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4 **CLINICOPATHOLOGICAL CHARACTERIZATION OF BREAST CANCER PATIENTS IN A**
5 **SECONDARY-LEVEL UNIT.**
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8 **ABSTRACT: Background:** Breast cancer is the most common malignant neoplasm among
9 women; the World Health Organization notes that incidence rates are 88% higher in developed
10 countries than in developing ones. Ductal carcinoma is the most common type of breast cancer,
11 accounting for 70% to 80% of all invasive cases, while lobular carcinoma is the second most
12 frequent, making up 10% to 15% of diagnoses. Biological and sociodemographic factors are the
13 primary risk factors for the development of breast cancer.

14 **Objective:** To identify the clinical-pathological characteristics of breast cancer patients in a
15 secondary-level care unit.

16 **Materials and Methods:** A cross-sectional, observational, descriptive, and analytical study was
17 conducted among patients diagnosed with breast cancer attending the oncology service at the
18 General Zone Hospital No. 8 (HGZ No. 8, IMSS) in Córdoba, Veracruz, Mexico. From an initial
19 universe of 497 clinical and electronic medical records registered between January 1, 2020, and
20 December 31, 2025, consecutive cases were screened; 414 records were excluded due to missing
21 clinical data (<80% completeness) or loss to follow-up, resulting in a final analytical sample of
22 83 fully documented cases. Sociodemographic, histopathological, and immunohistochemical
23 variables (estrogen/progesterone receptors, HER2) were recorded. Data were analyzed using
24 IBM SPSS (v.22) and GraphPad Prism (v.10). Categorical associations were assessed using the
25 Chi-square test (χ^2), and linear correlations between hormone receptor expression levels were
26 determined using Pearson's correlation coefficient ($p \leq 0.05$). The protocol was approved by
27 Institutional Ethics and Research Committee No. 3101 (Registration No. R-2025-3101-012).

28 **Results:** The total clinical population (N=497) underwent a methodological screening process
29 that resulted in the final study sample (n=83 medical records containing $\geq 80\%$ of the required
30 information). Data obtained included mean age (58.52 ± 10.26 years), prevalence by histological
31 subtype (65.1% infiltrating ductal and 34.9% lobular carcinoma), statistical independence values
32 from the bivariate analysis ($\chi^2=0.517$, $p=0.472$ for age and histology), and a highly significant
33 biological correlation between estrogen and progesterone receptors ($\rho=0.657$, $p<0.001$).

34 **Conclusions:** This study demonstrates strong biological consistency regarding estrogen and
35 progesterone receptors; however, the critical findings highlight institutional gaps—specifically
36 loss to follow-up, delayed results, loss of immunohistochemistry specimens, and under-reporting.
37 The study concludes by emphasizing the need to transition toward logistical optimization,
38 digitization, and a timely, patient-centered care model within the secondary-level care unit.

39
40 **Key words:-**
41 Clinicopathological characteristics, breast cancer, risk factors.

43 **Introduction:**

44 Breast cancer constitutes the most frequently diagnosed malignant neoplasm and the primary
 45 cause of cancer-related mortality among women worldwide.¹ Global estimates indicate an
 46 annual burden exceeding 2.3 million new cases (accounting for 11.7% of all oncological
 47 diagnoses), with incidence rising by approximately 1% annually, predominantly driven by
 48 localized hormone receptor-positive tumors.¹ In Latin America, breast cancer represents the
 49 leading female malignancy, with over 152,000 annual diagnoses and an incidence of 27 cases per
 50 100,000 women, where endocrine and hormonal imbalances have increasingly been implicated
 51 in therapeutic resistance.² Although breast cancer is predominantly driven by advanced age
 52 and female sex, distinct clinicopathological profiles emerge across different patient subsets; for
 53 instance, human epidermal growth factor receptor 2 (HER2) overexpression delineates an
 54 aggressive disease entity requiring standardized clinical consensus,³ alongside rigorous
 55 evaluation guidelines defined by the ASCO/CAP panels.⁴

56 Nodal involvement and intrinsic molecular classification serve as fundamental determinants of
 57 patient survival,⁵ while achieving a pathological complete response (pCR) following
 58 neoadjuvant therapy provides a robust surrogate endpoint for favorable outcomes, particularly in
 59 Luminal B and triple-negative subtypes.⁶ In developing countries, breast cancer mortality rates
 60 are approximately 17% higher than in developed nations, reflecting disparities in early screening,
 61 infrastructure, and institutional programs such as *PrevenIMSS*.⁷ In Mexico specifically, breast
 62 cancer has been the leading cause of oncological death among women since 2006,
 63 disproportionately affecting economically active women aged 30 to 54 years and necessitating
 64 dedicated financial protection mechanisms for catastrophic healthcare expenses.⁸

65 Disease progression during systemic therapy remains a decisive marker of poor clinical
 66 outcome,⁹ prompting ongoing research into independent prognostic biomarkers such as
 67 minichromosome maintenance complex component 6 (MCM6) to refine risk stratification.¹⁰
 68 Other validated indicators of adverse prognosis include young age at presentation, large tumor
 69 dimensions, lack of estrogen receptor expression, and extensive axillary lymph node
 70 involvement (>3 positive nodes), especially in locally advanced or inflammatory
 71 presentations.¹¹ Conversely, although male breast cancer represents only 1% of all cases, it
 72 predominantly expresses hormone receptors (>90%) but frequently presents at advanced stages,
 73 compromising overall survival.¹² At the other end of the molecular spectrum, triple-negative
 74 breast cancer exhibits a unique risk factor profile and striking biological aggressiveness,¹³
 75 characterized by extensive intratumoral heterogeneity and distinct genetic drivers—such as
 76 *ITGB1* and *ACTN1*—that promote cell survival and multidrug resistance.¹⁴

77 Tumor proliferation, assessed via Ki-67 expression ($\geq 18\%$), along with cell-cycle dysregulation
 78 involving the cyclin D/CDK4/6 pathway, plays a pivotal role in mediating endocrine resistance
 79 in invasive carcinomas.¹⁵ Concurrently, modifiable nutritional and metabolic factors influence
 80 cancer biology; while dietary epidemiology has shifted from isolated food items toward overall
 81 dietary patterns,¹⁶ high-fat diets and obesity have been demonstrated to accelerate malignant
 82 progression and promote adverse clinicopathological phenotypes.¹⁷ Modern management of

high-risk, hormone receptor-positive, HER2-negative early-stage breast cancer has been transformed by the addition of CDK4/6 inhibitors such as abemaciclib to adjuvant endocrine therapy, significantly improving invasive disease-free and distant relapse-free survival.¹⁸ Longitudinal biomarker analyses, such as those from the MONARCH studies, highlight the clinical utility of circulating tumor DNA (ctDNA) dynamics,¹⁹ demonstrating that necessary dose adjustments to manage adverse events do not compromise long-term therapeutic efficacy.²⁰

A comprehensive oncological approach must also account for early genetic susceptibility (e.g., *BRCA1*, *BRCA2*, *TP53*, and *PALB2* mutations) and environmental exposures in young cohorts,²¹ while actively managing cancer-related symptoms. Pain is among the most prevalent manifestations—arising from tumor infiltration, diagnostic procedures, or treatment toxicities²² and often persists as an underdiagnosed neuropathic sequela that diminishes physical functionality and long-term quality of life in survivors.²³ Furthermore, systemic cytotoxic regimens frequently induce chemotherapy-related amenorrhea, autonomic dysfunction, and neuromuscular weakness, which elevate secondary cardiovascular and metabolic risks.^{24,25}

In terms of histological diversity, invasive ductal carcinoma (IDC) and invasive lobular carcinoma (ILC) present distinct biological and surgical considerations; ILC often demonstrates differential chemosensitivity that directly impacts surgical margins and conservative resections.²⁶ Risk prediction tools, such as the Nottingham Prognostic Index (NPI), integrate tumor size, histological grade, and lymph node burden to predict locoregional recurrence risk and guide clinical decisions.²⁷ Downstaging locally advanced tumors with neoadjuvant systemic therapy enables oncologically safe breast-conserving surgery, particularly when residual tumor size is ≤ 4 cm and Ki-67 levels are carefully monitored.²⁸ Pathological assessments must accurately document histological nuances, including mixed or transition phenotypes identified after neoadjuvant exposure.²⁹ Epidemiological studies have also established that combined hormone replacement therapy selectively increases the relative risk of lobular and mixed carcinomas compared to pure ductal histologies.³⁰ Nevertheless, in early-stage lobular disease, systemic cytotoxic chemotherapy does not always confer a clear long-term survival advantage, reinforcing the need for strict mammographic and ultrasound surveillance (BIRADS stratification).³¹

Consequently, managing breast cancer requires an integrated, multidisciplinary approach supported by precise immunohistochemical profiling to define tailored treatment strategies.³² Postnatal mammary development and carcinogenesis are fundamentally driven by estrogen and progesterone signaling within the terminal ductal lobular units,³³ underscoring the clinical importance of quantitative hormone receptor analysis. Furthermore, national multidisciplinary guidelines, such as the Mexican Consensus on Breast Cancer Diagnosis and Treatment, highlight the logistical importance of minimizing delay across the referral chain and securing clear surgical margins.³⁴

In secondary care hospital facilities (*unidades de segundo nivel de atención*), clinical reality often presents operational obstacles—such as administrative loss to follow-up, paper and digital record fragmentation, and prolonged turnaround times for immunohistochemistry reports—that undermine statistical documentation and patient continuity. Within the regional catchment area

of the Hospital General de Zona No. 8 (HGZ No. 8, IMSS) in Córdoba, Veracruz, characterizing the specific clinical, histological, and molecular features of breast cancer patients is essential to evaluate biological concordance with international standards and identify administrative areas of opportunity. Therefore, the objective of this study was to characterize the clinical and pathological profile of breast cancer patients treated at HGZ No. 8 IMSS in Córdoba, Veracruz, determine the relationship between clinical and histopathological variables, and outline institutional strategies to strengthen regional oncology care.

Materials and Methods:

A cross-sectional, observational, descriptive, and analytical study was carried out at the Oncology Outpatient Service of the Hospital General de Zona No. 8 (HGZ No. 8), belonging to the Instituto Mexicano del Seguro Social (IMSS), Decentralized Administrative Operation Body (OOAD) Veracruz Sur, located in Córdoba, Veracruz, Mexico.

The study universe comprised all adult patients with a confirmed diagnosis of invasive breast cancer who received medical care at HGZ No. 8 between January 1, 2020, and December 31, 2025 ($N=497$).

Sampling was non-probabilistic and conducted via consecutive case selection. Strict data curation criteria were applied: medical records (both physical charts and institutional electronic records) were evaluated for completeness. Records with less than 80% of the core study variables available or with loss to clinical/administrative follow-up ($n=414$) were excluded. Consequently, the final evaluated sample consisted of 83 validated clinical records ($n=83$) exhibiting $\geq 80\%$ complete data integrity across all primary endpoints.

Data were systematically collected using a structured collection instrument and entered into a dedicated database. Variables were classified into three core operational domains:

1. **Clinical and Sociodemographic Variables:** Age at diagnosis (years completed), age at menarche, and municipality of permanent residence.
2. **Biological and Histopathological Variables:** Histological subtype (infiltrating ductal carcinoma vs. infiltrating lobular carcinoma), histological grade (Grades 1, 2, and 3), and pathological axillary lymph node status (positive vs. negative).
3. **Immunohistochemical and Molecular Profiles:** Human epidermal growth factor receptor 2 (HER2) status (positive vs. negative), quantitative expression levels of estrogen receptors (ER) and progesterone receptors (PR), cell proliferation index (Ki-67 percentage), and first-degree family history of breast cancer.

Data curation and organization were performed in Microsoft Excel. Statistical analyses were computed using IBM SPSS Statistics for Windows (Version 27.0; IBM Corp., Armonk, NY, USA), and graphical representations were generated using GraphPad Prism (Version 10.0; GraphPad Software, San Diego, CA, USA).

- **Descriptive Statistics:** Categorical variables were reported as absolute frequencies and percentages ($n, \%$). Continuous variables were summarized using measures of central

tendency and dispersion, specifically mean $\pm$ standard deviation ($\bar{x} \pm SD$) along with minimum and maximum values.

- **Inferential Bivariate Analysis:** The Chi-square test of independence (χ^2) and likelihood ratio were employed to evaluate associations between categorical variables (including histological subtype across age groups and lymph node involvement). Pearson's correlation coefficient (ρ/r) with 95% confidence intervals (95% CI) was calculated to evaluate the linear relationship between estrogen and progesterone receptor expression levels.
- **Significance Threshold:** In all analyses, a two-tailed p -value ≤ 0.05 was established as statistically significant.

Ethical Approval and Patient Confidentiality

This protocol was reviewed and formally approved by the Local Health Research and Ethics Committee No. 3101 (Comité Local de Investigación en Salud No. 3101) of IMSS, under institutional approval register **R-2025-3101-012** (COFEPRIS 17 CI 30 118 018; CONBIOÉTICA 30 CEI 005 2018082).

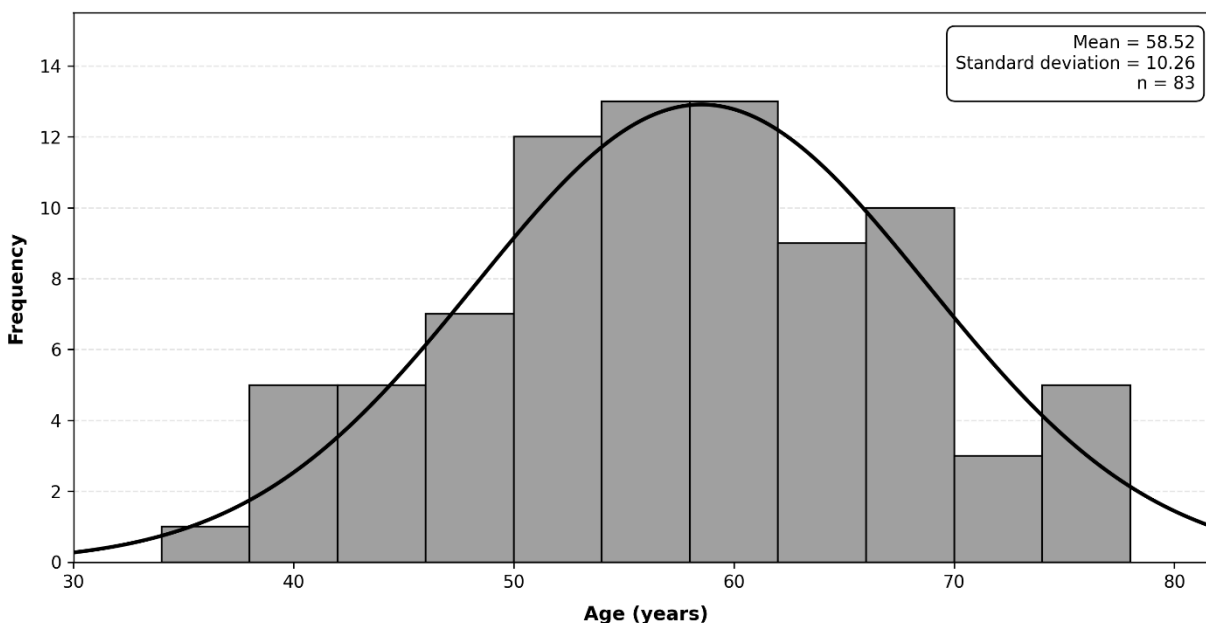
The research was conducted in full compliance with the ethical tenets of the Declaration of Helsinki (Fortaleza revision, 2013), Good Clinical Practice guidelines established by the Pan American Health Organization (PAHO), and the Mexican General Health Law in the Field of Health Research (*Reglamento de la Ley General de Salud en Materia de Investigación para la Salud*). In accordance with Article 17, Section I of the aforementioned regulation, this study was categorized as **research without risk** (*investigación sin riesgo*) as it exclusively involved retrospective/documentary review of existing medical records. An informed consent waiver was granted by the institutional ethics committee. Strict confidentiality and data anonymization procedures were maintained throughout all stages of data extraction and analysis to ensure participant privacy.

Results:

From an initial clinical universe of 497 medical records identified with a breast cancer diagnosis at the oncology outpatient service of HGZ No. 8 between 2020 and 2025, a strict data curation process was applied. A total of 414 records were excluded due to incomplete clinical information (<80% completeness) or administrative loss to follow-up. Consequently, comprised 83 validated patients ($n=83$) fulfilling the required $\geq 80\%$ data integrity threshold for clinical, histopathological, and molecular variables.

Among the 83 patients evaluated, the mean age at diagnosis was 58.52 ± 10.26 years, spanning an age range from 34 to 78 years (Figure 1). The highest concentration of cases occurred between the fifth and seventh decades of life, with 31 patients (37.3%) clustered between 50 and 69 years, consistent with a postmenopausal clinical presentation. Only one patient (1.2%) was diagnosed before the age of 35 years.

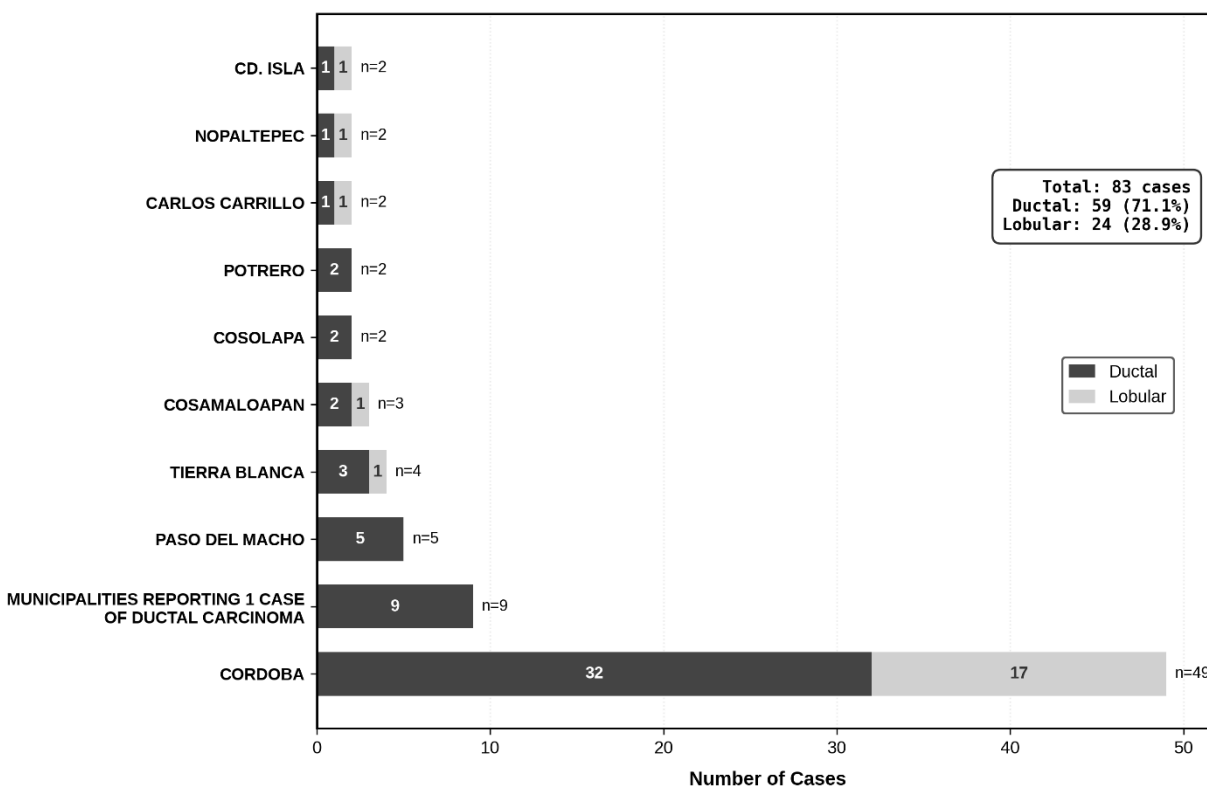
Figure 1. Age distribution of patients with breast cancer.



Age distribution with fitted normal curve ($n=83$; 58.52 ± 10.26 years).

The municipality of Córdoba accounted for the highest absolute frequency of cases for both subtypes, showing a marked difference favoring ductal carcinoma. In contrast, the remaining municipalities exhibited considerably lower frequencies, characterized by low and dispersed records, each reporting a single case of ductal carcinoma (Carlos Carrillo, Cd. Isla, Coatzacoalcos, Cosolapa, Cuitlahuac, Paraje Nuevo, Paso del Macho, Potrero). Lobular carcinoma showed a more limited distribution and lower variability across the 18 municipalities. Overall, a heterogeneous distribution is evident, with case clustering in a predominant municipality and a lower disease burden across peripheral localities, consistently maintaining the higher prevalence pattern of ductal carcinoma. (Figure 2)

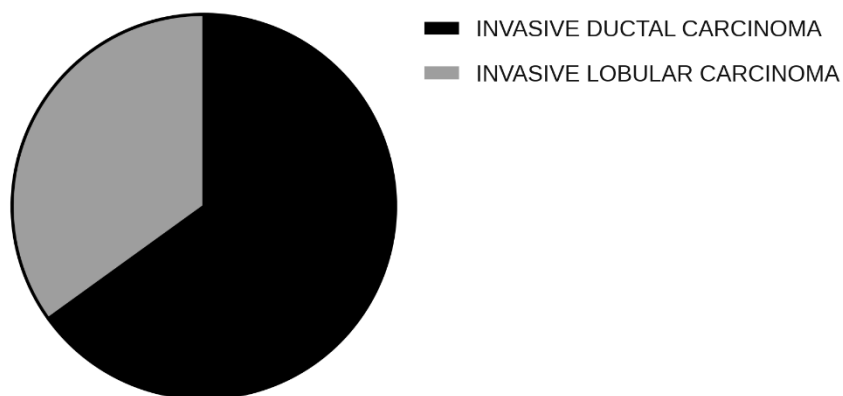
Figure 2. Frequency of humoral subtype by municipality of residence.



Córdoba = 49, Paso del Macho = 5, Tierra Blanca = 4, Cosamaloapan = 3. n = 83.

In the study population, all cases were cases of infiltrating breast carcinoma, classified according to histopathological subtype. Of these, 54 cases (65.1%) were infiltrating ductal carcinoma, while 29 cases (34.9%) were classified as lobular carcinoma. A clear predominance of infiltrating ductal carcinoma is observed, with an absolute difference of 25 cases compared to lobular carcinoma and a relative difference of 30.2 percentage points. (Figure 3)

Figure 3. Frequency of breast cancer cases by histological subtype.



Predominance of histological subtypes: ductal = 54 (65.1%), lobular = 29 (34.9%); n = 83.

An association analysis was carried out using X², between the age group and the histological subtype of the tumor in a sample of 83 patients. Ductal carcinoma was the most significant in both age groups, representing 64.5% of the cases. However, a low. (Table 1)

Table 1. Humoral subtype table by age.

Age Group	Histological Subtype		χ^2	df	p
	Ductal Carcinoma f (%)	Lobular Carcinoma f (%)			
45 to 60 years	23 (30.3)	15 (19.7)	0.517	1	0.472
61 to 78 years	26 (34.2)	12 (15.8)			

p=0.472, χ^2 0.517, n=83

The results showed a χ^2 value of 0.0184 with 1 degree of freedom and a two-tailed statistical significance of p = 0.892 in a sample of 83 valid cases; thus, no significant association was demonstrated between the humoral subtype and nodal status, a finding supported by the likelihood ratio (LR), which yielded a value of 0.0178 (df = 1; p = 0.892). (Table 2)

Table 2. Cross-tabulation of nodal status according to humoral subtype.

Lymph Status	Node	Histological Subtype		χ^2	df	p
		Ductal Carcinoma f (%)	Lobular Carcinoma f (%)			
Positive		16 (64.0)	9 (36.0)	0.0184	1	0.892
Negative		38 (65.5)	20 (34.5)			

χ^2 = 0.0184, p = 0.892, gl = 1 LR (+) 0.0178, n=83.

The results demonstrated a moderate-to-high positive correlation between estrogen receptors (ER) and progesterone receptors (PR) (ρ = 0.586), with a two-tailed statistical significance of p < 0.001 and a sample size of 83 participants. As ER values increase, PR values also tend to increase. (Table 3)

Table 3. Correlation coefficient of PR and ER in breast cancer patients.

	Mean	Pearson Correlation	95% CI
Estrogen Receptors (ER)	53.98	0.586	0.421 – 0.710
Progesterone Receptors (PR)	31.41		

IC 0.421 – 0.7110, ρ =0.586, p < 0.001, n=83.

DISCUSSION

This study provides epidemiological data; the mean age at diagnosis observed in our cohort was 58.52 ± 10.26 years, with the highest concentration occurring during the postmenopausal stage (50 to 70 years of age). This finding is entirely consistent with the analysis of global trends reported by Giaquinto et al. (conducted in the USA), which indicates that the majority of invasive breast cancer cases (84%) and deaths (91%) occur among women aged 50 or older, with approximately half (52%) of all deaths occurring in women aged 70 or older; the study describes advanced age and the postmenopausal transition as the primary determinants of cumulative risk, closely correlated with greater cumulative exposure to ovarian hormones.

Infiltrating ductal carcinoma clearly predominated, accounting for 65.1% ($n = 54$) of cases, while the rate of infiltrating lobular carcinoma reached a notable 34.9% ($n = 29$). In this regard, O'Connor et al. reported findings from a systematic review of 40 studies conducted in Ireland, which included 87,303 patients (7,596 with invasive lobular carcinoma [8.7%] and 79,708 with invasive ductal carcinoma [91.3%]). The figures observed in the present study are high compared to those reported by O'Connor et al.

This overrepresentation of the lobular subtype in the Córdoba area and the peripheral municipalities of the IMSS Veracruz Sur delegation suggests the existence of local factors (genetic, environmental, or specific lifestyle factors) favoring this histological pattern, or alternatively, a substantial variation associated with under-reporting and the forced purging of incomplete physical and electronic records, which limited our final sample.

Finally, the moderate-to-high positive correlation identified between Estrogen Receptors (ER) and Progesterone Receptors (PR) ($\rho=0.657$, $p<0.001$) is perfectly consistent with the endocrine carcinogenesis model detailed by Gruszka et al. (2025). These authors reaffirm that the expression of both receptors is functionally coupled under the transcriptional control of estrogenic stimulation.

Consequently, the high prevalence of tumor positivity for both receptors in our sample supports the feasibility of implementing long-term maintenance endocrine therapies—such as the use of CDK4/6 inhibitors described by Alexiou et al. (2025) in a study conducted in Greece, where 34% of patients in both the intervention and control groups had Ki-67 levels $<20\%$, while 45% in the intervention group and 44% in the control group had Ki-67 levels $\geq 20\%$. These therapies have been shown to substantially increase invasive disease-free survival in hormone-dependent tumors with clinical and biological profiles comparable to those characterized in the present study.

Conclusion:

The analysis conducted in this study identified clinical, histological, and molecular patterns consistent with international literature. The most significant finding lies not only in the clinical results obtained but also in the identification of structural limitations within the healthcare system that directly impact the quality of epidemiological data and the continuity of oncological care. The exclusion of a substantial number of patients due to incomplete medical records

highlights critical issues regarding data recording, follow-up, and the availability of ancillary tests—particularly those involving immunohistochemistry.

The analysis identified key weaknesses, including the loss of clinical follow-up, under-reporting of key variables, inadequate management of biological specimens, and prolonged turnaround times for molecular test results. These factors also directly affect timely clinical decision-making and patient prognosis.

Despite these limitations, the complete data available demonstrate strong biological coherence—evidenced by the significant correlation between hormone receptors—which supports the validity of the findings. Furthermore, identified opportunities—such as digitizing pathology systems, implementing sample traceability strategies, and updating institutional guidelines—represent key areas for intervention that could significantly improve the quality of data recording and patient follow-up.

Consequently, it is essential to improve data recording by capturing specific details, such as the exact location of the lesion and a detailed transcription of imaging reports. It is also a priority to ensure timely documentation and continuous follow-up after surgery and subsequent histopathological analysis; this ensures that all necessary information is available to implement treatments promptly and substantially improve each patient's prognosis.

This study highlights the urgent need to improve the administrative and logistical processes of the healthcare system. Optimizing the collection, integration, and availability of clinicopathological information is essential to ensure quality oncological care and to strengthen epidemiological research. Addressing these areas of opportunity will not only improve health outcomes but also advance a more efficient, timely, and patient-centered care model. In conclusion, the alternative hypothesis is rejected.

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