Original article

Clinical-epidemiological characterization of patients under or equal to 40 years old with breast cancer

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Caracterización clínica-epidemiológica de pacientes menores o iguales a 40 años con cáncer de mama

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Abstract
Introduction. Breast cancer is among the first three cancers diagnosed in women worldwide. In women younger than 40 years old it occupies the first place in incidence. About 146 000 new cases are diagnosed globally in women under 40 years old. **Objective.** To identify the epidemiological and clinical characteristics of patients under or equal to 40 years old, diagnosed with breast cancer in a tertiary hospital specialized in women's care. **Methodology.** Descriptive cross-sectional study. Information was collected from 60 clinical records of patients diagnosed with breast cancer with an age less than or equal to 40 years old, between January 2019 and December 2020. **Results.** The highest number of cases was found in women between 39 and 40 years old (18.3 % each). Sixty percent were from the urban area; 80 % of the patients had parity between one and four children; 40 % were overweight and 58 % had no family history of breast cancer. The most frequent clinical stage was IIIA. The most common histopathological diagnosis was invasive breast carcinoma of non-special type (91.6 %), poorly differentiated with positive estrogen and progesterone receptors. **Conclusion.** Women aged less than or equal to 40 years old, with breast cancer, are patients from urban areas, overweight, with one to four children and no family history of breast cancer, with initial clinical presentation in locally advanced stages, with a diagnosis of invasive breast carcinoma of non-special type, poorly differentiated and positive estrogen and progesterone receptors.

Keywords
Breast neoplasms, female, risk factor, epidemiology.

Resumen
Introducción. El cáncer de mama se encuentra dentro de los tres primeros cánceres diagnosticados en las mujeres a nivel mundial. En las mujeres menores de 40 años ocupa el primer puesto de incidencia. Alrededor de 146 000 nuevos casos son diagnosticados en mujeres menores de 40 años a nivel global. **Objetivo.** Identificar las características epidemiológicas y clínicas de las pacientes con edad menor o igual a 40 años con diagnóstico de cáncer de mama en un hospital de tercer nivel especializado en la atención de la mujer. **Metodología.** Estudio transversal descriptivo. Se recolectó información de 60 expedientes de pacientes con diagnóstico de cáncer de mama con edad menor o igual de 40 años diagnosticados entre enero 2019 y diciembre 2020. **Resultados.** El mayor número de casos se encontró en las mujeres entre 39 y 40 años (18,3 %, cada uno). El 60 % era del área urbana; el 80 % de las pacientes tenía una paridad entre uno a cuatro hijos; el 40 % de se encontraba con sobrepeso y el 58 % no tenía antecedentes familiares de cáncer de mama. El estadio clínico más frecuente fue IIIA. El diagnóstico histopatológico más común fue carcinoma de mama invasivo de tipo no especial (91,6 %), pobremente diferenciado, con receptores para estrógeno y progesterona positivos. **Conclusión.** Las mujeres con edad menor o igual a 40 años, con cáncer de mama, son pacientes procedentes del área urbana, con sobrepeso, con uno a cuatro hijos y sin antecedentes familiares de cáncer de mama; con presentación clínica inicial en etapas localmente avanzadas, con diagnóstico de carcinoma de mama invasivo de tipo no especial, pobremente diferenciado y receptores para estrógeno y progesterona positivos.

Palabras clave
Neoplasias de la mama, mujer, factor de riesgo, epidemiologia.

Introduction

Breast cancer is one of the best-known malignancies. It is among the first three cancers diagnosed in women in both developed and developing countries[1,2]. Despite high incidence rates, the five-year survival of women diagnosed with breast cancer is about 90 % in developed countries[3]. Advances in treatment and early detection, have decreased breast cancer mortality in all age groups, nevertheless for women of younger age it remains a risk factor for lower survival worldwide[4].

According to the Global Cancer Observatory[2], about 247 953 new cases of breast cancer were detected in 2020 in women under 40 years old globally[2]. The trend of breast cancer in young women is variable in different parts of the world. In women under 40 years old, breast cancer ranks first in incidence worldwide at 27.9 %, and third in women under 30[2,4]. The age-standardized incidence in women under 40 years old is slightly higher in developed countries (8.8) than in developing countries (5, 4)[5]. The lowest rates of breast cancer in young women are from East and Southern African countries, while the highest rates are from Europe and North America[4,5].

In the Latin American and the Caribbean region a total of 210 100 cases of breast cancer was registered in 2020, representing 9.3 % of the total number of cases in the world. Breast cancer in women under 40 years old in this region accounts for 25.8 %, and ranks first among all cancers in this age group[2,4].

By the year 2020, breast cancer cases in El Salvador represented 16.4 % of all cancers, at an incidence rate of 40.5 cases per 100 000 inhabitants[2]. From data obtained in a study conducted in the country in 2018, it was evidenced that the incidence of breast cancer in women under 40 years old amounted to 13.1 %[6].

Early breast cancer has a low incidence compared to breast cancer in postmenopausal patients and is associated with a more aggressive clinical presentation, delayed diagnosis due to low suspicion of malignancy at the time of clinical assessment, and poorer treatment outcomes[7,8].

Between 2019 and 2020, the National Women's Hospital admitted 392 patients diagnosed with breast cancer. Of these, 60 patients were women under the age of 40 years, and were in advanced localized clinical stages with histologically aggressive subtypes, which can compare with international results in this age group.

This study allows to know the epidemiological and clinical characteristics of patients under 40 years old diagnosed with breast cancer in a third level hospital specialized in women's care, during the years 2019 and 2020, in order to contribute to early diagnosis, which is the basis for adequate treatment.

Methodology

A descriptive cross-sectional study was conducted at the National Women's Hospital, a tertiary health care facility specializing in women's care, in San Salvador. Sixty patients with breast cancer were identified through the review of clinical records, in the period from January 2019 to December 2020.

Inclusion criteria were: patients aged 40 years or younger, seen for the first time in the breast or oncology service, diagnosed with breast cancer for the first time, with histopathology and immunohistochemistry report. Exclusion criteria were: patients with non-primary breast cancer and clinical records with incomplete information.

The variables included in the study were: age, marital status, schooling, area of origin, age at menarche, parity, age at first birth, lactation time, body mass index (BMI), family history, initial clinical stage, histopathologic outcome, degree of histologic differentiation and molecular classification.

With the support of the Department of Statistics and Medical Documents of the National Women´s Hospital, the clinical records of the patients included in the study were reviewed. Data collection was carried out by the researcher using a digital data collection form, previously designed based on the identified variables, using the Microsoft Forms application. Each form could only be viewed by the researcher, to guarantee the confidentiality of the patients' data. The data from each document were analyzed with the Microsoft Excel program, through measures of central tendency and expressed through tables and graphs.

The research complied with the ethical principles established in the Declaration of Helsinki. The clinical records for data collection were used within the hospital facilities. With the data obtained, a database was created without identifying the patients' names, using only the file number, which was managed solely by the researcher.

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Results

Epidemiological profile

71.6 % of the patients diagnosed were over 34 years old. The most frequent ages were 39 and 40 years with 18.3 % each. The youngest patient diagnosed with breast cancer was 25 years old (Figure 1).

The geographical distribution of the patients showed that 60 % were from urban areas. The marital status of free union represented the highest percentage (41.6 %), followed by married women (35.0 %) and single women (23.4 %).

The average age of menarche in the patients was 12 years in 30 %; 10.0 % at 11 years and 1.7 % at 16 years. 85 % of the patients had at least one child; one was gestational and only 13.3 % were nulliparous (Figure 2). The 3.3 % reported breastfeeding for a period

between six months and one year; 28.3 % between one and two years; 10 % for more than two years and 1.6 % did not breastfeed.

The nutritional condition of 33 % of the patients was obese: 20 % were obese grade I, 8 % were obese grade II, and 5 % were obese grade III. 40 % were overweight and 27 % were of normal weight.

Fifty-eight percent of the patients reported no family history of breast cancer; 8.3 % reported having this history in a first-degree relative; 11.6 % in second-degree relatives and 1.6 % with a third-degree relative. 20 % of the women did not specify this data.

According to staging by clinical examination and TNM[9], patients were classified as stage IA (3.3 %), IIA (11.6 %) and IIB (20 %). 30 % were stage IIIA, 26.6 % were stage IIIB, 3.3 % were stage IIIC and 5 % were stage IV (Figure 3).

The most frequent histological type of cancer was non-special type invasive breast carcinoma (91.6 %), followed by 5 % of carcinoma with apocrine differentiation; invasive lobular carcinoma with 1.7 %, and carcinoma with medullary pattern with 1.7 % (Figure 4).

According to the degree of histologic differentiation, 48 % were poorly differentiated (grade 3), 42 % moderately differentiated (grade 2) and 10 % (grade 1) well differentiated.

Regarding the molecular subtype obtained by immunohistochemistry tests, 40 % were reported as luminal B, 37 % as triple negative, 15 % as HER2/Neu receptor positive, and 8 % as luminal A (Figure 5).

Discussion

Recent studies describe that the diagnosis of breast cancer in patients under 35 years old increases the risk of death by 5 % per year[7], which has led to study the epidemiological and clinical characteristics of breast cancer in patients 40 years old or younger, who are considered young patients[4,7]. The patients presented mainly locally advanced clinical stages, with histological diagnosis of non-special type invasive breast carcinoma, poorly differentiated and positive estrogen and progesterone receptors.

In a study conducted at the Cancer Institute of El Salvador in 2018, it was evidenced that breast cancer is diagnosed more frequently in women after the age of 50 years (62.5 %), with a low frequency in women between 20 and 39 years (13.1 %), but a significant increase of this disease is observed from the age of 40 years (8.1 %) and 45 years (16.3 %)[2,6].

The results of this research are related to the findings of the Cancer Institute of El Salvador, since a low incidence is reported in younger patients and an increase is presented after 35 years of age with a higher frequency in women between 39 and 40 years old, which is evidence of the exponential incidence of breast cancer.

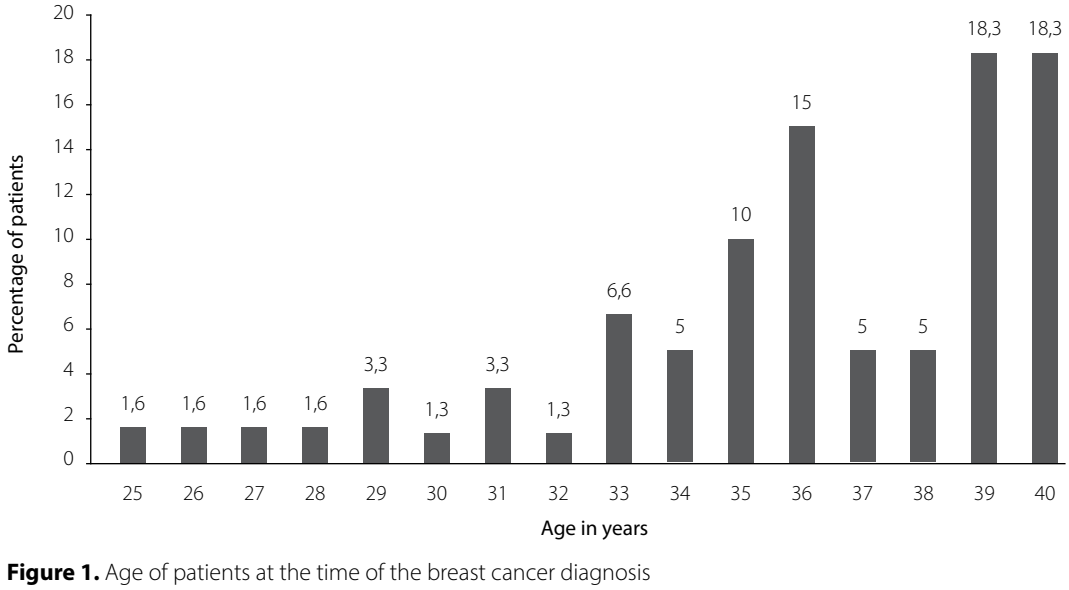

Figure 1. Age of patients at the time of the breast cancer diagnosis

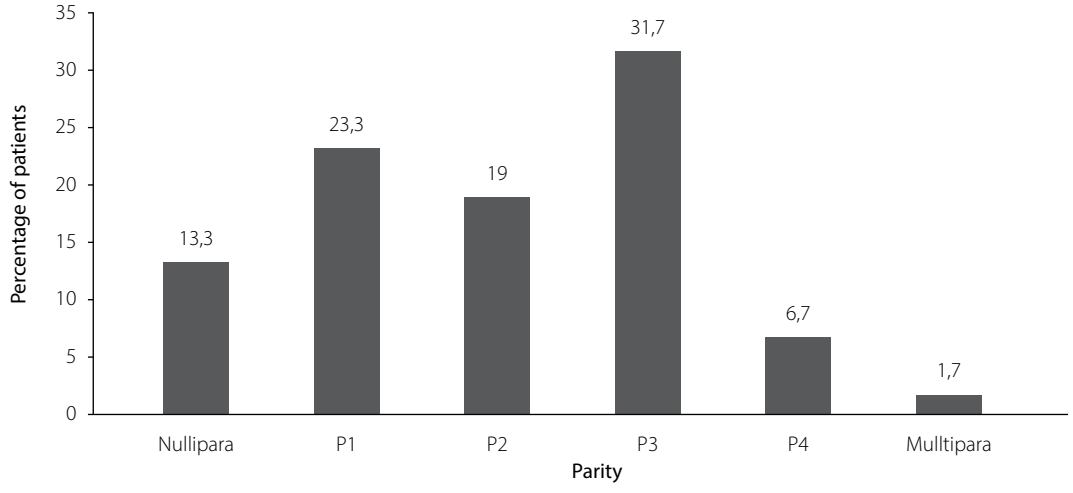

Figure 2. Population distribution according to parity

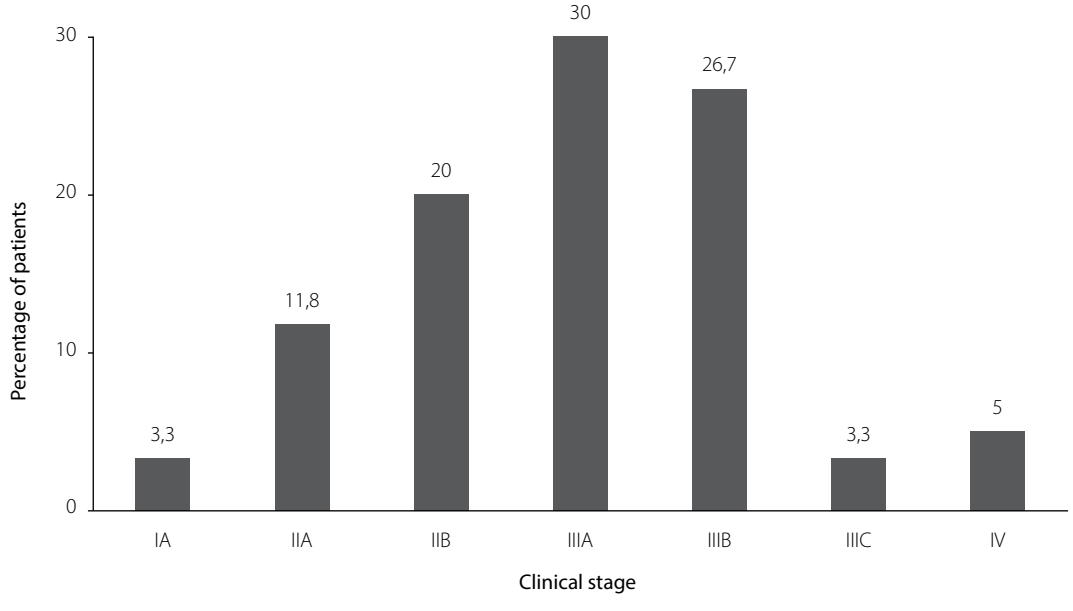

Figure 3. Population distribution according to breast cancer clinical stage at the time of diagnostic

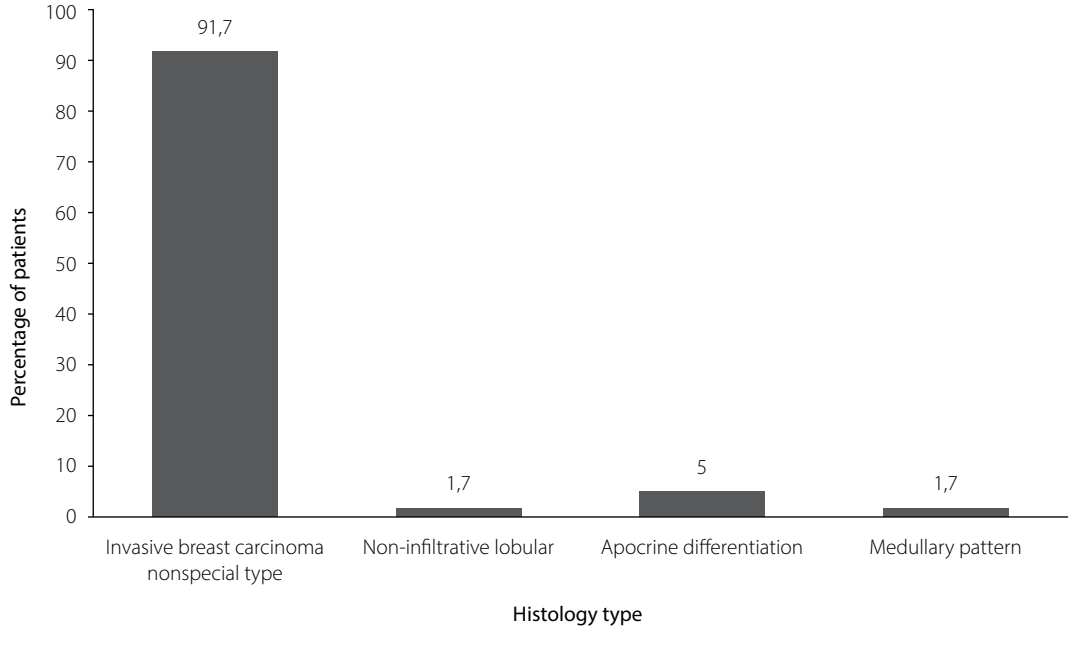

Figure 4. Distribution according to histology type of population under study

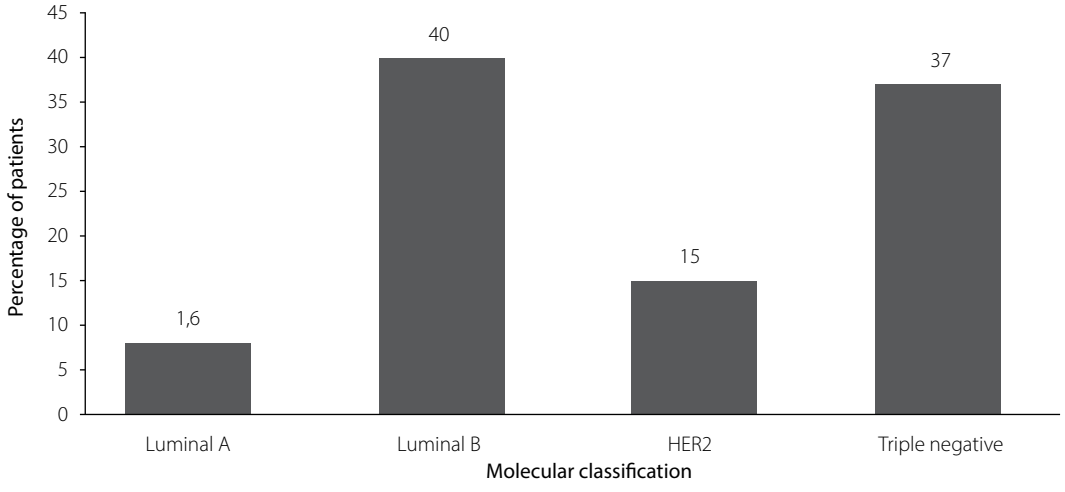

Figure 5. Frequency of determined molecular subtypes according to immunohistochemistry

Most of the patients come from urban areas. This may be related to the place where the study was conducted, given that 70.9 % of the population of San Salvador is from urban areas[10]. However, the delay in diagnosis may be related to the waiting time between the patient's identification of the condition and the request for medical attention[11], i.e., patients are diagnosed at more advanced stages and more aggressive treatments are necessary.

Among other factors related to breast cancer, hormonal stimulation has a great influence; therefore, the age of menarche is an important factor[12]. It is estimated that the risk of breast cancer decreases by about 9 % for each year of delay in menarche[12,13]; in the population studied, it was observed that the highest percentage of patients had menarche at an average age between 12 and 13 years.

The American Cancer Association has reported that having children before the age of 30 decreases the incidence of breast cancer[3]. In fact, there is considered to be a 3 % risk reduction for each full-term pregnancy a woman has and there is a 5 % increased risk for each year of delay in the first full-term birth[3,12]. Similarly, for each year of cumulative breastfeeding, the risk of breast cancer is reduced by 4.3 %[1,13]. It can be observed that, in spite of being young patients, most of them had between one and four children; more than 50 % of the patients were under 30 years old. Twenty-eight percent breastfed between one and two years. The presence of all these protective factors in the group of patients differs from the data obtained in some developed countries due to cultural differences[7,14,15]. In Latin America, the fertility rate is higher as patients are younger[16].

Family history in young patients is the main risk factor for breast cancer, especially when diagnosed in a first-degree blood relative at an early age[1,14]. The findings in this study differ from that premise, as 58 % of the patients had no family history of breast cancer.

Recent studies have shown that overweight is one of the main exogenous risk factors for breast cancer in both premenopausal and postmenopausal women[17]. A diet high in animal fat from mainly red meat and high-fat dairy shows up to a 50 % increased risk for breast cancer[18].

Excess adipose tissue generates an increased risk of breast cancer through several pathways: increased sex hormone levels through increased aromatase and 17-β-hydroxysteroid dehydrogenase activity, reduced glucose uptake and, therefore, generation of a hyperinsulinemic state. Consequently, there was a reduction in sex hormone-binding hormone (SHBG) levels, increased release of IL-6, TNF-α, leptin and decreased adiponectin[19,20].

In premenopausal patients, physical exercise has been associated with a 23 % reduction in breast cancer risk[12,20]. In this investigation, the highest percentage of patients were overweight and with some degree of obesity.

Based on the TNM21 staging in the initial clinical evaluation, it is evident that advanced localized stages predominate in this group of patients, which present with palpable tumor, this being the main cause of consultation[7,22,23] and with lymph node involvement, both factors related to poor prognosis due to late diagnosis and advanced stages[22,24,25].

Many studies have shown that breast cancer in young patients presents in more advanced stages[26,27], since the low suspicion of this pathology, due to the age of the patients, is one of the main factors in the diagnostic delay[23,28].

The lack of a routine mammographic study in patients younger than 40 years

contributes to this, as it presents more often with a palpable mass than with a screening mammography finding[22,25].

Similarly, in premenopausal patients, imaging studies may be reported with probably benign findings, thus contributing to the delay in diagnosis[23], which is the reason some authors recommend the use of breast tomosynthesis as a more accurate diagnostic method[29,30].

A study conducted at St. Louis Hospital, Missouri, showed that patients under 40 years old had palpable tumors larger than two cm (T2/T3) in 50.4 % and nodal involvement in 44 %[26,28]. A study at Mount Sinai Medical Center, New York, showed that patients younger than 35 years of age had larger tumors, more lymph node involvement (50 % vs. 37 %) and a higher probability of being diagnosed with stage II or III cancer (60 % vs. 43 %) than patients older than 36 years[12].

The most common histological type was invasive breast carcinoma of non-special type in 91.6 % of the studied patients. In a study conducted between 2002 and 2010 at the Central University Hospital in Osijek, Croatia, in which the characteristics of breast cancer in patients under 40 years of age and postmenopausal patients were compared, it was shown that invasive breast carcinoma of non-special type was the most frequent histological type in both groups: 70 % in young patients and 59.8 % in postmenopausal patients[27,31].

In terms of histologic grade, poorly differentiated or grade III tumors were the most common, occurring in 28 % of the patients. This is comparable with the results obtained in the study carried out at the University Clinical Hospital of Valencia, Spain, in which 36.4 % of patients under 35 years old with a diagnosis of breast cancer presented poorly differentiated tumors[7].

At present it is important to classify tumors at the molecular level, since each subtype presents different behavior and aggressiveness. According to the different patterns of gene expression, so will be the impact on prognosis[8,31,32]. Based on immunohistochemical expression according to HER2, estrogen receptor (ER), progesterone receptor (PR) and Ki67 markers, and following the criteria of the St. Gallen International Expert Consensus of 2011, the tumors were classified according to their molecular level. Following the 2011 St. Gallen International Expert Consensus criteria, tumors were classified as triple negative (ER-/PR-/HER2-), HER2 overexpressed, Luminal A (ER+/PR+/HER2-/Ki 67< 14 %), Lu - minal B (ER+/PR+/HER2-/Ki-67 > 14 %)[33,32].

Molecular subtypes in patients younger than 40 years old have been shown to be variable according to the type of population studied[24,34]. The results of the study performed in Valencia, Spain, in which the molecular subtype was compared in premenopausal versus postmenopausal patients, showed that estrogen and progesterone receptor expression was similar in both groups (70 % and 59.3 % premenopausal and 71 % and 68 % in postmenopausal). HER2 overexpression predominated in young patients (28 % vs. 22 %). In contrast, the triple-negative subtype occurred more frequently in postmenopausal patients (16.8 %) than in premenopausal patients (13.5 %)[7].

In a study conducted in Croatia, a higher incidence of triple-negative breast cancer was found in patients younger than 40 years old compared to patients older than 60 (32 % and 10 %, respectively), HER2-positive tumors in both groups without statistical significance (20 % and 24 %). The presence of estrogen and progesterone receptors was higher in patients over 60 years old (67 % and 54 %), compared to 43 % and 44 % in patients younger than 40 years old[35].

In the results obtained, the most common molecular subtype (40 %) was luminal B, a subtype with positive hormone receptors and a high rate of cell proliferation, followed by triple negative, with 37 %. Triple-negative cancer correlates with a shorter survival time[36]. Despite the obtained information on clinical presentation and histopathological report, some files lacked important information on risk, lifestyle, biological and reproductive factors, which became one of the limitations for the research.

Results achieved from this study show the heterogeneity of breast cancer, in terms of its presentation and behavior in this stage group of patients with age less than or equal to 40 years old. It is evident that most of the patients have overweight and obesity as a risk factor, therefore, strategies of food education and promotion of physical activity should be implemented, since they contribute to prevent the development of breast cancer, as these actions are associated to weight loss. This reduces the inflammatory microenvironment, improves antitumor immunity and lowers estrogen levels[20].

The data gathered established that the majority of patients had some conditions that are considered important for reducing the risk of breast cancer: factors such as menarche, parity, breastfeeding period and family history, which suggests studying the genetics of tumors in young women, since BRCA 1 and BRCA 237 gene mutations have

a greater association with breast cancer and occur in a higher percentage in premenopausal patients (3 %) than in postmenopausal patients (6 %)[31,32,36].

Therefore, it is important to strengthen the health system with the accessibility to genetic studies that can be used for this age group of patients, to establish the origin of the disease and to be able to predict the behavior, since these factors directly influence the treatment and prognosis of this group of patients. By knowing the genetic behavior, it will be possible to individualize each case and thus improve the prognosis.

Conclusions

The characteristics of the patients with breast cancer were: patients older than 35 years old, from the urban area, with low schooling, overweight, and without family history of breast cancer; in advanced localized stages; with histological diagnosis of invasive breast carcinoma of non-special type, poorly differentiated and positive estrogen and progesterone receptors.

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References

1. Lee H-B, Han W. Unique Features of Young Age Breast Cancer and Its Management. J Breast Cancer. 2014;17(4):301. DOI: 10.4048/jbc.2014.17.4.301
2. Global Cancer Observatory. International Agency for Research on Cancer. Francia. 2018. Available in: https://gco.iarc.fr/
3. American Cancer Society. Estados Unidos. 2000. Available in: https://www.cancer.org
4. Castro Reyes B. Características del cáncer de mama en la mujer joven. Revista de Senología y Patología Mamaria. 2021;34(2):116-120. DOI: 10.1016/j.senol.2020.06.007
5. Anders CK, Johnson R, Litton J, Phillips M, Bleyer A. Breast Cancer Before Age 40 Years. Seminars in Oncology. 2009;36(3):237-249. DOI: 10.1053/j.seminoncol.2009.03.001
6. Orellana Beltrán JA, Valladares Martínez OM. Caracterización clínica epidemiológica del cáncer de mama en mujeres mayores de 20 años en El Salvador. Alerta. 2021;4(3):126-134. DOI: 10.5377/alerta.v4i3.10952
7. Martínez MT, Oltra SS, Peña-Chilet M, Alonso E, Hernando C, Burgues O, *et al.* Breast Cancer in Very Young Patients in a Spanish Cohort: Age as an Independent Bad Prognostic Indicator. Breast Cancer (Auckl). 2019;13:1-10. DOI: 10.1177/1178223419828766
8. Collins LC, Marotti JD, Gelber S, Cole K, Ruddy K, Kereakoglow S, *et al.* Pathologic features and molecular phenotype by patient age in a large cohort of young women with breast cancer. Breast Cancer Res Treat. 2012;131(3):1061-1066. DOI: 10.1007/s10549-011-1872-9
9. American Society of Clinical Oncology. Cáncer de mama: Estadios. 2022. Fecha de consulta: 25 de enero de 2023. Available in: https://www.cancer.net/es/tipos-de-c%C3%A1ncer/c%C3%A1ncer-de-mama/estadios
10. Estimaciones y proyecciones de población, Urbano-Rural, 1985-2030. Ministerio de Economía. San Salvador, El Salvador. 2009. Available in: https://www.transparencia.gob.sv/institutions/minec/documents/12874/download
11. Martínez-Pérez DC, Gómez-Wolff LR, Ossa-Gómez CA, Hernández-Herrera GN, Rivas-Bedoya Y, García-García HI. Asociación entre retraso en el diagnóstico y estadio clínico avanzado de cáncer de mama al momento de la consulta en cuatro centros oncológicos de Medellín, Colombia, 2017. Estudio de corte transversal. Rev. Colomb. Obstet. Ginecol. 2020;71(2). DOI: 10.18597/rcog.3410
12. Assi H, Khoury K, Dbouk H, Khalil L, Mouhieddine T, El Saghir N. Epidemiology and prognosis of breast cancer in young women. Journal of Thoracic Disease. 2013;5(51):52-58. DOI: 10.3978/j.issn.2072-1439.2013.05.24
13. Brinton LA, Sherman ME, Carreon JD, Anderson WF. Recent Trends in Breast Cancer Among Younger Women in the United States. JNCI: Journal of the National Cancer Institute. 2008;100(22):1643-1648. DOI: 10.1093/jnci/djn344
14. Sofi N, Jain M, Kapil U, Yadav C. Epidemiological characteristics of breast cancer patients attending a tertiary healthcare institute in the National Capital Territory of India. J Can Res Ther. 2019;15(5):1087. DOI: 10.4103/jcrt.JCRT_868_16
15. Bray F, Colombet M, Mery L, Piñeros M, Znaor A, Zanetti R, *et al.* Cancer incidence in five continents. International Agency

for Research on Cancer. Volumen XI. 2021. Available in: https://publications.iarc.fr/597
16. América Latina y el Caribe alcanzará sus niveles máximos de población hacia 2058. Comisión Económica para América Latina. Chile. Available in: https://www.cepal.org/
17. Maleki F, Fotouhi A, Ghiasvand R, Harirchi I, Talebi G, Rostami S, *et al.* Association of physical activity, body mass index and reproductive history with breast cancer by menopausal status in Iranian women. Cancer Epidemiology. 2020;67:101738. DOI: 10.1016/j.canep.2020.101738
18. Brenner DR, Brockton NT, Kotsopoulos J, Cotterchio M, Boucher BA, Courneya KS, *et al.* Breast cancer survival among young women: a review of the role of modifiable lifestyle factors. Cancer Causes Control. 2016;27(4):459-472. DOI: 10.1007/s10552-016-0726-5
19. Cho E, Spiegelman D, Hunter DJ, Chen WY, Stampfer MJ, Colditz GA, *et al.* Premenopausal Fat Intake and Risk of Breast Cancer. JNCI Journal of the National Cancer Institute. 2003;95(14):1079-1085. DOI: 10.1093/jnci/95.14.1079
20. Marco Continente C, Luesma Bartolomé MJ, Santander Ballestín S. Influencia de la actividad física en la prevención, tratamiento antineoplásico y supervivencia de pacientes con cáncer de mama. Revista de Senología y Patología Mamaria. 2021;34(4):220-235. DOI: 10.1016/j.senol.2020.05.011
21. Edge SB, Compton CC. The American Joint Committee on Cancer: the 7th edition of the AJCC cancer staging manual and the future of TNM. Surgicaloncology Official Journal of the Society of Surfical Oncology. 2010;17:1471-1474. DOI: 10.1245/s10434-010-0985-4
22. Gajdos C, Tartter PI, Bleiweiss IJ, Bodian C, Brower ST. Stage 0 to stage III breast cancer in young women. Journal of the American College of Surgeons. 2000;190(5):523-529. DOI: 10.1016/S1072-7515(00)00257-X
23. Lee KA, Talati N, Oudsema R, Steinberger S, Margolies LR. BI-RADS 3: Current and Future Use of Probably Benign. Curr Radiol Rep. 2018;6(2):5. DOI: 10.1007/s40134-018-0266-8
24. Azim HA, Michiels S, Bedard PL, Singhal SK, Criscitiello C, Ignatiadis M, *et al.* Elucidating Prognosis and Biology of Breast Cancer Arising in Young Women Using Gene Expression Profiling. Clinical Cancer Research. 2012;18(5):1341-1351. DOI: 10.1158/1078-0432.CCR-11-2599
25. Hindle WH, Davis L, Wright D. Clinical value of mammography for symptomatic women 35 years of age and younger. American Journal of Obstetrics and Gynecology. 1999;180(6):1484-1490. DOI: 10.1016/S0002-9378(99)70043-8
26. Bharat A, Aft RL, Gao F, Margenthaler JA. Patient and tumor characteristics associated with increased mortality in young women (≤40 years) with breast cancer: Young Women With Breast Cancer. J. Surg. Oncol. 2009;100(3):248-251. DOI: 10.1002/jso.21268
27. Fredholm H, Magnusson K, Lindström LS, Garmo H, Fält SE, Lindman H, *et al.* Long-term outcome in young women with breast cancer: a population-based study. Breast Cancer Res Treat. 2016;160(1):131-143. DOI: 10.1007/s10549-016-3983-9
28. Kroman N. Factors influencing the effect of age on prognosis in breast cancer: population based study Commentary: much still to learn about relations between tumour biology, prognosis, and treatment outcome in early breast cancer. BMJ. 2000;320:474-479. DOI: 10.1136/bmj.320.7233.474
29. Basha MAA, Safwat HK, Alaa Eldin AM, Dawoud HA, Hassanin AM. The added value of digital breast tomosynthesis in improving diagnostic performance of BI-RADS categorization of mammographically indeterminate breast lesions. Insights Imaging. 2020;11(1):26. DOI: 10.1186/s13244-020-0835-2
30. Suleimenova D, Eghtedari M, Rakow-Penner R, Lim V, Ladd W, Ojeda-Fournier H. Breast Cancer in Patients Younger Than 40 Years: Imaging, Assessment, and Management. Contemporary Diagnostic Radiology. 2020;43(18):1-7. DOI: 10.1097/01.CDR.0000695664.82022.6b
31. Anders CK, Fan C, Parker JS, Carey LA, Blackwell KL, Klauber-DeMore N, *et al.* Breast Carcinomas Arising at a Young Age: Unique Biology or a Surrogate for Aggressive Intrinsic Subtypes? JCO. 2011;29(1):18-20. DOI: 10.1200/JCO.2010.28.9199
32. Goldhirsch A, Wood WC, Coates AS, Gelber RD, Thürlimann B, Senn H-J. Strategies for subtypes—dealing with the diversity of breast cancer: highlights of the St Gallen International Expert Consensus on the Primary Therapy of Early Breast Cancer 2011. Annals of Oncology. 2011;22(8):1736-1747. DOI: 10.1093/annonc/mdr304
33. Waks AG, Winer EP. Breast Cancer Treatment: A Review. JAMA. 2019;321(3):288. DOI: 10.1001/jama.2018.19323
34. Lovelace DL, McDaniel LR, Golden D. Long-Term Effects of Breast Cancer Surgery, Treatment, and Survivor Care. Journal of Midwifery & Women's Health. 2019;64(6):713-724. DOI: 10.1111/jmwh.13012
35. Erić I. Breast Cancer in Young Women: Pathologic and Immunohistochemical

Features. ACC. 2018;57(3):497-502 DOI: 10.20471/acc.2018.57.03.13
36. Harbeck N, Thomssen C, Gnant M. St. Gallen 2013: Brief Preliminary Summary of the Consensus Discussion. Breast Care. 2013;8(2):102-109. DOI: 10.1159/000351193
37. Manual de práctica clínica en senología 2019. Sociedad Española de Senología y Patología Mamaria. España. 2019. Available in: https://www.sespm.es/wp-content/uploads/2020/02/MANUAL-SESPM-2019-web-protegido.pdf