

Correlation between Cancer Breast Subtypes and Age at Presentation in Egyptian Patients; Single Institution Experience

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Abstract

Background: Breast cancer is defined according to molecular subtypes. Each molecular subtype defines different disease behavior and requires different treatment. The different molecular subtypes have different risk factors and different distribution across age classes. **Aim of the study:** To detect the incidence of cancer breast subtypes by age among Egyptian patients treated at the Clinical Oncology Department, Faculty of Medicine, Ain Shams University, in the period between April 2016 and December 2018. **Patients and Methods:** Inclusion criteria: Cases with proven pathological diagnosis and underwent IHC studies for the molecular subtype while exclusion criteria were: Bilateral cases, cases with unknown molecular subtype or age at presentation, cases with multiple primaries, cases with in situ cancer, male breast cancer cases, and cases diagnosed during pregnancy. Age classes were computed in four groups: from 20 - 35, >35 - 50, >50 - 65 and those older than 65 years of age. Immunohistochemical studies were done; ER, PR and HER2 were recorded for each case, Molecular subtypes were defined as follows: HR+/HER2-, HR+/HER2+, HER2 overexpressed (HER2 positive, HR-) and Triple Negative Breast Cancer; TNBC (HER2 negative, ER negative and PR negative). **Results:** one thousand and two cases were included in the study. The median age was 51 years and the mean age was 51.64 ± 11.74 , with range from 24 to 85 years. The total number of ER positive patients was 706 patients (70.5%), the total number of PR positive patients was 667 (66.6%), and the total number of Her2 positive patients was 286 patients (28.5%). While there were no statistically significant differences in the incidence of ER and PR positivity among all age classes, Her2 over expression decreased with age and the difference was statistically significant (P-value: 0.012). Her2 overexpression subtype incidence decreased by age and it was highest in the younger age group 17.6% compared to 8.2% in the older age group and the difference was statistically significant. Similarly,

HR+/HER2- tumors incidence were higher in patients older than 65 (57.4%) and lower in the younger age group (40.5%) (P-value: 0.031). Triple negative tumors incidence ranged from 14.9% for those younger than 35 to 17.2% for those older than 65 years. **Conclusion:** This study shows that there are significant differences in the age distribution by molecular subtype and the incidence of Her2 overexpression subtype decreases by age. The study also shows that the nature of the breast cancer in the group of Egyptian patients studied is more of the favorable hormonal positive subtype.

Keywords

Breast Cancer, Molecular Subtypes, Egyptian, Age

1. Introduction

Breast cancer is the most frequent cancer in women worldwide and though incidence rates are lower in Africa compared to the rest of the world, mortality is high [1] [2] [3]. In Egypt, breast Cancer represented 38.8% of cases in 2007 [4].

Every patient should undergo prognostic factors analysis among which the most important are, Estrogen Receptor (ER), Progesterone Receptor (PR), Human epidermal growth factor receptor (Her2/neu) [5]. Each of these parameters shares in the determination of tumor behavior and accordingly is treated in a different way [6]. Hormonal receptors (HRs) are also a fundamental characteristic of the epidemiology of this malignancy [7] and those tumors have better prognosis and are responsive to hormonal therapy [8]. Accordingly, breast cancer is defined according to molecular subtypes [9]. These molecular subtypes are identified by immunohistochemical studies which became an essential assessment tool [10]. Recurrence in terms of progression free survival and site of recurrence is affected by the molecular subtype, and each of them has different risk factors, and different distribution across age classes [11]. Some studies showed that the proportion of luminal A subtype increased with age, whereas triple negative tumors decreased with age [12]. Analysis of molecular subtypes is important to evaluate and compare survival of patients and plane resources for treatment [13].

Whether genetic and racial factors are controlling prevalence of molecular subtypes is an open question. It was reported that; 79% of breast cancer in white American women are ER+, while the percentage is lower among black Americans (about 61%) [14] [15]. Some studies [16] [17] reported higher proportion of basal-like subtype in African patients, while others suggest that it is not different from that reported worldwide [18] [19].

Aim of the study:

To detect the incidence of cancer breast subtypes by age among Egyptian patients treated at the Clinical Oncology Department, Faculty of Medicine, Ain

Shams University, in the period between April 2016 and December 2018.

2. Patients and Methods

This retrospective study was carried out by comprehensive review of the files of cases of cancer breast treated at the clinical oncology department, Faculty of Medicine, Ain Shams University, in the period between April 2016 and December 2018 regarding age of the patients and their molecular subtypes.

Inclusion criteria were: Cases with proven pathological diagnosis and underwent IHC studies for the molecular subtype while exclusion criteria were: Bilateral cases, cases with unknown molecular subtype or age at presentation, cases with multiple primaries, cases with in situ cancer, male breast cancer cases, and cases diagnosed during pregnancy.

Age classes were computed in four groups: from 20 - 35, >35 - 50, >50 - 65 and those older than 65 years of age. Immunohistochemical data namely; Estrogen receptor (ER), progesterone receptor (PR) and human epidermal growth factor receptor (HER2) were recorded for each case. Ki 67 being not routinely performed for the patients was not included in the classification. Analysis included only cases confirmed to be Her2/neu positive by FISH or SISH as per the routine laboratory studies of the breast unit at our institute.

Molecular subtypes were defined as follows: HR+/HER2-, HR+/HER2+, HER2+ overexpressed (HER2 positive, HR-) and Triple Negative Breast Cancer; TNBC (HER2 negative, ER negative and PR negative), HR was considered positive if any of ER or PR were found to be positive as per the guidelines of the breast clinic.

Statistical Analysis

Data were collected, revised, coded and entered to the Statistical Package for Social Science (IBM SPSS) version 23. Quantitative data were presented as mean, standard deviations, median with inter-quartile range (IQR) and range while qualitative variables were presented as number and percentages. The comparison between groups with qualitative data was done by using Chi-square test. The confidence interval was set to 95% and the margin of error accepted was set to 5%. So, the P-value was considered significant at the level of <0.05.

3. Results

In the allocated period 1636 cases were recorded in the files among whom 634 cases were excluded as per the exclusion criteria of the study and 1002 cases were included in the study. The median age was 51 years and the mean age was 51.64 ± 11.74 , with range from 24 to 85 years (**Table 1**).

The total number of patients below 35 years of age was 74 (7.4%) patients while those more than 65 years of age were 244 patients (24.4%). In the whole study group the total number of ER positive patients were 706 patients (70.5%) and the total number of PR positive patients were 667 (66.6%), the total number of Her2 positive patients were 286 patients (28.5%) (**Table 2**).

Table 1. Mean and Median age of patients included in the study.

Age	Total No. = 1002
Median (IQR)	51 (43 - 60)
Mean \pm SD	51.64 \pm 11.74
Range	24 - 85

Table 2. Correlation between age groups and IHC data of the patients.

		Age groups				Total	Chi-square test		
		(20 - 35)	(35 - 50)	(51 - 65)	>65		χ^2	P-value	Sig.
		No. (%)	No. (%)	No. (%)	No. (%)				
ER	Negative	25 (33.8%)	92 (26.7%)	114 (33.6%)	65 (26.6%)	296 (29.5%)	5.717	0.126	NS
	Positive	49 (66.2%)	253 (73.3%)	225 (66.4%)	179 (73.4%)	706 (70.5%)			
	Total	74 (7.4%)	345 (34.4%)	339 (33.8)	244 (24.4%)	1002 (100%)			
PR	Negative	31 (41.9%)	101 (29.3%)	122 (36.0%)	81 (33.2%)	335 (33.4)	6.059	0.109	NS
	Positive	43 (58.1%)	244 (70.7%)	217 (64.0%)	163 (66.8%)	667 (66.6)			
	Total	74 (7.4%)	345 (34.4%)	339 (33.8%)	244 (24.4%)	1002 (100%)			
HER2	Negative	41 (55.4%)	249 (72.2%)	243 (71.7%)	183 (75.0%)	716 (71.5%)	10.945	0.012	S
	Positive	33 (44.6%)	96 (27.8%)	96 (28.3%)	61 (25.0%)	286 (28.5%)			
	Total	74 (7.4%)	345 (34.4%)	339 (33.8%)	244 (24.4%)	1002 (100%)			

ER: Estrogen Receptor, PR: Progesterone Receptor, HER2: Human Epidermal Growth Factor Receptor, NS: not significant, S: significant.

While there were no statistically significant difference in the incidence of ER and PR positivity among all age classes, Her2 over expression decreased with age and the difference was statistically significant (P-value: 0.012) (**Table 2** and **Figure 1**).

Regarding distribution of molecular subtypes by different age groups (**Table 3** and **Figure 2**), there was a statistically significant difference (P-value: 0.031), as Her2 overexpression subtype incidence decreased by age (17.6% compared to 8.2% in the younger and older age groups respectively) and HR+/Her+ were also higher in the younger age group 27% compared to 17.2% in both groups respectively. Meanwhile, HR+/HER2- tumors incidence were higher in patients older than 65 (57.4%) and lower in the younger age group (40.5%). Regarding the TNBC the incidence ranged from 14.9% for those younger than 35 to 17.2% for those older than 65 years.

4. Discussion

The current study aimed at exploring the patterns of molecular subtypes and its age distribution among patients treated at our department, and though seems to be easy information to get, there is actually no enough studies to answer the question what is the actual age distribution of Egyptian breast cancer patients as defined by molecular subtypes and whether there is a specific molecular subtype that is more prevalent among those patients.

Table 3. Correlation between age and molecular subtypes of the patients.

Molecular subtype	(20 - 35)	(35 - 50)	(51 - 65)	>65	total	Chi-square test	
	No. (%)	No. (%)	No. (%)	No. (%)	No (%)	χ^2	P-value Sig.
HR+/Her-	30 (40.5%)	189 (54.8%)	187 (55.2%)	140 (57.4%)	546 (54.5%)		
HR+/Her+	20 (27.0%)	70 (20.3%)	51 (15.0%)	42 (17.2%)	183 (18.3%)		
HER2	13 (17.6%)	27 (7.8%)	44 (13.0%)	20 (8.2%)	104 (10.3%)	18.391	0.031 S
TNBC	11 (14.9%)	59 (17.1%)	57 (16.8%)	42 (17.2%)	169 (16.9%)		
Total	74 (7.4)	345 (34.4)	339 (33.8)	244 (22.4)	1002 (100%)		

HR+/HER2- (HR positive, HER2 negative), HR+/HER2+ (HR positive, HER2 positive), HER2+ overexpressed (HR negative, HER2 positive) and Triple Negative Breast Cancer; TNBC (HR negative, HER2 negative), S: Significant.

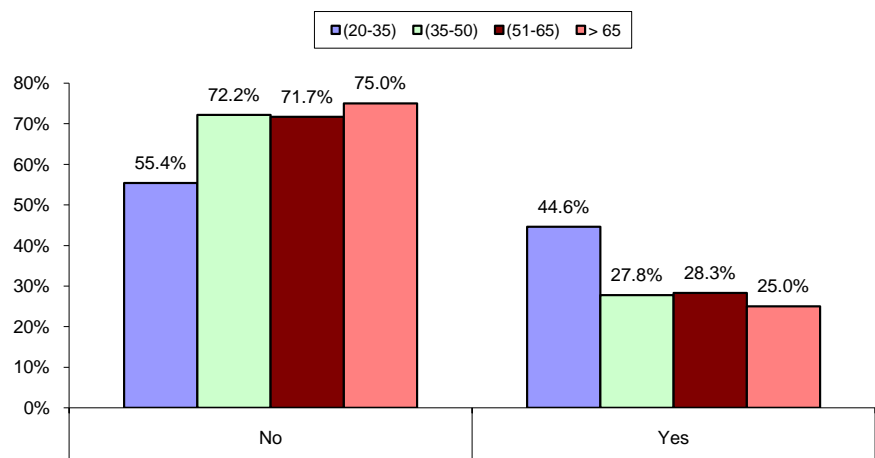


Figure 1. Percentage of Her2 over expression in the studied patients.

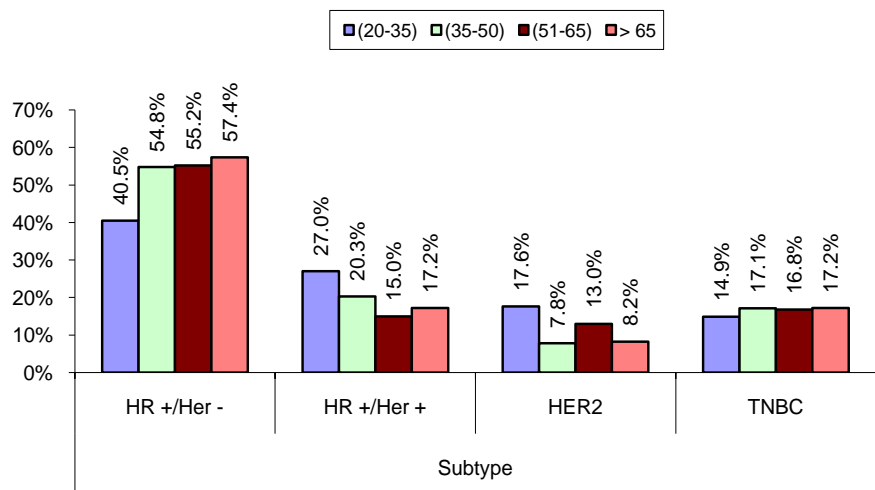


Figure 2. Distribution of molecular subtypes by age class.

The median age of patients was 51 years with an IQR (43 - 60) and the mean was 51 years which goes in accordance with that reported in other studies on Egyptian patients that reported a mean age of 53 years and a median of 52 years

in one study of 263 patients [20], and a mean age of 51.3 years in another one [21]. However, lower Median age of 46 years was reported in Hospital-based reports of The National Cancer Institute of Egypt [22]. In Egypt, though some reports suggest age distribution shift towards early sixties, median age at diagnosis is believed to be younger than that reported in Western data [22] [23] [24]. Regarding the Arab countries, a comprehensive literature review of reports of breast cancer in Arab countries, reported on an average age of 48 with a range of 43 - 52 years and a median of 48.5 years [23].

In the current study ER+ tumors dominated with an incidence of 70.4% followed by PR+ tumors with 66.5% incidence compared to 65% and 43% respectively for another report of Egyptian patients [21]. Gharbia cancer registry in Egypt reported an incidence of 69% HR+ in all cases with known receptor status [25]. Regarding other countries, lower incidence of 51.5% HR positive tumors was reported in 194 Tunisian patients with breast cancer [26]. It was also reported that, luminal subtype was predominant in African post-menopausal North Americans [21] [27]. Additionally, luminal subtype was also predominant in those of Sudanese and Tunisian descent [26].

The incidence of Her2 positive tumors in the current study was 28.5% but this figure has to take into consideration that our institute is a referral center for the targeted therapy trastuzumab so though our results were in accordance with Salhia *et al.* [21] who reported on an incidence of 25.1%, it was different from Hussein *et al.* who reported on an incidence as low as 14.1% [20].

In the current study there was a statistically significant difference in distribution of molecular subtypes by age (P-value: 0.031), so though Hormonal positive tumors (luminal subtype) in general was the predominant subtype among all age groups, HR+/Her+ were higher in the younger age group (27% compared to 17.2%) and Her2 overexpression subtype was higher in the younger age group (17.6% compared to 8.2%). Triple negative tumors had the incidence of 16.7% in the current study compared to 19.0% reported by Hussein *et al.* [20], and 28.5% in a report of Elhawary *et al.* who reported on 274 surgical specimens [28]. High frequency of the basal-like subtype has been reported in about 40% of young premenopausal African North American women [29].

It was also reported that triple negative tumors decreased with age [12]. This finding was neither supported in the current study nor by Cortet *et al.* [13]. In the current study, the distribution of the TNBC was consistent among all age classes which suggest that the nature of the disease in the Egyptian patients could be the same as that reported elsewhere.

This study was limited by the fact that there is no cancer patients' registry in Egypt and the measurement of Ki 67 is not done routinely for patients in our department so the luminal subtype could not be further subdivided in most of the cases.

5. Conclusion

This study shows that there are significant differences in the age distribution by

molecular subtype and the incidence of Her2 overexpression subtype decreases by age while the incidence of TNBC is consistent among all age classes. The study also shows that the nature of the breast cancer in the group of Egyptian patients studied is more of the favorable hormonal positive luminal subtype and the more aggressive triple negative subtype is not of higher incidence compared to other reports worldwide.

Ethics approval

The authors made the necessary regulatory arrangements to use the data from patients' records.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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