

Breast Cancer Molecular Subtypes in Relation to Age, Stage and Grade among Sudanese Women Patients in Khartoum Oncology Hospital (2013 – 2017)

Abstract

Background: - Sudan has no screening program for breast cancer & delayed presentation.

There are few studies about molecular subtypes of breast cancer among Sudanese patients. No data had correlated the molecular subtypes with age, stage and grade till our data had been collected.

The aim of this study is to determine breast cancer molecular subtype among Sudanese women in relation to age, stage and grade.

Methods: We extracted data from 255 files of Sudanese female diagnosed with breast cancer between september2013- August 2017 in Khartoum Oncology Hospital.

Results: luminal B was most commonly diagnosed subtype 89 cases :(34.9%) followed by triple negative 80cases :(31.4%), then HER-2 enriched 49 cases :(19.2%) lastly luminal A 37cases: (14.5%).131 cases: (54.4%) of women were grade: 3 and 57 cases :(22.4%) of women diagnosed as stage IIIb.

Conclusion: luminal B was most commonly diagnosed subtype and were more common in younger age groups as compared to luminal A. Majority of Sudanese women in the study were grade 3 and stage IIIb .Most of them diagnosed at age 41-50 years, triple negative subtype was high among Sudanese women and significantly associated with high grade breast cancer.

Key words: Subtypes, Breast Cancer, Sudanese, Women

1. Introduction:

Breast cancer consider the most common cancer among females with global health concern leading to 327000 deaths annually [1, 2] .WHO reported, about 2.1 million newly diagnosed female with breast cancer In 2018 [3] comprise 11.6% of the total cancer incidence burden globally [4]. The latest data according to Globocan 2018, Sudan breast cancer ranked as the most frequent cancer among women and 5 677 women diagnosed with breast cancer accounts for 36.69% of all new cancer cases among women living in Sudan [5].

Molecular subtypes of breast cancer have been recognized as recent and advanced in the field and focused on patient care based on early detection and better prognosis and management [6,7].Breast cancer divided to four major molecular intrinsic molecular subtypes: luminal A, is most frequent and has better prognosis account of fifty to sixty percent of all breast cancers while luminal B in compare to luminal A associated with higher histological grade which account for 15%-20% [8]. Triple negative breast cancer (TNBC) varies in relation to patient racial and ethnicity, it has impact in patient's survival variation and may has role in treatment options [9] HER2-enriched subtype (previously the HER2+/ER- subtype) is characterized by aggressive behaviour [10]There is variation of molecular subtypes worldwide. Luminal A tumors were the most common subtype among some Middle East countries Like Saudi Arabian [11], Jordon [12] and Egypt [13] and also common among some western countries like Italy [14], Germany [15] and Atlanta (America) [16] studies in some Asian countries revealed that luminal A was high among Iranian patients [17] while Luminal B was found high prevalence among Japanese [18] and Pakistani patients [19].

Studies in some African countries demonstrated that: Luminal B was high prevalence in Morocco (North Africa) [20] while Triple negative had high prevalence among some African countries like Nigeria (West Africa) [21] , Uganda (sub-Saharan Africa) [22] and Sudan and Eretria (North East and East Africa)[23]. African-American women also showed high prevalence of TNBC [24]. Study conducted to compare molecular subtypes between Sudanese and German

women, revealed that: triple-negative subtype was more prevalent in Sudanese than German women [25].

2. Methods

This is a retrospective descriptive cross sectional study, of 255 women with breast cancer, done at Khartoum hospital oncology Sudan. . The inclusion criteria: patients with proofed breast cancer, period (September 2013- August 2017) .The data was collected by reviewing patient's medical records.

2.1 Setting

Khartoum oncology hospital, is specialized and classified as tertiary level providing chemotherapy, targeted therapy and radiotherapy services, located in capital Khartoum, it had capacity to accommodate patient from other states.

2.2 Data collection methods & tools

The data was collected by reviewing patient's medical records. We used summary sheets for data collection.

2.3 Ethical Issue

The study was approved by the ethical committee of Khartoum state ministry of health ethical committee.

3. Results:

255 women were enrolled in this study 135 women age group ≤ 50 years: (52.9%) while 120 women age grouped >50 years: (47.1%). Majority of women were diagnosed with breast cancer before age of sixty years. The luminal B subtype is most commonly diagnosed, 89 cases: (34.9%) of all cases, followed by triple negative, 80 cases: (31.4%), HER-2 enriched, 49 cases: 19.2% and luminal A, 37 cases :(14.5%)

Cross tabulation showed age ($p = 0.162$), tumor stage ($p = .0.257$), and histological grade ($p = .0.012$) were significantly associated with intrinsic subtypes.

Table1: frequency distribution of breast cancer according to age of diagnosis

Age group	Frequency	Percent
<30	7	2.7
30-40	54	21.2
41-50	74	29.0
51- 60	67	26.3
>60	53	20.8
Total	255	100.0

As shown in table:1 With regard to breast cancer stage, majority of women were diagnosed with breast cancer before age of sixty years, 74 cases, age (41-50) :(29.0. %), 67 cases, age :(51-60): 26.3%, 54 cases, age (30-40): (21.2 %.).Only 7cases diagnosed before age 30 years: (2.7%) and 53cases: (20.8%) diagnosed at age >60.

Table2: frequency distribution of breast cancer according to stage

<i>stage</i>	<i>frequency</i>	<i>Percent</i>
<i>Ia</i>	17	6.7
<i>II a</i>	54	21.2
<i>IIb</i>	54	21.2
<i>III a</i>	40	15.7
<i>IIIb</i>	57	22.4
<i>IIIc</i>	11	4.3
<i>IV</i>	22	8.6
<i>Total</i>	255	100.0

table: 2 above showed that: 57 cases :(22.4%) of women diagnosed as stage IIIb followed by stage IIb

& IIa 54 :(21.2%).

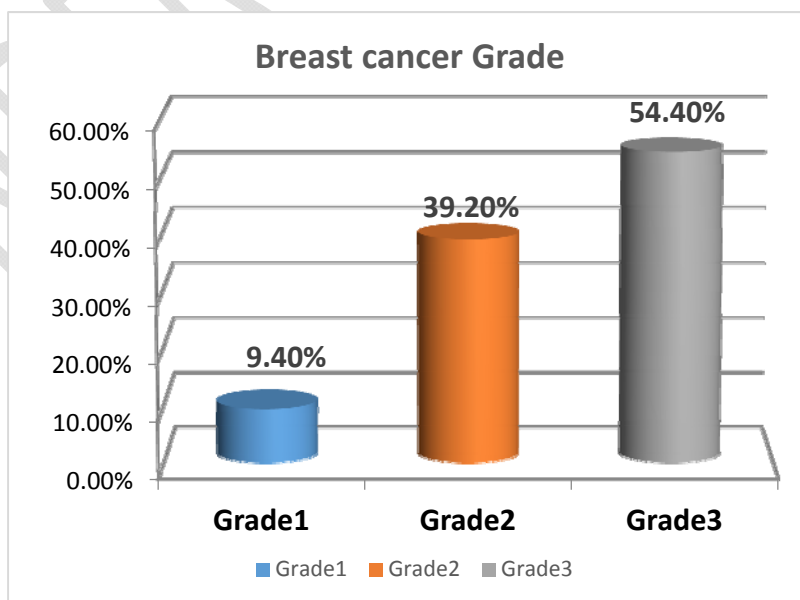


Fig.1: Frequency distribution of breast cancer according to grade.

131 cases :(54.4%) of women were grade: 3, 100 cases: (39.2 %) were grade: 2 and the .least were grade: 1, 24 cases: (9.4%)

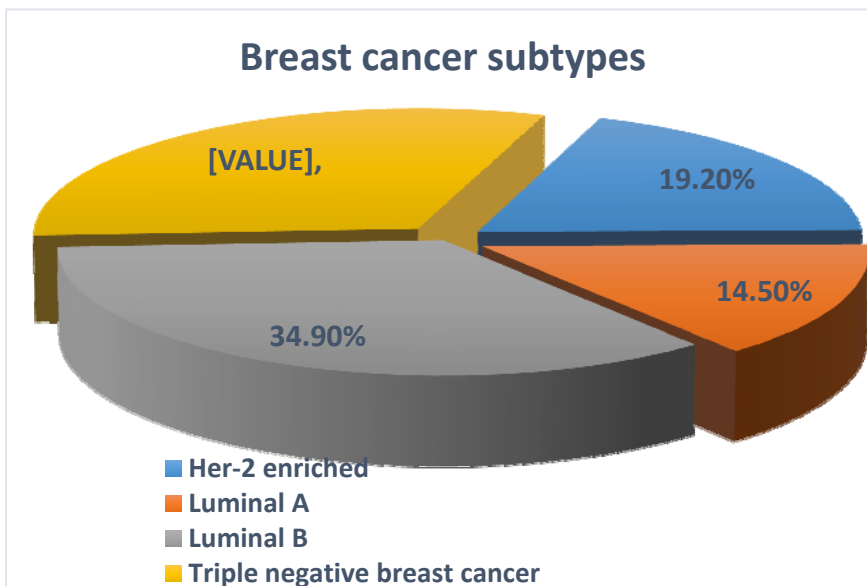


Fig.2: Frequency distribution of breast cancer according to molecular subtype

As figure: 2 shown, luminal B subtype is most commonly diagnosed, 89 cases: (34.9%) of all cases, followed by triple negative, 80 cases: (31.4%), HER-2 enriched, 49 cases: (19.2%) and luminal A, 37 cases :(14.5%).

Table 3: The relationship between Molecular subtype of breast cancer and age

	<u>Cases <50 years</u>		<u>cases >50 years</u>		P
	N	percent	N	percent	
Her-2 enriched	30	61.2	19	38.8	
Luminal A	14	37.8	23	62.7	
Luminal B	46	51.7	43	48.3	

Triple negative breast cancer	45	56.3	35	47.7	0.162
Total	135		120		

As table: 3 above, (51.7%) of luminal B subtype were distributed among age ≤ 50 while (48.3%) were distributed among age grouped >50 years. (62.2%) of Luminal A subtypes were distributed among age >50 years while (37.8 %) were distributed among age grouped ≤ 50 . (56.3%) of triple negative breast cancer distributed among age grouped ≤ 50 and (43.7%) were distributed among age >50 years. (61.2%) of Her-2 enriched subtypes were distributed among age grouped ≤ 50 while (38.8%) were distributed among >50 years.

Table4: The relationship between Molecular subtype of breast cancer and stage.

			Stage							total	P	
			Ia	II a	IIb	III a	IIIb	IIIc	IV			
Molecular subtype	Her-2 enriched	Count	1	8	12	9	13	1	5	49		
		% of Total	.4%vs. 2%	3.1%vs. 16%	4.7%vs. 24.4 %	3.5%vs. 18.3%	5.1%vs. 26.5%	.4%vs. 2%	2.0%vs. 10. %	19.2%	100%	
	Luminal A	Count	6	12	7	4	6	1	1	37		
		% of Total	2.4%vs. 16.2%	4.7%vs. 32.4%	2.7% 18.9%	1.6%vs. 10.8%	2.4%vs. 16.2%	.4% vs. 2.7%	.4%vs. 2.7%	14.5%	100%	
	Luminal B	Count	5	20	17	12	20	3	12	89		

	Triple negative breast cancer	% of Total	2.0%vs. 5.6%	7.8%vs. 22.4%	6.7%vs. 19%	4.7% 13.4%	7.8%vs. 22.4%	1.2%vs. 3.4%	4.7%vs. 13.4%	34.9%	
		Count	5	14	18	15	18	6	4	80	
		% of Total	2.0% vs. 6.25%	5.5%vs. 17.5%	7.1%vs. 22.5%	5.9%vs. 18.75%	7.1%vs. 22.5%	2.4%vs. 7.5%	1.6%vs. 5%	31.4%	
Total	Count	17	54	54	40	57	11	22	255	0.257	
	% of Total	6.7%	21.2%	21.2%	15.7%	22.4%	4.3%	8.6%	100.0%		

Regarding molecular subtype in relation to breast cancer stage, (22.4% vs.7.8%) of luminal B subtype were distributed among stage: IIIb while (19% vs.6.7%) of luminal B subtype were distributed among stage: Iib, while only (16.2% vs.2.4%) of luminal A were stage: IIIb and (32.4%vs.4.7%) were stag: Iia. (22.5% vs.7.1%) of TNBC were stage IIIb, (18.8%vs.5.9%) was stage: IIIa, (7.5% vs.2.4%): stage IIIc and (5%vs.1.6%) stage: IV. (26.5%vs.5.1%) of Her-2 enriched were stage: IIIb and (24.4 %vs.2.7%) were stage: Iib and (18.3vs.3.5%) stage: IIIa. (10. % vs.2%) stage IV.

Table 5: The relationship between Molecular subtype of breast cancer and histologic grade.

			Grade			Total	P
			1	2	3		
Molecular subtype	Her-2 enriched	Count	3	14	32	49	
		% of Total	1.2% Vs. 6.1%	5.5% vs.28.6%	12.5% 65.3%	19.2%	
	Luminal A	Count	6	20	11	37	
		% of Total	2.4% Vs.16.2%	7.8% Vs. 54.1%	4.3% Vs.29.7	14.5%	
	Luminal B	Count	9	41	39	89	

		% of Total	3.5% <i>Vs.10.1%</i>	16.1% <i>Vs.46.1</i>	15.3% <i>Vs.43.8%</i>	34.9%	
	Triple negative breast cancer	Count	6	25	49	80	
		% of Total	2.4% <i>Vs.7.5%</i>	9.8% <i>Vs.31.2%</i>	19.2% <i>Vs.61.3</i>	31.4%	0.012
	Total	Count	24	100	131	255	
		% of Total	9.4%	39.2%	51.4%	100.0%	

Regarding the relation between Breast cancer subtypes and grade, The subtypes are significantly associated with Breast cancer grade, for Luminal B distribution of grade 1, 2 and 3 was (10.1%vs.3.5%), (46.1%vs.16.1%) and (43.8% vs.15.3%) respectively while for Luminal A for 1, 2 and 3was (16.2%vs.2.4%), (54.1% vs.7.8 %) and (29.7% vs.4.3% respectively. (61.3%vs.19.2%) of triple negative were grade: 3, (31.2% vs.9.8%) were grade: 2 while (7.5% vs.2.4%) were grade: 1. (65.3% vs.12.5) of Her-2 enriched were grade: 3, (28.6% vs5.5%) grade: 2 and only (6.1 % vs.1.2%) Were grade: 1

4: Discussion

In this study the age group ≤ 50 women was higher percentage (52.9%) than age group > 50 (47.1%).

Most of women diagnosed breast cancer at age (41-50) similar to finding by study done in Nigeria [21]. Most of the cases were of grade; 3(54.4%) and (39.9%) grade: 2 this differed from the finding reported by Nigerian, Sudanese and German women, among Sudanese grade: 2 was (54.6%) while grade:3 was(41.8%), for German women grade 2,3 was(60%) and (22%) respectively while Nigerian women Grade 2 was slightly higher (48.57%) than grade 3 (43.57%). [21, 25].That indicate late detection of cases in Sudan.

(22.4%) of women diagnosed as stage IIIb that may due to lack of awareness, lack of screening program and accessibility of services.

Majority of the cases were classified as luminal B (34.9%) and only (14.5%) luminal A, this disagree with the literature fifty to sixty percent luminal A and luminal B (15%-20%) of all breast cancers [8] This is at variance with reported by studies in Middle East countries luminal

A was found in Saudi Arabian, Jordan and Egypt was (58.5%), (60%) and (45%) respectively.[11,12 and 13]and also differed with the result obtained by studies in western countries Italy, Germany and Atlanta : (34%), (44.7%) and (51.1%) respectively [14, 15 and 16]. Also differed from finding registered by Iranian study (63.8%) [17]. Luminal B in t Japan, Pakistan and Morocco (71%), (69%) and (41.8%), respectively [18, 19and 20] which higher than our finding. May be the Variance due to different age groups distribution by the studies.

The study found that: (31.4%) of breast cancers were triple negative subtypes. In Nigeria: (26.53%) and (21.2%) among African-American women, which was lower than our finding [21, 24]. TNBC was (34%) in Uganda, Sudanese Eritrean and (34.5) among Sudanese women which slightly similar to our finding [22, 23 and 25]. HER-2 enriched was: (19.2%), which was higher when compared by the finding reported by studies done among Jordanian women :(12%) [12], Sudanese women: (15.7%), German women :(6.8%) [25], Sudanese Eritrean women: (16%) and Moroccan women: (9.2%) [20,23]. (51.7%) of luminal B subtype were distributed among age \leq 50 and (48.3%) were distributed among age grouped $>$ 50 years.(62.2%) of Luminal A subtypes were distributed among age $>$ 50 years while(37.8. %) were distributed among age grouped \leq 50.That indicate most that indicate most of Luminal A distributed among old ages group, this agree with the result obtained by the study among Jordanian women, in older age group, the most common subtype was luminal A (72%) [12].

(56.3%) of triple negative breast cancer distributed among age grouped \leq 50 and (43.7%)were distributed among age $>$ 50 years.(61.2%) of Her-2 enriched subtypes distributed among age grouped \leq 50 while 38.8 was distributed among age grouped $>$ Triple negative and HER-2 enriched subtype was more prominent in the younger age. Similar finding was obtained by study done among Sudanese and German women [25].

(22.4% vs.7.8%) Luminal B was stage: IIIb while only (16.2% vs.2.4%) of Luminal A, which indicate that: Luminal A is less aggressive than Luminal B.

(43.8% vs.15.3%) of luminal B were grade: 3 and (46.1%vs.16.1%) were grade: 2while (54.1% vs.7.8 %) of luminal A was grade: 2 indicate that: luminal B associated with higher histological grade [8]. (61.3%vs.19.2%)Triple negative were grade: 3, and (65.3% vs.12.5) f Her-2 enriched were grade: 3 Indicate that most Triple negative and Her-2 enriched characterized by aggressive and advance breast cancer[10] the result was similar to which was reported among Sudanese women and slightly differed to reported among German women [25].

4: Conclusion and recommendation:-

Most of Sudanese women Diagnosed with breast cancer at age 41-50 years most of them presented with grade 3 and stage IIIb. Luminal B molecular subtypes was the commonest followed by Triple negative, Luminal A was commonly distributed among old age groups.

Most of Her-2 enriched and TNBC subtypes were grad: 3 and distributed more among younger Sudanese women.

Detecting the subtype of breast cancer is essential for disease prognosis, and management planning.

Screening program for early detection of breast cancer and study to address survival rate in relation to molecular subtypes is highly recommended.

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