

REVIEWER'S REPORT

Manuscript No.: IJAR-59279

Title: CLINICOPATHOLOGICAL CHARACTERIZATION OF BREAST CANCER PATIENTS
IN A SECONDARY-LEVEL UNIT

Recommendation:

Accept as it is

Accept after minor revision.....

Accept after major revision ...YES.....

Do not accept (*Reasons below*)

Rating	Excel.	Good	Fair	Poor
Originality			☐	
Techn. Quality				☐
Clarity			☐	
Significance		☐		

Reviewer's ID: JPR-094

Detailed Reviewer's Report

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Manuscript Title

Clinicopathological Characterization of Breast Cancer Patients in a Secondary-Level Unit

Overall Assessment

The manuscript addresses a clinically relevant topic by describing the clinicopathological characteristics of breast cancer patients treated at a secondary-level hospital in Córdoba, Veracruz, Mexico. The use of institutional medical records covering 2020–2025 and the inclusion of histopathological and immunohistochemical variables are potentially valuable. The study also identifies important limitations in clinical record completeness and patient follow-up.

However, several important methodological, statistical, reporting, and interpretational problems require attention. In particular, there are inconsistencies between the Abstract and Methods/Results, discrepancies in the reported Pearson correlation coefficient, insufficient explanation of the exclusion of

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414 of 497 records, unclear statistical methodology, incomplete presentation of important clinicopathological variables, and some conclusions that extend beyond what the presented data can establish.

Recommendation: MAJOR REVISION

1. Strengths of the Manuscript**1.1 Clinically relevant topic**

Breast cancer is an important public-health problem, and characterization of patients at the secondary-care level can provide useful information for local oncology services.

1.2 Clearly identified study setting

The manuscript identifies the study institution, geographic location, study period, and oncology service. This improves reproducibility and helps readers understand the healthcare context.

1.3 Defined study population and study period

The study considers patients diagnosed between January 2020 and December 2025, providing a six-year institutional observation period.

1.4 Ethical approval is reported

The manuscript provides an institutional ethics committee number and registration number and describes the retrospective nature of the study and confidentiality procedures.

1.5 Multiple clinicopathological variables were considered

The investigators attempted to evaluate demographic, histopathological, lymph-node, HER2, ER, PR, Ki-67 and family-history variables. This multidimensional approach is a positive feature.

1.6 The manuscript identifies important data-quality problems

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The large number of incomplete records and reported problems with follow-up, documentation, immunohistochemistry and specimen management could be valuable findings for institutional quality improvement.

1.7 ER–PR association is potentially useful

The reported positive relationship between estrogen- and progesterone-receptor expression is clinically relevant and could constitute one of the useful findings of the study if the statistical analysis and numerical reporting are corrected.

2. Major Weaknesses

2.1 Very high exclusion rate and potential selection bias

The study began with **497 records but excluded 414**, leaving only 83 records for analysis. Thus, approximately 83.3% of the initial records were excluded.

The manuscript states that records were excluded because of incomplete information or loss to follow-up.

This is a major methodological concern because the final 83 patients may not adequately represent the original 497-patient population.

Required revision:

The authors should:

- Provide a detailed flow diagram of patient selection.
- Report the exact number excluded for each reason.
- Clarify how many were excluded for incomplete records and how many for loss to follow-up.
- Explain whether some patients had more than one exclusion reason.
- Discuss the possibility of selection bias.
- Explain whether the characteristics of included and excluded patients could differ systematically.

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2.2 Study design is inconsistently described

The Abstract describes the study as:

"cross-sectional, observational, descriptive, and analytical"

However, the study is based on retrospective medical-record review over 2020–2025. The authors should clearly define the design as a **retrospective observational study** and explain whether the analysis is cross-sectional or retrospective cohort/record-based descriptive analysis.

The terminology should be standardized throughout the manuscript.

2.3 Major discrepancy in statistical software reporting

The Abstract states that IBM SPSS **version 22** was used, whereas the Methods section states that IBM SPSS Statistics **version 27.0** was used.

This must be corrected.

Required revision:

State one correct SPSS version consistently throughout the manuscript.

2.4 Major discrepancy in the ER–PR correlation coefficient

This is one of the most important problems in the manuscript.

The Abstract reports:

$\rho = 0.657$, $p < 0.001$

The Results section reports:

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$\rho = 0.586, p < 0.001$

The table also reports:

Pearson correlation = 0.586; 95% CI 0.421–0.710

while the Discussion again reports:

$\rho = 0.657$.

The authors must determine which value is correct by returning to the original statistical output.

Required revision:

- Recalculate the correlation.
- Report the correct coefficient consistently.
- Specify whether it is **Pearson's r** or **Spearman's rho (ρ)**.
- Provide the exact 95% confidence interval.
- Explain how ER and PR percentages were measured and whether the data fulfilled the assumptions for Pearson correlation.

2.5 Problems with the age-group table

The reported Table 1 contains:

45–60 years: 23 ductal + 15 lobular = 38

61–78 years: 26 ductal + 12 lobular = 38

Therefore, the table accounts for **76 patients**, whereas the stated sample size is **83**.

Seven patients are therefore apparently missing from this analysis.

This needs explicit explanation.

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Required revision:

State whether:

- seven patients had missing age/subtype information,
- seven patients were excluded from this particular analysis,
- the age categories are incorrect, or
- the table contains transcription errors.

The denominators should be clearly reported for every statistical analysis.

2.6 Inappropriate use of the term "prevalence"

The manuscript describes 65.1% ductal and 34.9% lobular carcinoma as "prevalence by histological subtype." In this institutional sample, these are better described as **proportions, frequencies, or distributions of histological subtypes**, rather than population prevalence.

Required revision:

Replace "prevalence" with appropriate terminology unless the authors have a clearly defined population denominator allowing calculation of prevalence.

2.7 Important variables are listed but not adequately reported

The Methods state that the study collected:

- age at menarche,
- histological grade,
- lymph-node status,

HER2,

- ER,

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- PR,

Ki-67,
- family history.

However, many of these variables are not adequately presented in the Results.

For example, the manuscript should provide descriptive results for:

- Histological grade 1/2/3
- HER2 positive/negative
- ER positive/negative
- PR positive/negative
- Ki-67 categories or continuous distribution
- Family history
- Lymph-node involvement
- Age at menarche

Required revision:

Provide a comprehensive baseline/clinicopathological characteristics table.

2.8 Statistical analysis is too limited for the stated objective

The stated objective includes determining relationships between clinical and histopathological variables. However, only a small number of bivariate analyses are presented.

No multivariable analysis is reported.

Given the sample size of 83, sophisticated multivariable modeling may be limited, but the authors should nevertheless justify the statistical strategy and explain why only the reported analyses were performed.

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2.9 The manuscript makes causal or speculative statements not supported by the study design

The Discussion states that the high proportion of lobular carcinoma may suggest:

genetic, environmental, or lifestyle factors

However, these factors were not demonstrated by the presented analysis.

This is speculative.

Required revision:

Present this only as a hypothesis and explicitly state that the study did not evaluate genetic, environmental, or lifestyle determinants.

2.10 The discussion overinterprets endocrine treatment implications

The manuscript suggests that the receptor findings support the feasibility of long-term endocrine therapies and discusses CDK4/6 inhibitors.

However, this retrospective descriptive study does not appear to have evaluated treatment allocation, treatment response, progression-free survival, overall survival, or treatment outcomes.

Therefore, the receptor correlation should not be used to infer therapeutic efficacy or treatment feasibility.

Required revision:

Restrict the conclusion to the observed clinicopathological findings and avoid implying treatment effectiveness unless treatment-outcome data are actually analyzed.

3. Key Points Requiring Correction

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1. **SPSS version discrepancy:** Abstract says v22; Methods says v27.
2. **Correlation discrepancy:** 0.657 versus 0.586.
3. **Pearson versus Spearman terminology:** standardize the statistical test and notation.
4. **Age-table denominator:** Table 1 accounts for 76 rather than 83 patients.
5. **Reasons for exclusion of 414 records:** must be separately quantified.
6. **Selection bias:** must be discussed prominently.
7. **Missing variables:** several variables described in Methods are absent or inadequately reported in Results.
8. **Terminology:** "prevalence" should generally be replaced with "proportion/distribution" for histological subtypes.
9. **Speculative explanations:** genetic/environmental/lifestyle explanations require appropriate qualification.
10. **Therapeutic conclusions:** should not exceed the data.
11. **Conclusion statement:** the sentence "**the alternative hypothesis is rejected**" is statistically and scientifically unclear and should be removed or rewritten.
12. **Figures/tables:** all figures should contain sufficient legends, denominators and clearly defined variables.
13. **Reference formatting:** references should be checked carefully for consistency, completeness, author names, journal titles, volume/pages and DOI information.
14. **Language editing:** several sentences require substantial English-language and scientific editing.

4. Significance of the Study

The study has potential local and institutional significance.

Its principal value is the characterization of breast cancer cases in a secondary-level Mexican healthcare setting and the identification of deficiencies in medical-record completeness and continuity of care. The study reports that only 83 of 497 identified records met the predefined completeness criterion, highlighting a substantial data-quality problem.

The local finding of a relatively high proportion of lobular carcinoma may also be worth reporting, but it requires cautious interpretation because the final sample is small and heavily affected by exclusions.

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The ER–PR relationship is potentially informative but should be presented as an association rather than evidence of causality or therapeutic effectiveness.

5. Minor Comments**Title**

The title is appropriate but could be made more precise by specifying that this is a retrospective institutional study.

Abstract

The Abstract should be revised after all statistical discrepancies are resolved.

Keywords

The keywords are too limited. Consider including terms such as:

- Breast neoplasms
- Histopathology
- Immunohistochemistry
- Estrogen receptor
- Progesterone receptor
- Secondary healthcare

Introduction

The Introduction is extensive and covers many topics that are not directly investigated, including CDK4/6 inhibitors, ctDNA, chemotherapy-related amenorrhea, pain, genetic mutations and several treatment issues.

The Introduction should be shortened and focused on:

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1. breast cancer burden,
2. clinicopathological classification,
3. importance of ER/PR/HER2,
4. relevance of secondary-care data,
5. existing knowledge gap,
6. study objective.

Methods

The authors should provide:

- precise inclusion criteria,
- exclusion criteria,
- definition of complete record,
- definition of ER/PR positivity,
- HER2 classification criteria,
- Ki-67 methodology,
- histological classification system,
- method of handling missing data.

Results

Results should be presented in a logical sequence:

1. patient selection,
2. demographics,
3. histopathology,
4. lymph-node status,
5. immunohistochemistry,
6. statistical associations.

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Discussion

The Discussion should distinguish clearly between:

- findings directly demonstrated by the study,
- comparison with previous literature,
- possible explanations,
- hypotheses requiring future research.

6. Recommendation to the Editor

Recommendation: MAJOR REVISION

The manuscript addresses a relevant clinical and institutional problem and contains potentially useful local epidemiological data. The retrospective dataset, ethical approval, defined study setting, and inclusion of histopathological and immunohistochemical variables are strengths.

However, the current version has several substantive problems that prevent confident interpretation of the results. The most important issues are the **very high exclusion rate, potential selection bias, inconsistent statistical reporting, contradictory ER–PR correlation values, incomplete reporting of collected variables, discrepancy in the age-group table, and overinterpretation of some findings.**

These issues appear potentially correctable through careful re-analysis of the original dataset and thorough revision of the manuscript.

The manuscript should not be accepted in its present form. A major revision with verification of the original statistical dataset is recommended.

Priority before reconsideration

The authors should first:

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- (1) verify the raw dataset,
- (2) recalculate all statistical analyses,
- (3) resolve the 0.586/0.657 discrepancy,
- (4) correct Table 1 and all denominators,
- (5) provide a patient-selection flowchart,
- (6) report all major variables described in Methods,
- (7) strengthen the limitations section, and
- (8) revise the conclusions so that they do not exceed the evidence.

Overall reviewer recommendation: Major Revision. The manuscript has a publishable research question, but the statistical and reporting inconsistencies should be resolved from the original patient-level dataset before acceptance.