ISSN: 2697-3391
Vol. 7 No. 2, pp. 6 – 22, April - June 2024

www.anatomiadigital.org

Frecuencia de las mutaciones en genes brca1 y brca2 y factores de riesgo relacionados con el padecimiento de cáncer de mama en mujeres que asisten al Instituto Del Cáncer Solca

Frequency of brca1 and brca2 gene mutations and risk factors related to breast cancer in women attending the Solca Cancer Institute

[1] Jasmine Estefania Barros Illescas https://orcid.org/0009-0004-6220-3548
Catholic University of Cuenca, Cuenca, Ecuador.
jazmin.barros.99@est.ucacue.edu.ec
[2] Ruth Noemi Carpio Suarez. https://orcid.org/0009-0000-7383-109X
Catholic University of Cuenca, Cuenca, Ecuador.
ruth.carpio.18@est.ucacue.edu.ec
[3] Jonnathan Gerardo Ortiz Tejedor. https://orcid.org/0000-0001-6770-2144
Catholic University of Cuenca, Cuenca, Ecuador.
jonnathan.ortiz@est.ucacue.edu.ec
[4] Andrés Fernando Andrade Galarza. https://orcid.org/0000-0001-5598-8165
Solca CANCER Institute – Cuenca, Cuenca, Ecuador.
toandrade@institutodelcancer.med.ec

Scientific and Technological Research Article
Sent: 12/01/2024
Revised: 09/02/2024
Accepted: 05/03/2024
Published:05/04/2024
DOI: https://doi.org/10.33262/anatomiadigital.v7i2.2979

Please quote: Barros Illescas, JE, Carpio Suárez, RN, Ortiz Tejedor, JG, & Andrade Galarza, AF (2024). Frequency of mutations in brca1 and brca2 genes and risk factors related to breast cancer in women attending the Solca Cancer Institute. Digital Anatomy, 7(2), 6-22.https://doi.org/10.33262/anatomiadigital.v7i2.2979

DIGITAL ANATOMY is an electronic, quarterly journal that will be published in electronic format and has the mission of contributing to the training of competent professionals with a humanistic and critical vision who are capable of presenting their investigative and scientific results to the same extent that positive changes in society are promoted through their intervention.https://anatomiadigital.org
The journal is published by Editorial Ciencia Digital (a prestigious publisher registered with the Ecuadorian Book Chamber with membership number 663).www.celibro.org.ec

ISSN: 2697-3391
Vol. 7 No. 2, pp. 6 – 22, April - June 2024

www.anatomiadigital.org

Palabras claves:
BRCA1, BRCA2, Cáncer de Mama, mutaciones, genes.

Resumen

Introducción: El cáncer de mama ha sido establecido como un problema de salud pública y es el más común a nivel mundial, es una enfermedad heterogénea que consiste principalmente en el crecimiento anormal, multiplicación y proliferación de las células sanas hasta transformarse en un tumor. Los genes BRCA1 y BRCA2 están en estrecha relación, pues son los encargados de inhibir los tumores malignos y una mutación de estos produce este tipo de carcinoma. **Objetivo:** Caracterizar la frecuencia de las mutaciones en genes BRCA1 y BRCA2 en mujeres con cáncer de mama atendidas en el Instituto de Cáncer SOLCA Cuenca en el periodo 2019 – 2023. **Metodología:** El presente artículo está basado en un enfoque cuantitativo de tipo descriptivo no experimental, documental secundario y de corte transversal. La información se recopiló de fuentes secundarias ingresadas en la base de datos del departamento de secuenciación genética del Instituto del Cáncer SOLCA – Cuenca; se elaboró una base de datos mediante el empleo del programa Microsoft Excel y SPSS. **Resultados:** De 188 pacientes con cáncer de mama (correspondientes al 100%), apenas el 4% de casos es debido a una mutación en los genes BRCA1 o BRCA2, con un rango de edad de diagnóstico de 25 a 62 años. **Conclusión:** Los datos recopilados en este estudio determinaron que la frecuencia de las mutaciones en genes BRCA1 o BRCA2 en mujeres con cáncer de mama atendidas en el Instituto de Cáncer SOLCA Cuenca en el periodo 2019 – 2023 es baja. **Área de estudio general:** Medicina (biología molecular). **Área de estudio específica:** Oncología. **Tipo de estudio:** Artículo Original.

Keywords:
BRCA1, BRCA2, Breast cancer, mutations, genes.

Abstract

Introduction: Breast cancer has been established as a public health problem and is the most common worldwide. It is a heterogeneous disease that consists of abnormal growth, multiplication, and proliferation of healthy cells until it transforms into a tumor. The BRCA1 and BRCA2 genes are closely related since they are responsible for inhibiting malignant tumors, and a mutation of these genes produces this type of carcinoma. Objective: To characterize the frequency of mutations in BRCA1 and BRCA2 genes in women with breast

cancer treated at the SOLCA Cancer Institute in Cuenca in 2019 – 2023. Methodology: This article uses a non-experimental descriptive, secondary documentary, and cross-sectional quantitative approach. The information was collected from secondary sources and entered the database of the genetic sequencing department of the SOLCA Cancer Institute. A database was developed using Microsoft Excel and Spss. Results: Out of 188 patients with breast cancer (corresponding to 100%), only 4% of cases were due to a mutation in the BRCA1 or BRCA2 genes, with an age range of diagnosis from 25 to 62 years old. Conclusion: The data collected in this study determined that the frequency of mutations in BRCA1 or BRCA2 genes in women with breast cancer treated at the SOLCA Cancer Institute in Cuenca in 2019 – 2023 is low.

Introduction

Breast cancer (BC) is the most common cancer worldwide; it is a heterogeneous disease, which consists mainly of the abnormal growth, multiplication and proliferation of healthy cells until they become a tumor.(1)Various factors influence the origin of this pathology and include aspects such as: age, early menstruation or late menopause, absence of pregnancies, smoking, family history (genetics), among others.(2).

CM has been established as a public health problem, despite the great advances in medicine, it is the first cause of mortality in women in Latin America and even worldwide.(3). Therefore, in recent years, both the incidence and mortality of breast cancer have been highly prevalent in North America and Northern Europe, while in Southern Europe and Latin America the frequency is at an intermediate level, and in Asia and Africa the frequency is minimal.(4).

In North America, the United States accounts for more than 260,000 cases each year and is responsible for approximately more than 40,000 deaths.(5). On the other hand, in South America, Uruguay leads the list of countries, with 40.1 deaths per 100,000 inhabitants. Continuing the trend, Argentina is ranked second with a mortality rate of 29.5(6).

According to statistical data obtained from Globocan, in Ecuador during 2020, 3,563 cases of BC were diagnosed and more than 29% of them died. At the national level, 1,287

new cases are diagnosed annually, breast cancer represents the first morbidity in women, in addition to that, it produces 3.99 deaths per 100 thousand inhabitants.(7, 8).

The BRCA1 and BRCA2 genes have among their normal functions the repair, transcription and recombination of DNA, due to which they are closely related to this cancer, for the same reason they are responsible for inhibiting malignant tumors and a hereditary mutation of these produces breast cancer.(9).

BRCA1 and BRCA2 are autosomal dominant inheritance. In the female population, it is estimated that up to the age of 70 there is a 50 to 95% risk of acquiring BC due to the mutation of the BRCA1 or BRCA2 gene, while in the male population there is only a 1% risk for developing this malignant neoplasm.(10, 11).

The BRCA1 gene, cloned in 1994 and located on chromosome 17, may be involved in approximately 45% of cases of hereditary breast cancer. Similarly, the BRCA2 gene, cloned in 1995 and located on chromosome 13, may contribute to around 35% of cases of hereditary breast cancer.(12).

Due to the dimension of this public health problem, the objective of this article was based mainly on characterizing the frequency of mutations in BRCA1 and BRCA2 genes in women with breast cancer treated at the SOLCA Cuenca Cancer Institute in the period 2019 - 2023; and is aimed both at the benefit of women suffering from breast cancer, as well as for the health personnel working at SOLCA - Núcleo de Cuenca.

Methodology

This article is based on a quantitative, non-experimental, descriptive, secondary documentary, and cross-sectional approach. The study universe was made up of the set of women with breast cancer who attend the SOLCA Cuenca Cancer Institute, in the period 2019 - 2023. For the entire sample, a full coverage sampling was used, from the records of patients diagnosed with breast cancer due to the mutation in BRCA1 or BRCA2 genes. The information was collected from secondary sources entered into the database of the genetic sequencing department.

The inclusion criteria in this study were records of only female patients diagnosed with breast cancer due to mutations in the BRCA1 and BRCA2 genes; the exclusion criteria were: patients diagnosed with breast cancer due to mutations in other genes, or due to prolonged use of estrogens and hormones, and finally, patients diagnosed with breast cancer outside the period 2019 - 2023. At the same time, the main variables analyzed were chronological age, family history, and finally the production of mutated genes, these being BRCA1 and BRCA2.

A database was created using the Microsoft Excel program and for statistical analysis a database was generated in the SPSS program, as well as descriptive statistics, central tendency measures (mean, median and mode), frequency analysis and cross tables.

Tables were used to present the results and graphs were represented using bars and pie charts.

This article is based on the ethical principles for research with human subjects established in the Declaration of Helsinki Addendum of Taiwan. The data obtained by the researchers were anonymized and coded to maintain the dignity, confidentiality and integrity of the patient at all times; it should be emphasized that the use of the present data is being derived solely for the total benefit of society.

Results

From an anonymized database of 188 patients, corresponding to 100% of the female population studied who presented breast cancer and attended the SOLCA Cuenca Cancer Institute in the period 2019 - 2023, 4% presented a mutation in the BRCA1 or BRCA2 genes, this being the cause of BC, on the other hand, 96% suffer from BC due to other factors (Figure 1). Likewise, through the results obtained from the database of the aforementioned Institution, it was possible to corroborate that the age range of diagnosis for BC due to mutations in the BRCA1 or BRCA2 genes ranges from a minimum of 25 years to 62 years, with an average of 44 years. However, through the bibliographic review carried out previously, it was evident that up to the age of 70, women have a higher risk of suffering from BC due to mutations in the BRCA1 or BRCA2 genes.

In Solca, to determine the degree of CM involvement, Birads 2 mammograms are used to monitor the patient, as the results are usually benign. Similarly, Birads 3 mammograms are performed, where findings are also probably benign, requiring check-ups every 3 months. In the case of diagnosing breast carcinoma, Birads 4 mammography is used, as it reveals some suspicious abnormality and a biopsy is necessary. Birads 5 and Birads 6 classifications, on the other hand, indicate a high degree of suspicion of malignancy or, equivalently, a histologically confirmed lesion.

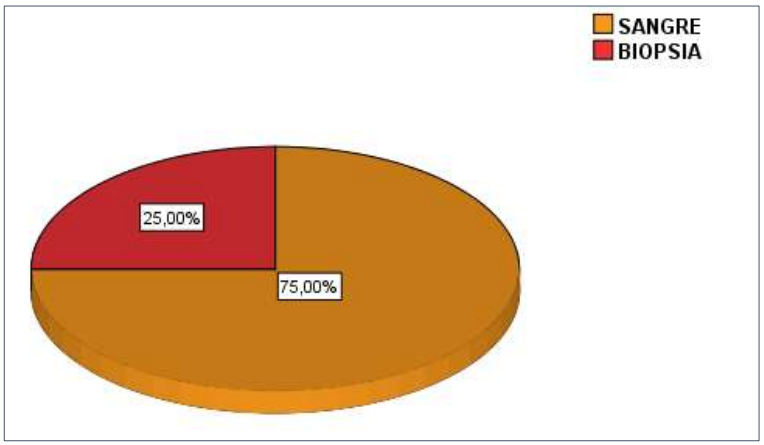
Anatomía Digital
ISSN: 2697-3391
Vol. 7 No. 2, pp. 6 – 22, April - June 2024
www.anatomiadigital.org

Figure 1.*Percentage of female patients with breast cancer who attend the SOLCA Cuenca Cancer Institute in the period 2019 - 2023*

Note: Database (SOLCA - Cuenca)

For a diagnosis of a mutation in the BRCA1 or BRCA2 genes, at the Solca Cancer Institute - Cuenca, a sample is taken, either from blood or from a biopsy; in the case of the present study population, 25% underwent a biopsy and 75% underwent a blood sample (figure 2).

Figure 2. Percentage of sample type performed on female patients with breast cancer due to mutations in BRCA1 or BRCA2 genes who attend the SOLCA Cuenca Cancer Institute in the period 2019 - 2023



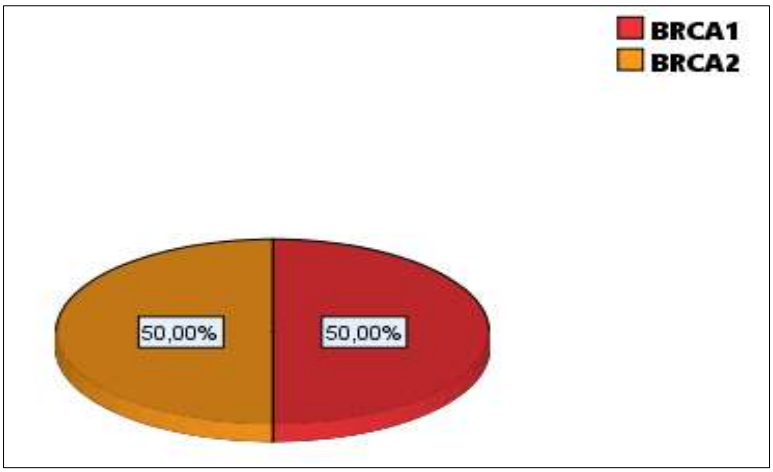
Note: Database (SOLCA - Cuenca)

As can be seen in Figure 3, there is a 50% equality regarding the mutation in the different genes, whether it is BRCA1 or BRCA2, considering that the BRCA1 gene can originate in 45%, while BRCA2 in approximately 35% of breast cancer cases.

Figure 3. Percentage of mutations in the BRCA1 or BRCA2 genes in female patients with breast cancer who attend the SOLCA Cuenca Cancer Institute in the period 2019 - 2023

ISSN: 2697-3391
Vol. 7 No. 2, pp. 6 – 22, April - June 2024

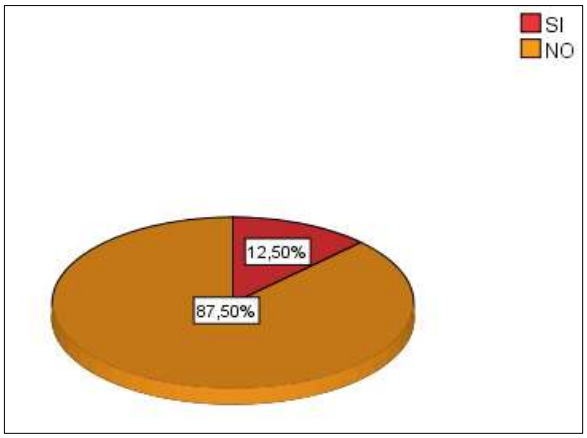
www.anatomiadigital.org



Note: Database (SOLCA - Cuenca)

Regarding CM mortality due to mutations in the genes mentioned, according to our study, it is evident that only 12.50% of the population studied died, and 87.50% managed to survive with adequate treatment (Figure 4).

Figure 4. Mortality rate in female patients with breast cancer attending the SOLCA Cuenca Cancer Institute in the period 2019 - 2023.



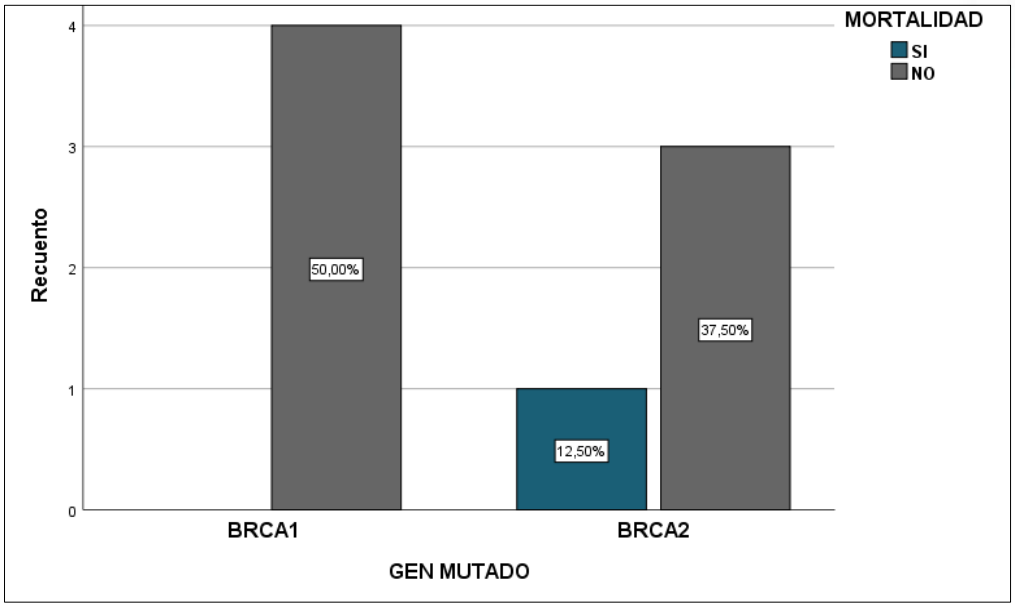
Note: Database (SOLCA - Cuenca)

As previously mentioned, there is a 50% equality regarding the mutation in the different genes. Based on the data obtained, 50% who have BRCA1 survived, and of the other 50% who have BRCA2, 12.50% died and 37.50% managed to survive (Figure 5).

ISSN: 2697-3391
Vol. 7 No. 2, pp. 6 – 22, April - June 2024

www.anatomiadigital.org

Figure 5. Mortality rate in female patients with breast cancer who have mutations in BRCA1 or BRCA2 genes and attend the SOLCA Cuenca Cancer Institute in the period 2019 - 2023



Note: Database (SOLCA - Cuenca)

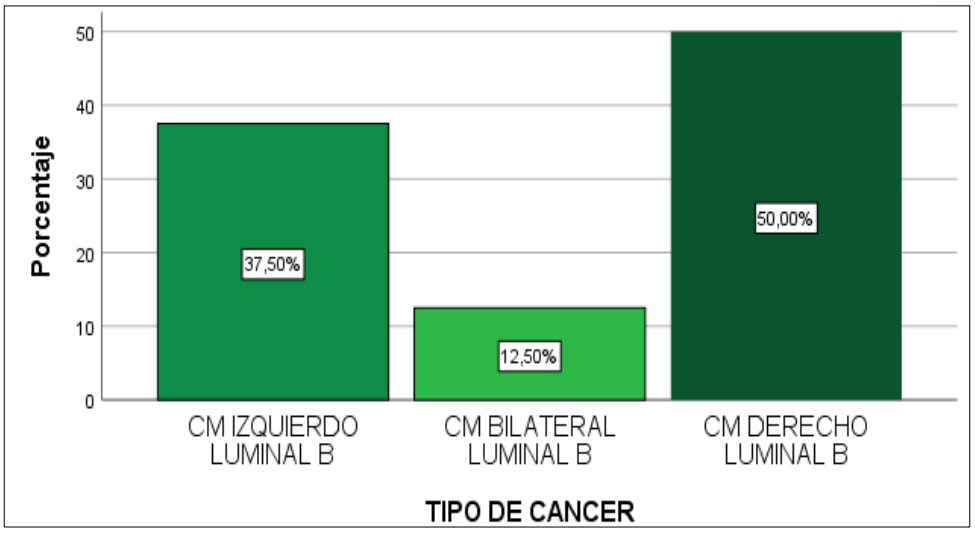
Regarding the frequency of the type of cancer presented by female patients with breast cancer with BRCA1 and BRCA2 mutations who attend the SOLCA Cuenca Cancer Institute in the period 2019 - 2023, it is shown that 37.50% had left luminal B CM, 12.50% bilateral luminal B CM and 50% right luminal B CM (Figure 6), thus demonstrating that bilateral CM is rare.

The relationship between genes and type of breast cancer in the patients studied shows that, on the one hand, 25% of patients with BC due to mutations in the BRCA1 and BRCA2 genes have an infection in the right breast; likewise, patients with a mutation in the BRCA2 gene have an infection in the left breast in 25% of cases, while those patients with a mutation in the BRCA1 gene have an infection in the left breast in 12.50% of cases. Finally, only 12.50% of the population studied with a mutation in the BRCA1 gene have bilateral breast cancer.

ISSN: 2697-3391
Vol. 7 No. 2, pp. 6 – 22, April - June 2024

www.anatomiadigital.org

Figure 6. Frequency of the type of cancer presented in female patients suffering from BC due to mutations in BRCA1 or BRCA2 genes who attend the SOLCA Cuenca Cancer Institute in the period 2019 - 2023



Note: Database (SOLCA - Cuenca)

By analyzing the anonymized database, among the possible risk factors being genetic or hormonal, it was determined that all patients with BC and an affection in some gene (BRCA1 or BRCA2), have relatives from the first to fourth degree of consanguinity who have presented BC and have even died because of it, and at the same time they have presented an early menarche (9 years of age) in 25%, and others have presented a late menarche (17 years of age) in 12.50%.

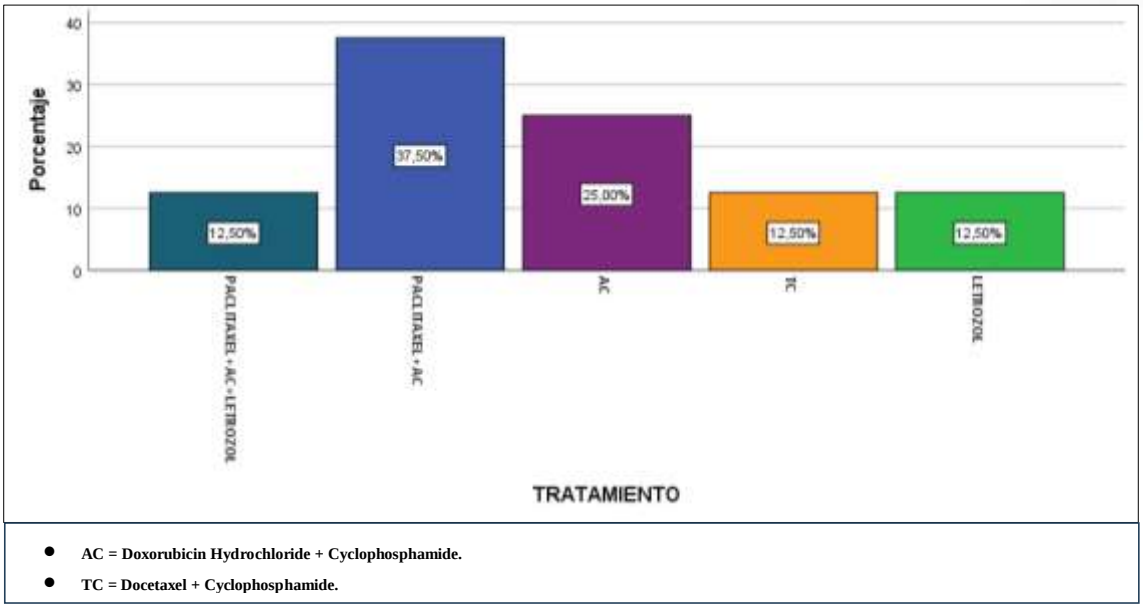
On the other hand, in Figure 7 you can see different types of treatments which will help female patients with CM, the most commonly used being paclitaxel + doxorubicin hydrochloride (Adriamycin) and cyclophosphamide (AC) + Letrozole at 12.50%, paclitaxel + AC at 37.50%, AC at 25%, docetaxel and cyclophosphamide (TC) at 12.50% and Letrozole at 12.50%.

As previously mentioned, treatment for CM will help prevent the spread of cancer cells and prevent a long-term increase in the risk of mortality. Therefore, with the treatments used in the patients, there was no mortality with paclitaxel + AC + letrozole at 12.50%, paclitaxel + AC 37.50%, AC 25%, TC 12.50%. However, with letrozole there was a 12.50% mortality rate.

ISSN: 2697-3391
Vol. 7 No. 2, pp. 6 – 22, April - June 2024

www.anatomiadigital.org

Figure 7. Frequency of treatment in female patients with breast cancer attending the SOLCA Cuenca Cancer Institute in the period 2019 - 2023



- **AC = Doxorubicin Hydrochloride + Cyclophosphamide.**
- **TC = Docetaxel + Cyclophosphamide.**

Note: Database (SOLCA - Cuenca)

Discussion

In SOLCA, blood or a biopsy of the affected patient can be used, and through this type of sample, immunohistochemical studies are performed to determine the presence or absence of cancer cells. If cancer cells are present, a massive gene sequencing study (NGS) is performed.(15,16)In the present data analysis, all patient samples underwent NGS to determine the type of mutation, which could be BRCA1 or BRCA2.

In the present study, mutations in the BRCA1 and BRCA2 genes that cause BC are rare, since of the 188 patients only 4% have a mutation in the genes in question, and the presence of both BRCA1 and BRCA 2 are equal in 50%. In Mexico, a case-control study of breast cancer was reported from 12 hospitals in three cities, where 810 blood samples were obtained from women with cancer, of which 334 (41%) were premenopausal and 476 (59%) were postmenopausal. Likewise, 35 mutations were identified in 34 of the 810 (4.3%) women analyzed, including 8 unique BRCA1 mutations in 20 women and 11 unique BRCA2 mutations in 14 women.(13).

On the other hand, in Colombia, a study was carried out to measure the frequency of the BRCA1 and BRCA2 genes in 43 patients who were referred for suspected breast cancer syndrome, of these, 48.8% had the BRCA1 gene and 51.2% had mutations in the BRCA2 gene.(14).

As is known, breast cancer can occur due to different factors, such as: age, late menarche or menopause, lack of pregnancies, smoking, family history (genetics), among others. A

mutation in the BRCA1 or BRCA2 genes produces BC, but this is a purely genetic factor. However, the factors mentioned above may be the cause of activating or triggering a mutation in these genes early.(2); and according to the present study, it was determined that all patients have first to fourth degree relatives who have presented CM.

Likewise, some of the patients studied presented an early menarche (9 years), and others presented a late menarche (17 years); corroborating that the literature tells us that normally a menarche occurs between 10 to 15 years.(23); therefore, the menarche of these patients in question may or may not have been a trigger that accelerated the mutation factor of the BRCA1 or BRCA2 genes.

Analyzing the anonymized database of the SOLCA Institute, 12.50% of those with a BRCA 2 gene condition died, and those with a BRCA1 gene condition did not show a death rate; considering that, according to research, 26% die from BC due to a mutation in the BRCA1 gene and 21% of the population can die due to a mutation in the BRCA2 gene.(20).

Of the female patients with breast cancer with BRCA1 and BRCA2 mutations who attend the SOLCA Cuenca Cancer Institute in the period 2019 - 2023, right luminal B CM occurred more frequently, however, in studies previously carried out according to its classification, luminal A type breast carcinomas occur in 62.5% while luminal B type occurs in 18%.(21); at the same time it was determined that bilateral CM is rare in these patients, which, like the literature, tells us that bilateral breast cancer is rare, since it occurs in approximately 1-2.5% of all patients.(22).

As previously mentioned, in terms of results, treatment for BC will help prevent the spread of cancer cells and avoid a long-term increase in the risk of mortality, and in SOLCA, polypharmacotherapy is the most commonly used because it has a high possibility of making BC treatment more effective.

Although the tumor may become resistant to a specific drug, the effectiveness of the treatment may still be maintained thanks to the tumor's response to another drug within the combination used.(24).

In conjunction with treatment, early detection using mammography has reduced mortality in patients with BC by more than 30%. The Breast Imaging Reporting and Data System (BI-RADS) was developed, which is a widely used method for categorizing mammography findings.(17,18).

For the management of breast lesions, BI-RADS 0 is categorized as: Inconclusive study, additional images required; BI-RADS 1: Negative mammography, annual control; BI-RADS 2: Benign findings, annual control; BI-RADS 3: Probably benign findings (<2% risk of malignancy), control in 6, 12, 18, 24 months; BI-RADS 4: Suspicious abnormality,

positive predictive value between 29-34% up to 70%); BI-RADS 5: Highly suggestive of malignancy, biopsy, malignancy between 81-97%; BI-RADS 6: histologically confirmed lesion.(18, 19).

Conclusions

- Risk factors related to BC are obesity, smoking, family history, among others; in the present study, mutations in the BRCA1 and BRCA2 genes were analyzed, these being the ones that cause BC. It was possible to demonstrate that this mutation is rare, since according to the literature it tells us that 5 to 10% of BC cases are due to hereditary conditions; and at the SOLCA Cuenca Cancer Institute, of the 188 female patients with BC, only 4% presented a mutation in the genes in question.

- The mutated genes in these patients are found in a 50/50 ratio, however, the literature indicates that the gene that mutates most frequently is the BRCA1 gene; also, in these patients the main risk factor is due to a family inheritance, but whether the mutation occurs at an early age or not, can go hand in hand with menarche, since, corroborating with some studies carried out, an early or late menarche can be a risk factor for the suffering of BC.

- Likewise, the therapeutic regimen used at SOLCA Núcleo de Cuenca is the same for most patients; early diagnosis along with appropriate treatment can reduce the mortality rate of CM.

- Finally, it is correct to state that in Ecuador the genetic determination of BRCA1 and BRCA2 is restricted due to the associated costs and the availability of the necessary technology. This situation makes it difficult to obtain an accurate understanding of the percentage of patients nationwide who present these genetic alterations. In the specific case of the city of Cuenca, it is noteworthy to highlight that the SOLCA Cancer Institute is the only center in the region with the capacity to carry out these analyses, highlighting the concentration of this service in a single medical establishment in that locality.

Conflict of interest

The authors of this scientific research declare that there is no conflict of interest in relation to the presented article.

Authors' contribution statement

The authors Jazmín Estefanía Barros Illescas and Ruth Noemí Carpio Suárez contributed to the writing and preparation of the scientific article.

Authors Jonnathan Gerardo Ortiz Tejedor and Andrés Fernando Andrade Galarza contributed to the writing, statistical analysis and final review of the scientific article.

Bibliographic References

1. Senkus-Konefka E., Cardoso F., Douillard JY., Bramley C., Longo F., Jezdic S. Breast Cancer. ESMO [Internet]. 2018 [cited October 14, 2023]. Available in:https://www.esmo.org/content/download/6594/114963/1/ES-Cancer-de-Mama-Guia-para-Pacientes.pdf

2. Calero Cuerda F. Risk factors in breast cancer. Elsevier [Internet]. 2017 [cited 14 October 2023]. 42(90):9065-9088. Available at:https://www.elsevier.es/es-revista-progresos-obstetricia-ginecologia-151-articulo-factores-riesgo-el-cancer-mama-13009702

3. Knaul M., López Carrillo L., Lazcano Ponce E., Gómez Dantés H., Romieu I., Torres G. Breast cancer: a challenge for society and health systems. Public Health of Mexico [Internet]. 2009 [cited 14 October 2023]. 51(2):138-140. Available at:https://www.redalyc.org/articulo.oa?id=10616164002

4. Lazcano EC., Tovar V., Alonso P., Romieu I., López L. Breast cancer. A historical, present and future common thread. Public Health of Mexico [Internet]. 1996 [cited 14 October 2023]. 38(2):139-152. Available at:https://www.redalyc.org/pdf/106/10638208.pdf

5. Chavarría Campos G., Blanco Naranjo E., Garita Fallas Y. Breast cancer associated with mutation in BRCA-1 and BRCA-2 genes. Sinergica Medical Journal [Internet]. 2021 [cited 14 October 2023]. 6(3):650. Available at:https://www.medigraphic.com/pdfs/sinergia/rms-2021/rms213b.pdf

6. Rojas Cabrera E. Argentina and Uruguay: a comparison of the mortality rate from sexually transmitted diseases in people aged 50 years and older during the five-year periods 1997-2001 and 2010-2014. Semiannual electronic journal of the Central American Population Center [Internet]. 2019 [cited October 14, 2023]. 17(1):15. Available at:https://www.scielo.sa.cr/pdf/psm/v17n1/1659-0201-psm-17-01-041.pdf

7. Age-standardized rate (global) per 100 000 population, incidence, both sexes, in 2022. World Health Organization [Internet]. 2022 2019 [cited 13 October 2023]. Available at:https://gco.iarc.fr/today/en/dataviz/bars?mode=population

8. Pazmiño C. Genetic and genomic progress in breast cancer. Metro Ciencia [Internet]. 2022 [cited 13 October 2023]. 30(2):8 – 13. Available

at:https://www.revistametrociencia.com.ec/index.php/revista/article/view/446/462

9. Orland Díez G. Hereditary breast-ovarian cancer syndrome: Molecular aspects. Letrame [Internet]. 2018 [cited 13 October 2023]. Available at:https://seom.org/seomcms/images/stories/recursos/infopublico/publicaciones/cancerHereditario/modulo3.pdf

10. Narod S., Rodriguez A. Genetic predisposition to breast cancer: BRCA1 and BRCA2 genes. Salud Publica Mex [Internet]. 2011 [cited 13 October 2023]. 53(5):420-429. Available at:https://www.scielo.org.mx/scielo.php?script=sci_abstract&pid=S0036-36342011000500010&lng=es&nrm=iso&tlng=es

11. Fernández A., Reigosa A. BRCA1 expression in benign and malignant breast lesions.Public Health Mex [Internet]. 2016 [cited 13 October 2023]. 57(4):330 - 351. Available at:https://ve.scielo.org/scielo.php?script=sci_abstract&pid=S0535-51332016000400003&lng=es&nrm=iso&tlng=es

12. García Cornejo C., Gamarra Cabezas E., Layana D. Breast Cancer and BCRA1 and BCRA2 Genes. Catholic University of Santiago de Compostela [Internet]. 2019 [cited 16 October 2023]. 23(3):156-158. Available at:https://rmedicina.ucsg.edu.ec/archivo/10.2/RM.10.2.10.pdf

13. Torres Mejía G., Royer R., Llacuachaqui M., Akbari M., Giuliano A., Martínez. Matsushita L. Recurrent BRCA1 and BRCA2 mutations in Mexican women with breast cancer. AACR [Internet]. 2015 [cited October 16, 2023]. 24(3):498-505. Available in:https://aacrjournals.org/cebp/article/24/3/498/115382/Recurrent-BRCA1-and-BRCA2-Mutations-in-Mexican

14. Cifuentes L., Rivera Herrera A., Barreto G. Mutations in the BRCA1 and BRCA2 genes in a sample of families with breast and/or ovarian cancer from the Colombian Pacific.Colombia Médica [Internet]. 2019 [cited 14 October 2023]. 50(3):163-175. Available at:http://www.scielo.org.co/pdf/cm/v50n3/es_1657-9534-cm-50-03-00163.pdf

15. Vega L. Immunohistochemistry in dermatopathology: review of the most frequently used antibodies (part i). AEDV [Internet]. 2013 [cited 14 October 2023]. 104(2):99.127. Available at:10.1016/j.ad.2012.02.015

16. Valderrama Martín J., Ortigosa F. Sequencing methods: third generation. EB [Internet]. 2020 [cited 28 December 2023]. 13(175):15-21. Available at:https://encuentros.uma.es/assets/journals/13/175singles/175.4_secuenciacion.pdf

17. Méndez Rondón O., Salazar W., Reyna Villasmil E., Mejía Montilla J. BI-RADS classification and biopsy results in patients with breast pathology. INSPILIP [Internet]. 2017 [cited 14 October 2023]. 1(1):1-14. Available at:https://docs.bvsalud.org/biblioref/2019/04/987851/33-clasificacion_bi-rads_y_resultado_.pdf

18. Aibar L, Santalla A, Criado MSL, González–Pérez I, Calderón MA, Gallo JL, et al. Radiological classification and management of breast lesions. Elsevier [Internet]. 2010 [cited 14 October 2023]. 38(4):141-149. Available at: 10.1016/j.gine.2010.10.016

19. Poveda C. Birads system: Deciphering the mammographic report. Repertorio de Medicina Y Cirugía Journal [Internet]. 2010 [cited 14 October 2023]. 19(1):18-27. Available at:https://revistas.fucsalud.edu.co/index.php/repertorio/article/view/566/606

20. Orozco Hernandez J., Marin Medina S., Martinez Muñoz M., Martinez J. A View of Breast Cancer Predisposition Genes. PKP [Internet]. 2017 [cited 14 October 2023]. 34(3):766-783. Available:https://rcientificas.uninorte.edu.co/index.php/salud/article/view/10311/214421443478

21. Molecular subtypes of breast cancer: prognostic implications and clinical and immunohistochemical characteristics. PKP [Internet]. 2011 [cited 19 October 2023]. 34(2):219-233. Available at: dx.doi.org/10.4321/S1137-66272011000200008

22. Ajá L., Sánchez J., Avilés C. Synchronous bilateral breast cancer. Literature review and case presentation. Finlay [Internet]. 2012 [cited 19 October 2023]. 2(2):129-133. Available at:https://revfinlay.sld.cu/index.php/finlay/article/view/94/1292

23. Leal F., Stuardo A., Molina G., González A. Early menarche and its association with risk behaviors in adolescents. Chil Obstet Ginecol[Internet].2015[cited October 19, 2023]. 80(1):41-47.Available in:https://www.scielo.cl/scielo.php?script=sci_arttext&pid=S0717-75262015000100006

24. Memorial Sloan Kettering Cancer Center. Chemotherapy for Breast Cancer. MSKCC [Internet]. 2019 [cited 14 October 2023]. Available at:https://www.mskcc.org/es/cancer-care/types/breast/treatment/systemic-therapy/chemotherapy

ISSN: 2697-3391
Vol. 7 No. 2, pp. 6 – 22, April - June 2024

Indexaciones