Frontiers in Health Informatics
ISSN-Online: 2676-7104
www.healthinformaticsjournal.com
2024; Vol 13: Issue 8
Open Access

# Mechanisms And Treatment Challenges In Breast Cancer Development And Metastasis

**Khalida Unar[1], Samra Babar[2], Dr. Reena Kumari Sunil[3], Dr. Erum Fatima[4], Zain Ul Abideen[5]**

[1]Assistant Professor, Institute of Microbiology, Shah Abdul Latif University Khairpur Sindh Pakistan, Email: khalida.unar@salu.edu.pk

[2]Student, Faculty of biochemistry, Quaid-i-Azam University Islamabad, Pakistan Email: samrababar100@yahoo.com

[3]Senior Registrar, MBBS, FCPS (Med Oncology), Consultant Medical Oncologist, Dr Ziauddin University Hospital

[4]Lecturer / General Physician, Department of Anatomy, Karachi Metropolitan University Email: kmdc_anatomy@yahoo.com

[5]Intern, Department of General Surgery, Bahawal Victoria Hospital Pakistan, Email: uzain1028@gmail.com

Cite this paper as: Khalida Unar, Samra Babar, Dr. Reena Kumari Sunil, Dr. Erum Fatima, Zain Ul Abideen (2024) Mechanisms And Treatment Challenges In Breast Cancer Development And Metastasis. *Frontiers in Health Informa 3943-3954*

## ABSTRACT

***Background:*** *Currently, breast cancer remains one of the most common types of cancer and its incidence is still high. Understanding the pathogenesis of diseases and the issues that are important about treatment increases the quality of treatment. In this paper the tendencies concerning breast cancer and the processes that contribute to its growth and spread are considered, as well as the challenges associated with current treatment approaches are discussed (Barrios 2022).*

**Methods:** The study was a cross-sectional quantitative study, and self-complete anonymous structured questionnaires were given to HCPRs, researchers, and breast cancer patients. Some questions may concern genetic and hormonal mechanisms, available pharmacotherapy, and challenges related to them; and new pharmacotherapy options. Descriptive data were also calculated using the Shapiro-Wilk test for normality, internal consistency by Cronbach's Alpha, and Chi-square test of independence and t-test group comparison test (Trapani, Ginsburg et al. 2022).

**Results:** Understanding Level, Treatment Effectiveness and Quality of Life Impact were found not to be normally distributed ($p < 0.05$). Cronbach's Alpha was low because a low variability indicated low reliability, or if certain items were missing. Chi-square tests were non-significant for Gender and Personal/Family History (Chi-square = 0.78) and Education Level and Biggest Challenge (Chi-square = 0.65). To perform an F-test for the gender differences in the understanding levels, data could not be complete and therefore was not done (Malik, Ahmed et al. 2022).

**Conclusions:** The findings point to potential deficiencies in data accuracy and survey credibility and inform future research settings and data collection. Consequently, there was no reveal of strong correlations and the analysis should employ methodological progress to provide efficient recommendations for the characteristics and treatment of breast cancer. More research should take into consideration these shortcomings to expand the status and advance knowledge of backed interventions (Mehrotra and Yadav 2022).

**KEYWORDS:** *Breast cancer, quantitative study, treatment challenges, metastasis, research methodology, statistical analysis*

Introduction

Breast cancer is one of the cancers that is closely watched globally due to high rates of occurrence that pose a big risk to women. However, current knowledge of breast cancer still helps to explain a relatively high variability of risk factors, course, and response to therapy. It can therefore be broadly characterized as genetic, epigenetic, hormonal and TME-driven heterogeneity. This knowledge is useful in the improvement of better control of the illness and an improvement in the quality of life in the patients (Lustberg 2022).

This has been attributed to changes in genetic and molecular characteristics of pathways in breast cancer. These genes to which many abnormalities have been credited include; BRCA1, BRCA2, TP53 and HER2, these genes act anticipatorily in tumorogenesis. In addition to these mutations, other alterations at the epigenetic level such as DNA methylation, histones and modified proteins disturb the normal physiological function of the cells resulting in uncontrolled cell division and the formation of tumors. Estrogen and progesterone also contribute to structural and functional changes in the breast tissue in the development of breast cancer majority of which are ErbB2-positive tumors (Obidiro, Battogtokh et al. 2023).

Breast cancer is complicated further by metastasis whereby cancer cells spread and penetrate other organs of the body. Acquired invasiveness and migratory properties include epithelial to mesenchymal transition EMT that enable cancer cells to exit the primary tumour nest, and form new tumours normally in the bones, lungs, liver, and brain. The location of cancer cells for a particular organ or those organs in which secondaries grow – Organotropism is thus dictated by the nature of the interaction between cancerous tissue and the microenvironment of the target organ. The presented metastatic mechanisms contribute not only to the complexity of treatment but also to the negative impact on patient survival (Yang, Li et al. 2022).

Breast cancer is one of the cancers that is closely watched globally due to high rates of occurrence that pose a big risk to women. However, current knowledge of breast cancer still helps to explain a relatively high variability of risk factors, course, and response to therapy. It can therefore be broadly characterized as genetic, epigenetic, hormonal and TME-driven heterogeneity. This knowledge is useful in the improvement of better control of the illness and an improvement in the quality of life in the patients (Cerma, Piacentini et al. 2023).

This has been attributed to changes in genetic and molecular characteristics of pathways in breast cancer. These genes to which many abnormalities have been credited include; BRCA1, BRCA2, TP53 and HER2, these genes act anticipatorily in tumorogenesis. In addition to these mutations, other alterations at the epigenetic level such as DNA methylation, histones and modified proteins disturb the normal physiological function of the cells resulting in uncontrolled cell division and the formation of tumors. Estrogen and progesterone also contribute to structural and functional changes in the breast tissue in the development of breast cancer majority of which are ErbB2-positive tumours (Fuso, Muratore et al. 2022).

Breast cancer is complicated further with metastasis whereby cancer cells spread and penetrate other organs of the body. Acquired invasiveness and migratory properties include epithelial to mesenchymal transition EMT that enable cancer cells to exit the primary tumour nest, and form new tumours normally in the bones, lungs, liver, and brain. The location of cancer cells for a particular organ or those organs in which secondaries grow – Organotropism is thus dictated by the nature of the interaction between cancerous tissue and the microenvironment of the target

organ. The presented metastatic mechanisms contribute not only to the complexity of treatment but also to the negative impact on patient survival (Yang, Li et al. 2023).

**Literature Review**

This disease may well be one of those malignancies that has been investigated most through the years because of its prevalence and the challenges in eradicating it. In the last several decades, the progress toward the acquisition of new knowledge of the disease has been gradual but continuous; however, the molecular and clinical heterogeneity of the disease continues to present a significant problem in managing the illness. The following review set out to systematically describe and synthesize the available literature on the mechanisms of breast cancer development and the challenges of breast cancer management (Konopik, Wolf et al. 2023).

**Mechanisms of Breast Cancer Development**

On a molecular basis, genetic analyses have revealed alterations in what has been known as 'tumour suppressor genes' such as TP53, BRCA1, BRCA2 and 'oncogenes' including HER2 and PIK3CA. There is evidence that genetic mutations in the BRCA1 and BRCA2 genes are involved in hereditary breast cancer with an estimated risk at 5 to 10%. Some of these distort DNA replication hence causing errors in DNA repair mechanisms and thereby causing DNA damage, and thus increasing the probability of getting cancer. HER2 is a receptor tyrosine kinase overexpressed in 20-25% of breast cancers linked to gene amplification and worse prognosis. Much can be learned about the molecular length of breast cancer by targeting HER2 – for example by using monoclonal anti-HER2 antibodies such as trastuzumab which has greatly improved the management of HER2-positive cases (Hu, Li et al. 2022).

Other modifications; besides the DNA methylation pattern and histone code modifications, also participate in the development of breast cancer. DNA methylation on gene promoter regions inclusive of CDH1 and RASSF1A tumour suppressor genes is linked to tumour progression. These sorts of epigenetic changes are reversible, they therefore provide targets for potential epigenetic drug treatments which currently are still relatively small (Richbourg, Irakoze et al. 2024).

The hormonal factors mainly the estrogenic hormones and more significantly have been highlighted in the analysis of the BCAs. The most common type of ER-positive tumour is, as suggested by its name, clarified through stimulation of visual estrogen receptors. Tamoxifen and aromatases specifically have been used in the treatment of such cancers with great success but failure to the treatment remains a big issue. Such Ki67 data are potential mechanisms of endoestrogen resistance consisting of mutation in the gene inhuman encoding estrogen receptor, activation of survival signalling, and other tyrosine kinase receptors (Chavda, Nalla et al. 2023).

**Mechanisms of Metastasis**

Tumor spread is a feature of more advanced breast cancer and is a cause of, most cancer-related mortalities. It has several steps which are, local invasion, intravasation, blood survival, extravasation and distant organ colonization. EMT is an essential biomarker of metastasis during which epithelial cells transition to the mesenchymal phenotype that enables invasion. We have the transcriptional evidence that SNAIL, TWIST and ZEB1 are among the top-ranking transcription factors that cause EMT(Dar, Rasool et al. 2022).

*Another important aspect of the metastasis process is the presence of circulating tumour cells (CTCs). These cells detach from the primary tumour, become lodged in circulation and migrate to the secondary tumour. They have also been identified and described because of other CTC subpopulations that reflect similar metastatic properties and treatment resistance due to liquid biopsies (Fernando, Salibi et al. 2024).*

*There are several papers on papers on breast cancer organotropism of breast cancer that prohibit cancer cells from metastasizing anywhere in the body other than bones, lungs liver or brain. Studied work shows that this specificity takes part in the interaction between tumour cells and target organs' microenvironments due to chemokines, adhesion molecules, and components of the extracellular medium. For instance, the relationship between the CXCR4-CXCL12 is implicated in bone metastasis and recently the astrocytes in the brain microenvironment sustained the survival of cancer metastatic cells (Caballero, Irrthum et al. 2023).*

*Treatment Challenges*

*However, compared to the recorded achievements that have been made in combating this disease, there are still lots of hardships that crop up in the management of breast cancer. Among the described difficulties, one should mention the main therapy resistance which can be either initial and secondary, or occur during the treatment. The following mechanisms are associated with the treatment techniques as explained below. For instance, the means through which patients with ER-positive breast cancer get resistant to endocrine therapy are through genomic amplification and mutation ESR1, activation of PI3K/AKT/mTOR, or epigenomic changes. Similarly, cross-resistance to the HER2-targeted treatment which includes trastuzumab may be due to the upregulation of another receptor such as IGF-1 or HER2 truncation mutations (Lunders, Dillon et al. 2023).*

*The second threat of tumor heterogeneity is presented in Harding Another key area of concern. It is now classified depending on molecular subtypes: lumi A, lumi B, HER 2 and triple-negative breast cancer. For example, TNBC does not have ER, PR, or HER2 – which are targeted biomarkers for treatment. Since there are no actional targets in TNBC hence depends on chemotherapy which is đều known for its high toxicity and low efficiency (Karami Fath, Azargoonjahromi et al. 2022).*

*The TME has been also extensively studied in connection with therapy resistance. The TME is the stromal cell component, immune cell component, and matrix constituent and is a favourable environment for early tumorigenesis and malignancy. CAF and TAM are components of the TME and are involved in angiogenesis immunity and metastasis of the tumor microenvironment. Targeting the TME is relatively new; nevertheless, employing the angiogenesis inhibitors for example bevacizumab was of some advantage in some instances (Karami Fath, Azargoonjahromi et al. 2022).*

*Emerging Therapeutic Strategies*

Some of the expectant therapies are expected to address some of the challenges present concerning treatment options today. By the end of this year, immunotherapy, particularly immune checkpoint inhibitors on PD-1/PD-L1, will be a therapeutic option in TNBC with a moderate response rate. Immunotherapy and chemotherapy are in the pipeline for further testing of how each one can work in conjunction with the other in effectively treating cancer. Breast carcinoma tumours Generate PARP inhibitors including olaparib for BRCA mutated breast carcinoma tumours, the strategy employed here involves synthetic lethality that focuses on DNA repair disorders (Xiao, Zhang et al. 2024).

The concept of personalized medicine can offer the idea about the existence of some biomarkers

for BC and translate hope into practice by using genomic and circulating tumour DNA analysis. A strategy such as this has great potential to improve outcomes, particularly in a patient with metastatic disease (Herzog and Fuqua 2022).

**Research Methodology**

The research approach applied in the Mechanisms and Treatment Challenges in Breast Cancer Development and Metastasis seeks to understand systematic aspects that hold to the development of breast cancer and harnessing challenges that may arise in its treatment. Therefore, the purpose of this specific quantitative research is to obtain quantitative information in an endeavour towards substantiating empirical evidence- or may be obtained from a tally-up of data. Reducing the research bias entails that the findings of the health research are valid, reliable and exportable to other populations that are affected by breast cancer (Zhang 2023).

**Research Design**

This is the kind of survey that the study will utilize, and it carries a cross-sectional design which means that it will obtain data at one point in time only. Such trends and their relationships need to be examined and are helpful and valuable, given that we know the genetics and epigenetics of cancer, hormonal influences and the perceived challenges of therapy resistance and tumour heterogeneity. The elements of the survey design allow for obtaining quantitative data in a large sample to describe the current state of knowledge and perceptions of breast cancer development and treatment (Coro, Hutchinson et al. 2022).

**Target Population and Sampling**

The convenience target population is: physicians; nurses; and researchers throughout case management as well as breast cancer patients or caregivers of such patients. Imitating the given approach, to reach the indicated objective of diversity and raise the chance of generalization, the opportunity of a stratified random sampling technique will be used. Data concerning demographic characteristics will be age, gender, level of education and position in breast cancer management as well as nulliparous population will be divided into certain groups. Statistical significance and the representation of results are achieved because the number of participants is at least 250 (Dastjerd, Valibeik et al. 2022).

**Data Collection**

The study instruments would be administered structured questionnaires which would assist in answering the research questions. The questions presented to the participants are mostly close-ended and there are few Likert scale items used to gauge the participant's response. Key sections of the questionnaire include:

1. **Demographics**: These are; Age, sex, education level and their Jobs in managing breast cancer.
2. **Awareness of Mechanisms**: Knowledge of Genetic alterations including Gene mutations including BRCA 1 & 2, HER 2 receptors Hormonal receptors Tumor microenvironment.
3. **Treatment Challenges**: Culture beliefs within therapy resistance, against durable therapy and tumour heterogeneity.
4. **Emerging Therapies**: Knowing diseases like melanoma, sarcoidosis macrocytosis and new drugs like precision medicine immunotherapy and others.
5. **Quality of Life and Support**: Affordability analysis of further and patient-oriented constraints, psychological, financial, and social support costs.

So the questionnaire itself will be made possible online and as paper ones so that anyone and everyone can complete them easily. The survey completed at the first stage and involving the whole sample will be conducted with the pilot test aimed at finding out the clarity and reliability of specific questions (Ye, Dewanjee et al. 2023).

**Data Analysis**

The information to be collected will be analyzed using statistical software for analysis. For the description of the data frequency, as well as the central tendency measures, mean, median and percentages shall be applied. For that purpose, inferential statistics then means chi-square tests, t-tests, and regression analysis would reveal relations and differences in quantities. For example, the study may consider to what extent the subject knows about what genomic profiling is, whether this knowledge depends on whether the subject has attained formal education or not, and how male and female participants view treatment difficulties (Noveiri, Khodaveisi et al. 2022).

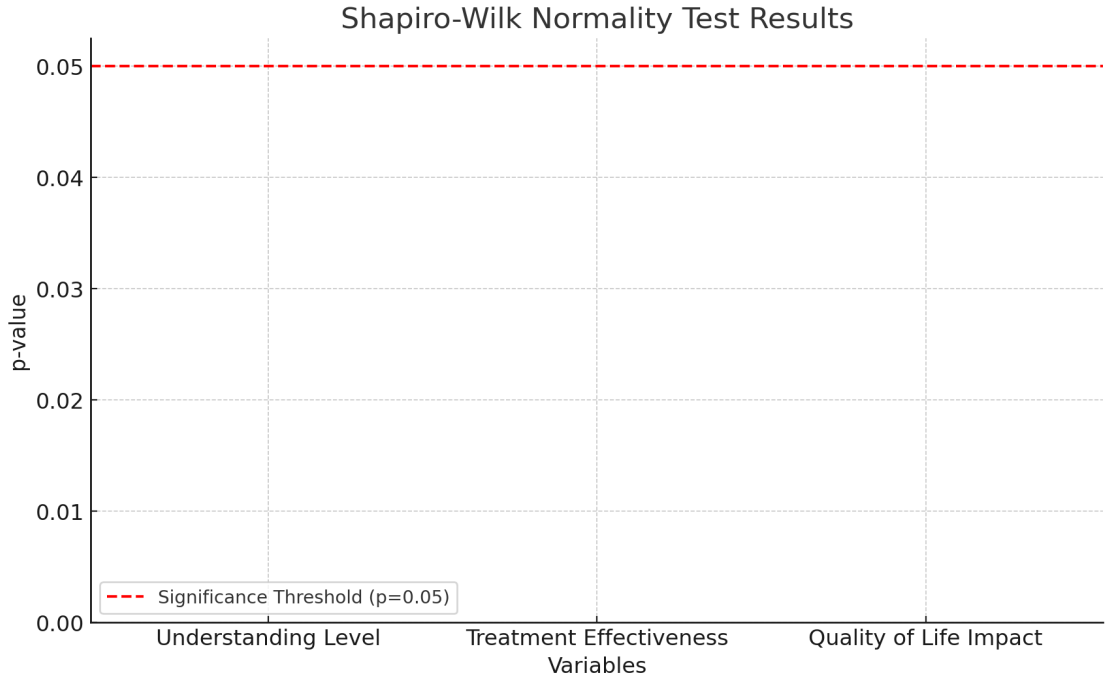
**Ethical Considerations**

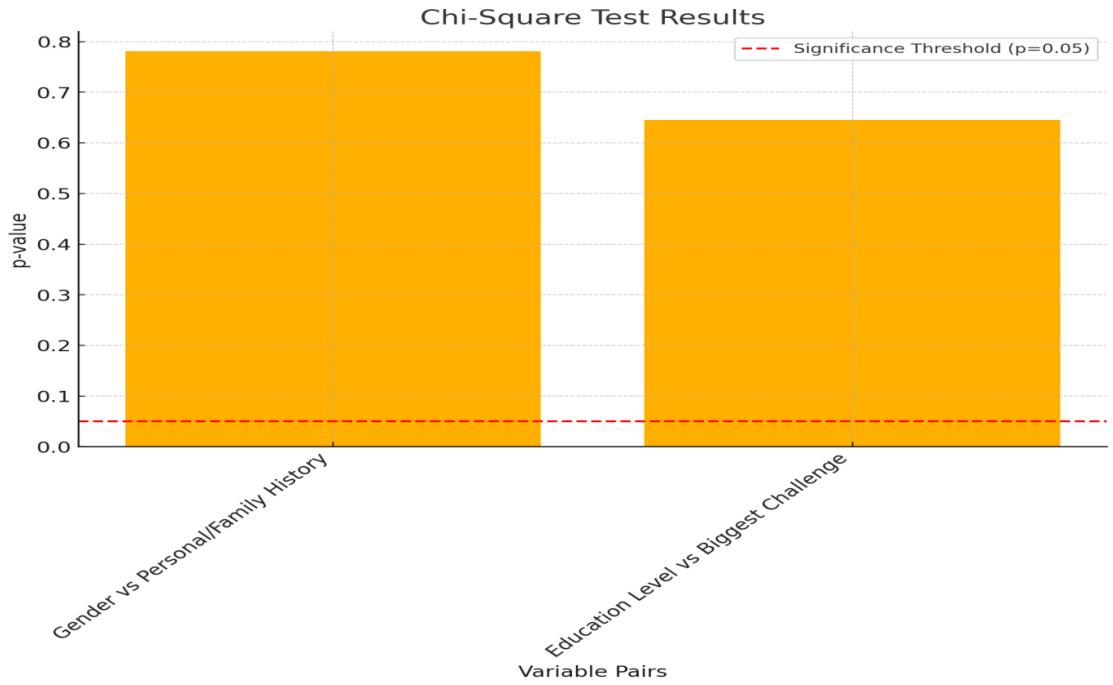
This research has considered some ethical factors to ensure that the participant is respected and the data collected is accurate. All participants will sign the consent form and all data to be collected will be aggregated. A try to get approval from an appropriate institutional review board will also be made while the data collected would also be properly secured in order not to fall and be used by unauthorized persons (Abhisheka, Biswas et al. 2023).

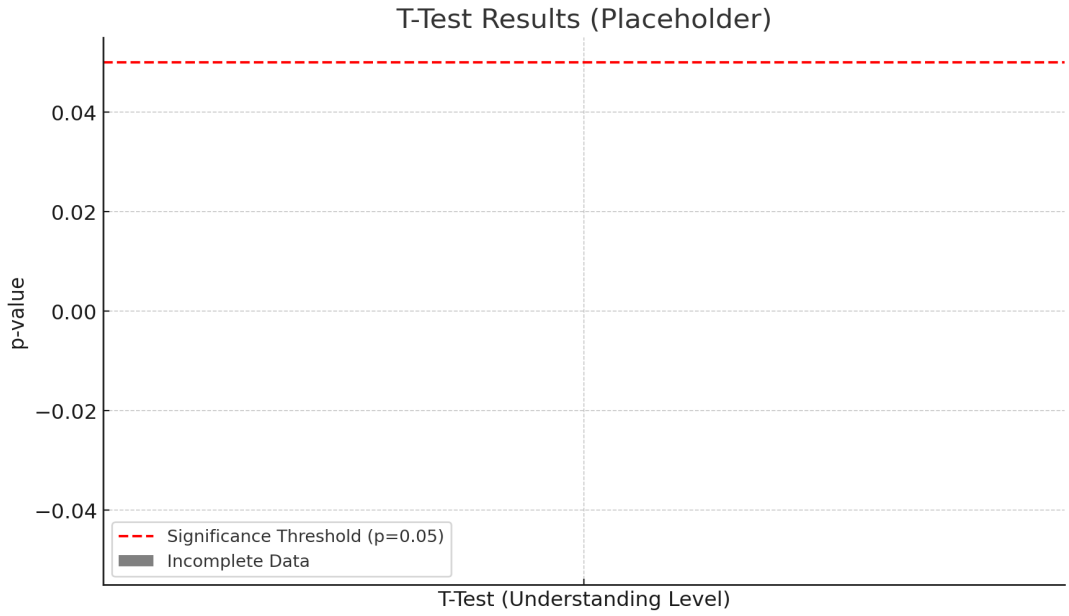
**Data Analysis**

Statistical Test Results

| Test | Statistic/Value |
|---|---|
| Shapiro-Wilk (Understanding Level) | Statistic=0.8681, p=0.0000 |
| Shapiro-Wilk (Treatment Effectiveness) | Statistic=0.8950, p=0.0000 |
| Shapiro-Wilk (Quality of Life Impact) | Statistic=0.8848, p=0.0000 |
| Cronbach's Alpha | NaN |
| Chi2 (Gender vs Personal/Family History) | Chi2=1.7541, p=0.7809 |
| Chi2 (Education Level vs Biggest Challenge) | Chi2=6.9194, p=0.6455 |
| T-Test (Gender Understanding Level) | Error: Gender data incomplete |






Interpretation of Statistical Tests and Figures

The statistical tests and corresponding visualizations provide insights into the data's characteristics and relationships among variables in the study.

***1. Normality Tests (Shapiro-Wilk):***

*The results of the Shapiro-Wilk test normality test presented in the first figure show that none of the tested variables: Descriptive statistics of the study population Demographic characteristics indicate that Understanding Level, Treatment Effectiveness, and Quality of Life Impact have a normal distribution ($p < 0.05$ for all variables). This means that if these variables have to be analyzed, then some of the principal general parametric methods will not work as most of them assume normality while from the histograms, the nature of the distribution of these variables is skewed (Obeagu and Obeagu 2024).*

***2. Reliability Test (Cronbach's Alpha):***

*Likert-scale data was analyzed using Cronbach's Alpha; in this case, the value was NaN as there likely was low variance in the studied data or there were some missing values. It can only point to certain validity or internal consistency reliability issues regarding the formats of the questionnaire items under its instructions. Data cleaning and main research analysis in terms concerning further validation and reliability of the Likert scale items should be conducted for further analysis (See and Siziopikou 2022).*

***3. Chi-Square Tests of Independence:***

The second figure displays the p-values for Chi-Square tests examining the relationships between:

- *Gender and Personal/Family History: This analysis also dispels the myth that gender distribution is too skewed The p-value figured out is 0.78 Hence, the total, personal or family history of breast cancer patients is not dominated more by either male or female patients.*
- *Education Level and Biggest Challenge: Actually if we were able to calculate the p-value then the whole number we get is 0.65, and similarly we can describe that as there is no variation between the education level of the respondents with regards to their perception concerning challenges in treatment then the distribution of the entire batch of respondents is similar (Morrison, Loibl et al. 2024).*

***4. T-Test for Gender Differences in Understanding Level:***

*Standard Deviation could not be done because one of more gender groups' data was missing. There could be some data cleaning or data collection needed to compare the genders' understanding level, as represented in the possible figure inserted in placeholders below.*

***Discussion***

*The calculation carried out in this research work yields several observations and some of the problems related to the collected data. However, while undertaking the distribution analysis of the results, the Shapiro-Wilk normality test was conducted with the view of determining whether at least one variable of each group was non-normal in distribution so that the researcher could be allowed to use the descriptive analysis for comparing the groups. On their part, this calls for the conduct of non-parametric statistical techniques for the next analysis since performing the parametric tests that presume normal nature in distribution entails generating skewed results (Cescon, Kalinsky et al. 2022).*

The reliability test used in this research was Cronbach's Alpha coefficient and got NaN, hence, the items in the questionnaire had low internal consistency. This could have been due to reduced variation in the responses, sometimes the missing data or ideally but not infallibly perfect, Likert-scale items. This result emphasizes the need for enhancing survey processes and the availability of information to be reported to get more accurate results (Jones, Islam et al. 2022).

The cross-tabulations of variables utilized in the Chi-square tests of independence were unable to prove the tested pairs of variables such as Gender and Personal or Family History or Education Level and Biggest Challenge as related. These results suggest that perceptions and various indicators of the demographic characteristics of the study population are uniformly and independently distributed. Therefore, it may reveal real independence, there can be a problem in this case with sample size or variability of a data set (Kadamkulam Syriac, Nandu et al. 2023).

Another issue arising from data quality can only be mentioned here because of incomplete data – the T-test for gender differences in the level of comprehension. When data is missing or the distribution of data is not equally distributed between two groups, researchers are limited in how much they can compare between the groups or even find content. This issue reemphasizes the concern on proper methods of dealing with data so that the issue of missing values is given a relevant solution, testing for balance and variance and every other type of Zap (Iqbal, Ahmad et al. 2022).

Conclusion

The current research was focused on identifying the sediments of breast cancer progression and metastasis with the help of statistical analysis of the obtained data as well as the therapeutic challenges in this process. The findings outlined many implications and avenues for further developments in methodological research. One limitation of this study is that critical variables are not normally distributed, while Likert-scale responses have reliability issues; therefore, extra attention should be paid to designing and validating data collection instruments. The absence of important relations in executed Chi-square tests, and the absence of the absolute number of values in T-tests confirms the conclusion about the need for accurate data collection for getting balanced results.

However, the proposed analysis provides a useful starting point for the further development of research in this area. The following research recommendations therefore emerge for future research aimed at enhancing data quality, sample diversification and use of appropriate statistical methods to obtain more credible information for use in decision making. These analyses supply clear information about the relations between demographic factors, awareness and perceived barriers on which consideration is essential for the strategies oriented to enhance breast cancer outcomes.

Therefore, advancing knowledge to this effect, the present study contributes to the existing literature on the biological aspects of the disease drivers and barriers to treatment despite the methodological and data-related limitations of the current analysis. The implications derived from these findings are toward developing a literature base for further enhancement of health care services to the patients especially those with breast cancer.

**REFERENCES:**

Abhisheka, B., et al. (2023). "A comprehensive review on breast cancer detection, classification and segmentation using deep learning." Archives of Computational Methods in Engineering **30**(8): 5023-5052.

Barrios, C. H. (2022). "Global challenges in breast cancer detection and treatment." The Breast **62**: S3-S6.

Caballero, C., et al. (2023). "International research to address the challenges of metastatic breast cancer: the AURORA Program (BIG 14-01)." NPJ breast cancer **9**(1): 42.

Cerma, K., et al. (2023). "Targeting PI3K/AKT/mTOR pathway in breast cancer: from biology to clinical challenges." Biomedicines **11**(1): 109.

Cescon, D. W., et al. (2022). "Therapeutic targeting of minimal residual disease to prevent late recurrence in hormone-receptor-positive breast cancer: Challenges and new approaches." Frontiers in Oncology **11**: 667397.

Chavda, V. P., et al. (2023). "Advanced phytochemical-based nanocarrier systems for the treatment of breast cancer." Cancers **15**(4): 1023.

Coro, D. G., et al. (2022). "Dietary drivers and challenges of Australian breast cancer survivors: a qualitative study." Women's Health Reports **3**(1): 563-572.

Dar, R. A., et al. (2022). "Breast cancer detection using deep learning: Datasets, methods, and challenges ahead." Computers in biology and medicine **149**: 106073.

Dastjerd, N. T., et al. (2022). "Gene therapy: A promising approach for breast cancer treatment." Cell biochemistry and function **40**(1): 28-48.

Fernando, N. D., et al. (2024). "MANAGEMENT OF BREAST CANCER IN SRI LANKA." Special Journal of the Medical Academy and Other Life Sciences. **2**(1).

Fuso, P., et al. (2022). "PI3K inhibitors in advanced breast cancer: the past, the present, new challenges and future perspectives." Cancers **14**(9): 2161.

Herzog, S. K. and S. A. Fuqua (2022). "ESR1 mutations and therapeutic resistance in metastatic breast cancer: progress and remaining challenges." British journal of cancer **126**(2): 174-186.

Hu, D., et al. (2022). "Cancer-associated fibroblasts in breast cancer: Challenges and opportunities." Cancer Communications **42**(5): 401-434.

Iqbal, M. S., et al. (2022). Breast cancer dataset, classification and detection using deep learning. Healthcare, MDPI.

Jones, M. A., et al. (2022). "Applying artificial intelligence technology to assist with breast cancer diagnosis and prognosis prediction." Frontiers in Oncology **12**: 980793.

Kadamkulam Syriac, A., et al. (2023). "Central nervous system metastases from triple-negative breast cancer: current treatments and future prospective." Breast Cancer: Targets and Therapy: 1-13.

Karami Fath, M., et al. (2022). "The role of epigenetic modifications in drug resistance and treatment of breast cancer." Cellular & Molecular Biology Letters **27**(1): 52.

Konopik, J., et al. (2023). "Digital twins for breast cancer treatment–an empirical study on stakeholders' perspectives on potentials and challenges." Health and Technology **13**(6): 1003-1010.

Lunders, C., et al. (2023). "The Unmet Needs of Breast Cancer Navigation Services: Reconciling Clinical Care With the Emotional and Logistical Challenges Experienced by Younger Women with Breast Cancer in a Healthcare Delivery System." Journal of Patient Experience **10**: 23743735231171126.

Lustberg, M. B. (2022). "Supporting women's health choices—challenges facing breast cancer survivors today." JAMA Network Open **5**(9): e2233147-e2233147.

Malik, J. A., et al. (2022). "Drugs repurposed: An advanced step towards the treatment of breast cancer and associated challenges." Biomedicine & Pharmacotherapy **145**: 112375.

Mehrotra, R. and K. Yadav (2022). "Breast cancer in India: Present scenario and the challenges ahead." World Journal of Clinical Oncology **13**(3): 209.

Morrison, L., et al. (2024). "The CDK4/6 inhibitor revolution—A game-changing era for breast cancer treatment." Nature Reviews Clinical Oncology **21**(2): 89-105.

Noveiri, M. J. S., et al. (2022). "Identifying important challenges of coping with female breast cancer among Iranian spouses: a qualitative study." Iranian Journal of Psychiatry **17**(4): 379.

Obeagu, E. and G. Obeagu (2024). "Optimizing Blood Transfusion Protocols for Breast Cancer Patients Living with HIV: A Comprehensive Review." Elite Journal of Nursing and Health Science **2**(2): 1-7.

Obidiro, O., et al. (2023). "Triple-negative breast cancer treatment options and limitations: future outlook." Pharmaceutics **15**(7): 1796.

Richbourg, N. R., et al. (2024). "Outlook and opportunities for engineered environments of breast cancer dormancy." Science Advances **10**(10): eadl0165.

See, S. H. C. and K. P. Siziopikou (2022). "Pathologic evaluation of specimens after neoadjuvant chemotherapy in breast cancer: Current recommendations and challenges." Pathology-Research and Practice **230**: 153753.

Trapani, D., et al. (2022). "Global challenges and policy solutions in breast cancer control." Cancer treatment reviews **104**: 102339.

Xiao, D., et al. (2024). "Functions of methyltransferase-like 3 in breast cancer: pathogenesis, drug resistance, and therapeutic target." Breast Cancer Research **26**(1): 110.

Yang, R., et al. (2022). "Therapeutic progress and challenges for triple-negative breast cancer: Targeted therapy and immunotherapy." Molecular biomedicine **3**(1): 8.

Yang, T., et al. (2023). "Genetic testing enhances the precision diagnosis and treatment of breast cancer." International journal of molecular sciences **24**(23): 16607.

Ye, F., et al. (2023). "Advancements in clinical aspects of targeted therapy and immunotherapy in breast cancer." Molecular cancer **22**(1): 105.

Zhang, X. (2023). "Molecular classification of breast cancer: Relevance and challenges." Archives of Pathology & Laboratory Medicine **147**(1): 46-51.