Analysis of breast cancer development in young women: An integrative review

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ABSTRACT
Breast cancer is the second most frequent type of cancer in the world and is a global public health problem due to its severity and magnitude, and despite being infrequent in younger women, it has recently been increasing in this age group. Breast cancer in young women stands out for presenting more aggressive histopathological aspects, are usually discovered as advanced disease, presenting worse prognosis and higher mortality rate. Objective: To analyze the scientific production regarding breast cancer in young women. Methodology: This is an Integrative Literature Review in the period from 2009 to 2018, being carried out by means of specific terms in the LILACS and Virtual Health Library databases. Articles that investigated breast cancer in young women were retrieved. Results and discussions: In the selected period, six studies were identified that met the established selection criteria, being four retrospective studies, one analytical-prospective and one did not discriminate the method. It was evidenced that after the year 2014 a deficit of publications with the specific theme, highlighting the need for more updated studies in addition to expanding the exploration of the subject to all geographic regions of Brazil, since the predominant regions in the studies found were the Southeast and South of the country. Conclusion: It is evident the limited exploration of the subject, being necessary to emphasize the need for expansion in scientific production, considering the greater aggressiveness, recurrence and worse prognosis of this disease in younger women.

Keywords: Cancer, Breast, Young Women.

1 INTRODUCTION

Breast cancer is the cancer that most affects women worldwide (PEREIRA, VIAPIRANA, & SILVA, 2017). It is the leading cause of death from cancer in women. Over the decades it has become a global public health problem due to its severity and magnitude (VARGENS et al., 2017). In Brazil, mortality rates remain high, most likely because the disease is still diagnosed in advanced stages. (ALMEIDA et al., 2015)

Breast cancer mainly affects women in perimenopause. However, those who are in full reproductive activity can also be affected (PINHEIRO et al., 2013). The involvement of this type of cancer in young women, i.e., those under 40 years of age, is still considered infrequent, however, it has been showing a slight growth in the country (VARGENS et al., 2017).

According to Pinheiro et al. (2013), the disease has a worse prognosis in young women. When young and diagnosed with the disease, they present an unfavorable prognosis, due to its

genetic instability, unusual pathological characteristics, difficult early diagnosis and high rates of morbidity and mortality, contributing to the greater potential for rapid growth and cell invasion. (SOUZA et al., 2015).

Young women are more vulnerable to advanced diagnosis, justified by the lack of screening actions and difficulty in reading and interpreting monographic results due to high breast density. Another factor that can collaborate is the false perception, by many health professionals, that young women have no risk of developing cancer, devaluing early signs and symptoms of the disease (PINHEIRO et al., 2013).

Therefore, these considerations justify the interest in performing an integrative review on the scientific production on breast cancer in young women for the interpretation of the knowledge produced in the area and with the purpose of helping in the development of future investigations and deepening of the theme.

Thus, the objective of this study was to analyze the scientific production regarding breast cancer in young women.

2 THEORETICAL FRAMEWORK

Breast cancer remains the second most frequent type of this disease in the world (SOUZA et al., 2017). In Brazil, it is the cancer that most affects women, except for non-melanoma skin cancer. In 2017, 57,960 new cases of the disease were estimated and in 2014 the Mortality Information System (SIM) recorded 14,622 cases of deaths in women due to breast cancer, being the leading cause of cancer death in women in Brazil (MIGOWSKI et al., 2018). It affects mainly women over 40 years, however, lately it has been affecting younger and younger women (SOUZA et al., 2015).

Despite being infrequent, breast cancer in young women should be highlighted (ALMEIDA, et al., 2015), because breast carcinomas in young women have more aggressive histopathological aspects and are usually discovered as advanced disease (VARGENS et al., 2017). Almeida et al. (2015) points out that systemic metastases occur in 55.3% of cases in young women and in 39.2% of cases in the elderly group, and the mortality rate in young people is 38% of cases and 33% in elderly women. Breast carcinoma constitutes between 5% and 7% of the cases in young women, presenting a worse prognosis, since, in most cases, the diagnosis is made when the patient is symptomatic and, therefore, has already evolved to a more advanced stage of the disease. Consequently, it is observed a higher mortality rate and lower disease-free survival when compared to patients in the postmenopausal period (PINHEIRO et al, 2013).

Breast cancer is considered the most feared by women, for affecting the perception of sexuality and of the body image itself (PESSOA et al, 2015). Pinheiro et al. (2013) shows that its occurrence causes great psychological, functional and social impact, acting negatively on issues related to self-image and sexuality. Young women suffer a psychosocial impact by the diagnosis and present more depression and worse quality of life than middle-aged women, due to the effects of treatment, being the mastectomy the most used (ALMEIDA, et al., 2015), besides offering great challenges for being in full reproductive and productive activity, in the biological, social and economic point of view, constituting family and consolidating her professional career (VARGENS et al., 2017). Studies suggest that early breast cancer differs from breast cancer at the usual age, regarding the etiology and clinical characteristics (SILVA et al., 2013).

Some histological characteristics of tumors in younger women have already been analyzed. Among the differences observed in relation to older patients, it is mentioned the higher histological grade, with a predominance of grade 3 in women under 25 years (MOURA, SANTOS and PARTELE, 2015), being the infiltrating ductal carcinoma (IDC), according to WHO, the most prevalent type among breast carcinomas, including cancers that affect young patients (SILVA et al., 2013). Also according to Silva et al. (2013), an important predisposing factor to be considered is the increased likelihood of the genetic character of the pathology, mutations in BRCA1 and 2 genes increase in early onset cancers. "Hence the importance of evaluating variables such as the genetic expression of tumors and staging" (PEREIRA, VIAPIRANA AND SILVA, 2017).

As for survival in younger women, there is a worse prognosis due to the aggressiveness of the tumors (SILVA et al., 2013). It is considered a complex disease, which requires painful treatments and generates uncertainties about its cure, causing impact on women's lives (ALMEIDA, et al., 2015). The treatment can combine different therapeutic modalities, associating surgical approach and systemic therapy (VARGENS et al., 2017). In addition to radiotherapy and physiotherapy (SOUZA et al., 2017). The approach to breast cancer treatment in young women is no different compared to older women. However, young women are susceptible to emotional and psychological problems, mainly related to body image arising from surgical treatment (PEREIRA, VIAPIRANA E SILVA, 2017).

Diagnosis at an early stage through screening favors women with better chances of curing cancer, in addition to providing less radical and systemic treatment, leading to a better recovery, faster and with minimal sequelae from the treatment (SOUZA et al., 2017). However, according to Pereira, Viapirana and Silva (2017) there is a tendency for late diagnosis in young women, either due to lower awareness of the physical examination and lower indication for mammography as

higher breast density, hindering the accuracy of mammography. It is essential to train health professionals for health education actions and active search for women prone to develop this disease, showing that early detection is essential for better chances of cure (SOUZA et al., 2017). Silva et al. (2013) emphasize that mammography should be the first imaging technique indicated to evaluate most clinical breast alterations, ultrasonography as the method of choice forevaluation of palpable lesions in women under 35 years of age, and core biopsy as the cheapestand least invasive method to obtain material for histological analysis. Although the incidence ofbreast cancer in developed countries is higher, its mortality is lower due to better efficiency bothin screening and treatment. In Brazil, however, there are still numerous barriers that persist from access to early detection actions to the difficulties of using diagnostic resources and indicated treatments (PINHEIRO et al, 2013).

3 METHODOLOGY

This review included studies on breast cancer in young women, identifying aspects considered relevant. The bibliographic survey occurred in the months from May to July 2018 and focused on studies published in the period from 2009 to 2018 and indexed in the electronic databases LILACS and Virtual Health Library - VHL. The descriptors "breast cancer" and "young women" in Portuguese were used, being combined with the Boolean operator "AND". The search was carried out in both databases. The articles were selected in Portuguese.

The searches resulted in a total of 157 articles containing the descriptors of interest, and 25 articles were excluded for duplicity. To pre-select the articles, the titles were read, and 21 publications were selected to read the abstracts. From these, 6 articles were selected to be read in full, since they met the inclusion criteria: original articles about breast cancer in young women. Case report studies, review studies, epidemiological studies, theses and dissertations were excluded, as well as those whose focus was not limited to investigating breast cancer in young women.

The analysis of the articles was carried out in two stages. In the first stage, data on the location of the article, year, author, objective, sample, and journal of publication were identified. In the second step, the articles were analyzed, and the results were synthesized and discussed.

4 DATA ANALYSIS AND INTERPRETATION

After a careful reading, the sample consisted of six studies developed in Brazil, all of which met the inclusion criteria and were classified according to the type of study. After a careful reading,

the study sample consisted of 06 studies, all developed in Brazil, which met the inclusion criteria and were classified according to the type of study. The selected articles were inserted into a table (Table 1) in order to compare them.

Table 1. Description of articles according to author, year, study type, study period, sample, study site, histological type, staging and phenotype of publications analyzed between 2009-2018 for the present study.

Autor/Ano	Aoki et al.2012	Bacchi et al.2009	Garicoche a et al.2009	Dutra et al.2009	Moura et al.2015	Stival et al.2014
Tipo de estudo	Estudo retrospectivo	Estudo retrospectivo	Estudo retrospectivo	Não descriminou	Estudo analítico prospectivo	Estudo retrospectivo
Período do estudo	1977 a 2007	1997 a 2007	1995 a 2000	Não citou	2001 a 2014	2001 a 2011
Amostra	86 pacientes abaixo 41 anos	315 pacientes abaixo 35 anos	54 pacientes abaixo 40 anos	106 pacientes abaixo 35 nos	40 pacientes abaixo 40 anos	65 pacientes abaixo 40 anos
Local do estudo	São Paulo	São Paulo	Rio Grande do Sul	Minas Gerais, Goiânia, São Paulo	Não citou	Paraná
Tipo histológico	Carcinoma mamário ductal invasor	Carcinoma mamário ductal invasor	Carcinoma mamário ductal invasor	Carcinoma mamário ductal invasor	Carcinoma mamário ductal invasor	Carcinoma mamário ductal invasor
Estadiamento	Grau II	Grau II	Grau II	Grau III	Grau II	Grau II
Fenótipo	Receptor hormonal negativo HER2 não realizou	Receptor hormonal positivo HER2 positivo	Receptor hormonal positivo HER2 não realizou	Receptor hormonal não claro HER2 negativo	Receptor hormonal positivo HER2 não realizou	Receptor hormonal positivo HER2 negativo

When examining the types of methodology most used in these studies, it was found that despite the extensive use of quantitative methods, one study did not discriminate a specific method. It is noteworthy that 4 studies used the retrospective methodological approach, being one case-control and one descriptive, and one with a prospective analytical approach.

Quantitative research works with variables expressed as numerical data and employs rigid resources and statistical techniques to classify and analyze them, due to their greater precision and reliability, they are more suitable for planning collective actions, because their results can be generalized, especially when the samples represent, with fidelity, the population from which they were taken, as for the development in time the retrospective research explores facts of the past,from the current moment to a certain point in the past, several years ago (FONTELES et al, 2009).Of the retrospective studies the one by Aoki et al. (2012) was conducted from 1977

to.

2007, the one by Garicochea et al. (2009) from 1995 to 2000, the one by Bacchi et al. (2009) from1997 to 2007, the one by Stival et al. (2014) from 2001 to 2011 and the prospective one by Mouraet al (2015) from 2001 to 2014. The study by Dutra et al. (2009) did not mention the research period. After the year 2014 there was no publication of articles with the specific theme. These data highlight the need for more updated studies since Abreu et al. (2016) highlights the significant increase in breast cancer in young women and that this is more aggressive, and the treatment is more intense and extensive, reducing the quality of life, which further reinforces the need for more detailed and expansive studies in this field of research.

When checking the sample as a whole, it was found that three studies divided the group of young women under 40 years old, two studies considered under 35 years old, and one under 41 years old. All the articles in their sample separated the groups of young women and those above this previously discriminated age group. Vieira et al. apud Batista et al. (2017) highlights that in recent decades, an increase in the incidence in younger age groups is observed worldwide, emphasizing lifestyle, environmental and genetic factors as risk factors for the development of breast cancer. Souza et al. (2017) also highlights significant incidence in younger age group: 32% from 20 to 40 years.

The data are similar to those of the National Cancer Institute (Inca) - which indicates a tendency for an increase in breast cancer cases in women up to the age of 50. The location of the studies was examined and it was identified that one study was conducted in Rio Grande do Sul, one in Paraná, two in the state of São Paulo, one in the states of Minas Gerais, Goiânia and São Paulo, and the study by Moura et al. (2015) does not cite the location of the database used. The study by Dutra et al. (2009) is the most comprehensive one carried out in the laboratory of the Federal University of Minas Gerais and in hospitals in Goiânia and São Paulo.

The quantity of articles found related to the study of breast cancer in young women presents the predominant regions in the studies, Southeast and South of the country, evidencing the limited exploration of the theme in other geographical regions of Brazil. In a study by Martins et al. (2013), during the period from 1980 to 2011, an increase in breast cancer mortality in women up to 50 years of age was observed, highlighting the difference between regions, with special emphasis on the North, Northeast and Midwest regions, showing a tendency to increase. In the light of a deeper study about genetic characteristics, family history, and behavioral aspects potentially influenced

by regional issues, one must consider that Brazil has enormous diversities among its regions in terms of socioeconomic and cultural aspects that can directly impact health and quality

of life. Inthis study, it was notable the clarity of the objectives of all the articles found, facilitating the reader's understanding.

Another result obtained is regarding the histological types of breast carcinomas identified in the groups of young women, the predominance of the invasive ductal type was found in all the studies analyzed, resembling the study conducted by Pessoa et al. (2015), which shows the characteristics of neoplastic tumors in young patients studied in 2008 and 2009, highlighting that in 87% of them the infiltrating ductal carcinoma was observed, reaching an undisputed majority, similar to data presented by the Ministry of Health, where this was also the most frequent, with a percentage of 68%. According to Pereira, Viapiana and Silva (2017) the predominant histological type was also the invasive ductal carcinoma in 76.9% of cases and in the study by Pinheiro et al. (2013), in which they analyzed 12,689 young women aged up to 39 years in the period from 2000 to 2009, the data showed that invasive ductal carcinoma was prevalent in 90.7% of cases.

Regarding the clinical staging found in young women, there was a dominance of grade II and only the research of Dutra et al. (2009) highlights grade III. This result corroborates Pereira, Viapiana and Silva (2017) in which they demonstrate that the most common clinical stage found in the patients studied, equal to or younger than 40 years, was IIA. These data disagree with the research conducted by Pessoa et al. (2015) in which the breast cancers surveyed in women under 40 years 56.5% were diagnosed in stages III and IV. Thus, young women more often presented advanced clinical staging when compared to older women (PEREIRA, VIAPIANA and SILVA, 2017).

Regarding the assessments of phenotypes in breast carcinomas in young women the results showed most studies with a predominance of hormone receptor positive, only one, Aoki et al (2012), predominated hormone receptor negativity and one study was unclear about the outcome of the hormone receptor assessment.

The study by Moura et al. (2015) performs a comparison between two groups, one under 40 years and one over 40 years, concluding that "There was no significant difference in the occurrence rate regarding the presence of positive Hormone Estrogen Receptor and presence of overexpression of C-erb 2 Mutation between the Groups." Although Moura et al. (2015) cites that there is no difference between the two groups, he does not cite the results to justify this statement. As for the evaluation of HER-2 protein (human epidermal growth factor receptor 2) three studies did not analyze this protein, two studies prevaled HER2 negative in young patients and one, in the study by Bacchi et al. (2009) highlights HER 2 positive and triple negative molecular type as a more frequent trend in young patients.

After the analysis of these studies, it was found that the HER-2 research was deficient in three studies, which weakens the classification of molecular subtypes of breast cancer. This classification is essential because, according to Perruzi and Andrade (2016), breast cancer is a complex disease that has histological and molecular differences responding to different therapies and prognoses.

5 FINAL CONSIDERATIONS

The number of articles found related to the investigation of breast cancer in young women showed the limited exploration of the subject, which is perhaps justified by the lower incidence in this age group compared to older age groups; however, one must consider the greater aggressiveness, recurrence, and worse prognosis of this disease in younger women, besides the fact that there is a gap in the production of knowledge in the North, Northeast, and Midwest regions, drawing attention to the need to expand research on this subject, especially in the regions mentioned.

Considering the aspects of molecular subtypes in the scientific articles studied it was evident the deficiency in the results, reinforcing the need for further research on the phenotype of breast cancers, since breast cancer in young women is increasing progressively and the effectiveness of the diagnosis defines the most targeted treatment, determining the prognosis and improving the treatment with consequent improvement in quality of life. It is concluded that the expansion in scientific production is important to achieve the purpose of providing the knowledge base, which can promote the effectiveness of care.

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