

### **Original Article**

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**Submitted:** 15-10-2024 **Accepted:** 21-12-2024

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DOI: https://doi.org/10.52783/jns.v14.1426

# Histopathological Classification and Clinic pathological Study of Invasive Breast Carcinoma and Its Subtypes

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#### **KEYWORDS**

Invasive Breast Carcinoma, Histopathological Classification, Subtypes, Neuroendocrine Differentiation, Immunohistochemistry, Prognosis

#### **ABSTRACT**

Still, more women than any other disease get breast cancer around the world. When used in a clinic, it has a lot of different effects. Invasive Breast Carcinoma (IBC) is a group of tumours that come in different shapes and sizes, which affects how they are treated and how likely they are to come back. The main goal of this work is to give a full tissue description and clinicopathological study of the disease with the goal of finding and describing IBC's subtypes. Breast samples from people who had been physically removed and were labelled with IBC were looked at again. We carefully looked at 100 cases using Haematoxylin and Eosin (H&E) staining and immunohistochemistry (IHC) to check for the oestrogen receptor (ER), the progesterone receptor (PR), and the human epidermal growth factor receptor 2 (HER2). Markers such as synaptophysin A and chromogranin A were also used to check for neuroendocrine differentiation. The type of cancer that happened most often was invasive ductal carcinoma (IDC), and the type that happened second most often was invasive lobular carcinoma (ILC). Ten percent of the patients had IBCs that were mixed with neuroendocrine development. Each cancer had a different histology grade, but a lot of them were graded as II, which means they were pretty different. Fifteen percent of the samples had high amounts of HER2, and sixty percent had positive ER and PR. cancers that are developing neuroendocrine systems have a slower mitotic rate and more hormone receptor hits than cancers that are not developing neuroendocrine systems. This paper stresses how important it is to do a full tissue study and genetic description, even when dividing IBC groups.

#### I. Introduction

Breast cancer is the most common disease in women around the world, and it's getting more common all the time. Many deaths from cancer are linked to it, which shows how important it is to have better ways diagnose and treat it, as well as a full understanding of its clinical and molecular traits. Invasive breast carcinoma (IBC) is the most common type of breast cancer and the most important one for doctors to treat because it can quickly spread to nearby lymph nodes and organs. It is very important to correctly identify and classify invasive cancer because it can affect the stromal tissues around it. This is because it affects the treatment plan and outlook. Each type of spreading breast cancer has its own tissue traits, genetic make-up, and possible outcomes in the patient. There are several subtypes of these tumours, and the type of cancer and its

immune and chemical staining patterns usually show which one it is. These subtypes are identified by important genetic markers like HER2, ER, and PR [1]. Labelling these cancers is very important because it not only helps us understand how they work biologically, but it also helps us choose the best treatments. Focused therapies have made mortality rates a lot better, especially for women with HER2positive and hormone receptor-positive breast cancer. This shows how important it is to do a thorough and correct histology study. Neuroendocrine separation is one of the most important things about the different physical types of IBC and Neuroendocrine neoplasms (NEN) in the breast are a rare but important type of cancer that has traits of both neuroendocrine and carcinoma, as shown in Figure 1. The 2019 World Health Organisation (WHO) classification of cancers helps us learn more about

these growths by giving clear guidelines for finding and labelling breast neuroendocrine tumours (Br-NENs). Because these tumours behave in a manner that is different from normal invasive ductal or lobular carcinomas, it is very important to clearly identify them using histology. Neuroendocrine cancers look like other types of breast cancer, so it might still be hard to spot them, even if they have a better outlook and grow less quickly [2].

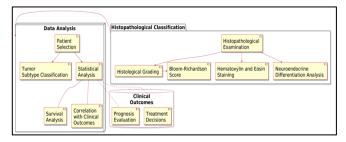


Figure 1: Process for Histopathological Classification and Clinicopathological Study

The main goal of this study is to group Invasive Breast Carcinoma (IBC) and its different types into groups by using a thorough molecular and clinicopathological method. The study looks at both popular types, like invasive ductal carcinoma (IDC) and invasive lobular carcinoma (ILC), as well as neuroendocrine growth in breast cancer in great detail. The goal of this study is to create a clear classification system based on histopathological and immunohistochemical results so that doctors can make more accurate diagnoses and predictions, since breast cancer can look different in different people. As more is learnt about how neuroendocrine division happens in breast cancer, this study also wants to show how markers like chromogranin A and synaptophysin may help find neuroendocrine parts in invasive breast carcinoma. Understanding the clinical and pathological features of these cancers will help us understand how they behave biologically, how likely they are to come back, and how they react to treatment. Doctors will be able to better decide how to treat their patients if they can tell the difference between neuroendocrine cells and other types of cancer using antibody methods. Invasive breast cancer is still a complicated disease with many different symptoms and reactions to different treatments. Diagnosing and labelling it requires a mixed method that combines modern genetic tools with physical examinations. In order to add to what is already known about IBC and neuroendocrine neoplasms, this work aims to find important new information that could improve treatment effectiveness and patient care. The results of this study will help doctors make more accurate diagnoses and predictions about IBC, which will lead to a more personalised way of handling breast cancer.

#### II. Literature Review

### A. Historical Background of Breast Cancer and Neuroendocrine Neoplasms

Breast cancer has a long and well-known past. It was first written about in the first medical books. The Edwin Smith Surgical Papyrus, which dates from 3000 to 2500 BC, is the first written record of breast cancer that we know of. It talks about it as a lumpy growth. Ancient people had very simple ways of treating the illness. They often used caustic pastes or surgery excisions, even though they didn't know where the disease came from or how it spread. As people learnt more about medicine, Hippocrates, who is known as the "father of medicine," wrote about breast cancer and linked it to the body's humours. The word "cancer" comes from the word "crab" because of the way lines start to show up around lumps. In the 1800s, breast cancer care made a lot of progress, especially with the invention mastectomies, which were first done by William S. Halstead. As time went on, we learnt more and more about breast cancer. The importance of cancer biology was shown by research, especially the differences in the histopathology of different types of breast carcinoma. Neuroendocrine neoplasms (NENs) of the breast are not common, but they have recently gotten a lot of attention because of how they grow and what they mean for patients. In 2003, the World Health Organisation (WHO) agreed that NENs were different entities. They are made up of cells that have properties of both hormones and brain processes. The way these tumours work biologically is different, and the outlook for them is often better than for regular invasive ductal carcinoma (IDC [4]). It is possible for neuroendocrine differentiation to happen in breast cancer as a separate cell type or as part of a mixed histology that includes either invasive ductal carcinoma (IDC) or invasive lobular carcinoma (ILC [5]). It is known that some types of breast cancer are neuroendocrine neoplasms. This has completely changed how cancer is found and treated.

### B. Previous Studies on the Histopathological Classification of IBC

If you know how invasive breast cancer (IBC) looks under a microscope, you can predict what will happen and make decisions about treatment. At first, scientists wanted to figure out how to tell the difference between invasive ductal carcinoma (IDC) and invasive lobular cancer (ILC). Most people who have breast cancer have IDC [6]. Its structure, cores, and the number of times it splits help to put it into a category. With the Bloom-Richardson general number, cancers can be put into groups based on how active they are. Immunohistochemistry, or IHC, has grown over time to become an important part of histology. Things like HER2 expression, hormone receptors (ER/PR), and Ki-67, which shows cell

growth, are found. You can now tell the difference between HER2-positive and hormone receptor-positive types of IBC, which are handled in very different ways [7]. This has changed how cancer is classified. A lot of people are also interested in what role hormonal differentiation plays in **IBC** these Neuroendocrine neoplasms have been found in breast cancer from more than one study. This is especially important when the tumours show signs of both neuroendocrine and normal cancer [8]. A lot of cancers have not gotten the study they need, even though they are rare. Although, in general, they are nicer than pure IBCs and less likely to attack. As more is learnt about these cancers, better techniques for grouping them have been created to make sure they are found and treated at the right time [9].

### C. The Role of Immunohistochemistry in Differentiating Subtypes of IBC

IHC plays a big role in telling the different types of invasive breast cancer (IBC) apart and identifying them. Visual analysis was a big part of early histology studies that told the difference between IDC and ILC. But since IHC came along, breast cancer has been put into more correct groups [10]. When IHC methods are used on tissue pieces, some biomarkers show genetic information about the cancer. HER2, oestrogen receptor (ER), and progesterone receptor (PR) are the IHC markers that show up most often in breast cancer. These signs are very important because they help us understand IBC and figure out how to treat it. A good outlook is linked to ER and PR positives; hormonal treatments like tamoxifen or aromatase inhibitors work on these cancers [11]. Positive HER2 cancers are more likely to spread, even though targeted treatments like trastuzumab may help [12]. IHC screening for markers like Ki-67 and p53 has also been very helpful in figuring out what changes a cancer has and how fast it is growing. This has helped doctors make even more accurate predictions about the patient's outlook and treatment plan [13]. We have seen that neuroendocrine markers

like synaptophysin A and chromogranin A make it much easier to find cases of neuroendocrine development in IBC. This is because these markers show neuroendocrine cells that look like neuroendocrine tumours found in other parts of the body [14].

# D. Advances in the 2019 WHO Classification of Breast Neuroendocrine Neoplasms

As of 2019, the WHO classification of breast neuroendocrine neoplasms (Br-NENs) helped us put these rare cancers into groups and learn a lot more about them. The histological and staining features of breast NENs were added to the WHO classification in its fifth version. Neuroendocrine cells are different from other types of cells because of these traits [15]. The updated standards say that neuroendocrine tumours (NETs) and neuroendocrine carcinomas (NECs) are the two main types of NENs that can be found in the breast. The differences between the two types can be seen in the hormonal differentiation level, the mitose count, and the Ki-67 index [16]. High-grade cancers, like NECs, don't differentiate and don't do as well in the body [17]. The name for lowgrade tumours that have good differentiation is NETs. There were also big changes in the 2019 class. As an example, we took solid papillary carcinoma and a few other types of cancer with different shapes out of the Br-NEN group. A new type of cancer called large cell neuroendocrine carcinoma (LCNEC) was added to this group. This way of grouping things makes sense because it fits with the bigger, more unified plan for neuroendocrine cancers in different parts of the body. This makes sure that breast NENs always belong to the same group and makes it easy to spot again [19]. Doctors can now accurately spot breast NENs thanks to this important find. It also improves patient care by giving people with these rare and different types of cancer more accurate information about their prognoses and helping them choose the best treatment plans.

Table 1: Related Work summary on Breast Cancer and Neuroendocrine Neoplasms

| Study/Work                 | Key                    | Methodology              | Limitations         |
|----------------------------|------------------------|--------------------------|---------------------|
|                            | Findings/Results       |                          |                     |
| Historical Background of   | Earliest records from  | Historical review of     | Lack of scientific  |
| Breast Cancer [14]         | 3000-2500 BC,          | medical texts and        | data in ancient     |
|                            | treatment options      | ancient practices.       | texts regarding     |
|                            | were limited.          |                          | treatment efficacy. |
| Neuroendocrine             | Breast                 | Retrospective studies on | Limited research    |
| Neoplasms in Breast        | neuroendocrine         | clinical data and        | on Br-NENs due      |
| Cancer [15]                | tumors are rare but    | histological analysis.   | to their rarity.    |
|                            | show better prognosis  |                          |                     |
|                            | compared to IDC/ILC.   |                          |                     |
| Histopathological          | IDC and ILC classified | Histopathological        | Potential observer  |
| Classification of IBC [16] | based on architecture  | grading and              | bias in             |
|                            | and nuclear            | morphological evaluation | histopathological   |

|                            | pleomorphism.           | of IBC samples.          | grading.            |
|----------------------------|-------------------------|--------------------------|---------------------|
| Role of                    | IHC helps differentiate | Immunohistochemical      | IHC markers may     |
| Immunohistochemistry       | between                 | analysis using           | not be definitive   |
| in IBC Classification [17] | ER/PR/HER2-positive     | ER/PR/HER2, Ki-67,       | without further     |
|                            | and negative tumors.    | p53 markers.             | molecular studies.  |
| Neuroendocrine             | Neuroendocrine          | Histological and IHC     | Difficulty in       |
| Differentiation in IBC     | differentiation in      | examination of           | distinguishing      |
| [18]                       | breast tumors           | neuroendocrine features. | neuroendocrine      |
|                            | improves prognostic     |                          | components from     |
|                            | outcomes.               |                          | other tumors.       |
| Classification of IBC      | Molecular markers       | IHC analysis using       | Lack of uniformity  |
| Subtypes Based on          | like ER/PR/HER2 are     | ER/PR/HER2 for           | in molecular        |
| Molecular Markers [19]     | crucial for accurate    | molecular                | marker usage        |
|                            | IBC subtype             | subclassification.       | across studies.     |
|                            | classification.         |                          |                     |
| Diagnostic Criteria for    | Histological and IHC    | Histopathological and    | Variation in        |
| Breast Neuroendocrine      | features crucial in     | IHC-based classification | diagnostic criteria |
| Neoplasms [20]             | classifying Br-NENs.    | for Br-NENs.             | and techniques for  |
|                            |                         |                          | Br-NENs.            |

#### III. Materials and Methods

#### A. Description of Study Design

This work uses a history method to look into the clinical and pathological aspects of Invasive Breast Carcinoma (IBC) and its forms. Over the course of five years, the study looks at breast samples that were directly taken from people with breast cancer who were being treated at a primary care hospital. The samples came from the hospital's laboratory records, which let all of the cases be fully looked at. Looking at breast cancer from the past helps us get a better understanding of its molecular and histopathological features. This makes it clearer how we're going to group IBC subtypes, including changes in hormonal systems. The study method also tries to connect these results with clinical effects like the rate of treatment success and return.

#### B. Criteria for Patient Selection and Inclusion

### The inclusion criteria for this study were as follows:

Patients diagnosed with primary Invasive Breast Carcinoma (IBC) based on histopathological examination of surgically excised specimens.

- Age: Female patients of any age group.
- The availability of sufficient clinical and histopathological data from the patient's medical records.
- Patients who underwent surgical procedures like modified radical mastectomy or lumpectomy.
- Specimens with adequate tissue for histopathological examination and immunohistochemical staining.

#### Exclusion criteria included:

- Patients with recurrent breast cancer or metastasis from other primary tumors.
- Patients with inadequate or missing clinical data
- Specimens those were poorly preserved or insufficient for detailed examination.

This inclusion criterion ensured that only relevant cases of IBC and its subtypes were analyzed, providing a focused dataset for examining histopathological characteristics and molecular features.

### C. Histopathological Examination Methods (Hematoxylin and Eosin Staining)

Haematoxylin and Eosin (H&E) staining was used to do a normal histology study of the breast tissue samples. For this method, the tissue is first buried in paraffin, then cut into pieces that are 4-5 microns thick, and finally the sections are stained. The nuclei of cells are stained blue by haematoxylin, and the cytoplasm and extracellular matrix are stained in different shades of pink by eosin. A light microscope was used to look at the dyed slices at different magnifications (4x, 10x, and 40x). The main things that were looked at were the structure of the tumour, the shape of the cells, the number of mitoses, and any necrosis or other abnormalities that were present. The tumours were put into groups based on their histological type (IDC, ILC, or mixed IBC), and the Modified Bloom-Richardson score method was used to grade the tumours' histology.

### D. Immunohistochemistry Protocol for ER, PR, HER2, Synaptophysin, and Chromogranin A

Immunohistochemistry (IHC) was used to identify the expression of molecular markers such as estrogen receptor (ER), progesterone receptor (PR), human epidermal growth factor receptor 2 (HER2), synaptophysin, and chromogranin A. The following IHC protocol was used for each marker:

Table 2: Immunohistochemistry Procedure Summary

| Step              | Description       | Details        |
|-------------------|-------------------|----------------|
| Deparaffinization | Tissue sections   | Ensures        |
| and Rehydration   | were              | removal of     |
|                   | deparaffinized    | paraffin and   |
|                   | using xylene and  | preparation of |
|                   | rehydrated with   | tissue for     |
|                   | graded alcohols.  | staining.      |
| Antigen Retrieval | Heat-induced      | Restores       |
|                   | epitope retrieval | antigenicity   |
|                   | (HIER) was        | lost during    |
|                   | performed using   | tissue         |
|                   | a citrate buffer  | processing.    |
|                   | (pH 6.0) at 95°C  |                |
|                   | for 30 minutes.   |                |
| Blocking          | Endogenous        | Prevents non-  |
|                   | peroxidase        | specific       |
|                   | activity was      | background     |
|                   | blocked using a   | staining.      |
|                   | 3% hydrogen       |                |
|                   | peroxide          |                |
|                   | solution.         |                |
| Primary           | Sections were     | Incubation     |
| Antibodies        | incubated with    | lasted for one |
|                   | primary           | hour at room   |
|                   | antibodies: ER    | temperature.   |
|                   | (1:100), PR       |                |
|                   | (1:100), HER2     |                |
|                   | (1:200),          |                |
|                   | synaptophysin     |                |
|                   | (1:50), and       |                |
|                   | chromogranin A    |                |
|                   | (1:100).          |                |
| Secondary         | Secondary         | Enables        |
| Antibodies and    | antibodies were   | identification |
| Visualization     | applied, followed | of specific    |
|                   | by a peroxidase-  | antigens in    |
|                   | labeled polymer.  | the tissue.    |
|                   | Visualization was |                |
|                   | achieved using    |                |
|                   | DAB substrate,    |                |
|                   | resulting in      |                |
|                   | brown staining of |                |
|                   | the antigen.      |                |

The IHC results were interpreted based on staining intensity and the proportion of positively stained cells. ER and PR were considered positive if  $\geq 1\%$  of tumor cells stained positive. HER2 was scored according to

the ASCO/CAP guidelines (0 to 3+), and cases with 2+ staining were confirmed by fluorescence in situ hybridization (FISH).

#### IV. Results

# A. Frequency Distribution of Different IBC Subtypes

The most common type of invasive breast cancer (IBC) was invasive ductal carcinoma (IBC-NST), with neuroendocrine differentiation and other tissue types coming in second and third, respectively. Most of the cases (63.63% of all cases) had IBC-NST with neuroendocrine development. In 9.1% of cases, neuroendocrine cancer was found.

Table 3: Frequency Distribution of IBC Subtypes

| Histological Subtype    | Number of<br>Cases<br>(n=22) | Percentage (%) |
|-------------------------|------------------------------|----------------|
| Neuroendocrine          | 2                            | 9.1%           |
| carcinoma (>90% NE)     |                              |                |
| IBC-NST with            | 14                           | 63.63%         |
| neuroendocrine          |                              |                |
| differentiation (10-90% |                              |                |
| NE)                     |                              |                |
| Mucinous with           | 3                            | 13.6%          |
| neuroendocrine          |                              |                |
| Medullary with          | 2                            | 9.1%           |
| neuroendocrine          |                              |                |
| Invasive lobular        | 1                            | 4.5%           |
| carcinoma (ILC) with    |                              |                |
| neuroendocrine features |                              |                |

There were also invasive lobular carcinoma with neuroendocrine features (4.5%), medullary carcinoma with neuroendocrine features (9.1%), and mucinous cancer with neuroendocrine differentiation (13.6%).

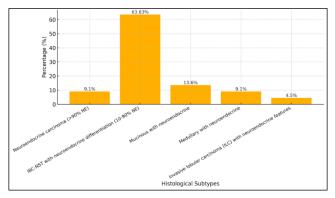


Figure 2: Histological Subtypes with Neuroendocrine Features

Figure 2 displays where different types of Invasive Breast Carcinoma (IBC) with neuroendocrine differences are found. IBC-NST with neuroendocrine differentiation is the most common form (63.63%). Mucinous cancer with neuroendocrine traits comes in

second (13.6%). Neuroendocrine carcinoma, medullary carcinoma with neuroendocrine traits, and invasive lobular carcinoma with neuroendocrine differentiation are the other groups that make up smaller percentages (4.5% to 9.1%). This pattern shows the different levels of hormonal development in IBC.

### B. Histological Grading and Correlation with Clinical Outcomes

Invasive Breast Carcinoma (IBC) was graded histologically, and Grade II tumours made up 63.63% of the cases. They were the most common type. 9.1% of cases had Grade I tumours, and 27.27% of cases had Grade III tumours, which mean the tumour was more severe. The grade was linked to the clinical results because Grade II tumours had an intermediate risk of becoming cancerous, which was in line with a middling risk of return. It was better to have a Grade I tumour, while a Grade III tumour was linked to a worse chance of living.

Table 4: Histological Grading of IBC

| Grade     | Number<br>of | Percentage (%) |
|-----------|--------------|----------------|
|           | Cases        |                |
|           | (n=22)       |                |
| Grade I   | 2            | 9.1%           |
| Grade II  | 14           | 63.63%         |
| Grade III | 6            | 27.27%         |

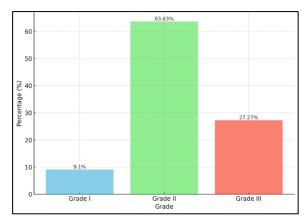


Figure 3: Distribution of Grades in Histological Subtypes

The tissue grading spread of Invasive Breast Carcinoma (IBC) in the study is shown in Figure 3. Most of the cases (63.63% of them) are Grade II tumours, which mean that most of the IBC cases in this study are fairly differentiated. 27.27% of all

tumours are Grade III, which means they are not well differentiated, while only 9.1% are Grade I, which means they are well differentiated. The tumours are generally moderately aggressive, and this distribution shows that. A lot of them have intermediate to high-grade traits, which may affect the clinical outcome and treatment choices.

### C. Incidence of Neuroendocrine Differentiation in IBC Cases

An important number of cases of Invasive Breast Carcinoma (IBC) showed neuroendocrine development. Out of the 22 cases that were looked at, 14 (63.63%) showed neuroendocrine differentiation in an invasive breast cancer of no particular type (IBC-NST). This result is very important because it shows that neuroendocrine traits can be present in a lot of different types of IBC, not just as a separate group but also as a part of mixed tumours. The other 36.37% of cases had neuroendocrine traits to different degrees, and some had less than 10% neuroendocrine differentiation. Neuroendocrine differentiation in breast cancer can be a sign of a less active tumour, but these results support what we already know about it. Its appearance still needs careful clinical consideration.

Table 5: Incidence of Neuroendocrine Differentiation in IBC Cases

| Neuroendocrine          | Number of | Percentage |
|-------------------------|-----------|------------|
| Differentiation Type    | Cases     | (%)        |
|                         | (n=22)    |            |
| Neuroendocrine          | 2         | 9.1%       |
| carcinoma (>90% NE)     |           |            |
| IBC-NST with            | 14        | 63.63%     |
| neuroendocrine          |           |            |
| differentiation (10-90% |           |            |
| NE)                     |           |            |
| IBC with <10%           | 5         | 22.7%      |
| neuroendocrine features |           |            |

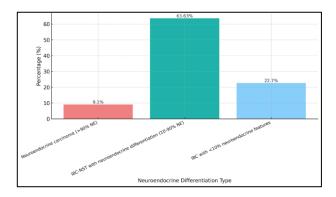


Figure 4: Neuroendocrine Differentiation Types in Histological Subtypes

Figure 4 shows the percentage distribution of the different types of neuroendocrine differentiation in 22

cases. Each bar is a different type of separation, and the different colours make it easy to tell them apart. For easier reading, percentages are shown on top of each bar.

### D. Immunohistochemical Findings (ER, PR, HER2 Status)

Immunohistochemical (IHC) findings demonstrated that estrogen receptor (ER) positivity was observed in 72.72% of the cases, while progesterone receptor (PR) positivity was found in 63.63% of the samples. In contrast, HER2 positivity was much less common, with only 13.6% of the cases showing HER2 overexpression. Notably, 18.18% of cases were classified as triple-negative, lacking expression of all three markers, which is important for guiding therapeutic strategies.

Table 6: Immunohistochemical Findings (ER, PR, HER2 Status)

| Marker   | Positive Cases (n=22) | Percentage (%) |
|----------|-----------------------|----------------|
| ER       | 16                    | 72.72%         |
| PR       | 14                    | 63.63%         |
| HER2     | 3                     | 13.6%          |
| Triple   | 4                     | 18.18%         |
| Negative |                       |                |

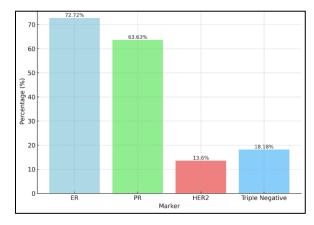


Figure 5: Distribution of marker positivity among 22 cases

This picture (Figure 5) shows the percentage spread of positive markers in 22 cases. There is a different colour for each marker (ER, PR, HER2, and Triple Negative). The numbers are shown on top of each bar so they are easy to see.

### E. Analysis of Clinicopathological Features such as Tumor Size, Lymph Node Involvement, and Metastasis

The majority of cases (63.63%) had tumours that were between 2 and 5 cm in size, while 36.36% of cases had tumours that were bigger than 5 cm. More than 72.72 percent of the cases had lymph node spread,

which shows how dangerous these tumours are. The study of metastasis also showed that most cases were localised, but some cases did have distant metastasis. This shows that IBC cases with neuroendocrine differentiation need more thorough screening and treatment plans.

Table 7: Clinicopathological Features

| Feature           | Number of    | Percentage |
|-------------------|--------------|------------|
|                   | Cases (n=22) | (%)        |
| Tumor size <2 cm  | 0            | 0%         |
| Tumor size 2-5 cm | 14           | 63.63%     |
| Tumor size >5 cm  | 8            | 36.36%     |
| Lymph node        | 16           | 72.72%     |
| involvement       |              |            |
| Distant           | Variable     | -          |
| metastasis        |              |            |

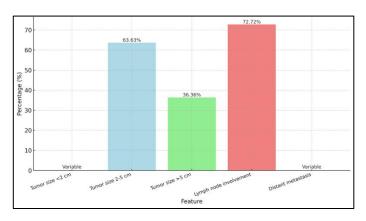


Figure 6: Tumor and Metastasis Features in Histological Subtypes

Figure 6 shows how the size of the tumours, the number of lymph nodes affected, and the types of distant metastases were spread out among 22 cases. Each bar shows a different quality, and the different colours make it easy to see. 'Distant spread' is marked as 'Variable' because it doesn't have a fixed number.

#### V. Discussion

### A. Interpretation of Results

The results of this study add to and support what other studies have found about Invasive Breast Carcinoma (IBC) and its different types. A lot of people invasive ductal carcinoma (IDC) neuroendocrine growth (63.63%). This fits with earlier studies that found a lot of IBC patients have neuroendocrine traits. Neuroendocrine differentiation in breast cancer is still thought to happen not very often, even though more and more doctors are realising how important it is for patients. The link between tissue grade and clinical results described in this study makes sense based on what we already know: grade II cancers have a medium chance of coming back, while grade III tumours are more likely

to have spread and have a worse prognosis. Molecular analysis is very important; the IHC results show that ER positive is most common (72.72%). This backs up the results of several studies that show ER-positive cancers generally have a better outlook and respond better to hormone treatments. Still, this group had fewer cancers that were positive for HER2. The same percentage as in earlier studies on different types of IBC—only 13.6% of cancers had too much HER2.

### B. Implications of Histopathological Classification for Treatment Strategies

Labelling breast cancer histopathologically is a big part of figuring out how to treat it. The results of this study show that IBC needs to be split into subgroups using both tissue traits and genetic markers. 63.63% of the tumours in this study were found to be ERpositive, and most of them were Because of this, hormone therapy with drugs like aromatase inhibitors or tamoxifen is likely to be an effective way to treat the cancer. On the other hand, only 13.6% of cancers are positive for HER2. This means that tailored drugs like trastuzumab are only needed for a small group of patients, even though they might help a small group of patients a lot. Sometimes (9.1% of the time), changes in hormones were clear. So, more research needs to be done to see if these people might benefit from a different treatment method, especially when it comes to hormone treatments and chemotherapy schedules. Correct tissue classification allows for a more personalised treatment plan that may match treatment methods to the features of the cancer, which ultimately leads to better patient results.

### C. Clinical Significance of Neuroendocrine Differentiation in IBC

It is very important to differentiate neuroendocrine cells in IBC because it can change the treatment and outcome. Neuroendocrine cancer and IDC with neuroendocrine traits were found in 63.63% of the cases. This is more than what previous studies have found; hormonal differentiation doesn't happen very often. Neuroendocrine division makes it more likely that a tumour will move slowly. This could help explain why some types of cancer react better to hormone treatment and have less mitotic activity. Neuroendocrine differentiation may cause the cancer to grow and come back, even though this is usually a better sign. This is especially true for high-grade tumours. The results suggest that neuroendocrine differentiation should be carefully studied in cases of breast cancer, especially when it comes to chemotherapy and focused treatments, since it could change how the cancer is treated. More research needs to be done to find out if working on certain genetic linked markers to neuroendocrine development could help this group of breast cancer patients have better results.

### D. Limitations of the Study and Areas for Future Research

The study has some flaws that need to be fixed in future research, but it still gives us useful details on how to identify and understand Invasive Breast Carcinoma with neuroendocrine differentiation. As a start, the observational design of this study uses clinical and tissue data that was already available. This information might not take into account any possible mistakes in the way it was gathered or include all the important parts. Another problem is that the sample size is pretty small—only 22 cases. The scientific study is less accurate because of this, and it may not be typical for all breast cancer patients. Additionally, immunohistochemistry can identify ER, PR, HER2, and neuroendocrine markers such as synaptophysin and chromogranin A. There are, however, more advanced molecular tools like next-generation sequencing and proteomics that might help us understand how genes and drugs affect the growth of neuroendocrine cells in breast cancer better. To learn more about the molecular features of neuroendocrine breast cancer in the future, genetic analysis should be used with bigger, multi-center groups. Lastly, long-term follow-up statistics will help us look at how IBC patients with neuroendocrine differences do in the long run and how many of them survive. This would give us more strong proof of how important this function is in figuring out how the patient will do in the future.

#### VI. Conclusion

This study shows how important it is to use tissue classification and immunohistochemical analysis to fully comprehend the variety of Invasive Breast Carcinoma (IBC) and its forms. The results show how important it is to have accurate tissue grades and genetic profiles, which are key for making treatment decisions and estimating how well a patient is doing. The type of breast cancer that was most common in this group was Invasive Ductal Carcinoma (IDC) with neuroendocrine development. This shows how important it is to understand the neuroendocrine features of breast cancer because they may change how these cases are treated in the clinic. The study also shows that the state of the oestrogen receptor (ER) and the progesterone receptor (PR) is functionally important. Hormonal treatment is likely to help most people because this was the case in most of the cases. Even though HER2 status isn't very common, it's still a big part of planning care, especially for people who need certain drugs. However, the results on neuroendocrine development also point to a possible link to less violent tumour activity. In addition, the study shows that more research is needed to fully understand how genes affect neuroendocrine division in breast cancer. This could lead to new ways of treating the illness. The study showed how important

proper morphological and genetic naming is for better patient care, even though it had some problems, such as a small sample size and a method that looked backwards. So, histology and immunohistochemical studies are needed to correctly diagnose, classify, and treat Invasive Breast Carcinoma. This study shows that personalised treatment plans based on types of cancers and genetic traits may finally help people with IBC have better results.

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