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FREQUENCY OF ER, PR, AND HER2 POSITIVE CARCINOMA IN OPD SETTING AT JINNAH POSTGRADUATE MEDICAL CENTRE (JPMC), KARACHI

Dr. Ghazala Rafique[*1], Dr. Dileep Kumar[2], Dr. Irfan Ali Sahito[3], Dr. Kanwal Soomro[4], Dr. Soha Nazeer[5], Dr. Maham Atta[6]

[*1,3]*Postgraduate Trainee, at Department of, General Surgery, Jinnah Postgraduate Medical Centre (JPMC), Karachi, Pakistan*

[2]*Professor and Head of Department, at Department of General Surgery, Jinnah Postgraduate Medical Centre (JPMC), Karachi, Pakistan*

[4]*Assistant Professor at Department of General Surgery, Jinnah Postgraduate Medical Centre (JPMC), Karachi, Pakistan*

[5]*Post Graduate Traine*

[6]*Surgical Resident at, Department of general surgery, Jinnah Postgraduate Medical Centre (JPMC), Karachi, Pakistan*

[*1]drghazalarafique@gmail.com, [2]dileep123-kumar@gmail.com, [3]efyali8@yahoo.com, [4]dr.kanwalhameed@gmail.com, [5]mahamqureshi530@gmail.com

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Corresponding Author: *
Dr. Ghazala Rafique

Abstract

Objective:

To determine the frequency of estrogen receptor (ER), progesterone receptor (PR), and HER2/neu positivity and molecular subtypes of breast carcinoma among patients presenting to the outpatient department of a tertiary care public hospital.

Study Design:

Descriptive cross-sectional study.

Place and Duration of Study:

General Surgery Unit, Jinnah Postgraduate Medical Centre (JPMC), Karachi, from July 2024 to December 2024.

Methods:

A sample population of 57 women with a history of breast carcinoma, which was histologically confirmed, was gathered using non-probability consecutive sampling method. Immunohistochemical testing was done to establish the expression of estrogen receptor (ER), progesterone receptor (PR) and HER2/neu. Operation of HER2 overexpression was based on the intensity of 3+ on immunohistochemistry. Based on this, molecular subtypes were given. The statistical tests were conducted with SPSS 25, and frequencies and percentages of receptor status and molecular subtypes were calculated.

Results:

The mean age of patients was 48.6 ± 11.2 years. ER positivity was observed in 43 (75.4%) patients, PR positivity in 40 (70.2%), and HER2 positivity in 18 (31.6%). Luminal A was the most common molecular subtype, found in 27 (47.4%) cases, followed by Luminal B in 11 (19.3%), HER2-enriched in 7 (12.3%), and triple-negative breast cancer in 12 (21.0%) patients.

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Conclusion:

The most common phenotype among patients who came to the outpatient department included hormone receptor positive breast cancer most commonly Luminal A subtype. Systematic receptor profiling is unavoidable in the development of proper therapeutic plans, especially when dealing with resource limited settings of the public sector.

INTRODUCTION

The most diagnosed cancer in women across the globe is breast cancer and one of the most prevalent cancer causes of morbidity and mortality in humans, especially in low- and middle-income countries. It is a significant burden to the population, as it causes about 25% of all cancer among women in the world. The country has one of the highest rates of breast cancer incidence based on age in Asia, so it is evident that the disease is increasingly affecting this country. [1-3] Further developments in molecular biology have transformed the knowledge and treatment of breast cancer. Estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor-2 (HER2/neu)-based classification has become the key to prognostication and treatment planning since breast cancer has become classified into biologically disparate molecular subtypes, i.e., luminal A, luminal B, HER2-enriched, and triple-negative cancer [4,5]. The hormone-receptor positive tumors are usually associated with good prognosis and sensitivity to endocrine therapy, but the HER2-positive tumors are associated with an aggressive behavior but with significant response to targeted anti-HER2 therapy [6,7]. This has made molecular profiling an essential part of modern-day breast cancer management and personalized treatment regimen. Although the clinical significance of receptor-associated classification is well established, there is limited local information on the distribution of the ER, PR and HER2 subtypes in the outpatient department (OPD) of the public-sector hospitals in Pakistan. These settings often have patients with high levels of advancement, and they have minimal access to early diagnostic profiling and targeted therapies[8]. These findings make the local distribution of molecular subtypes essential in maximizing treatments, resource distribution, and enhancing the management of breast cancer in resource-limited health systems. The proposed study will identify the prevalence of ER, PR and HER2/neu and distribution of molecular subtypes among breast cancer patients with the outpatient department of a tertiary-care state-run hospital in Karachi.

METHODOLOGY

The study was carried out in General Surgery Unit out patient department (OPD) at JPMC in Karachi. The study was conducted over a six-month period, from July to December 2024. A total of 57 participants were recruited using non-probability sequential sampling. Participants in the trial had to be at least 20 years old, diagnosed with breast cancer, and undergoing histological testing, including IHC analysis for ER, PR, and HER2 positivity. Patients without complete immunohistochemistry (IHC) data and those with male breast cancer were not included in the study. All participants provided written informed consent after the Institutional Ethics Committee approved it.

We collected and recorded the patients' clinicopathological characteristics as well as the laboratory data. The receptor status was determined using information from immunohistochemistry reports. The presence of receptor expression on 1% or more of tumor cells was interpreted as a positive finding for both hormone receptors. HER2 expression was determined according to standard guidelines. Only those with a score of 3+ were deemed to have positive receptor status while appearances classified as 2+ were excluded because no FISH testing was performed. The results were carried out with the help of SPSS software (version 25). Data were summarized by computing frequencies

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and percentages of each receptor state. The proportion and frequency of patients with different receptor expressions were determined. The distribution of patient ages and the extent of their variability were calculated.

RESULTS

A total of 57 female patients with histologically confirmed breast carcinoma were included in the study. The age of the patients ranged from 28 to 72 years, with a mean age of 48.6 ± 11.2 years. The majority of patients (56.1%) were between 41 and 60 years of age.

Estrogen receptor (ER) positivity was observed in 43 patients (75.4%), while progesterone receptor (PR) positivity was noted in 40 patients (70.2%). HER2/neu overexpression (3+ on immunohistochemistry) was identified in 18 patients (31.6%).

Based on molecular classification, Luminal A subtype (ER+/PR+/HER2−) was the most frequent, identified in 27 patients (47.4%). Luminal B subtype (ER+/PR+/HER2+) was observed in 11 patients (19.3%). HER2-enriched subtype (ER−/PR−/HER2+) was present in 7 patients (12.3%). Triple-negative breast cancer (ER−/PR−/HER2−) was identified in 12 patients (21.0%).

Hormone receptor–positive breast cancer constituted the predominant molecular category in the study population. The detailed distribution of hormone receptor expression and molecular subtypes is presented in **Table 1**.

Table 1. Distribution of Hormone Receptor and HER2 Status (n = 57)

Receptor / Subtype	Frequency (n)	Percentage (%)
ER Positive	43	75.4
PR Positive	40	70.2
HER2 Positive	18	31.6
Luminal A (ER+/PR+/HER2−)	27	47.4
Luminal B (ER+/PR+/HER2+)	11	19.3
HER2-enriched (ER−/PR−/HER2+)	7	12.3
Triple-Negative (TNBC)	12	21.0

DISCUSSION

This paper evaluated the expression of estrogen receptor (ER), progesterone receptor (PR) and HER2/neu on breast carcinomas that had been reported to the outpatient department of a key public-sector tertiary care hospital in Karachi. The findings showed that the prevalence of hormone-receptor-positive disease was strong, with ER and PR positive results in 75.4% and 70.2% prevention of the statistical indicators respectively, and the overexpression of HER2/neu in 31.6% of patients. These results support that hormone-receptor-positive tumors are the main categories of the molecular types of breast cancer in this cohort that corresponds to the world-wide and the regional epidemiological trends [8-10]. Luminal A was the most prevalent molecular subtype, of 47.4% as in this cohort, which was then succeeded by Luminal B (19.3%), HER2-enriched (12.3 %), and triple-negative breast cancer (TNBC) (21.0%). This distribution complies with the global data that point at luminal subtypes as the most common biological phenotype in the world with its characteristic of good prognostic outcomes and sensitivity to endocrine treatment [11-13]. The positive correlation between hormone-receptor-positive tumours and better survival highlights the importance of routine receptor profiling to form the foundation of modern-day treatment of breast-cancer [14]. The HER2-positive rate in this study is consistent with national through Pakistan and South Asia where HER2 overexpression was reported ranging between

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2535 per cent of breast-cancer cases [15,16]. Similar trends have been observed in other institutional research of Lahore and Karachi, and this implies biological similarity in molecular-subtype distribution of various geographical areas within the country [17]. These data support the need to implement standardized HER2 testing guidelines and to increase availability to targeted anti -HER2 treatment schemes across the healthcare systems of the general population. TNBC was reported as 21.0% in the current study, which is at the regional and prevalence range of 18-24% but higher than the global one of 10-15% [12,18,19]. TNBC is a biologically aggressive subtype with early metastasis, few treatment options with targets, and worse clinical outcomes. The high rate of occurrence of TNBC in the low- and middle-income states is a therapeutic challenge, and it is mostly relevant in the resource-poor environment whereby the resource-poor countries still lack access to advanced chemotherapy and immunotherapy [20]. These findings highlight the fundamental need to implement early molecular profiling in the outpatient clinical context, in a public-health perspective. In resource-constrained health care systems, the delayed diagnosis and limited access to diagnostic services are often the reasons behind the late presentation of condition [21]. Regular immunohistochemical profiling assists in risk stratifying, selecting appropriate therapy, and rational resource allocation of limited oncologic resources that ultimately lead to increased treatment efficiency and patient outcome [22]. The research has several limitations. The small size of the sample and a cross-sectional design limit the possibility of making general conclusions about the relationship between receptor status and long-term clinical outcomes, including survival and response to treatment. Besides, equivocal HER2 (2+) cases were excluded by the lack of fluorescence in situ hybridization (FISH) testing, which might under- or overestimate the actual burden of HER2-positive disease [23, 24]. Studies in the future that are massive, cross-centered, longitudinal and include survival analyses, treatment-response data and whole-scale molecular profiling are necessary to better outline the prognostic and therapeutic implications of receptor status in the Pakistani population [25].

Limitations

This single-center, cross-sectional study with a relatively small sample size limits generalizability and causal inference. Use of non-probability sampling and exclusion of complex cases may underestimate bile duct injury. Intraoperative assessment without routine preoperative imaging may introduce observer variability.

Conclusion:

Most patients who report to the outpatient section at the Jinnah Postgraduate Medical Centre have hormone-receptor positive breast cancers with a significant number of the tumours being of the Luminal A type. These results highlight the significance of a systematic review of estrogen receptor, progesterone receptor and HER -2 status in order to provide an individualised breast-cancer treatment. Prompt identification of molecular subtype brings great advantages to patients who are treated in hospitals with limited resources. The use of immunohistochemical profiling therefore should be an essential part of oncological diagnosis to ensure that the right treatment is given to the patient in due time. In addition, larger-scale research is needed to clarify the effect of these parameters on survival rates and to improve national quality of cancer care.

Author contribution:

1. Dr. Ghazala Rafique: Contributed to the conception and design of the study, drafting of the manuscript, and final approval of the version to be published.
2. Dr. Dileep Kumar: Contributed to study supervision, critical revision of the manuscript for important intellectual content, and final approval of the version to be published.
3. Dr. Irfan Ali: Contributed to data collection, patient recruitment, and data acquisition.

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4. Dr. Abdul Waheed: Contributed to data analysis and interpretation and critically revised the manuscript.
5. Dr. Tanweer Ahmed: Contributed to data interpretation and critically revised the manuscript for important intellectual content.
6. Dr. Maham Atta: Contributed to data collection, patient recruitment, and initial data organization.
All authors read and approved the final manuscript and agree to be accountable for all aspects of the work in accordance with ICMJE guidelines.

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