writer’s name, year of study, the location of study, the name of the journal, year of publication, and writer’s address. Specific information included: the period of study, sampling method, sample size, number of breast cancer cases, and data collection source; studied results: crude incidence rate and ASR of breast cancer 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 breast cancers where the number of breast cancer cases was not reported. In the cases which dispersion index (SD, SE, or CI) was not available and we had the number of breast cancer cases Keyfitz formula used to estimate the SE [9]. In cases where neither the dispersion index (such as SE) and nor the number of breast cancer cases reported, SE was obtained using MICE (Multiple Imputation via Chained Equations)[10]. SE was calculated by this method in approximately 13% of the cases.

In cases where a study was conducted during a few 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 included as a data point. All processes of search, quality assessment of studies, and extraction of data were done by two investigators (ZR & TF) independently. Disagreement between investigators was resolved through discussion and review, or by referring to a third author (ZF).

2.5. Final Data Used in the Analysis

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

2.6. Data Analysis

All analysis were run based on SQRT (Square Root) regarding the ASR index, due to the positive skewness of studied variables according to Poisson distribution [12]. Considering high values of I square index (68.4%, P value<0.001) and Tau2 = 2.2; and based on the initial meta-regression analyses results the variables such as: time, location, quality of cancer registry system were significant. Therefore, in order to reduce the heterogeneity, subgroup analysis was done: first, based on four separate time periods including: 1998–2000, 2000–2005, 2006–2010, and 2011–2018; and second, based on three categories of the quality of cancer registry system. Considering that 96% of data was reported based on cancer registry data therefore the extracted data categorized according to the quality of cancer registry system in each country. The data quality categories were formed based on Group1 (High quality of data) in which population-based registry of cancer was over50% including Qatar, Kuwait, Bahrain and Oman, Group2 (Medium quality of data) that population-based registry of cancer was lower than 10%: Iran, Morocco, Saudi Arabia, Libya, Tunisia, Egypt, Jordan, Group3(Low quality of data): Afghanistan, Pakistan, Iraq, Yemen, Djibouti, Somalia, Syria, Sudan, UAE, Lebanon based on pathology, treatment centers or survey.

Based on the study's objective, a meta-analysis was done in three parts:

2.6.1. Determining the Current Status of Breast Cancer

The data on the ASR of breast cancer between 2011 and 2018 was used to determine the current status of breast cancer. The pooled ASR of breast cancer was calculated separately for each country of EMR by random-effect meta-analysis method.

2.6.2. Studying the ASR Trend of Breast Cancer

In order to find out the trend of breast cancer, data was analyzed based on the whole region from 1998 to 2018 and then based on the quality of data groups 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 the quality of data.

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

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

Considering that about 60% of data points were related to Iran, therefore, the sensitivity analysis method was used in order to estimate the pooled ASR of breast cancer in EMR. In the sensitivity analysis the first results reported by including the studies related to Iran, and once by excluding those studies. All the analyses were done using STATA 12.0 software (StataCorp, College Station, TX, USA). All P values were two-sided with a significance level of less than 0.05.

Results

In the initial search, 3,980 papers, international and national reports were identified, among which 76 studies possessed the criteria to be included in the analysis.[1, 6, 13–86] The search processes are illustrated in flowchart 1 and summarized characteristics of included studies can be found in appendix1 (webtable2). The average agreement between investigators

(ZR&TF) was good (Cohen's unweighted κ = 0·87) for deciding which studies to include, quality assessment of studies, and extraction of data. 499 data points of breast cancer incidence were extracted from these 76 studies, among them 57% (285 data points) were related to Iran. Most of the data (82%) was related to the national cancer registration system and 43% was related to the third period of the study, during 2006–2010. In terms of quality of analyzed data, 66% was related to the countries of the second group (Table 1).

3.1. The Current Status of ASR Breast Cancer in EMR and Countries within that Region, from 2011 to 2018

Pooled ASR of breast cancer in EMR was about 39.8 per 100,000 person-years (95% CI,36, 43.9) between 2011 and 2018, and after removing the data from Iran, the estimated number was 45.1 per 100,000 person-years (95% CI,39.9, 50.6); this difference is statistically significant (P value<0.001) (Table 2).

According to the meta-analysis of the existing reports on the ASR of breast cancer, Lebanon had the highest rate of breast cancer incidence with 81.8 (95% CI, 56.1, 112.4) and Syrian had the lowest rate with 23.6 (95% CI, 15.8, 32.9) per 100,000 person-years, among the 21 countries of this region from 2011 to 2018 (Table 2). Lebanon was in the highest group between EMR countries regarding ASR of breast cancer during the fourth period of the study (in appendix1, Fig.1.).

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

The pooled ASR of breast cancer in EMR from 1998 to 2005 had a constant trend followed by an increasing trend was observed [23.7 (95% CI, 17.9, 30.2) to 23.7 (95% CI, 20.7, 26.9)], whereas it showed an upward trend later on to 39.8 (95% CI, 36, 43.9) per 100,000 person-years in the fourth period. (Table 3, in appendix1, Graph1).

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

3.3.1. Countries of High Quality Data (Group 1)

Pooled ASR of breast cancer in highest quality of data registration had an upward trend in the first two time periods [19.6 (95% CI, 13.1, 27.4) to 40.1 (95% CI, 31.5, 49.8)], whereas it showed a decline later on to 37.7 (95% CI, 28.3, 48.4) per 100,000 person-years in the fourth period of the study (Table 3& in appendix1, Graph2).

3.3.2. Countries of Medium Quality Data (Group 2)

On the contrary to high quality data group, a downward trend followed by an increasing trend was observed in this group; 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-years respectively (Table 3& in appendix1, Graph2). The similar trend was seen through exclusion of Iran, merely the pooled ASR had been increased 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].

3.2.2.3. Countries of Low Quality Data (Group 3)

The trend of breast cancer incidence in the countries of this group that had the lowest quality of data registration in EMR was unstable, had a significant increase in the second period [29.9 (95% CI, 14.4,50.9) to 41.8 (95% CI, 32.2,52.7)], then in the third period, the incidence of cancer decreased considerable and increased again to 48.3 (95% CI, 41.01,56.3) per 100,000 person-years in the fourth period of the study (Table 3& in appendix1, Graph2).

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

The initial analysis showed that variables such as the location of study, year of study, and quality of data had significant effects on the heterogeneity of data, and tau2 index [from 2.2 to 1.01] was decreased significantly after insertion of these variables in the meta-regression model (Table4).

In the univariate and multivariate methods, 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 breast cancer incidence (Table4).

Discussion

The pooled ASR of breast cancer occurrence was estimated to be about 40 per 100,000 person-years in this region during 2011 −2018. After excluding Iran from the region, sensitivity analysis showed that this quantity had a somewhat increase, and this change was significant. The ASR of breast cancer in Lebanon is almost four times than that of Syria which these countries had the highest and lowest value regarding breast cancer incidence in this region respectively during 2011 - 2018. There is an upward trend for ASR of breast cancer in EMR from 1998 to 2018; however, this pattern of breast cancer incidence has been somewhat different in various regions based on the quality of data groups in EMR for the above-mentioned years. The results of study show the significant association between ASR of breast cancer, HDI and obesity in adjusted models.

The studies performed on Asian and EMR countries in recent years, showed an increasing trend regarding the occurrence of breast cancer in most countries [42, 53, 79, 81–83, 87]. WHO predicted that this increasing trend in EMR countries will continue in the next decade[78].

This study showed average of breast cancer incidence in EMR between 2011 and 2018 has been lower than the global average of breast cancer in women in 2015[42], but it was higher than GLOBOCAN in 2012 [88]. According to this result, the global rate of breast cancer in EMR has increased over the last decade generally.

Lebanon has the highest incidence of breast cancer in EMR between 2011 and 2018. The high incidence of breast cancer in Lebanon was confirmed by another study conducted in 2004, in which the ASR of breast cancer was higher than other Arab countries and Iran[85].

The highest value regarding ASR of breast cancer in the last period, as well as the highest increase in the incidence of breast cancer for the last two period of the study, is related to the low-quality data countries. The fact is that only in 4 countries (Kuwait, Oman, Jordan and Tunisia) there had been population-based cancer registry before 1998(11). Furthermore cancer registration system in the countries such as Bahrain, Qatar, Morocco, Egypt, Iran, and Libya had been changed from pathological data collection to a population-based registration system during 1998 - 2005. Considering the stable statistic in cancer incidence in group 1 with high-quality data since 2001 and reverse pattern in the low-quality data group, therefore changes in the quality of cancer registration systems may be justified the inconstancy of breast cancer for the low quality data group [41]. Besides the diversity in the increasing patterns of breast cancer in various Eastern

Mediterranean regions is probably due to the difference at the beginning of upgrading in cancer registration system of countries.

HDI showed a negative association with incidence of breast cancer in the adjusted and unadjusted model, that it has been significant in adjusted model; the negative association of HDI with breast cancer incidence is discordance to other studies [1, 42, 79, 89]. Lebanon, Pakistan and Iraq which had the highest ASR of breast cancer during the recent years belong to the middle, low and middle HDI countries respectively[5]. HDI could not lead to increased breast cancer directly, but the factors that are related to socioeconomically developed countries such as increased longevity, decreased fertility, increased obesity or changes in lifestyle, which increased the incidence rate of breast cancer [79, 90]. Several studies suggested the higher incidence of breast cancer in countries such as Pakistan and Iraq may be less affected by hormonal and parity related factors, but may be due to genetic and environmental factors [91–92]. Besides that these countries had low quality of data in this study, and to consider breast cancer incidence predicted in some cases[6], therefore the estimated data may be inexact. The ASR of breast cancer show a positive association with obesity as this association is confirmed by other studies [1, 42, 79, 90]. The association between ASR of breast cancer and TFR was positive in unadjusted and negative in the adjusted model but it was not significant, which means the positive association in the unadjusted model may be due to the confounder effect of other variables such as quality of data, location and time of the study, HDI and obesity. The other studies have reported a negative and significant association between TFR and ASR of breast cancer[93–94]; this discordance may be due to the fact that there has been a decline in TFR in all of the EMR countries[11].

Limitations of the Study

Considering that there has not been a comprehensive study in terms of the incidence rate of breast cancer and its trend in EMR, thus the results of this study can help in health-policy making of the region. Although, performing the current study had certain limitations that should be taken into consideration at the time of interpreting the results such as: The low number of studies and lack of availability of adequate data in some counties, especially in recent few years and the mere use of English papers. On the other hand, we could not investigate some other risk factors of breast cancer such as breastfeeding, diet, hormone therapy, physical activity that may justify incremental trend of breast cancer incidence. To consider the ecological method used to study the association between breast cancer incidence and risk factors, thus limitations of such studies should be taken into account for interpreting the results.

Conclusion

Based on the results of study, pooled ASRs of breast cancer in EMR is lower than the global average; the highest and lowest value of ASR is belonged to the countries of low-quality data, during 2011 - 2018. Furthermore, there is an increasing trend in the ASR of this cancer in EMR in recent years, especially in the low-quality data group. The possible reasons for the incremental trend of breast cancer incidence can be data availability and quality or physiological ones such as increasing obesity. Interms of data there has been an improvement in the cancer registry, but the published data on the incidence of breast cancer in EMR countries has been limited in recent years. Therefore, considering that a number of countries still do not have a national registry system or population-based system, it is expected that following improvements in registry systems, the upward trend will continue in EMR in the coming years.

Declarations

Availability of data and materials

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

Acknowledgments

This study is a part of a PhD scholarship provided by Modeling in Health Research Center, Kerman University of Medical sciences, Iran, which funded this project is gratefully acknowledged.

Funding

The funder of this study in the design and collection of data was, Modeling in Health Research Center in Kerman University of Medical sciences, Iran, NO 96000531.

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.

Competing interests

The authors declare no conflict of interest.

Ethics approval

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.

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.

References

[1] Fitzmaurice C, Allen C, Barber RM, et al. Global, regional, and national cancer incidence, mortality, years of life lost, years lived with disability, and disability-adjusted life-years for 32 cancer groups, 1990 to 2015: a systematic analysis for the global burden of disease study. JAMA oncol.3(4),524-48(2017).

[2] Forouzanfar MH, Foreman KJ, Delossantos AM, et al. Breast and cervical cancer in 187 countries between 1980 and 2010: a systematic analysis. The lancet.378(9801),1461-84(2011).

[3] Baschieri A. Health inequities in the Eastern Mediterranean Region Selected country case studies. (2014).

[4] Ghoncheh M, Soltani S, Salehiniya H. Disparities in incidence and mortality of breast cancer. Iran J Public Health.45(2),270-1(2016).

[5] Jahan S. Human development report 2016: human development for everyone: United Nations Publications; 2016.

[6] Organization WH. GLOBOCAN 2012: Estimated cancer incidence, mortality and prevalence worldwide in 2012. Breast cancer fact sheet[Citated 2018Aug 1] Available at http://globocan iarc fr/Pages/fact_sheets_cancer aspx. (2015).

[7] Institute TJB. The Joanna Briggs Institute Reviewers' Manual 2014 The Systematic Review of Prevalence and Incidence Data. The Joanna Briggs Institute Reviewers'; 2014.

[8] Hoy D, Brooks P, Woolf A, et al. Assessing risk of bias in prevalence studies: modification of an existing tool and evidence of interrater agreement. J Clin Epidemiol.65(9),934-9(2012).

[9] Keyfitz N. Sampling variance of standardized mortality rates. Am J Hum Biol.38(3),309-17(1966).

[10] Furukawa TA, Barbui C, Cipriani A, et al. Imputing missing standard deviations in meta-analyses can provide accurate results. J Clin Epidemiol.59(1),7-10(2006).

[11] Barzin M, Valizadeh M, Serahati S, et al. Overweight and obesity: Findings from 20 years of the Tehran Lipid and Glucose Study. International journal of endocrinology and metabolism.16(4 Suppl)(2018).

[12] von Bortkiewicz L. Das gesetz der kleinen zahlen: BG Teubner; 1898.

[13] Iranian Annual of National Cancer Registration Report 2003-2004. Tehran: Ministry of Health Center for Disease Control& Prevention Non-Communicable Deputy Cancer Office; 2005.

[14] Iranian Annual of National Cancer Registration Report 2010-2011. Ministry of Health Center for Disease Control& Prevention Non-Communicable Deputy Cancer Office; 2013.

[15] Al-Bahrani B, Al-Busaidi A, Al-Lawati NA, et al. Cancer Incidence in Oman 2013. Ministry of Health Soltanate of Oman.

[16] Al-Madouj AN, Eldali A, Al-Zahrani AS. Ten-Year Cancer Incidence Among Nationals Of The GCC States 1998-2007. GCC; 2011.

[17] Al-Masri A, Kofahi S, Al-Ruhaibeh M, et al. Epidemiology of breast cancer in the North Jordan. RMJ.35(2),168-72(2010).

[18] Asgarian F, Mirzaei M, Asgarian S, et al. Epidemiology of breast cancer and the age distribution of patients over a period of ten years. Iran J Breast Dis.9(1),31-6(2016).

[19] Babaei M, Mousavi S, Malek M, et al. Cancer occurrence in Semnan Province, Iran: results of a population-based cancer registry. Asian Pac J Cancer Prev.159-64(2005).

[20] Badar F, Mahmood S, Yusuf MA, et al. Epidemiology of cancers in Lahore, Pakistan, 2010–2012: a cross-sectional study. BMJ open.6(6),e011828(2016).

[21] Basaleem H, Al-Sakkaf K, editors. Trends of breast cancer in Aden Cancer Registry, Yemen (1997-2011). Eur J Cancer; 2016: ELSEVIER SCI LTD THE BOULEVARD, LANGFORD LANE, KIDLINGTON, OXFORD OX5 1GB, OXON, ENGLAND.

[22] BEN ABDALLAH M, BEN AYOUB WH. Registre Des Cancers NORD-TUNISIE Données 2004 – 2006. MINISTERE DE LA SANTE PUBLIQUE Institut Salah AZAIEZ Institut National de la Santé Publique & MINISTERE DE L'ENSEIGNEMENT SUPERIEUR DE LA RECHERCHE SCIENTIFIQUE ET DE LA TECHNOLOGIE Unité de Recherche en Epidémiologie des Cancers en Tunisie.

[23] Bener A, Ayub H, Kakil R, et al. Patterns of cancer incidence among the population of Qatar: a worldwide comparative study. Asian Pac J Cancer Prev.9(1),19-24(2008).

[24] Benider A, Harif M, Karkouri M. Registre des cancers de la region du grand Casablanca (2005.2006. 2007). Association Lalla Salma de lutte contre le Cancer. (2012).

[25] Bhurgri Y. Karachi cancer registry data–implications for the national cancer control program of pakistan. Asian Pac J Cancer Prev.5(1),77-82(2004).

[26] Bhurgri Y, Bhurgri H, Ajam A, et al. Cancer patterns in Quetta (1998-1999). J Paki Med Assoc.52(12),560(2002).

[27] Bhurgri Y, Naseeruddin S, Zaidi S, et al. Cancer patterns in Karachi division (1998-1999). J Paki Med Assoc.52(6),244(2002).

[28] Bodalal Z, Azzuz R, Bendardaf R. Cancers in eastern Libya: First results from Benghazi medical center. World journal of gastroenterology: WJG.20(20),6293(2014).

[29] Bouchbika Z, Haddad H, Benchakroun N, et al. Cancer incidence in Morocco: report from Casablanca registry 2005-2007. Pan Afr Med J.16(1)(2014).

[30] Curado M-P, Edwards B, Shin HR, et al. Cancer incidence in five continents, Volume IX: IARC Press, International Agency for Research on Cancer; 2007.

[31] Dey S, Soliman AS, Hablas A, et al. Urban–rural differences in breast cancer incidence in Egypt (1999–2006). Breast J.19(5),417-23(2010).

[32] El Mistiri M, Salati M, Marcheselli L, et al. Cancer incidence, mortality, and survival in Eastern Libya: updated report from the Benghazi Cancer Registry. Ann Epidemiol 25(8),564-8(2015).

[33] El Mistiri M, Verdecchia A, Rashid I, et al. Cancer incidence in eastern Libya: the first report from the Benghazi Cancer Registry, 2003. Int J Cancer.120(2),392-7(2007).

[34] El-Zaemey S, Nagi N, Fritschi L, et al. Breast cancer among Yemeni women using the national oncology centre registry 2004–2010. J Cancer Epidemiol.36(3),249-53(2012).

[35] Etemad K, Goya M, Ramazani Darya Sary R, et al. Iranian Annual of National Cancer Registration Report 2007-2008. Tehran: Ministry of Health Center for Disease Control& Prevention Non-Communicable Deputy Cancer Office; 2010.

[36] Etemad K, Goya M, Ramazani Darya Sary R, et al. Iranian Annual of National Cancer Registration Report 2008-2009. Tehran: Ministry of Health Center for Disease Control& Prevention Non-Communicable Deputy Cancer Office; 2011.

[37] Etemad K, Goya M, Ramazani Darya Sary R, et al. Iranian Annual of National Cancer Registration Report 2009-2010. Tehran: Ministry of Health Center for Disease Control& Prevention Non-Communicable Deputy Cancer Office; 2012.

[38] Faramarzi H, Bagheri P, Farahmandfar M, et al. Cancer occurrence in the south of Iran based upon pathology reports (2001–2009) Cas de cancer dans le Sud de l'Iran selon des rapports de pathologie (2001–2009). Afr J Cancer.5(3),137-43(2013).

[39] Fararouei M, Parisai Z, Farahmand M, et al. Cancer incidence appears to be rising in a small province in Islamic Republic of Iran: a population-based cohort study. East Mediterr Health J.21(5),319(2015).

[40] Fateh M, Emamian MH. Cancer incidence and trend analysis in shahroud, iran, 2000-2010. Iran j cancer prev.6(2),85(2013).

[41] Ferlay J, Bray F, Steliarova-Foucher E, et al. Cancer incidence in five continents, CI5plus. IARC CancerBase. (9)(2014).

[42] Fitzmaurice C, Dicker D, Pain A, et al. The global burden of cancer 2013. JAMA oncol.1(4),505-27(2015).

[43] Forman D, Bray F, Brewster D, et al. Cancer incidence in five continents, vol. X (electronic version) Lyon, IARC. 2014.

[44] Ghiasvand R, Adami H-O, Harirchi I, et al. Higher incidence of premenopausal breast cancer in less developed countries; myth or truth? BMC cancer.14(1),343(2014).

[45] Habib OS, Al-Diab J, Mohsin AA, et al. Experience and outcome of population-based cancer registration in Basrah-Southern Iraq in 2005-2008. Asian Pac J Cancer Prev.11(4),1151-4(2010).

[46] Habib OS, Hameed LA, Ajeel NA, et al. Epidemiology of breast cancer among females in basrah. Asian Pac J Cancer Prev.17,91-5(2016).

[47] Hagh Azali M, Ramazani Darya Sary R, DonLoo M, et al. Iranian Annual of National Cancer Registration Report 2002007-6. Tehran: Ministry of Health Center for Disease Control& Prevention Non-Communicable Deputy Cancer Office; 2008.

[48] Hanif M, Sabeen B, Maqbool A, et al. Breast cancer: Incidence (Thirteen year data analysis) and one year clinicopathological data of patients in a tertiary care cancer hospital. Int J Biol Biotech.12(3),373-9(2015).

[49] Hanif M, Zaidi P, Kamal S, et al. Institution-based cancer incidence in a local population in Pakistan: nine year data analysis. Asian Pac J Cancer Prev.10(2),227-30(2009).

[50] Hashemzadeh S, Maleki RA, Golzari SE. The incidence of breast cancer in northwest iran (2003-2008). J Cardiovasc Thorac Res.4(1),5(2012).

[51] Hussain A, Ahmad SB, Muhammad W, et al. Epidemiology of the breast cancer patients registered at Institute of Radiotherapy and Nuclear Medicine, Peshawar, Pakistan. Eur J Cancer Care.17(5),469-76(2008).

[52] Ibrahim AS, Khaled HM, Mikhail NN, et al. Cancer incidence in Egypt: results of the national population-based cancer registry program. J Cancer Epidemiol.2014(2014).

[53] Ismail SI, Soubani M, Nimri JM, et al. Cancer incidence in Jordan from 1996 to 2009: a comprehensive study. Asian Pac J Cancer Prev.14(6),3527-34(2013).

[54] Khoshnaw N, Mohammed HA, Abdullah DA. Patterns of cancer in Kurdistan-results of eight years cancer registration in Sulaymaniyah Province-Kurdistan-Iraq. Asian Pac J Cancer Prev.16(18),8525-31(2015).

[55] Majid RA, Mohammed HA, Hassan HA, et al. A population-based study of Kurdish breast cancer in northern Iraq: hormone receptor and HER2 status. A comparison with Arabic women and United States SEER data. BMC women's health.12(1),16(2012).

[56] Mashhadi M, Zakeri Z, Abdollahinejad M. Cancer incidence in South East of Iran: results of a population-based cancer registry. Shiraz E Med J.11(3),148-55(2010).

[57] Masoompour SM, Lankarani KB, Honarvar B, et al. Changing epidemiology of common cancers in southern iran, 2007-2010: A cross sectional study. PloS one.11(5),e0155669(2016).

[58] Mehrabani D, Almasi A, Farahmand M, et al. Incidence of breast cancer in Fars province, southern Iran: A hospital-based study. World j plast surg.1(1),16(2012).

[59] Mohagheghi S, MOUSAVI JS, Malekzadeh R, et al. Cancer incidence in Tehran metropolis: the first report from the Tehran Population-based Cancer Registry, 1998–2001. (2009).

[60] Moosavi S, DonLoo M, Hajsadeghi N, et al. Iranian Annual of National Cancer Registration Report 2005-2006 Ministry of Health Center for Disease Control& Prevention Non-Communicable Deputy Cancer Office; 2007.

[61] Moradpour F, Fatemi Z. Estimation of the projections of the incidence rates, mortality and prevalence due to common cancer site in Isfahan, Iran. Asian Pac J Cancer Prev.14(6),3581-5(2013).

[62] Mousavi SM, Mohaghegghi MA, Mousavi-Jerrahi A, et al. Burden of breast cancer in Iran: a study of the Tehran population based cancer registry. Asian Pac J Cancer Prev.7(4),571(2006).

[63] Mzayek F, Asfar T, Rastam S, et al. Neoplastic diseases in Aleppo, Syria. Eur J Cancer Prev.11(5),503-7(2002).

[64] Nimri O, Al-Sayaideh A. Cancer Incidence in Jordan-2012.

[65] Qureshi MA, Mirza T, Khan S, et al. Cancer patterns in Karachi (all districts), Pakistan: first results (2010–2015) from a Pathology based cancer registry of the largest government-run diagnostic and reference center of Karachi. Cancer epidemiol.44,114-22(2016).

[66] Ramazani Darya Sary R, Moosavi S, DonLoo M, et al. Iranian Annual of National Cancer Registration Report 2004-2005. Tehran: Ministry of Health Center for Disease Control& Prevention Non-Communicable Deputy Cancer Office; 2006.

[67] Sadjadi A, Nouraie M, Ghorbani A, et al. Epidemiology of breast cancer in the Islamic Republic of Iran: first results from a population-based cancer registry. (2009).

[68] Sadjadi A, Zahedi M, Nouraie M, et al. The first population-based cancer survey in Kerman Province of Iran. Iran J Public Health.36(4),26-34(2007).

[69] Saeed IE, Weng HY, Mohamed KH, et al. Cancer incidence in Khartoum, Sudan: first results from the Cancer Registry, 2009–2010. Cancer med.3(4),1075-84(2014).

[70] Sellami A, Sellami Boudawara T. Incidence des cancers dans le Gouvernorat de Sfax: 2000–2002. Institut National de la Santé Publique. (2007).

[71] Shamseddine A, Sibai A-M, Gehchan N, et al. Cancer incidence in postwar Lebanon: findings from the first national population-based registry, 1998∗. Ann Epidemiol.14(9),663-8(2004).

[72] Somi MH, Farhang S, Mirinezhad SK, et al. Cancer in East Azerbaijan, Iran: results of a population-based cancer registry. Asian Pac J Cancer Prev.9(2),327-30(2008).

[73] Taheri NS, Nosrat SB, Aarabi M, et al. Epidemiological pattern of breast cancer in Iranian women: is there an ethnic disparity? Asian Pac J Cancer Prev.13(9),4517-20(2012).

[74] TAZI MA, BENJAAFAR N, ER-RAKI A. Incidence des cancers a Rabat – anne´e2005. Assocition scientifique de l,Institu National d,oncologie (ASINO) & Direction deL,Epidemiologie et de lutte contre les Maladies (DELM); 2009.

[75] Tazi MA, Er-Raki A, Benjaafar N. Cancer incidence in Rabat, Morocco: 2006–2008. Ecancermedicalscience.7(2013).

[76] Yavari P, Hislop TG, Bajdik C, et al. Comparison of cancer incidence in Iran and Iranian immigrants to British Columbia, Canada. Asian Pac J Cancer Prev.7(1),86(2006).

[77] Zanetti R, Tazi MA, Rosso S. New data tells us more about cancer incidence in North Africa. European Journal of Cancer.46(3),462-6(2010).

[78] Organization WH. Towards a strategy for cancer control in the Eastern Mediterranean Region. (2009).

[79] Ghoncheh M, Mohammadian-Hafshejani A, Salehiniya H. Incidence and mortality of breast cancer and their relationship to development in Asia. Asian Pac J Cancer Prev.16(14),6081-7(2015).

[80] Hamadeh RR, Abulfatih NM, Fekri MA, et al. Epidemiology of breast cancer among Bahraini women: data from the Bahrain cancer registry. Sultan Qaboos Univ Med J.14(2),e176(2014).

[81] Al-Hashimi M, Wang XJ. Breast cancer in Iraq, incidence trends from 2000-2009. Asian Pac J Cancer Prev.15(1),281-6(2014).

[82] Jazayeri SB, Saadat S, Ramezani R, et al. Incidence of primary breast cancer in Iran: Ten-year national cancer registry data report. Cancer epidemiol.39(4),519-27(2015).

[83] Missaoui N, Trabelsi A, Parkin DM, et al. Trends in the incidence of cancer in the Sousse region, Tunisia, 1993–2006. Int J Oncol.127(11),2669-77(2010).

[84] Shamseddine A, Saleh A, Charafeddine M, et al. Cancer trends in Lebanon: a review of incidence rates for the period of 2003–2008 and projections until 2018. Popul Health Metr.12(1),4(2014).

[85] Lakkis NA, Adib SM, Osman MH, et al. Breast cancer in Lebanon: incidence and comparison to regional and Western countries. Cancer epidemiol.34(3),221-5(2010).

[86] Roshandel; Gholam Reza, Ghanbari Motlagh; Ali, Partoi Poor; Elham, et al. Annual Report of Iranian National Population-Based Cancer Registry (2014). Tehran: Ministry of Health and Medical Education, Deputy of Health Non-Communicable Diseases Control Department Cancer Office, Secretariat of the National Cancer Registry Program; 2018.

[87] Zahmatkesh B, Keramat A, Alavi N, et al. Breast cancer trend in Iran from 2000 to 2009 and prediction till 2020 using a trend analysis method. Asian Pac J Cancer Prev.17(3),1493-8(2016).

[88] Montella M, Crispo A, D'aiuto G, et al. Determinant factors for diagnostic delay in operable breast cancer patients. European journal of cancer prevention.10(1),53-9(2001).

[89] Moraga-Serrano PE. Global, Regional, and National Cancer Incidence, Mortality, Years of Life Lost, Years Lived With Disability, and Disability-Adjusted Life-Years for 29 Cancer Groups, 1990 to 2016: A Systematic Analysis for the Global

Burden of Disease Study. JAMA Oncology. (2018).

[90] DeSantis CE, Bray F, Ferlay J, et al. International variation in female breast cancer incidence and mortality rates. Cancer Epidemiol Biomarkers Prev (2015).

[91] ZAHRA F, HUMAYOUN F, YOUSAF T, et al. Evaluation of risk factors for carcinoma breast in Pakistani women. Journal of Fatima Jinnah Medical University.7(1)(2013).

[92] Asif HM, Sultana S, Akhtar N, et al. Prevalence, risk factors and disease knowledge of breast cancer in Pakistan. Asian Pac J Cancer Prev.15(11),4411-6(2014).

[93] Rosero-Bixby L, Oberle MW, Lee NC. Reproductive history and breast cancer in a population of high fertility, Costa Rica, 1984–85. International journal of cancer.40(6),747-54(1987).

[94] Madigan MP, Ziegler RG, Benichou J, et al. Proportion of breast cancer cases in the United States explained by well-established risk factors. JNCI: Journal of the National Cancer Institute.87(22),1681-5(1995).

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

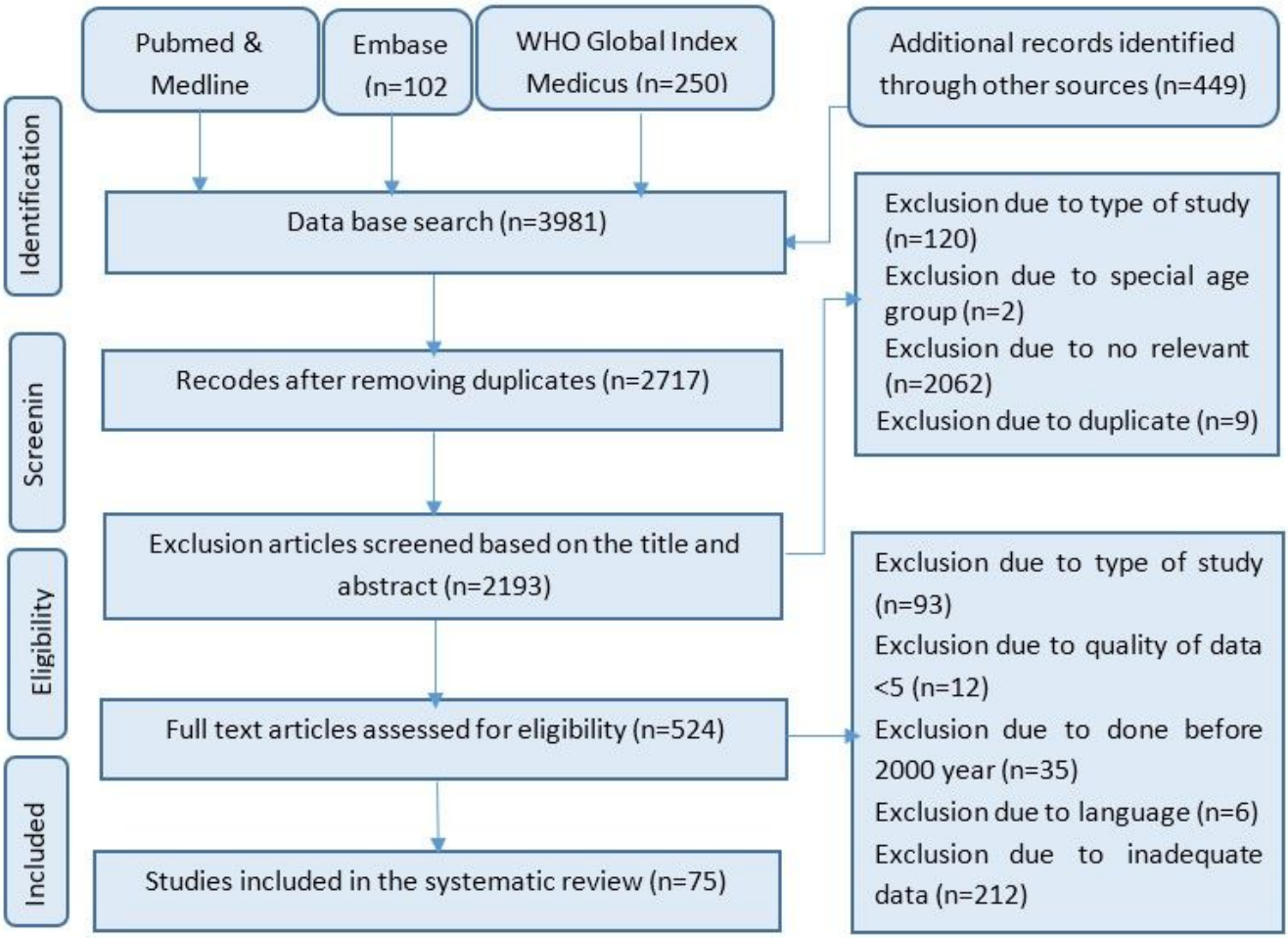

Figure 1

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

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- supplement1.docx