BMC Cancer

SYSTEMATIC REVIEW

Open Access

A systematic review and meta-analysis of pregnancy-associated breast cancer incidence rate

Mohammad Akhlaqi[1†], Amirali Ghofrani[1†], Nazila Najdi[2], Mohammadhosein Ranjkesh[3] and Amir Almasi-Hashiani[4,5*]

Abstract

Background Pregnancy-Associated Breast Cancer (PABC) is a special type of breast cancer that either occurs during pregnancy or one year postpartum. The aim of this systematic review and meta-analysis is to investigate the global incidence of PABC.

Methods In this meta-analysis, to find related studies, three international databases including PubMed (Medline), Scopus and Web of Science (Clarivate analytics) were explored. An additional search was also carried out using Google Scholar in December 2023 looking for any new relevant article, and the list of references for all new supposedly relevant papers were manually searched for and investigated as well. The required data were extracted from retrieved studies and the quality of the studies was evaluated using the Newcastle–Ottawa scale checklist. Heterogeneity among studies was assessed by I-square statistic and chi-square test and due to presence of a significant heterogeneity among studies, a random-effects model was used to pool the data.

Results Twenty-two studies were included in this meta-analysis. Among 51,944,490 number of female individuals included in the study, a total number of 7,267 cases of PABC were identified. Based on these results, the global incidence of PABC was estimated 19.2 cases per 100,000 pregnancies (95%CI: 16.1–22.2, I-square = 98.9%). The results of cumulative analysis showed that the incidence rate of PABC has risen over decades, as it increased from 13.3 cases (in 1969) to 19.2 cases (in 2022) per 100,000 pregnancies. The lowest incidence rate belonged to the American continent with 14.4 (95%CI: 9.8–19) cases per 100,000 pregnancies.

Conclusions The results obtained from this study demonstrates that the global incidence of PABC amounts to 19.2 cases per 100,000 pregnancies and it has been increasing slowly during the last few decades as time went by. The incidence rate in developing countries seem to be higher than in the developed countries. However, more studies are required in order to reach a better conclusion on this issue.

Keywords Breast neoplasm, Pregnancy associated breast cancer, Meta-analysis, Gestational breast cancer

†Mohammad Akhlaqi and Amirali Ghofrani contributed equally to this work.

*Correspondence:
Amir Almasi-Hashiani
Amiralmasi2007@gmail.com
Full list of author information is available at the end of the article

Introduction

Pregnancy-Associated Breast Cancer (PABC) is a special type of breast cancer that occurs either during pregnancy or within 1 year postpartum [1–3]. However, the period of time by which pregnancy-related breast cancer is defined varies among studies, ranging from 1 year after pregnancy in some studies up to 5 years postpartum in some others [4]. PABCs can occur during pregnancy or lactation period and is responsible for 0.2% to 3.8% of all breast cancers cases (accounting for 10% to 20% of all breast cancers in patients under 30 years of age) [5, 6]. The evidence available suggest that 1 for every 10,000 up to 1 for every 3,000 births is complicated by PABC in Western countries [7–9]. Meanwhile, about two-thirds of PABC cases are diagnosed after delivery and the other one-third of them are diagnosed during pregnancy [8].

Although certain risk factors for PABC have not been well established up until this point, older age at the time of first pregnancy, having a positive family history for BRCA1/2 gene mutations, having no history of breastfeeding the newborn as well as racial factors seem to play a role, the data available suggest; with the first pregnancy in older ages being mentioned as the most important factor [8].

PABC is notoriously known as an aggressive type of malignancy for plenty of reasons, which include relatively younger age of patients and a more advanced tumor stage at the time of diagnosis, higher rates of lymph node metastases, higher rates of estrogen receptor-negative (ER-negative) and progesterone receptor-negative (PR-negative) cases, and higher rates of HER2 expression [10]. In addition, patients with PABC may be more likely to suffer from delays in diagnosing their condition, considering the fact that changes in their breast tissue can easily be attributed to their pregnancy or lactation period rather than the underlying malignancy, which subsequently leads to a more advanced stage of the disease when the initial diagnosis is finally made. Furthermore, previous findings have clearly shown that women with PABC seem to have higher mortality rates compared to their non-PABC peers who were diagnosed at the same age and calendar period [11, 12]. To understand another reason responsible for a relatively worse prognosis of PABC compared to non-pregnancy associated breast cancers, one should appreciate that many women postpone taking recommended measures for breast cancer screening, the diagnostic mammography more precisely said, until after their course of pregnancy; On the other hand, the early detection of breast cancer could generally be more challenging during gestation and breastfeeding periods, since with the two latter conditions the breast tissue naturally grows in its density [13].

PABC usually affects young mothers with young children and does not pursue a good prognosis. Therefore, it imposes an extreme social, psychological and economic burden on the public. Taking its challenging nature into account when it comes to diagnosing this condition during pregnancy, it turns this matter into a demanding hurdle for society, seeking remarkable attention from the experts. Many information available addressing this very matter are equivocal. Due to a general increase in the mean age of marriage and pregnancy, which could be a potential cause of soaring PABC incidence rates during the last few decades, the need for more comprehensive and accurate information about the global incidence of this condition is felt more than ever. Therefore, the aim of this systematic review and meta-analysis was to investigate the global incidence rate of PABC.

Methods

Study design

This study is considered a systematic review and meta-analysis in terms of its study design. PRISMA guidelines and Cochrane Handbook for Systematic Reviews of Interventions were utilized to carry out this study and to report the ultimate results [14]. The protocol for the study has been registered in PROSPERO with the following ID number: CRD42023484980.

Search strategy

In order to find all related studies, a comprehensive search was carried out exploring three international databases including PubMed, Scopus and Web of Science (Clarivate analytics). Finally, a complementary search was also conducted using Google Scholar in order to find any new relevant article if present. By checking the filters, the obtained studies where limited to human studies only which comprised female individuals as participants and had a full-text in English language. The keywords used in the search strategy are listed as the following:"Pregnancy","Breast Tumor","Breast Cancer","Mammary Cancer","Breast Carcinoma","Pregnancy associated breast cancer","incidence","epidemiology", and"frequency". No time limit filter was applied to the search strategy, therefore all relevant articles from any time to the date of our search could be obtained and were reviewed.

Inclusion and exclusion criteria

Any study which met all of the following criteria was included in this study: 1) Having an available full-text in English language, 2) Being a cohort study (longitudinal study) in terms of study design, 3) Containing any data related to PABC incidence (number of assessed female individuals and number of PABC cases identified).

Any article which met one or more of the following criteria was excluded from the study: repetitive articles (duplicates), review studies, clinical trials, case reports, editorials, any study with no full-text available in English language, and articles which did not contain the required data.

Study selection and data collection process

After exploring the above-mentioned databases, obtained articles were transferred to EndNote20 software and all Duplicate studies were omitted from the library. All articles were initially screened, by which irrelevant studies with respect to our inclusion or exclusion criteria were identified and removed by either their title or abstract. The full-text for every single remaining article was explored intently and the required data were extracted from eligible studies.

Data features

The data included the following features for each study: year of publication, name of the first author, the country of origin where the study was conducted, studied population, study design, sampling method, the exact definition of PABC defined by that particular study, sample size (the number of people included), number of identified PABC cases, PABC incidence rate and the lower limit and upper limit of their 95% confidence interval (CI).

Risk of bias in individual studies

The Newcastle–Ottawa scale (NOS) checklist was employed in order to assess all included studies in regard to their methodological quality [15]. Based on this method, each article is graded a score from 0 to 9 points (stars), which the score can be further interpreted, and the study can be further classified as low quality if the score is a number between 0 and 3 points, moderate quality with 4 to 6 points, and high quality if the score is 7 or above, respectively.

Statistical analysis

Finally, the extracted data were integrated using the meta-analysis method. To check the heterogeneity among studies, I-square statistic was calculated using chi-square test at first. A random-effects model was also utilized to pool the data in case of any significant heterogeneity detected among the studies afterward. Furthermore, subgroup analysis was performed based on the country of origin and PABC definition for each specific study. Funnel plot, Egger's test and Begg's test were also used to check the publication bias. In addition, cumulative analysis (based on year) was performed to investigate the time trend. Sensitivity analysis was also performed to investigate the effect of each study on the estimated incidence rate as well. In the sensitivity analysis, individual studies were excluded from the meta-analysis, and the incidence of PABC was calculated, and the lowest and highest incidence rates were reported. This analysis shows which studies have the greatest impact on the calculated incidence rates. All data were analyzed using Stata software version 17 (Stata Corp, College Station, TX, USA).

Results

Study selection

A flowchart which shows the evaluation process for studies retrieved is shown in Fig. 1. Based on our search in multiple databases and Google Scholar, 5501 studies were found, and 4416 studies remained after removing the duplicates (n = 1085 studies). In the next step, the screening phase, 4223 presumably irrelevant studies were further removed by either title or abstract. A scrupulous exploration was carried out to explore the remaining 193 articles and to extract the required data from those eligible. Ultimately 22 studies were qualified to enter the meta-analysis.

Study characteristics

Twenty-two studies [16–37] were finally included in this meta-analysis. The total number of female individuals investigated equaled to 51,944,490 women and the total number of identified PABC cases amounted to 7267. The smallest sample size among all studies comprised 50,412 female individuals and the largest one belonged to a study with a total number of 11,846,300 female individuals. The oldest study reviewed was published in 1969 and the most recent one was published in year 2022. The most included articles were originated from the USA and Australia (with 4 articles each). The incidence of PABC were examined during pregnancy and within one year postpartum in most studies, in a few of other studies, however, the incidence rate data was limited to the pregnancy period only. More details for the included studies are available in Table 1.

Results of syntheses

The incidence rate data reported in twenty-two articles were pooled with random-effects model. The relevant Forest plot is shown in Fig. 2. Based on these results, the global incidence of PABC amounts to 19.2 per 100,000 pregnancies (95%CI: 16.1–22.2).

Risk of bias in studies

The NOS checklist was employed to classify the studies with regard to their quality. Consequently, 6 (27.3%) and 16 (72.7%) studies were classified as being moderate quality and good quality respectively. Most of the studies, however, took advantage of a population-based type

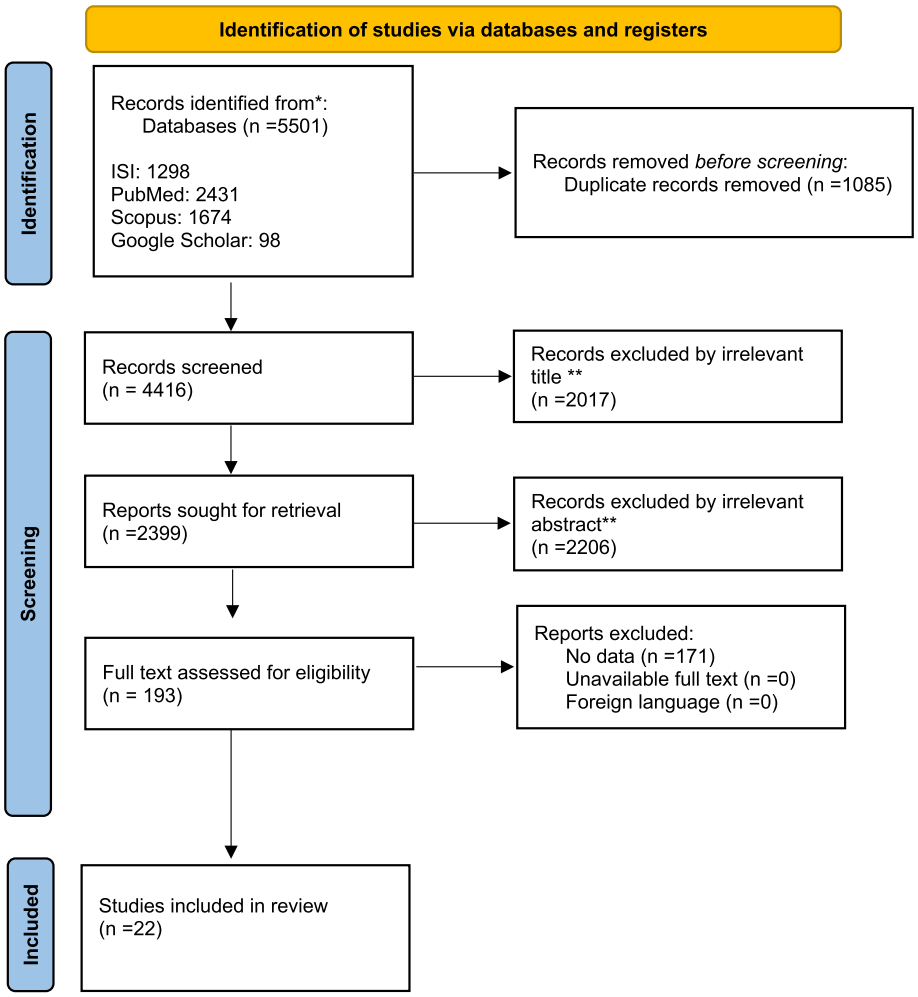

Fig. 1 Flow diagram of the literature search for studies included in meta-analysis

of data, which can explain the reason why the majority of studies stand in the high-quality group.

Heterogeneity between studies

Heterogeneity between studies was measured using the I-square statistic (variation in incidence rate attributable to heterogeneity) and its significance was checked using the chi-square test. According to the I-square statistic, a substantial heterogeneity was observed between the included studies (I-square = 98.9%), which was statistically significant (heterogeneity chi-square = 1983.03, (d.f. = 21), $p < 0.001$). For this reason, random-effects model was used to perform meta-analysis. In addition, subgroup analysis was also performed based on the location of the study and PABC definition.

Publication bias

Three methods were used to investigate the possibility of publication bias. The funnel plot (Fig. 3) showed a significant asymmetry. In addition, Egger's test also showed significant publication bias ($z = 4.73$, $p = 0.001$), while Begg's test did not support the existence of publication bias ($z = 0.56$, $p = 0.573$). Therefore, in general, the current evidence seems to be in favor of the presence of publication bias.

Cumulative meta-analysis

As an additional analysis, cumulative analysis over time was performed in order to investigate the time trend. The results of this analysis showed that the PABC incidence rate has risen over time, by which means that it has increased from 13.3 (in 1969) to 19.2 cases (in 2022) per 100,000 pregnancies (Fig. 4).

Sensitivity analysis

Based on the sensitivity analysis, the highest rate of PABC incidence rate was observed after the exclusion of Shechter Maor G et al.'s study [33] (19.92, 95%CI: 16.4–23.4 per

Table 1 Characteristics of the primary studies included in the meta-analysis

ID	Country	First Author	Year	Included Population	Sample size	BC Number	Study design	Sampling Method	PABC definition	Risk score	Ref
1	South Korea	Kang EJ	2016	Women who had given birth during the 2010–2012	1,384,551	317	Cohort	Not mentioned	Within 1 year after delivery (and not the pregnancy period)	6	[27]
2	Italy	Parazzini F	2017	Not mentioned	1,200,263	479	Population-based linkage study	All registered cases	During pregnancy (3-month before delivery for abortions and 9-month before delivery for normal deliveries) and 1 year after delivery	8	[30]
3	USA	Smith LH	2003	A group of women with 4,846,505 obstetric deliveries in California	4,846,505	935	Population-based retrospective review of cases	All registered cases	During pregnancy or within 1 year after delivery	7	[19]
4	Australia	Lee YY	2012	Women who gave birth in New South Wales	1,309,501	377	Population-based cohort study	All registered cases	During pregnancy or within 1 year after delivery	9	[22]
5	Australia	Lee YY	2013	Not mentioned	679,736	218	Validation study	Not mentioned	During pregnancy or within 1 year after delivery	6	[25]
6	South Korea	Park S	2022	Women under the age of 50 who experienced their first childbirth	1,528,152	334	NIH data registry	All registered cases	Within 1 year after delivery (and not the pregnancy period)	7	[36]
7	Italy	Murgia F	2019	Pregnant women	682,173	257	Population based linkage study	All registered cases	During pregnancy (3-month before delivery for abortions and 9-month before delivery for normal deliveries) and 1 year after delivery	9	[32]
8	Canada	Abenhaim HA	2012	Women who delivered during the admission to hospital	8,826,137	573	Population-based cohort	All registered cases	GBC (only during pregnancy and not afterwards)	6	[21]
9	South Korea	Shim MH	2016	Women who were diagnosed with cancer during pregnancy at a tertiary academic hospital	50,412	20	Retrospective cohort study	All registered cases	GBC (only during pregnancy and not afterwards)	6	[28]
10	Denmark	Eibye S	2013	Patients aged 15–44 years at first primary cancer diagnosis	2,427,670	489	Using data from the nationwide Danish registries	All registered cases	During pregnancy or within 1 year after delivery	8	[24]

Table 1 (continued)

ID	Country	First Author	Year	Included Population	Sample size	BC Number	Study design	Sampling Method	PABC definition	Risk score	Ref
11	USA	Cottreau CM	2019	Pregnancies among women aged 10–54 years during 2001–2013	775,709	208	Population based	All registered cases	During pregnancy or within 1 year after delivery	7	[31]
12	Northern Ireland	Lynch GA	1969	Not mentioned	337,342	45	Not mentioned	Not mentioned	Not defined	4	[16]
13	Sweden	Andersson TM	2015	Identified live births in women aged 15–44 years from 1963 to 2007	4,580,005	677	Population-based Swedish Cancer Register	All registered cases with live births	During pregnancy or within 1 year after delivery	8	[26]
14	USA	Tharmaratnam U	2012	all patients with a diagnosis of cancer, who delivered after 12 weeks of gestation	116,474	17	Retrospective data collection	Retrospective data collection of pregnant cancer patients	GBC (only during pregnancy and not afterwards)	5	[23]
15	Sweden	Andersson TM	2009	Women aged 15–44 years at the date of breast cancer diagnosis	4,156,190	539	Population-based cohort study	All registered cases	During pregnancy or within 1 year after delivery	8	[20]
16	Nigeria	Aghadiuno PU	1983	Identified from the records of the Cancer Registry Nigeria	51,058	14	Retrospective data collection	All registered cases	During pregnancy or within 1 year after delivery	6	[17]
17	USA	Shechter Maor G	2019	All delivery records who delivered during their admission	11,846,300	772	Population based cohort study	All registered cases	GBC (only during pregnancy and not afterwards)	8	[33]
18	Norway	Albrektsen G	1995	Norwegian women born in 1935–71	802,457	121	Population based cohort study	All registered cases	During pregnancy or within 1 year after delivery	8	[18]
19	Australia and New Zealand	Sullivan E	2022	Women participated in the Australasian Maternity Outcomes Surveillance System	533,000	40	Population based prospective cohort study	All registered cases	GBC (only during pregnancy and not afterwards)	7	[37]
20	Sweden	Lu D	2017	Newborns	3,947,215	707	Swedish Medical Birth Register (MBR)	All registered cases	During pregnancy or within 1 year after delivery	9	[29]
21	Australia	Safi N	2021	All women with pregnancies that ended in live birth or stillbirth	1,783,116	122	Population-based cohort study	All registered cases	GBC (only during pregnancy and not afterwards)	8	[35]
22	China	Yp Z	2019	Pregnant women	80,524	6	Prospective, multicenter cohort study	All registered cases	GBC (only during pregnancy and not afterwards)	7	[34]

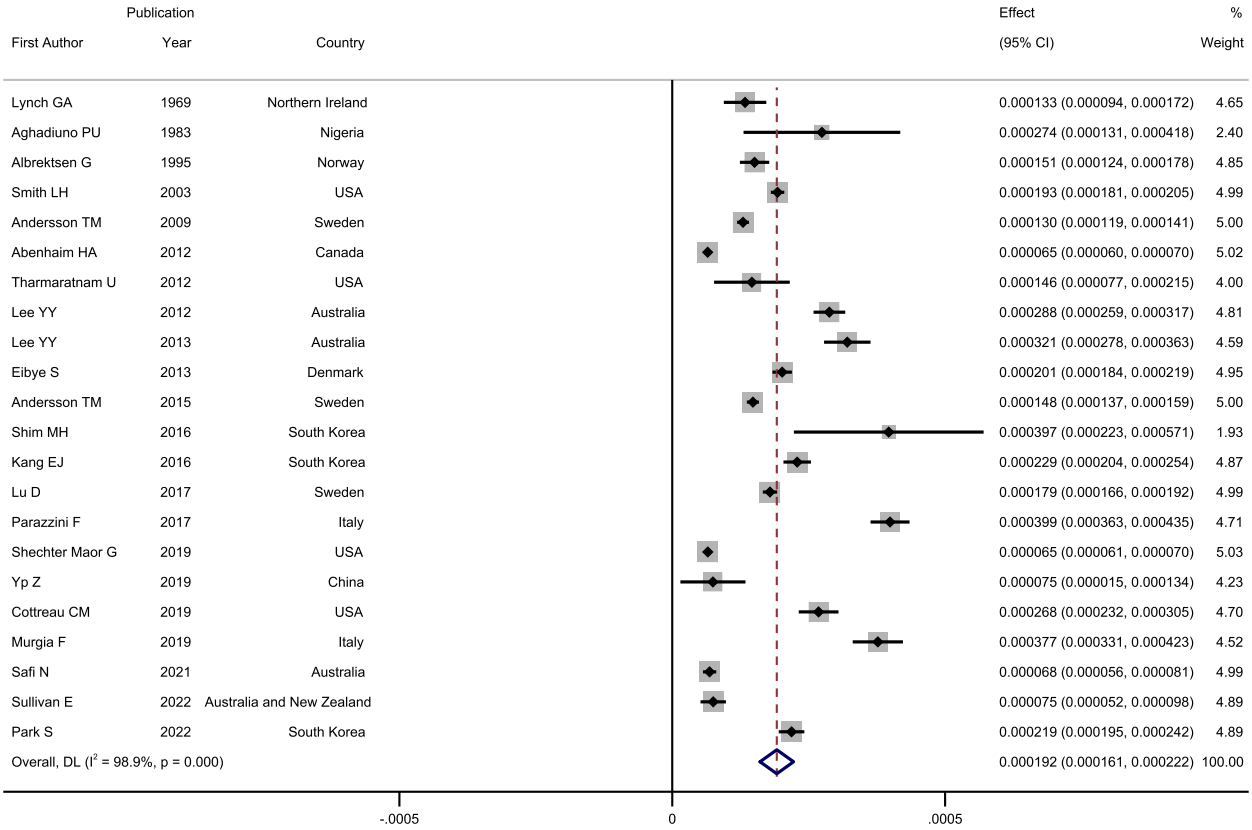

Fig. 2 Forest plot showing the incidence rate of pregnancy-associated breast cancer

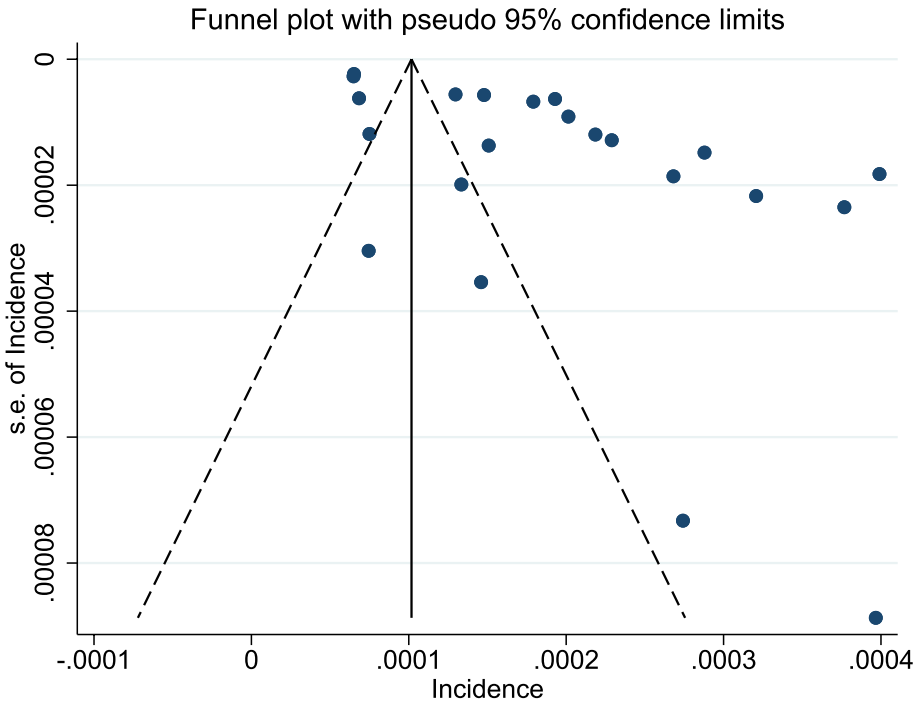

Fig. 3 Funnel plot assessing asymmetry of included studies

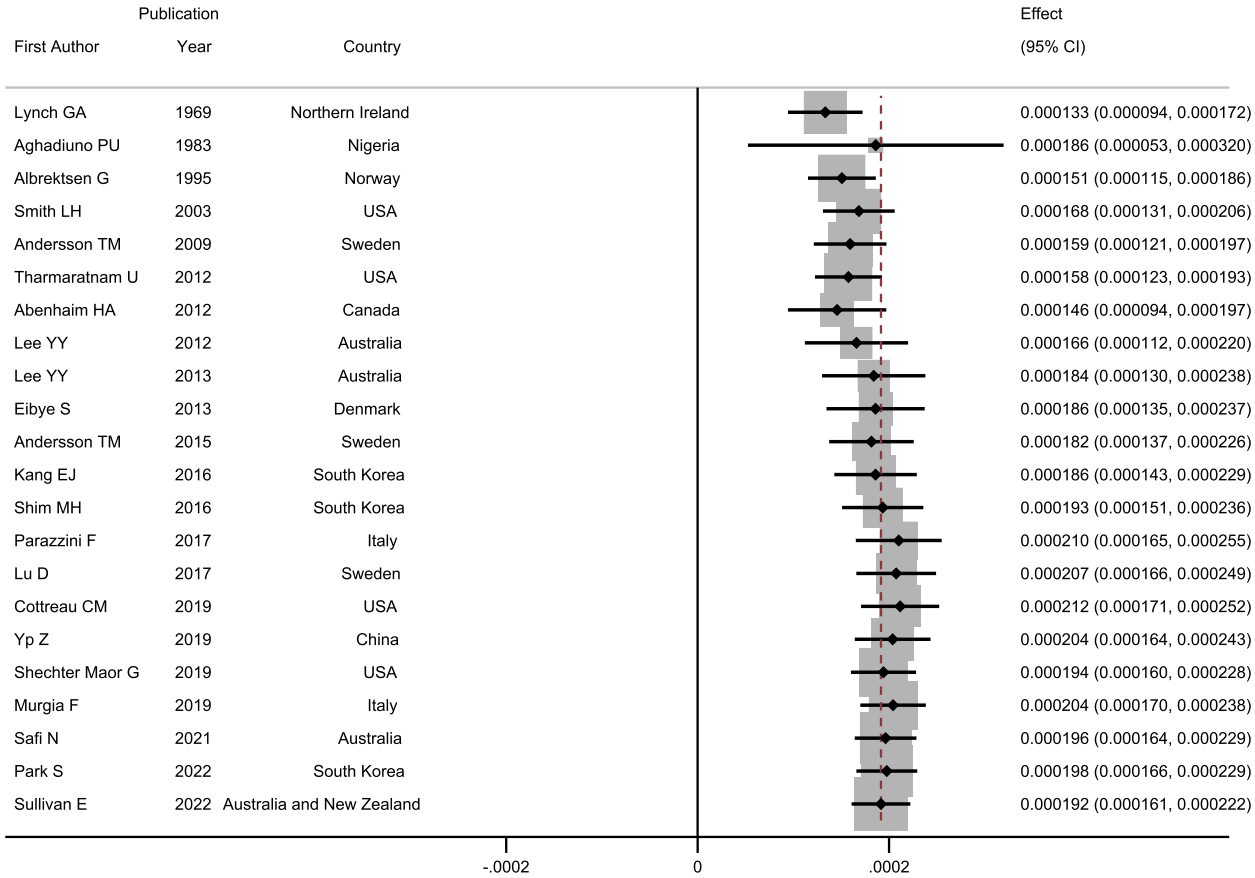

Fig. 4 Cumulative forest plot showing the incidence of pregnancy-associated breast cancer over time

100,000) and the lowest rate was observed after excluding Parazzini F et al.'s study [30] (18.07, 95%CI: 15.1–21.0 per 100,000) (Fig. 5).

Subgroup analysis

Subgroup analysis was carried out based on continents. There were 5 studies originating from America, 8 from Europe, 4 from Asia, 4 from Australia and Oceania, and 1 study from Africa. As shown in Fig. 6, the PABC incidence rate was estimated to be 14.4 (95%CI: 9.8–19.0) in America, 21.2 (95%CI: 16.9–25.5) in Europe, 20.1 (95%CI: 13.9–26.3) in Asia, 18.7 (95%CI: 7.1–30.3) in Australia and Oceania, and 27.4 (95%CI: 13.1–41.8) in Africa per 100,000 pregnancies.

The analysis displayed in Fig. 7 has been performed with respect to the PABC definition noted by each single study. In 12 studies, PABC was defined as breast cancer which is diagnosed either during pregnancy (gestational breast cancer (GBC)) or within one year postpartum (PP). In 7 studies, only cancers diagnosed during pregnancy period (GBC) were defined as PABC; and in two other studies data is limited to one year postpartum period (PP and not GBC) only. The authors of the one remaining study did not mention any clear definition of theirs for PABC. The incidence rate of pregnancy associated breast cancer was estimated to be 23.9 (95%CI: 20.3–27.6) in the PP + GBC group of studies, 7.0 (95%CI: 6.0–7.9) in the GBC-only group, and 22.3 (95%CI: 20.6–24.1) in the PP-only studies per 100,000.

Discussion

Breast cancer is one of the most common malignancies among women in reproductive age, with PABC being a subtype which carries a poor prognosis. Not only is there a less than needed amount of data available resulting from the very best efforts made by the experts trying to make an accurate estimation of PABC incidence rate, the numbers that have already been reported vary in different parts of the world as well. Which prompted the authors of the current study to comprehensively review the available literature addressing the issue, in order to reach an overall and hopefully close estimation of PABC incidence rate globally. Ultimately, 22 articles were included in this study and the incidence rate of PABC was estimated as being 19.2 cases per 100,000 pregnancies (95%CI: 16.1–22.2).

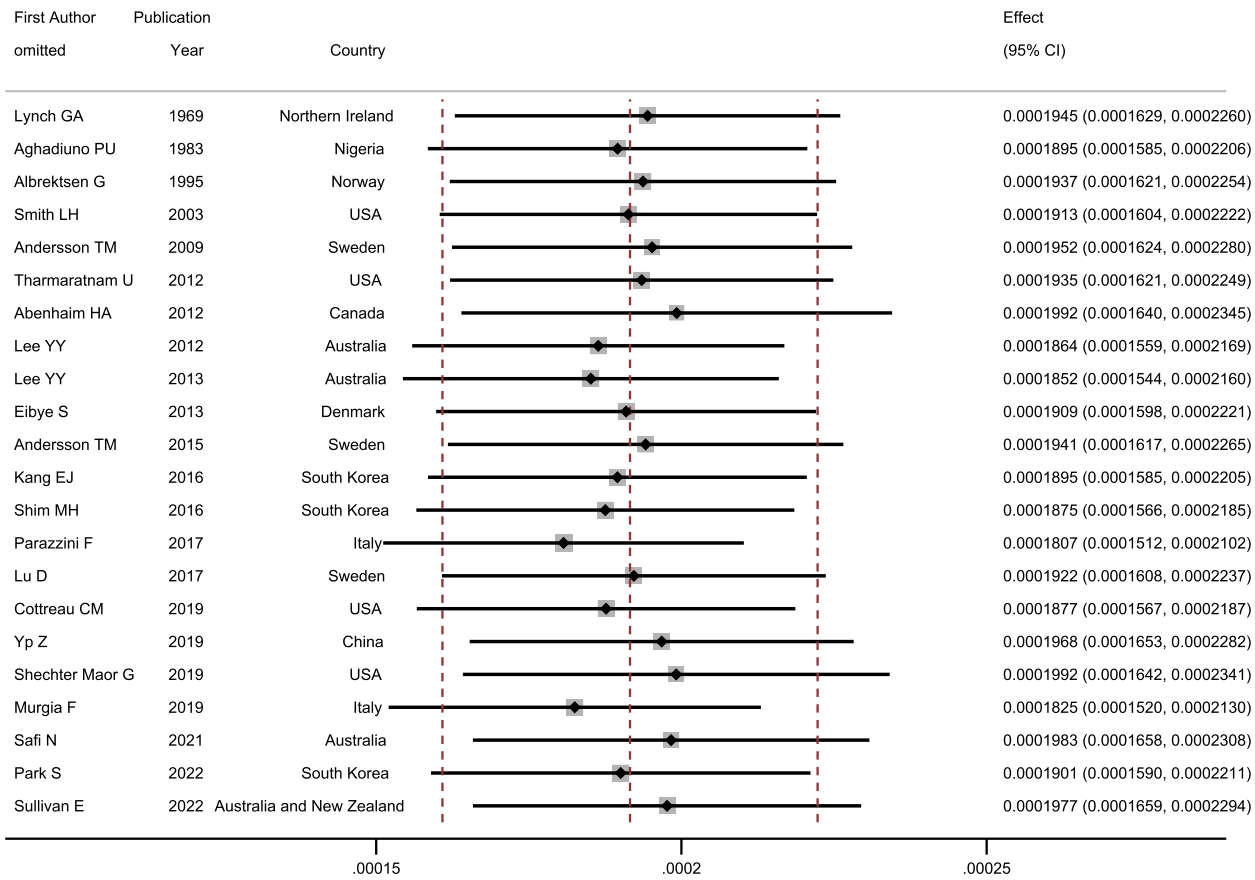

Fig. 5 Forest plot assessing sensitivity analysis

Additional analyzes showed that the incidence rate of PABC vary among continents all around the world, with the highest incidence rate being reported in Africa (27.4 per 100,000) and the lowest incidence rate being reported in America (14.4 per 100,000). However, in this meta-analysis, there was only one study from African countries, and the number of studies originating from Asia was limited as well, so that none of the studies included had originally taken place in central Asia, western Asia, or in the Middle East. Which may be the reason explaining the higher than global incidence of PABC in Asian and African countries being reported by some preliminary studies. Therefore, one should admit that more studies are required to reach an undisputed conclusion about the variations reported in different continents. Also, it might be noteworthy to mention that our study demonstrates a continuous mild increase in PABC incidence rate with a gentle slope during recent decades (raised from 13.3 (in 1969) to 19.2 cases (in 2022) per 100,000).

According to a study conducted in the USA, the incidence of breast cancer has been on the rise and increasing by 1% annually from 2012 to 2021. This increase was 1.4% annually in women under 50 years of age and 0.7% in women 50 years of age and older. The results showed that Asian American and Pacific Islander women had the fastest increases in both age groups (2.7% and 2.5% per year, respectively) [38]. The results of our study also showed an increasing trend in the incidence of breast cancer. Various factors have been identified as effective factors in the development of breast cancer, such as family history of breast cancer, BRCA gene mutations, the late menopause, late or no pregnancies, obesity, hormone replacement therapy, estrogen, alcohol consumption, use of oral contraceptives, smoking, and physical activity [39–41]. Given that the trend of these risk factors is also increasing in societies, the increase in cancer incidence can be justified. Differences in geographical areas can also be due to different prevalence of risk factors or the quality of breast cancer screening coverage in regions are different.

The global incidence of breast cancer in young women has increased by 16% since the 1990 s and is now the most common cancer in young women, with 244,000 cases per year [42] and according to GLOBOCAN 2022, breast cancer, thyroid and cervical cancer accounts for 47% of cancers in young women [43]. Breast cancer in

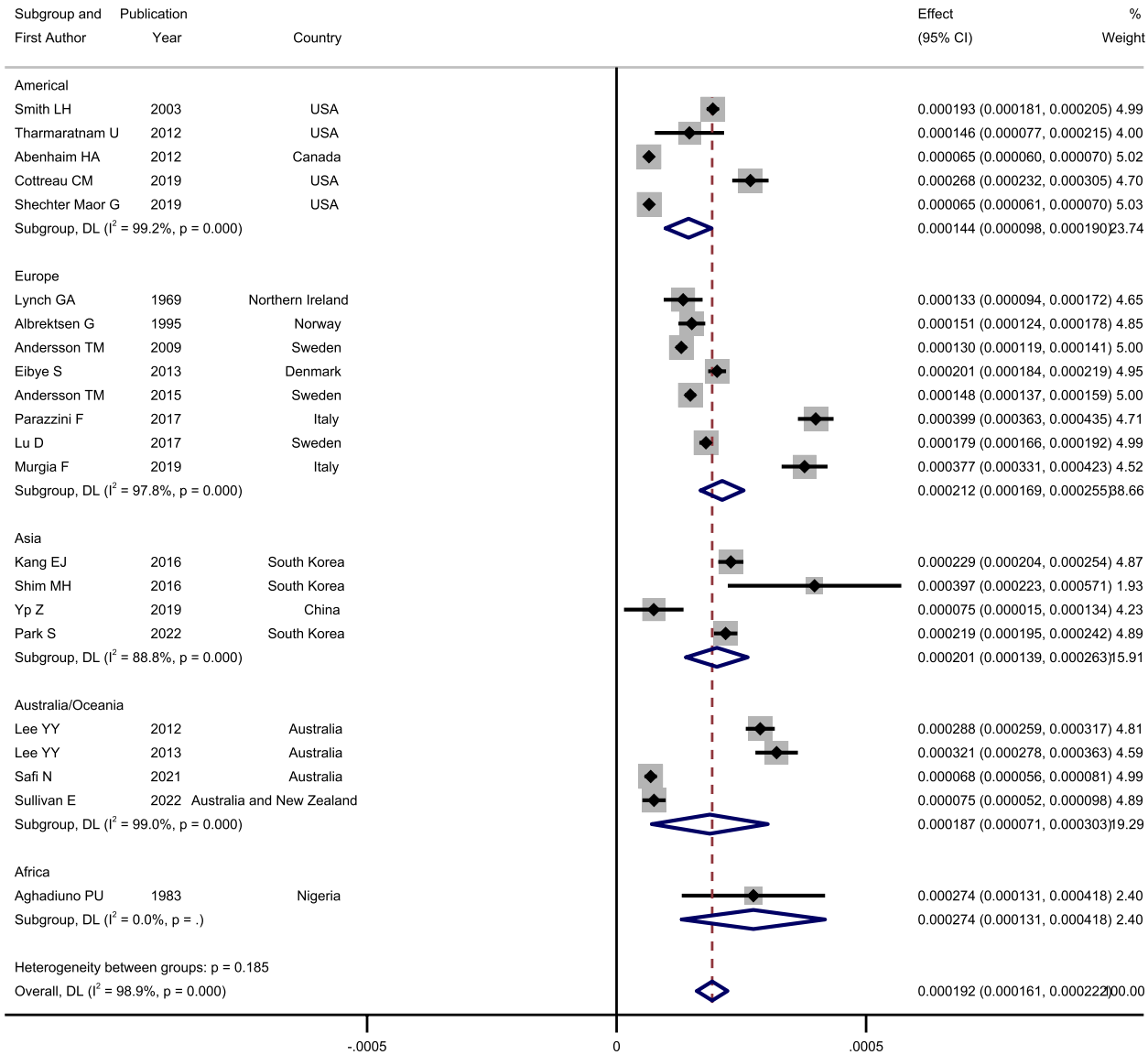

Fig. 6 Forest plot showing the incidence of pregnancy-associated breast cancer based on continents

young women (under 40 years of age) is much rarer and has a worse prognosis than breast cancer in older women. According to GLOBOCAN 2018, the age-standardized incidence rate of breast cancer in women under 40 years of age was 9.04 and in women over 40 years of age was 132 cases per 100,000 [42]. Part of the increase in breast cancer cases worldwide, especially in those under the age of 40, can be attributed to the increase in the number of PABC cases due to changing patterns of associated risk factors.

Many cases of breast cancer have a hormone-dependent nature, which means they rely on hormones in order to exist and grow, mostly estrogen and progesterone [44–46]. Although the exact underlying mechanisms are still poorly understood, breast cancer which occurs in association with pregnancy or breastfeeding has been proposed as a strong hypothesis since decades ago, considering the physiological effects of these two conditions on a woman's body, especially hormonal changes and breast tissue alterations which alter the breast tissue in favor of increasing the probability for a new malignancy to occur. Some of the risk factors for a malignant breast tumor growing during pregnancy can be outlined as the following: elevated levels of estrogen, progesterone and IGF- 1 hormones in the blood stream, elevated levels of estradiol which is already well-known for its mutagenic

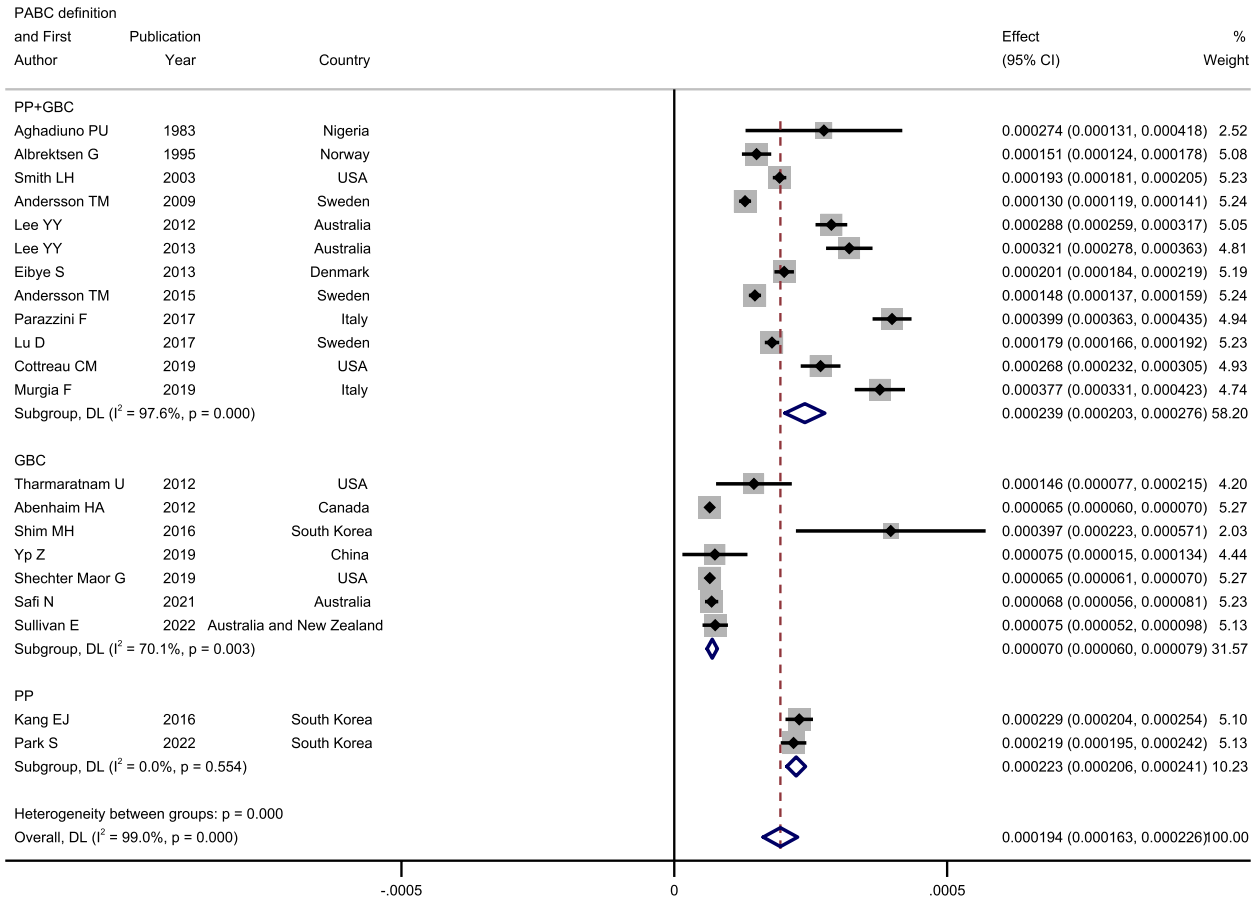

Fig. 7 Forest plot showing the incidence of pregnancy-associated breast cancer based on its definition

and carcinogenic effects, immune system alterations such as suppression of cellular immune system, increased overall immune tolerance and inflammatory responses in the breast tissue [8].

Breast cancers and cervical cancers are responsible for about 50% of pregnancies complicated by a malignancy. Even considering the relatively low incidence rate of PABC, the subsequent poor prognosis of the condition brings it into special attention inevitably [47]. The triple negative breast cancer phenotype (TNBC) accounts for about 30–40% of all PABC cases, which is slightly higher compared to those types of breast cancer affecting primiparous women, according to studies [48]. In addition, PABC is usually associated with a larger tumor size and has a higher tendency to involve the adjacent lymphatic system [47].

It seems that PABCs should be taken more seriously than other types of breast cancer. Worse prognosis and possibly higher mortality rates are among the several reasons which indicate the importance of this condition. Considering the fact that not only women affected by this condition are relatively young themselves, but they have also just given birth to a newborn, so it can be easily understood how important it is to approach this issue properly in order to avoid its devastating consequences for the individual, her family and the society she lives in. Hence, the current study provides valuable data, addressing the epidemiological aspect of the discussed condition which can be further utilized by major policymakers and healthcare experts from all around the globe, especially those with a robust intention of taking every possible measure in order to alleviate the heavy burden of health and social issues imposed by PABC on individuals and the public. However, the authors also admit that more primary and secondary studies are required for the scientific community to reach a more accurate and conclusive consensus on the incidence rate and the time trend of the explained condition.

It is worth mentioning that tactful measures taken by major policymakers in health care systems, in terms of facilitating new approaches which can lead to an earlier diagnosis of the condition, such as providing more comprehensive education programs for pregnant women, deployment of more accurate diagnostic tools

in medical care systems or running advanced training programs for healthcare personnel, may lead to even more favorable outcomes when it comes to reducing the burden of this condition.

To point out the strengths of this study, we can claim that no similar study has reported the global incidence rate for PABC so far, to our knowledge. Furthermore, time trends related to PABC have been assessed, and a comparison between different continents as well as a sensitivity analysis were performed in the current study.

In terms of limitations, it should be noticed that PABC had varied definitions among the reviewed studies. Also, it can be said that the limited number of studies originating from Africa and Asia could potentially cause errors when comparing the results related to different parts of the globe. In addition, this study had limited data from African and Asian countries, which could impact generalizability. Also, regarding publication bias, the results were in favor of the presence of publication bias among studies, which could affect the pooled estimates, suggesting that the results should be generalized with caution.

Conclusion

From the information provided by this study it can be concluded that the global incidence rate of PABC amounts to 19.2 cases per 100,000 pregnancies, and it has been increasing slowly during recent decades as time went by. The incidence rate of the discussed condition seems to be slightly higher in developing countries (Asian and African countries) in comparison with the developed countries (North American countries, Europe and Australia). However, more studies are required to reach more certain conclusions on this matter.

Abbreviations

PABC	Pregnancy-associated breast cancer
CI	Confidence Interval
PRISMA	Preferred Reporting Items for Systematic Review and Meta-Analysis
ER-negative	Estrogen receptor-negative
PR- negative	Progesterone receptor-negative
GBC	Gestational breast cancer
PP	Postpartum
NOS	Newcastle–Ottawa scale

Acknowledgements

We would like to thank the vice chancellor for the research of Arak University of Medical Sciences for their financial and scientific support.

Authors' contributions

AAH, MA, AGH, MHR and NN conceived the study. AAH, MA, AGH and MHR contributed to the title, abstract and full-text screening. Data extraction was done by AAH, MA, AGH and MHR and AAH analyzed the data. All authors contributed equally to the initial draft of the manuscript. All authors have read and approved the final version of the manuscript.

Funding

This study was funded by Arak University of Medical Sciences (Grant number: 4215). The funder had no role in the study design, data collection, analyses, and interpretation of the results.

Data availability

No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate

This study was approved by Ethical Committee of Arak University of Medical Sciences (ID: IR.ARAKMU.REC.1401.226).

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

Author details

[1]Student Research Committee, Arak University of Medical Sciences, Arak, Iran. [2]Department of Obstetrics and Gynecology, Arak University of Medical Sciences, Arak, Iran. [3]Student Research Committee, Baqiyatallah University of Medical Sciences, Tehran, Iran. [4]Department of Epidemiology, School of Health, Arak University of Medical Sciences, Golestan St., Arak, Iran. [5]Traditional and Complementary Medicine Research Center, School of Medicine, Arak University of Medical Sciences, Arak, Iran.

Received: 14 February 2024 Accepted: 4 April 2025
Published online: 10 April 2025

References

1. Jin YC, Du JX, Fu SM, Chen Q, Qiu YR, Pei A, Yao YJ, Zhu W, Wu KJ. A retrospective clinical study of patients with pregnancy-associated breast cancer among multiple centers in China (CSBrS-008). Chin Med J. 2021;134(18):2186–95.
2. Pyle C, Hill M, Sharafi S, Forton C, Sohaey R. Pregnancy-associated breast cancer: why breast imaging during pregnancy and lactation matters. J Breast Imaging. 2023;5(6):732–43.
3. Lundberg FE, Stensheim H, Ullenhag GJ, Sahlgren HM, Lindemann K, Fredriksson I, Johansson ALV. Risk factors for the increasing incidence of pregnancy-associated cancer in Sweden - a population-based study. Acta Obstet Gynecol Scand. 2024;103(4):669–83.
4. Lee GE, Mayer EL, Partridge A. Prognosis of pregnancy-associated breast cancer. Breast Cancer Res Treat. 2017;163(3):417–21.
5. Anders CK, Johnson R, Litton J, Phillips M, Bleyer A. Breast cancer before age 40 years. Semin Oncol. 2009;36(3):237–49.
6. Vinatier E, Merlot B, Poncelet E, Collinet P, Vinatier D. Breast cancer during pregnancy. Eur J Obstet Gynecol Reprod Biol. 2009;147(1):9–14.
7. Polivka J Jr, Altun I, Golubnitschaja O. Pregnancy-associated breast cancer: the risky status quo and new concepts of predictive medicine. EPMA J. 2018;9(1):1–13.
8. Ruiz R, Herrero C, Strasser-Weippl K, Touya D, St Louis J, Bukowski A, Goss PE. Epidemiology and pathophysiology of pregnancy-associated breast cancer: a review. Breast. 2017;35:136–41.
9. Kakoulidis I, Skagias L, Politi E. Pregnancy associated breast cancer (PABC): aspects in diagnosis. Breast Dis. 2015;35(3):157–66.
10. Wang B, Yang Y, Jiang Z, Zhao J, Mao Y, Liu J, Zhang J. Clinicopathological characteristics, diagnosis, and prognosis of pregnancy-associated breast cancer. Thorac Cancer. 2019;10(5):1060–8.
11. Azim HA Jr, Santoro L, Russell-Edu W, Pentheroudakis G, Pavlidis N, Peccatori FA. Prognosis of pregnancy-associated breast cancer: a meta-analysis of 30 studies. Cancer Treat Rev. 2012;38(7):834–42.
12. Woo JC, Yu T, Hurd TC. Breast cancer in pregnancy: a literature review. Arch Surgery. 2003;138(1):91–8; discussion 99.

13. Galati F, Magri V, Arias-Cadena PA, Moffa G, Rizzo V, Pasculli M, Botticelli A, Pediconi F. Pregnancy-associated breast cancer: a diagnostic and therapeutic challenge. Diagnostics (Basel). 2023;13(4):604.
14. Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. Annals of internal medicine. 2009;151(4):264–9, w264.
15. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses. http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp.
16. Lynch GA. Breast cancer associated with pregnancy. Ulster Med J. 1969;38(1):34–46.
17. Aghadiuno PU, Ibeziako PA. Clinicopathologic study of breast carcinoma occurring during pregnancy and lactation. Int J Gynaecol Obstet. 1983;21(1):17–26.
18. Albrektsen G, Heuch I, Kvåle G. The short-term and long-term effect of a pregnancy on breast cancer risk: a prospective study of 802,457 parous Norwegian women. Br J Cancer. 1995;72(2):480–4.
19. Smith LH, Danielsen B, Allen ME, Cress R. Cancer associated with obstetric delivery: results of linkage with the California cancer registry. Am J Obstet Gynecol. 2003;189(4):1128–35.
20. Andersson TM, Johansson ALV, Hsieh CC, Cnattingius S, Lambe M. Increasing incidence of pregnancy-associated breast cancer in Sweden. Obstet Gynecol. 2009;114(3):568–72.
21. Abenhaim HA, Azoulay L, Holcroft CA, Bure LA, Assayag J, Benjamin A. Incidence, risk factors, and obstetrical outcomes of women with breast cancer in pregnancy. Breast J. 2012;18(6):564–8.
22. Lee YY, Roberts CL, Dobbins T, Stavrou E, Black K, Morris J, Young J. Incidence and outcomes of pregnancy-associated cancer in Australia, 1994–2008: a population-based linkage study. BJOG. 2012;119(13):1572–82.
23. Tharmaratnam U, Balki M. Anesthetic management during labor and delivery: a 21-year review of women with cancer in a tertiary care center. J Clin Anesth. 2012;24(7):524–30.
24. Eibye S, Kjær SK, Mellemkjær L. Incidence of pregnancy-associated cancer in Denmark, 1977–2006. Obstet Gynecol. 2013;122(3):608–17.
25. Lee YY, Roberts CL, Young J, Dobbins T. Using hospital discharge data to identify incident pregnancy-associated cancers: a validation study. BMC Pregnancy Childbirth. 2013;13:37.
26. Andersson TM, Johansson AL, Fredriksson I, Lambe M. Cancer during pregnancy and the postpartum period: a population-based study. Cancer. 2015;121(12):2072–7.
27. Kang EJ, Seo JH, Kim LY, Park GU, Oh MJ, Park PJ, Cho GJ. Pregnancy-associated risk factors of postpartum breast cancer in Korea: a nationwide health insurance database study. PLoS One. 2016;11(12):e0168469.
28. Shim MH, Mok CW, Chang KH, Sung JH, Choi SJ, Oh SY, Roh CR, Kim JH. Clinical characteristics and outcome of cancer diagnosed during pregnancy. Obstetrics & gynecology science. 2016;59(1):1–8.
29. Lu D, Ludvigsson JF, Smedby KE, Fall K, Valdimarsdóttir U, Cnattingius S, Fang F. Maternal cancer during pregnancy and risks of stillbirth and infant mortality. J Clin Oncol. 2017;35(14):1522–9.
30. Parazzini F, Franchi M, Tavani A, Negri E, Peccatori FA. Frequency of pregnancy related cancer: a population based linkage study in Lombardy, Italy. International journal of gynecological cancer : official journal of the International Gynecological Cancer Society. 2017;27(3):613–9.
31. Cottreau CM, Dashevsky I, Andrade SE, Li DK, Nekhlyudov L, Raebel MA, Ritzwoller DP, Partridge AH, Pawloski PA, Toh S. Pregnancy-associated cancer: a U.S. population-based study. J Womens Health (Larchmt). 2019;28(2):250–7.
32. Murgia F, Marinaccio M, Cormio G, Loizzi V, Cicinelli R, Bettocchi S, Cicinelli E. Pregnancy related cancer in Apulia. A population based linkage study. Eur J Obstet Gynecol Reprod Biol X. 2019;3:100025.
33. Shechter Maor G, Czuzoj-Shulman N, Spence AR, Abenhaim HA. Neonatal outcomes of pregnancy-associated breast cancer: Population-based study on 11 million births. Breast J. 2019;25(1):86–90.
34. Zhang YP, Duan J, Zhu XW, Li J, Shi Y. Maternal and neonatal outcomes of cancer during pregnancy: a multi-center observational study. J Cancer. 2019;10(23):5727–34.
35. Safi N, Saunders C, Hayen A, Anazodo A, Lui K, Li Z, Remond M, Nicholl M, Wang AY, Sullivan E. Gestational breast cancer in New South Wales: a population-based linkage study of incidence, management, and outcomes. PLoS One. 2021;16(1):e0245493.
36. Park S, Lee JS, Yoon JS, Kim NH, Park S, Youn HJ, Lee JW, Lee JE, Lee J, Hur H, et al. The risk factors, incidence and prognosis of postpartum breast cancer: a nationwide study by the SMARTSHIP group. Front Oncol. 2022;12:889433.
37. Sullivan E, Safi N, Li Z, Remond M, Chen TYT, Javid N, Dickinson JE, Ives A, Hammarberg K, Anazodo A, et al. Perinatal outcomes of women with gestational breast cancer in Australia and New Zealand: a prospective population-based study. Birth. 2022;49(4):763–73.
38. Giaquinto AN, Sung H, Newman LA, Freedman RA, Smith RA, Star J, Jemal A, Siegel RL. Breast cancer statistics 2024. CA: a cancer journal for clinicians. 2024;74(6):477–95.
39. Łukasiewicz S, Czeczelewski M, Forma A, Baj J, Sitarz R, Stanisławek A. Breast cancer-epidemiology, risk factors, classification, prognostic markers, and current treatment strategies-an updated review. Cancers (Basel). 2021;13(17):4287.
40. Majeed W, Aslam B, Javed I, Khaliq T, Muhammad F, Ali A, Raza A. Breast cancer: major risk factors and recent developments in treatment. Asian Pac J Cancer Prev. 2014;15(8):3353–8.
41. Obeagu EI, Obeagu GU. Breast cancer: a review of risk factors and diagnosis. Medicine (Baltimore). 2024;103(3):e36905.
42. Sopik V. International variation in breast cancer incidence and mortality in young women. Breast Cancer Res Treat. 2021;186(2):497–507.
43. Li J, Kuang X. Global cancer statistics of young adults and its changes in the past decade: incidence and mortality from GLOBOCAN 2022. Public Health. 2024;237:336–43.
44. Emons G. Hormone-dependent cancers: molecular mechanisms and therapeutical implications. Cells. 2022;12(1):110.
45. Tavčar Kunstič T, Debeljak N, Fon Tacer K. Heterogeneity in hormone-dependent breast cancer and therapy: steroid hormones, HER2, melanoma antigens, and cannabinoid receptors. Advances in Cancer Biology - Metastasis. 2023;7:100086.
46. Miki Y. Hormone-dependent cancers: new aspects on biochemistry and molecular pathology. International journal of molecular sciences. 2023;24(13):10830.
47. Allouch S, Gupta I, Malik S, Al Farsi HF, Vranic S, Al Moustafa AE. Breast cancer during pregnancy: a marked propensity to triple-negative phenotype. Frontiers in Oncology. 2020;10:580345.
48. Pilewskie M, Gorodinsky P, Fought A, Hansen N, Bethke K, Jeruss J, Scholtens D, Khan SA. Association between recency of last pregnancy and biologic subtype of breast cancer. Ann Surg Oncol. 2012;19(4):1167–73.

Publisher's Note