ORIGINAL ARTICLE

Clinical Characteristics and Prevalence of Breast Cancer Molecular Subtypes: A Five-Year Retrospective Study at a Tertiary Care Center in Thailand

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Background: Breast cancer, the most common female cancer, has molecular subgroups that affect prognosis and treatment.

Objective: To determine the prevalence, clinicopathological factors, and the molecular subtypes of breast cancer patients at Rayong Hospital.

Materials and Methods: Data were collected from the medical records of Rayong Hospital regarding patients diagnosed between October 2018 and 2023. The present study covered demographics, tumor characteristics, staging, and molecular subtypes Luminal A, Luminal B, HER2-enriched, and TNBC based on ER, PR, HER2, and Ki-67. Pathological complete response (pCR) was also evaluated.

Results: Seven hundred thirty-one patients were included in the study, with a mean age of 54.17 years. Most patients were diagnosed in middle age, 55.4%. Predominant molecular subtypes were Luminal B at 35.0%, Luminal A at 34.6%, TNBC at 18.4%, and HER2-enriched at 12.0%. Younger patients were shown to be correlated with TNBC subtypes, and 48.14% of the patients were diagnosed at Stage II, followed by Stages III for 27.64%. The overall pCR rate for patients receiving neoadjuvant therapy was 20%.

Conclusion: Luminal B and Luminal A came out to be more predominant, whereas TNBC was associated with middle-aged patients. Most cases are diagnosed in the later stage, therefore, there is a need for early detection. Improved treatment with indications according to the individual and better screening will be necessary to better the outcomes of breast cancer.

Keywords: Breast cancer; Intrinsic subtypes; Epidemiology; Molecular subtype; Neoadjuvant therapy; Pathologic complete response

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Breast cancer is the most widely diffused cancer among females worldwide[1], with increasing incidence, particularly in Asia. Thailand had 34.2 cases per 100,000 between 2016 and 2018, while Rayong province had 29.5 cases per 100,000 people. The trend has increased in the past ten years. The diagnosis is usually made between the ages of 40 and 60[2].

Breast cancer includes various molecular subtypes associated with prognosis and treatment. The St. Gallen classification stratifies breast cancer according to immunohistochemical markers such as estrogen receptor (ER), progesterone receptor (PR), human epidermal growth factor receptor 2 (HER2), and Ki-67[3], delineating Luminal A, Luminal B as HER2-positive/-negative, HER2-enriched, and triple-negative breast cancer (TNBC). Subtype prevalence is important to understand to facilitate better treatment and outcomes.

Dialectical breast is Luminal A type, which is the most prevalent subtype, representing 50% to 70% of cases[4]. ER and PR define it as positivity, HER2 negativity, and low Ki-67 expression in 20%, indicating an indolent course and an excellent prognosis[5]. The benefits accrue to patients on endocrine therapy such as tamoxifen or aromatase inhibitors with little chemotherapy benefit[6]. This subtype is more common in postmenopausal women and in countries with early screening programs, like North America and Europe[7].

Luminal B-like breast cancer is attributable to 10% to 20% of cases, which are usually ER and/or PR positive with high levels of Ki-67 in more than 20%[8]. It has higher and rapid proliferation rate with worse prognosis than Luminal A-like tumors.

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Treatment typically encompasses endocrine therapy, chemotherapy, and HER2-directed therapy if HER2-positive[9]. This subtype is more prevalent in younger women and areas with high breast cancer mortality, such as sections of Latin America and Africa[10].

HER2-enriched breast cancer makes up 10% to 15% of cases and has HER2 overexpression and no hormone receptor expression[11]. It is also associated with worse prognosis. Survival has drastically changed with HER2-targeted therapies such as trastuzumab and pertuzumab[12]. Such subtypes are more frequently seen in younger patients and ethnic groups, such as Hispanic and Asian populations[13]. New research is underway to create novel HER2-targeting agents for treatment, including antibody-drug conjugates and tyrosine kinase inhibitors, to improve efficacy.

TNBC represents 10% to 20% of cases and does not express ER, PR, or HER2[14]. It is massively proliferative, frequently associated with mutations in TP53 and/or BRCA1, and has a very aggressive clinical course[15]. TNBC is particularly prevalent in premenopausal women and African American populations as well as in individuals with hereditary breast cancer syndromes. Aside from targeted therapies, chemotherapy is the mainstay of treatment, but there have been promising results with immunotherapy and PARP inhibitors[16].

The incidence of breast cancer varies in different regions. The distribution of subtypes is also quite different from place to place, and this fact highlights the necessity for a molecular approach to customization of treatment. St. Gallen 2013 consensus classification is useful to select the treatment, however, the data on subgroup classification in the Thai population is still limited.

Objective

To determine the incidence and clinical characteristics of breast cancer patients treated at Rayong Hospital between 2018 and 2023.

Materials and Methods

The investigators performed a retrospective study of breast cancer patients treated at Rayong Hospital between October 1, 2018, and September 30, 2023. Data was taken from electronic medical records and hospital databases.

Study population and criteria

Inclusion criteria:

1. Patients diagnosed with breast cancer at Rayong Hospital between October 1, 2018, and September 30, 2023.

Exclusion criteria:

1. Patients not treated at Rayong Hospital.
2. Patients without electronic medical records at Rayong Hospital.

Ethical approval

The present study protocol was approved by the Institutional Review Board of Rayong Hospital (number RYH REC No. E023/2567).

Statistical analysis

Patient characteristics were described using descriptive statistics. Numbers and percentages were given for categorical variables and mean ± standard deviation (SD) for continuous data.

Results

Seven hundred thirty-one breast cancer patients were included during the trial period. Among them, 727 (99.45%) were female. Patients ages were categorized into three groups, under 40 years with 80 patients (10.94%), between 40 and 60 years with 405 patients (55.4%), and over 60 years with 246 patients (33.65%). The mean age was 54.17±11.79 years. Table 1 describes the demographic data.

Cancer in the left breast was detected in 385 patients (52.67%) and in the right breast in 336 patients (45.96%). Of these, 619 patients (84.68%) had mastectomy, 71 patients (9.71%) received breast-conserving surgery, while 41 patients (5.61%) did not receive surgery. There were 630 cases (86.18%) confirmed to be invasive ductal carcinoma (IDC). Patients with tumor grading data were 43 (6.37%) Grade 1, 379 (56.15%) Grade 2, and 253 (37.48%) Grade 3.

Out of 673 cases of breast cancer, 108 (16.05%) were Stage I, 324 (48.14%) were Stage II, 186 (27.64%) were Stage III, and 55 (8.17%) were Stage IV. There were 679 patients tested for ER and 415 (61.12%) were positive and 264 (38.88%) were negative and PR results were found in 360 patients (53.02%) and 319 patients (46.98%), respectively. HER2 receptor status was assessable in 630 classified cases with 142 cases (22.54%) and 488 cases (77.46%) as HER2-positive and HER2-negative, respectively.

Note that the KI-67 proliferation index was only calculated in invasive tumors such as invasive carcinomas. Three hundred patients (43.92%) of all patients underwent this assessment. Of these,

Table 1. Demographic and clinical characteristics of breast cancer patients

Patient characteristics	n (%)
Sex	
Female	727 (99.45)
Male	4 (0.55)
Age (years)	
<40	80 (10.94)
40 to 60	405 (55.40)
>60	246 (33.65)
Mean±SD	54.17±11.79
Sides	
Left	385 (52.67)
Right	336 (45.96)
Bilateral	10 (1.37)
Type of surgery	
No	41 (5.61)
Mastectomy	619 (84.68)
Breast conserving surgery	71 (9.71)
Pathological report	
Invasive ductal carcinoma	630 (86.18)
Invasive mammary carcinoma	42 (5.75)
Invasive lobular carcinoma	11 (1.5)
Ductal carcinoma in situ	16 (2.19)
Phyllodes tumor	12 (1.64)
Other (e.g., mucinous, papillary)	29 (2.74)
Grading	
Grade 1	43 (6.37)
Grade 2	379 (56.15)
Grade 3	253 (37.48)
Stage	
I	108 (16.05)
II	324 (48.14)
III	186 (27.64)
IV	55 (8.17)
Estrogen receptor (ER)	
Positive	415 (61.12)
Negative	264 (38.88)
Progesterone receptor (PR)	
Positive	360 (53.02)
Negative	319 (46.98)
HER2 receptor	
Positive	142 (22.54)
Negative	488 (77.46)
Ki-67 status	
<20%	136 (19.91)
≥20%	164 (24.01)
Not performed	383 (56.08)
Imaging diagnosis	
Not performed	4 (0.55)
Yes	727 (99.45)
• Chest X-ray	364 (50.07)
• Ultrasound	146 (20.08)
• Computed tomography (CT)	347 (47.73)
• Bone scan	9 (1.24)

SD=standard deviation; HER2=human epidermal growth factor receptor 2

Table 2. Comparing the stages of breast cancer before and after neoadjuvant therapy

	Clinical TNM staging (n=40); n (%)	Pathological TNM staging (n=40); n (%)
Complete response	-	8 (20)
Stage 0	0 (0)	0 (0)
Stage I	0 (0)	4 (10)
Stage II	24 (60)	18 (45)
Stage III	16 (40)	10 (25)
Stage IV	0 (0)	0 (0)

136 (19.91%) had KI-67 of less than 20% and 164 (24.01%) had levels of 20% or above. But KI-67 was not performed in 383 patients (56.08%).

Nearly all patients, as 727 (99.45%), received at least one imaging procedure. Among those who were imaged, 364 (50.07%) received a chest X-ray, 347 (47.73%) had computed tomography (CT), 146 (20.08%) underwent ultrasound, and nine (1.24%) had bone scans.

The breast cancer stage and response to neoadjuvant chemotherapy is shown in Table 2. The 40 patients were staged according to the clinical TNM criteria. Of these, 24 patients (60%) were in Stage II and 16 (40%) in Stage III.

There was a pathologic downstaging of the tumor burden, following neoadjuvant chemotherapy. Some patients had a shrinkage of their tumors. More precisely, eight participants (20%) achieved a pathological complete response (pCR), defined as the absence of residual tumor. The majority of these were TNBC subtype in five out of eight patients (62.5%), followed by the Luminal B subtype in three out of eight patients (37.5%). In addition, four patients (10%) were downstaged to Stage I, and 18 patients (45%) were downstaged from 24 patients in Stage II. No one progressed to Stage IV following chemotherapy.

Among 40 patients receiving neoadjuvant

Table 3. Characteristics of breast cancer patients according to the intrinsic subtype (n=283)

	Luminal A (n=98); n (%)	Luminal B (n=99); n (%)	HER2-enriched (n=34); n (%)	TNBC (n=52); n (%)	Total (n=283); n (%)
Age at diagnosis					
<40	5 (5.1)	13 (13.1)	2 (5.9)	7 (13.5)	27 (9.5)
40 to 60	55 (56.1)	60 (60.6)	13 (38.2)	31 (59.6)	159 (56.2)
>60	38 (38.8)	26 (26.3)	19 (55.9)	14 (26.9)	97 (34.3)
Stage at diagnosis					
I	17 (17.4)	11 (11.1)	6 (17.7)	6 (11.5)	40 (14.1)
II	48 (49)	61 (61.6)	14 (41.2)	33 (63.5)	156 (55.1)
III	23 (23.5)	17 (17.2)	12 (35.3)	12 (23.1)	64 (22.6)
IV	10 (10.2)	10 (10.1)	2 (5.9)	1 (1.9)	23 (8.1)

HER2=human epidermal growth factor receptor 2; TNBC=triple-negative breast cancer

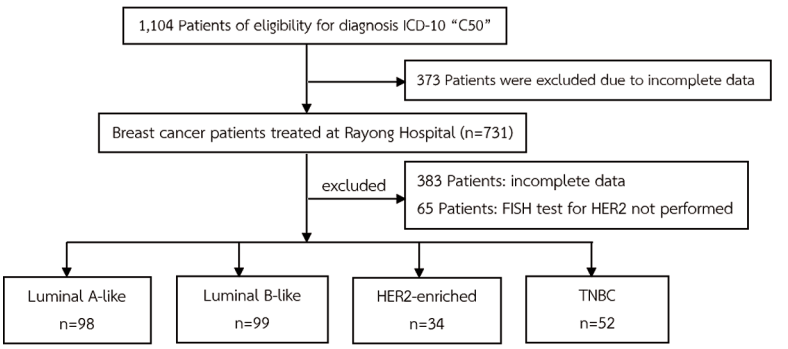

Figure 1. Study flow diagram of breast cancer patients treated at Rayong Hospital.

chemotherapy, regimens were categorized into standard chemotherapy and chemotherapy with anti-HER2 therapy, along with information on anti-hormone therapy. The majority, or 24 patients (60%), received Adriamycin plus Cyclophosphamide (AC) followed by a taxane, while six patients (15%) received AC alone. Anti-HER2 therapy was administered to three patients (7.5%) using the AC-taxane plus trastuzumab (TH) regimen.

Table 3 shows that 283 breast cancer patients were categorized according to intrinsic subtypes as Luminal A for 34.6%, Luminal B for 35%, HER2-enriched for 12%, and TNBC for 18.4% (Figure 1).

Stratified data regarding the age at diagnosis shows that 13.1% of Luminal B and 13.5% of TNBC subtypes are mostly present before 40 years. Furthermore, 60.6% of Luminal B diagnosis is done between 40 and 60 years. Most diagnoses (34.3%) were noted after attaining 60 years, with HER2-enriched at 55.9% as the highest percentage for this group. About the stage at diagnosis, 14.1% of the diagnosis was at Stage I, most diagnoses were from Luminal A at 17.4%. Stage II was the most prevalent at 55.1% and TNBC was the most common subtype at 63.5%. The second highest recorded was Stage III at 22.6% with HER2-enriched having 35.3% as the most common subtype. The least was Stage IV at 8.1%.

Discussion

A retrospective study was conducted at a tertiary care center about the prevalence of breast cancer subtypes, age, stage at diagnosis, and response to neoadjuvant therapy over five years. The mean age of the study population was 54.17 years, composed of 781 patients. In the present study, Luminal B was the most frequent molecular subtype at 35% followed by Luminal A at 34.6% according to the St. Gallen 2013 classification. This finding is consistent with international studies, as summarized in Table 4, which all showed a predilection toward hormone receptor-positive subtypes[13,17-23]. Given that the trend of Luminal B was quite high over this period, the present study findings support the previous argument that a substantial number of patients would need significantly more aggressive therapeutic intervention, including chemotherapy in addition to endocrine therapy[24].

Interestingly, there were 18.4% with TNBC and 12.0% with HER2-enriched breast cancer. The patients with TNBC were mainly young patients,

Table 4. Incidence of various subtypes based on international studies

Study	Luminal A	Luminal B	HER2-enriched	Basal-like	No.
Carolina breast cancer study[13]	51.4%	15.5%	6.6%	26.4%	496
Errahhali et al.[17]	61.1%	16.1%	8.6%	14.2%	2,260
Kumar et al.[18]	34%	18%	18%	25%	280
Mane et al.[19]	43.8%	14.8%	16.1%	25.3%	521
Pandit et al.[20]	37%	8%	11%	26%	2,062
Tubtimhin et al.[21]	31.6%	15.6%	9.9%	11.3%	523
Ditsatham et al.[22]	28.8%	36.4%	20.1%	14.7%	3,153
Leungsuwan et al.[23]	39%	24.4%	18.3%	18.3%	169
The present study	34.6%	35.0%	12.0%	18.4%	283

HER2=human epidermal growth factor receptor 2

especially the age group ranging between 40 and 60 years, whereas patients with HER2 enrichment were older. Prior literature was more likely to fit this data and previously provided evidence that TNBC typically occurred in younger women and was more associated with an aggressive disease course. These data confirm references[25].

Age differences among patients were indicated in the present study results, where TNBC was seen to be more prevalent in patients aged 40 to 60 years (59.6%). The present study results show TNBC to be more prevalent in 40 to 60-year-old patients and HER2-enriched found more in older patients aged older than 60 years with 55.9%, respectively. Younger patients with aggressive subtypes also may have been more amenable to early intervention and therapeutic strategies. At stage of diagnosis, the present study found the most common stage was II at 55.1%, which was followed by stage III at 22.6%. There continued to be a substantial challenge with late-stage diagnosis, stage II or III, with 8.1% of diagnosed cases at stage IV. This points to a need for early detection to increase the proportion of patients in an early state of disease.

Response to neoadjuvant chemotherapy and changes in TNM staging

Twenty percent of the patients showed pCR, a prognostic and predictive factor for disease-free survival and overall survival[26]. These results highlighted the impact of neoadjuvant therapy on response and surgical outcomes through the reduction of tumor burden[27].

Comparison with previous literature

The author analyzed the distribution of breast cancer subtypes in 283 cases. The results were Luminal A was seen in 34.6% of cases and Luminal B in 35.0%. The HER2-enriched subtype was represented in 12.0% of cases, while basal-like was noted in 18.4% of cases.

When comparing these findings with other international studies (Table 4), a relatively even distribution of Luminal A and Luminal B was evident in the present study, whereas this distribution in other studies favors Luminal A. The present study results regarding HER2-enriched cases at 12.0% also confirmed a mid-range where global reports varied from 6.6% to 20.1%. On the contrary, the frequency of basal-like breast cancer at 18.4% was also comparable with other studies but lower than the studies of Pandit et al. at 26%[20] and Kumar et al. at 25%[18].

Strength and limitation

A strength of the present study was the large sample size, enhancing the reliability of the findings. The inclusion of detailed molecular subtyping and TNM staging, pre- and post-neoadjuvant, reflected breast cancer trends at the author's center. However, a single-center, retrospective study limits generalizability. Variations in diagnosis and therapy over five years and insufficient data present problems. In addition, genetic profiling and long-term survival were not investigated.

Conclusion

In summary, the present study reported epidemiological trends of breast cancer molecular subtypes at a tertiary care institution over five years. Luminal B and Luminal A were the most common subtypes, whereas there was a predominance of TNBC in middle-aged patients. A large number of patients were diagnosed in later stages, stressing that improved early detection programs are essential. The results also highlighted the effectiveness of neoadjuvant treatment in downstaging the tumor, although there remained a need for further studies

to develop management protocols. In the future, personalized therapy strategies and improved screening methods will be important to increase breast cancer outcomes.

What is already known about this topic?

Breast cancer is a worldwide, highly heterogeneous disease with varying molecular subtypes that have different prognoses and treatment. Luminal A was usually the most common subtype, whereas TNBC and HER2-enriched subtypes were more aggressive and frequent in younger patients.

What does this study add?

This study revealed that Luminal B was the most common subtype, at 35%, in the cohort, which is contrary to the global trend that Luminal A was dominant. It also highlighted that middle-aged patients were more likely to show with aggressive TNBC subtypes and a higher proportion of late stage at diagnosis at 35.81% at stage III and IV.

Conflicts of interest

The author declares that there is no conflict of interest regarding the publication of this paper.

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