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Structural Determinants of Childbearing Challenges in Breast Cancer Survivorship: A Systematic Review

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Abstract

Objectives: A growing number of women of reproductive age are battling breast cancer. The younger the age of the breast cancer, the more aggressive gonadal toxic treatments are needed. A large number of younger women with breast cancer are childless and plan to become pregnant after treatment. Thus, this study aimed to understand the structural determinants of health associated with the challenges these women face as they navigate childbearing after breast cancer treatment.

Methods: PubMed, Scopus, Embase and Web of Science were searched up to July 2024. The review was preregistered (PROSPERO: CRD42024502269). We used "Newcastle-Ottawa Scale" for risk of bias assessment of studies.

Results: A total of nine studies met the inclusion criteria. They were all of high quality and had little chance of being biased. Breast cancer survivors' reproductive choices and childbearing are influenced by a number of structural determinants of health. These determinants include age, education level, socioeconomic status, housing, race, and ethnicity. Since age was a determinant in seven of eight studies reviewed (the lower the age, the greater the childbearing intention, fertility preservation, counseling, and pregnancy attempt), age appeared to be a more significant and influential factor.

Conclusions: This review analysis revealed a connection between the reproductive practices of surviving women and the structural determinants of health and fertility. Reproductive-aged women who have struggled with this condition in the past may face various difficulties because of their fertility problems. Therefore, it seems beneficial to understand these factors and develop strategies to address these obstacles. This will allow these women to live a happy and hopeful life.

Keywords: Social determinants of health, Structural determinants, Breast cancer, Survivorship, Childbearing, Reproductive behavior

Introduction

Breast cancer is the most common cancer in women worldwide, and is increasingly growing all around the world (1). Approximately 2.3 million new cases of breast cancer and 685 000 deaths from the disease were reported in 2020 (2). Breast cancer is also the most common cancer affecting Iranian women (3)

The incidence of breast cancer in women of reproductive age is increasing (4). According to National Cancer Institute surveillance data, 2.7% of breast cancer cases occur in women under the age of 35 (5). Evidence has shown that the younger the age of the breast cancer, the more aggressive gonadal toxic treatments are needed.

The global trend of delaying motherhood among young women has increased the number of young women diagnosed with breast cancer. This has led to a growing number of younger women with breast cancer who are childless and plan to become pregnant after treatment (6,7). In fact, young women who have survived breast cancer face a variety of health and life challenges related to fertility and motherhood (8-10). Accordingly, it is critical to focus on the factors that influence childbirth and infertility in breast cancer survivors.

Much attention is now being paid to the non-medical aspects of health decision making (11). The environments where people are born, grow, live, and work are known as social determinants of health. These determinants fall into two categories in the World Health Organization model: health-determining structural factors and mediating factors (12). Health inequalities are unfair and avoidable differences in health status that occur both within and between countries. The social determinants of health play a major role in these disparities. In countries with all income levels, health and disease follow a social gradient: the lower the socioeconomic condition, the worse is the health (12).

Factors that determine an individual's social class, including education, occupation, income level, ethnicity, and religion, are referred to as the structural determinants of health. These elements are sometimes referred to as

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societal determinants of health inequities (13).

A review of the literature shows that childbearing intention is associated with various parameters, including age, education, socioeconomic status, and occupation (14-16). According to a comprehensive review, the main structural characteristics associated with childbearing include education, occupation, income, culture, and ethnicity (17).

Income, education, improper housing, unemployment, racial discrimination, social support, and social network are the most important social determinants of health. All of these determinants have been studied concerning breast cancer incidence, stage of diagnosis, and survival (18). In fact, these factors have been shown to influence breast cancer risk (19). Based on literature reviews, factors such as socioeconomic status, race, education, poverty as measured by the census, and availability of preventative care and health insurance affect breast cancer survival rates (19).

No systematic review of the social determinants of health has hitherto been conducted to investigate the challenges of childbearing after breast cancer. Accordingly, the present study was conducted to determine the relationship between structural social determinants and childbearing among breast cancer survivors. This review was motivated by the importance of social determinants of health, such as structural factors of childbearing, especially in the breast cancer survivors.

Finding the relationship between the structural determinants of health and childbearing in women who have survived breast cancer is the main objective of this research.

Materials and Methods

The protocol of this systematic review was pre-registered in PROSPERO (CRD42024502269) and follows the reporting guidelines detailed in the PRISMA statement.

Sources Reviewed

For our review, we used the major databases and platforms such as PubMed, Scopus, Embase, and Web of Science.

Search Approach

The search strategy used in this review was based on the keywords obtained from the Medical Subject Headings (MeSH) thesaurus and Emtree in Embase. These keywords included "Breast Cancer", "Breast Neoplasms", "Breast Tumors", "Mammary Cancer", "Social Class", "Social Gradients", "Socioeconomic Status", "Social Inequality", "Ethnic Group", Racism, "Racial Discrimination", "Income Distribution", "Income Generation Programs", "Social Norms", "Reproductive Behavior", "compulsory fertility control". Moreover, non-Mesh and non-Emtree terms like "breast cancer survivorship", "survived breast cancer", "breast cancer, "childbearing desire", and "childbearing intention" were used. The Boolean operators of "AND" and "OR" were used to combine these terms. The latest search was done on July 2024

Inclusion Criteria

The inclusion criteria were as follows:

- Observational studies (cross-sectional, cohort, case-control) English articles
- Breast cancer survivors
- 20-45-year-old women
- History of chemotherapy or radiotherapy (gonad toxic treatment)
- Completed treatment

Exclusion Criteria

- The results obtained from theses, article summaries, and articles presented in conferences and websites
- Review articles, qualitative studies, interventional studies, case reports, case studies, and case series that were not suitable for the purpose of the study
- Studies in languages other than Persian or English
- Women newly diagnosed with breast cancer - Women who were not in the re-productive age group or were older than 45 of age
- Suffering from other types of cancer

Study Selection Process

Initially, duplicate citations were eliminated and all obtained publications were uploaded into the End Not program. Then, during the screening phase, titles and abstracts that were unrelated to the references were eliminated. Two authors then independently reviewed the entirety of the remaining references in accordance with the qualifying requirements

Data Extraction

Following full text review, data extraction was performed according to a checklist. The checklist included study characteristics such as first author, title, date of publication, design and sampling method, country, sample size and statistical analyses, instruments and questionnaire, and results. Two authors independently completed this step, and a third author resolved any discrepancies.

Quality Assessment

We utilized the New-Castle-Ottawa tool, which assesses the quality of cohort and cross-sectional studies, to determine the risk of bias in the included studies (20,21). The NOS evaluates cohort studies in three domains of selection, comparability, and outcome by asking nine specific questions. The scoring of this tool is determined by the creation of nine different questions: Studies with 3 or 4 stars in the selection domain, 1 or 2 stars in the comparability domain, and 2 or 3 stars in the outcome domain are of good quality. If studies receive 2 stars in the selection domain, 1 or 2 stars in the comparability domain, and 2 or 3 stars in the outcome domain, they are

considered to be of fair quality. Studies with 0 or 1 star in the selection domain, 0 stars in the comparability domain, and 0 or 1 star in the outcome domain are considered to be of poor quality (21). If the study received 2 stars in the selection domain, 1 or 2 stars in the comparability domain, 2 or 3 stars in the outcome domain, it was considered to be of good quality. If the study received 0 or 1 star in the selection domain, 0 stars in the comparability domain, 0 or 1 star in the outcome domain, it was considered to be of poor quality. The NOS for a cross-sectional study evaluates three domains of result, comparability, and selection, using eight different questions. With the exception of the comparability parameter, where each item can receive up to two stars, each question on this scale receives one star. Thus, the maximum score for studies was calculated to be 9, and studies with an estimated score of less than 5 stars were considered to have a high risk of bias or low methodological quality (22,23)

Results

Study Characteristics

Systematic searches retrieved 7449 articles (PubMed = 2679, Embase = 1262, other sources = 20, Scopus = 1579, Web of Science = 1872). After deletion of duplicate references (n = 4351), 3006 references remained for title and abstract screening to specify their compliance with the inclusion criteria. Consequently, 153 articles were reviewed for eligibility criteria. At this stage, 39 references due to unrelated community, 41references due to inappropriate design and method (review, qualitative, interventional, etc), 40 studies due to not addressing the main outcome of the study, and 24 studies due to the unavailability of the full text of the article were deleted. Subsequently, 9 references were included and investigated with regard to the relationship between structural determinants of health and childbearing in breast cancer survivors. The study selection and identification process is illustrated in the provided flowchart (Figure 1).

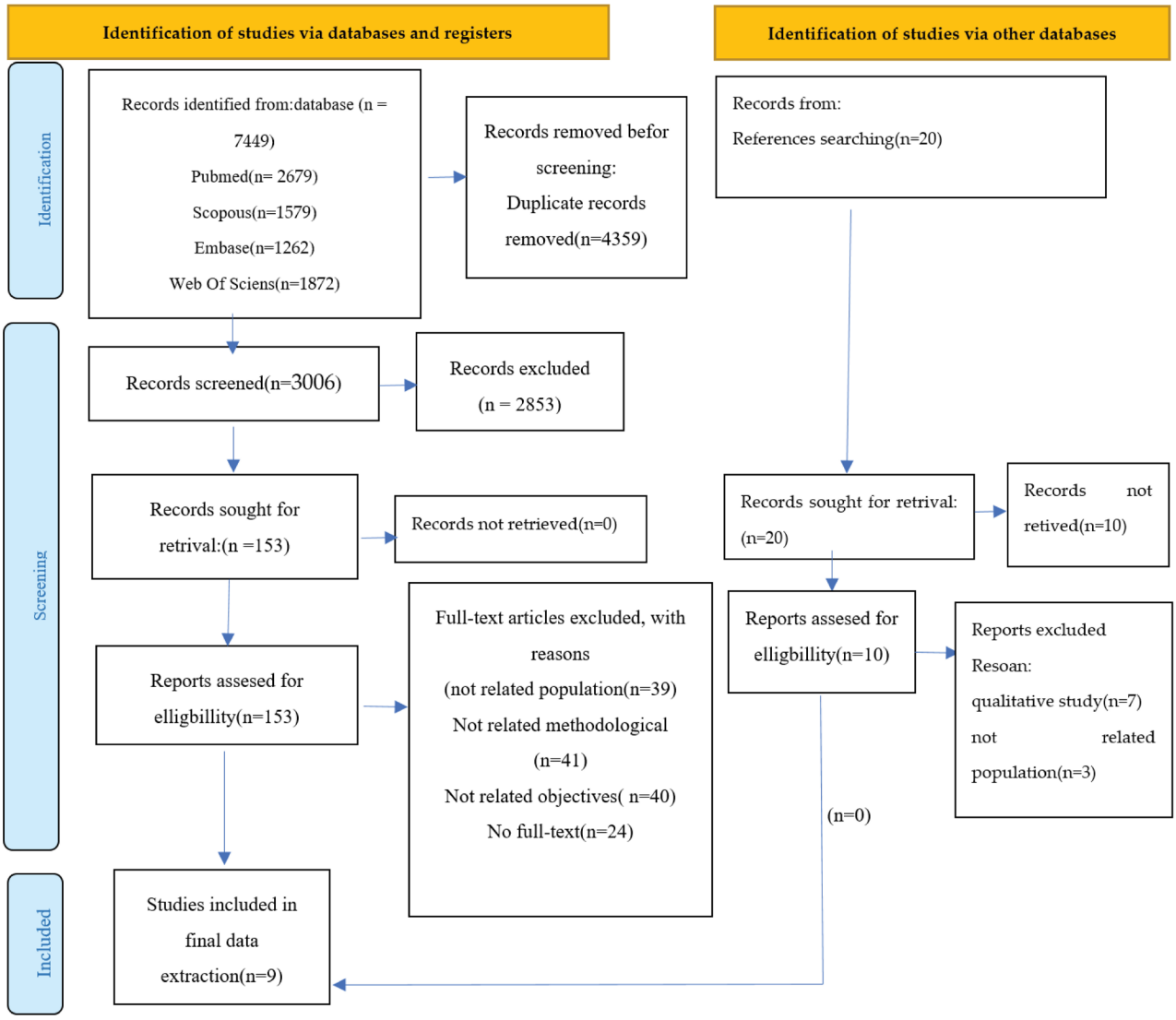

Figure 1. Flow Diagram of the Selection Process of Included Studies.

General Characteristics of the Selected Studies

Four cohort studies (24-27) and five cross-sectional studies (28-32) were included in this systematic review. Of these 9 studies, 5 studies were conducted in the United States (24,26,28,30,31), one study in California and Texas (29), one study in Taipei (25), one study in Portuguesa and USA (32), and one in France (27). The total sample size was 3,757 and the age of the participants varied from 20 to 45 years (Table 1).

Risk of Bias

The quality assessment of 4 studies was done using Newcastle-Ottawa for cohort studies. All four studies were of good methodological quality (24-27). Five cross-sectional studies included in this review were qualitatively assessed using the Newcastle-Ottawa Scale for cross-sectional studies. All five studies were of good methodological quality (28-32). The details of scoring articles are shown in Tables 2 and 3.

Structural Determinants of Childbearing in Breast Cancer Survivors

Age

Eight studies examined the relationship between fertility and childbearing age. The results of 6 studies indicated a significant association between age and childbearing. All showed that the lower the age, the greater the childbearing intention, fertility preservation, counseling, and pregnancy attempt (4,14,27,29,31,32). Two other studies found no statistically significant association between age and childbearing (24,30).

Education

Three of the nine studies that examined the relationship between education and childbearing found a significant relationship between these two factors (4,24,26).

Place of Residence

Only two studies examined the relationship between place of residence and reproduction, and both showed a significant relationship between these two factors (28,32).

Income/Socioeconomic Status

The association between childbearing and socioeconomic status was examined in three different studies and found to be significant in each (26,30,31).

Race and Ethnicity

The relationship between race/ethnicity and childbearing was also investigated in our study. There was a strong association between childbearing and race/ethnicity in two studies (28,32), and a non-significant association in two others (26,29). Table 4 shows the structural determinants of childbearing among breast cancer survivors.

Discussion

The aim of this study was to identify the structural factors that influence childbearing in women who have survived breast cancer.

Only nine studies were eligible for inclusion. What was fascinating, however, was that each study was of high quality and considered reasonably robust. Challenges of childbearing in women who have survived breast cancer were not specifically addressed in any of these studies. Thus, we also analyzed and included articles that addressed the topics of fertility and reproductive problems in breast cancer survivors.

According to this systematic review, age is one of the structural determinants of childbearing and fertility problems among women who have survived breast cancer. The majority of the studies found that unmet requirements for reproductive knowledge, pregnancy attempts, and fertility intentions increased with age. In fact, given the high caliber of these studies, it appears that women's age plays a major role in the difficulties associated with childbearing in this demographic factor. For this reason, young women are more receptive to information on fertility and attempting to conceive, since they are more likely to have not yet had the number of children they desire or have not completed their family.

Consistent with the results of this study, a retrospective cross-sectional analysis of breast cancer patients in their reproductive years by Ju et al found that 35-year-old and younger women had greater reproductive demands (33). However, the study of Dominick et al found that older cancer survivors take longer to recover from their illness and receive treatment. As a result, these younger women are more likely to become pregnant because they are more confident that their treatment will be completed and that their disease will not return (26). According to a systematic review that looked at fertility problems in young cancer survivors, older breast cancer survivors who are still fertile experience more fertility problems (34).

Education was the third structural factor that affected fertility and childbearing difficulties in breast cancer survivors. The studies included in the analysis showed that higher levels of education were associated with fewer unmet reproductive requirements and more reports of fertility preservation. The results of a cross-sectional study by Gorman et al indicated that one of the significant predictors of depression and reproductive concerns among cancer survivors was their educational level. Levels of depression and reproductive anxiety decrease with educational attainment (35). However, in the study by Kim et al, there was no correlation between educational attainment and the use of reproductive health services (36).

According to this comprehensive research, breast cancer survivors' reproductive and childbearing outcomes are also influenced by their housing and economic status. In the retrospective study of Paunescu et al, habitat

Table 1. Characteristics of Studies Included in the Synthesis (n = 9)

Author	Type of Study & Sampling Method	Location	Sample Size & Statistical Tests	Instruments	Main Results	Quality Assessment NOS Score
Chin et al (24)	Cohort, available sampling	Atlanta	1282, Bivariate and multivariate logistic model test	Self-designed questionnaire	Education level is related to not receiving fertility counseling.	7
Martinet-Kosinski et al (27)	Cohort Random sampling	France	575, Pearson's Chi2 and multivariate logistic model test	Self-designed questionnaire	Young age had a positive relationship with fertility preservation	8
Hawkins Bressler et al (28)	Cross-sectional study, available	United States of America	432, Logistic regression test	Self-designed Questionnaire	Young age had a positive relationship with fertility. Fertility issues were more prevalent in Hispanic women, and race was associated with fertility issues	7
Lam et al (29)	Cross-sectional study, available	California and Texas	431, Chi-square statistical test and multivariate regression	Self-designed Questionnaire	Age was related to desire to have children. Ethnicity, race and marital status were not related to desire to have children.	7
Mersereau et al (30)	Cross-sectional study, available	California	237, Statistical test of Pearson's correlation coefficient and regression	Decision conflict scale	Income and education had a significant relationship with decision conflict. Age had no significant relationship with decision conflict. Race, interest in having children in the future had no significant relationship with decision conflict. The elapsed time since diagnosis had no significant relationship with decision conflict.	9
Huang et al (25)	Longitudinal, available	Taipei	151 ,the generalized linear mixed model (GLMM) was used to perform multivariate analysis and evaluate the effect of time and burden of symptoms on fertility intention.	Taiwanese Anderson Symptom Inventory Questionnaire, Fertility Intention Questionnaire,	There was a significant relationship between age and fertility intention.	6
Dominick et al (26)	Cohort, available	California	251, statistical tests of bivariate analysis and binomial logistic regression	Self-designed questionnaire	There was a significant relationship between age, income level and trying to get pregnant (older age and more income, more trying to get pregnant)	6
Vânia Gonçalves, 2018	Cross-sectional study, available	Portugal and the United States of America	102, chi-square, Mann-Whitney U, correlation coefficient	Questionnaire of attitude towards fertility and parenting made by the researcher and obstetric and demographic information	Race and residence were associated with fertility preservation	7
Benedict et al (31)	Cross-sectional study, available	USA	3014, regression and Pearson	Reproductive concerns of cancer survivorships questionnaire, quality of life questionnaire, decisional conflict questionnaire	Age and socioeconomic status were associated with decisional conflict of fertility preservation and unmet fertility preservation informational needs	9

Table 2. Methodological Quality Assessment Through Newcastle-Ottawa Scale (for Cohort Studies)

Study	Selection				Comparability	Outcome			Total Score
	Representativeness of the exposed cohort	Selection of the non-exposed cohort	Ascertainment of exposure	Demonstration that outcome of interest was not present at start of study	Comparability of cohorts on the basis of the design or analysis	Assessment of outcome	Was follow-up long enough for outcomes to occur	Adequacy of follow up of cohorts	
Chin et al (24)	*	*	*	-	**	-	*	*	7
Dominick et al (26)	*	-	*	-	**	-	*	*	6
Huang et al (25)	*	-	*	-	**	-	*	*	6
Martinet-Kosinski et al (27)	*	*	*	-	**	*	*	*	8

* represents one score; ** represents two scores; - represents no score.

Table 3. Methodological Quality Assessment Through Newcastle-Ottawa Scale (for Cross-sectional Studies)

Study	Selection				Comparability	Outcome		Total Score
	Representativeness of the sample	Sample size	Non-respondents	Ascertainment of exposure	The subjects in different outcome groups are comparable, based on the study design or analysis. Confounding factors are controlled	Assessment of the outcome	Statistical test	
Gonçalves et al (32)	*	-	-	**	**	*	*	7
Hawkins Bressler et al (28)	*	-	-	**	**	*	*	7
Lam et al (29)	*	-	*	*	**	*	*	7
Mersereau et al (30)	*	*	-	**	**	**	*	9
Benedict et al (31)	*	*	*	*	**	**	*	9

.represents one score; ** represents two scores; - represents no score *

Table 4. Structural Determinants Health of Childbearing Among Breast Cancer Survivors

Author	Age	Education	Habitat	Income/Economic Statues	Race/Ethnicity
Hawkins Bressler et al (28)	*		*		*
Lam et al (29)	*				×
Chin et al (24)	×	*			
Mersereau et al (30)	×	*		*	×
Huang et al (25)	*				
Benedict et al (31)	*			*	
Gonçalves et al (32)			*		*
Dominick et al (26)	*	*		*	
Martinet-Kosinski et al (27)	*				

The cases where the relationship was found are marked with * and the cases where there was no relationship are marked with ×.

had an impact on the behavior of cancer survivors (37). This suggests that the reproductive behavior of survivors is influenced by their environment. Rodgers Moore demonstrated the impact of household income and socioeconomic conditions on the use of fertility services by reproductive-aged cancer survivors (38). Birth rates among female cancer survivors were found to be independently correlated with socioeconomic class in the study of Hartman et al. (39).

Race/ethnicity was another structural determinant identified in our systematic review. According to the study by Lawson et al, patients in racial and ethnic minority groups had less access to fertility preservation counseling, and race and ethnicity are related to fertility preservation counseling (40).

Conclusions

The results of this comprehensive analysis showed that the structural social determinants of age, education, place of residence, economic status, and race and ethnicity were associated with childbearing intentions among female breast cancer survivors. This study provided a unique perspective on the difficulties faced by childbearing survivors of breast cancer. The findings suggest that, in addition to physical aspects, structural factors that influence social health should be considered by healthcare systems when dealing with breast cancer survivors who wish to have children.

Limitations of the Study

A meta-analysis was not possible because of the significant heterogeneity among the studies included in this review. Furthermore, as mentioned in the previous sections, our comprehensive systematic review found no articles that directly addressed the determinants of fertility preferences among women surviving breast cancer. Therefore, we also included studies that examined factors related to fertility

Directions for Future Research

Given the limited studies conducted on the mediating determinants of fertility preferences among breast cancer survivors, it is recommended that more thorough and extensive studies be conducted in this area. Additionally, during our systematic review, we found that many studies addressing fertility and childbearing in women who have survived breast cancer were qualitative. It is also suggested that researchers conduct systematic reviews of qualitative studies in this area.

Authors' Contribution

Conceptualization: Behjat Khorsandi, Mahrokh Dolatian, Zohreh Mahmoodi.
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Funding acquisition: Mahrokh Dolatian.
Investigation: Behjat Khorsandi, Mahrokh Dolatian, Zohreh Mahmoodi.
Methodology: Hamid Alavi Majd, Behjat Khorsandi.
Project administration: Mahrokh Dolatian
Resources: Behjat Khorsandi, Mohammad Ali Broomand.
Software: Hamid Alavi Majd.
Supervision: Mahrokh Dolatian
Writing–original draft: Behjat Khorsandi.
Writing–review & editing: Behjat Khorsandi, Mahrokh Dolatian, Zohreh Mahmoodi and Leila Asadi.

Conflict of Interests

The authors declared that they have no conflict of interest.

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