Pattern Of Breast Cancer And Its Immune Stain Among Patients Registered To National Oncology Center ''NOC''- Mukalla, During Period 2008-2016

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Abstract:

Background: Breast cancer is the most common multifactorial cancer in women worldwide and usually hormonal related. It's typically detected either by notice a lump or during a clinical screening and confirmed by immune stain investigation.

Objective: To determine the patterns of breast cancer and its immune stain among patients registered to national oncology center at Mukalla-Hadramout (NOC) during period from 2008-2016 .

Methods: A retrospective descriptive study was conducted to determine the pattern of breast cancer and its immune stain among patients registered to NOC during 2008-2016.

Results: The most common age group affected was 41-50 years (32%) followed by 31-40 & 51-60 years (22.5% & 20% respectively).The most common type of breast cancer was infiltrating ductal carcinoma (IDC) (85%), followed by invasive lobular carcinoma (5.5%). There is statistical significant association between type of cancer and Estrogen receptor (ER) immune stain while no statistical significant association between type of cancer and state of metastasis, Progesterone receptor (PR), and HER2/NEW immune stain.

Conclusion: The breast cancer was mostly affect women during 41-50 years. The most type of breast cancer is IDC. There is statistical significant association between type of cancer and ER immune stain while no statistical significant association between type of cancer and state of metastasis, PR, and HER2/NEW immune stain.

keywords : Patterns, breast cancer, national oncology center, Mukalla.

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الخلاصة

الهدف: سرطان الثدي هو السرطان الأكثر شيوعا ومتعدد العوامل في النساء في جميع أنحاء العالم وعادة ما يرتبط بالهرمونات . غالباً ما يتم الكشف عنه إما بملاحظة ورم أو أثناء الفحص السريري ويؤكد بواسطة فحص الصبغة المناعية.

الهدف: لتحديد أنماط سرطانات الثدي وارتباطها بالصبغة المناعية للمرضى المسجلين بالمركز الوطني لعلاج الأورام للفترة من 2008 م - 2016 م.

الطرق: أجريت دراسة مرجعية وصفية حول مدى انتشار سرطان الثدي وارتباطه بالصبغة المناعية للمرضى المسجلين بالمركز الوطني لعلاج الأورام للفترة من 2008 م - 2016 م.

النتائج: أكثر فئة عمرية أصيبت بمرض السرطان كانت 41-50 بنسبة حوالي 32% متبوعة بـ 31-40 و 51-60 بنسبه 22.5% و 20% على التوالي . سرطان الأقنية الغازية هو أكثر أنواع سرطان الثدي انتشارا بنسبة 85 % متبوعا بسرطان الحويصلات الغازية بنسبة 5.5 % . توجد هناك علاقة احصائية بين انواع سرطان الثدي وصباغتها بهرمون الاستروجين بينما لا توجد علاقة احصائية بين انواع سرطان الثدي وحالة الانتشار او صباغتها بهرمون البروجسترون والهيرتونيو.

الاستنتاجات: من خلال الدراسة نجد ان سرطان الثدي غالبا ما يصيب الإناث في سن 41 الى 50 سنة. سرطان الأقنية الغازية هو أكثرأنواع سرطان الثدي انتشارا . توجد هناك علاقة احصائية بين انواع سرطان الثدي وصباغتها بهرمون الاستروجين بينما لا توجد علاقة احصائية بين انواع سرطان الثدي وحالة الانتشار او صباغتها بهرمون البروجسترون والهيرتونيو.

الكلمات المفتاحية: أنماط، سرطان الثدي، المركز الوطني لعلاج الأورام، المكلا.

Introduction:

Breast cancers are the most common cancer in women worldwide, many of them were hormone related(1). It's typically detected either during screening examination before symptoms have developed, or after a woman notices a lump in her breast and confirm by immune stain investigation (2).

The risk of breast cancer accumulates throughout woman's life. Many risk factors are not modifiable such as age, family history, early menarche, and late menopause while others are modifiable include postmenopausal obesity, use of combined estrogen and progestin menopausal hormones, and alcohol consumption. Some of these factors were related to life time exposure of breast tissue to the hormones. Hormones are thought to influence breast cancer risk by increasing cell proliferation, thereby increasing the likelihood of DNA damage, as well as promoting cancer growth(3).

Immunhistochemistry (immune stain) now a day becoming a standard investigation in pathology laboratories worldwide and can be used to provide substantial information with regard to diagnosis, therapeutic prediction and prognosis of breast cancer. There are an ever-increasing number of markers, the majority of them are antibodies that are suitable for use with formalin fixed paraffin embedded (FFPE) tissue. Changes in the non-operative diagnosis of breast cancer, with the greater use of tissue core biopsies, allow evaluation of predictive markers that can help in the selection of a more appropriate form of management for advanced disease or for the elderly(2).

The immune stain that can be used in the patient of breast cancer can be divided into diagnostic and prognostic one. One of diagnostic immune stain is GCDFP-15 that positive reaction for it is consistent with primary breast cancer, but a negative reaction is non-informative. The detection of basement membrane collagen IV can help in determining whether or not there is invasion in cases of ducal carcinoma in situ(2).

The identification of myoepithelial cells around small glands, particularly in sclerotic lesions such as radial scars, can differentiate between a tubular or grade I infiltrating ductal carcinoma and a benign lesion. It may also be of value in assessing invasion. This function can be done by cytokeratin14, CALLA, p-cadherin, P63 and caldesmon(4).

Another category is prognostic or therapeutic markers that can help us to characterize breast cancer and provide us with information about choice of therapy and prognosis as Estrogen receptor α (ER α), Progesterone receptor, pS2 protein and EGFR. The determination of ER α by immune histochemistry.

The ER antibody can give clear reproducible results in FFPE tissue. PR is induced by estrogen and is, therefore, a marker of a functioning ER. Some investigators have found that Progesterone status has a greater power than ER status in predicting the disease free interval(5-8).

EGFR is a member of the type1 tyrosine kinase receptor family and is also known as HER-2/new. It is present in normal breast. 30-40% of breast cancers have high levels of HER-2/new with an inverse relationship with ER. It can be detected immunohistochemically in FFPE tissue. Interest in this receptor has grown the development of inhibitors that can be used therapeutically, due to the recognized interaction between it and ER, and its possible role in endocrine response/ resistance(9,10).

The aim of study is to estimate the pattern of breast cancer and its correlation with immune stain among patients registered to NOC during period 2008-2016.

Patients and Methods:

Study design: This is a retrospective descriptive study was conducted at 2016-2017, to determine the pattern of breast cancer and its immune stain among patients registered to NOC during study period.

Study Population: The study population included all patients with breast cancer registered to NOC during the period from 2008 –2016 which were 506 cases.

Data Collection And Tools: The data obtained by a checklist from records of NOC included the following information:

1) Personal data: age, sex, region (Name not included).
2) Time of registration.
3) Breast cancer data:
- Site of cancer.
- Type of cancer.
- Grades of cancer.
- Metastasis of the cancer.
- Result of Immune Stain : [ER, PR & HER2/NEW] immune stain.

Data Analysis: Descriptive data were analyzed using descriptive statistical tools (frequency and percentage). Data are expressed as mean ± standard deviation. Data were analyzed using statistical package for social sciences program Version 20 (SPSS.V20).

Results:

The age distribution of breast cancer among patients registered to NOC was presented in (Table 1); The most common affected age group was 41-50 years which represented about 31.8%, while the lowest age group was > 80 years which represented 1.6%. The age groups of 31-40 years, 51-60 years, 61-70 years, 71-80 years, 21-30 years, and < 21 years was 22.5%, 20%, 11.3%, 6.3%, 5.7%, and 0.6% respectively .

Table 1: Frequency and percent of breast cancer according to age group.

Age groups	Freq. of patients	Percent%
>21	3	.6
21-30	29	5.7
31-40	114	22.5
41-50	161	31.8
51-60	101	20.0
61-70	57	11.3
71-80	32	6.3
<80	8	1.6
Total	**506**	**100.0**

The distribution of patients according to breast cancer types was presented in (Figure 1). The most common type of breast cancer was infiltrating ductal carcinoma (IDC) which represented 85%, followed by invasive lobular carcinoma which represent 5.5%. The third most common was medullary carcinoma followed by mucinous carcinoma and invasive papillary carcinoma which represent 2.2%, 2% & 0 .6% respectively, while the least common type was tubular carcinoma which represent 0.2%.
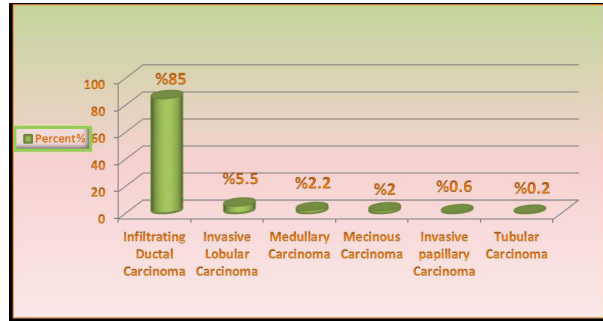
Fig.1: distribution of patients according to type of breast cancer

The correlation of types of breast cancer and metastasis was presented in (Table2); It shows that 183 cases of IDC were positive for metastasis, while 244 cases were negative; 11 cases of invasive lobular carcinoma were positive while 16 cases were negative; 3cases of medullary carcinoma were positive, while 6 cases were negative. There is no statistical significant association between type of cancer and state of metastasis with P value (0.862)

Table2: correlation of types of breast cancer and metastasis

Type of Cancer		Sate of Metastasis			Total	P
		Positive	Negative	Unknown		
Infiltrating Ductal Carcinoma	Frequency	183	244	3	430	
	% of Total	37.9%	50.5%	0.6%	89.0%	
Invasive Lobular Carcinoma	Frequency	11	16	1	28	
	% of Total	2.3%	3.3%	0.2%	5.8%	
Medullary Carcinoma	Frequency	3	8	0	11	
	% of Total	0.6%	1.7%	0.0%	2.3%	
Mucinous Carcinoma	Frequency	3	7	0	10	0.862
	% of Total	0.6%	1.4%	0.0%	2.1%	
Invasive papillary Carcinoma	Frequency	1	2	0	3	
	% of Total	0.2%	0.4%	0.0%	0.6%	
Tubular Carcinoma	Frequency	0	1	0	1	
	% of Total	0.0%	0.2%	0.0%	0.2%	
Total	Frequency	201	278	4	483	
	% of Total	41.6%	57.6%	0.8%	100.0%	

The correlation of types of breast cancer and ER ,PR and HER2/NEW immune stains was presented in (Table 3); 127 cases of IDC were positive for ER immune stain and 136 were negative, while ER immune stain not done for 176 of cases; 9cases of invasive lobular carcinoma were positive for ER immune stain and 8 cases were negative while ER immune stain not don for 11 cases; 3 cases of medullary carcinoma was positive for ER immune stain and 4

cases were negative while ER immune stain not done for 4 cases. There is statistical significant association between type of cancer and ER immune stain with P value (0.0478).

Regarding to the correlation of breast cancer types and PR immune stain:145 cases of IDC were positive for PR immune stain and 163 were negative, while PR immune stain not done for 122 of cases; 10 cases of invasive lobular carcinoma were positive for PR

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immune stain and 7 were negative, while PR immune stain not done for 4 cases. There is no statistical significant association between type of cancer and PR immune stain with P value (0.221.)

Table 3: Correlation between types of breast cancer and ER,PR and HER2/NEW immune stain

Type of Cancer * Estrogen immune stain							
Type of cancer	**Positive**		**Negative**		**Not Done**		**p**
	Freq.	**%**	**Freq.**	**%**	**Freq.**	**%**	
Infiltrating Ductal Carcinoma	127	26.3%	136	28.2%	167	34.6%	
Invasive Lobular Carcinoma	9	1.9%	8	1.7%	11	2.3%	
Medullary Carcinoma	3	0.6%	4	0.8%	4	0.8%	
Mucinous Carcinoma	3	0.6%	3	0.6%	4	0.8%	0.0478
Invasive papillary Carcinoma	3	0.6%	0	0.0%	0	0.0%	
Tubular Carcinoma	1	0.2%	0	0.0%	0	0.0%	
Total	**146**	**30.2%**	**151**	**31.3%**	**186**	**38.5%**	
Type of Cancer * Progesterone immune stain							
Type of cancer	**Positive**		**Negative**		**Not Done**		**p**
	Freq.	**%**	**Freq.**	**%**	**Freq.**	**%**	
Infiltrating Ductal Carcinoma	145	30%	163	33%	122	25.3%	
Invasive Lobular Carcinoma	10	2.1%	12	2.5%	6	1.2%	
Medullary Carcinoma	0	0%	7	1.4%	4	0.8%	
Mucinous Carcinoma	6	1.2%	2	0.4%	2	0.4%	0.221
Invasive papillary Carcinoma	2	0.2%	1	0.4%	0	0%	
Tubular Carcinoma	0	0%	1	0.2%	0	0%	
Total	**163**	**33.7%**	**186**	**38.5%**	**134**	**27.7%**	
Type of Cancer * HER2/NEW							
Type of cancer	**Positive**		**Negative**		**Not Done**		**p**
	Freq.	**%**	**Freq.**	**%**	**Freq.**	**%**	
Infiltrating Ductal Carcinoma	99	20.5%	184	38.1%	147	30.4%	
Invasive Lobular Carcinoma	7	1.4%	13	2.7%	8	1.7%	
Medullary Carcinoma	2	%0.4	4	0.8%	5	1.0%	
Mucinous Carcinoma	2	%0.4	6	1.2%	2	0.4%	0.924
Invasive papillary Carcinoma	1	%0.2	1	0.2%	1	0.2%	
Tubular Carcinoma	0	0.0%	0	0%	1	0.2%	
Total	**111**	**23%**	**208**	**43.1%**	**164**	**34%**	

Regarding to the correlation of breast cancer types and HER2/NEW immune stain :99 cases of IDC were positive for HER2/NEW immune stain and 184 were negative, while HER2/NEW immune stain not done for 147 of cases; 7cases of invasive lobular carcinoma were positive for HER2/NEW immune stain and 13 were negative, while HER2/NEW immune stain not don for 8 cases; 2cases of medullary carcinoma were positive for HER2/NEW immune stain and 4 were negative, while HER2/NEW immune stain not done for 5 cases. There is no statistical significant association between type of cancer and HER2/NEW immune stain with P value (0.924).

Discussion:

In this retrospective descriptive study we determined the pattern of breast cancer and its immune stain among patients registered to NOC. The mean age of patients were about 50 years (±14SD) and the most common affected age group was 41-50 years, by about 32%. In comparison with a study conducted in Northern Egypt, women aged between 45-60 years represented by 75% considered the peak incidence of age groups, with mean age of about 53 years (± 12SD). Another study in Iraq was done in 2016 indicate high incidence (about 35%) of studied population were 45-54 years age group.(11&12)

Also our study showed that the most common type of breast cancer was IDC which represents 85% and in other study of NOC was conducted in Yemen at 2010 clarify that the IDC represent 76%.(13,14)

Our study showed that most of breast cancer cases were express positivity for both ER immune stain and PR immune stain with 63.9%, and in American study it was 74%. The HER2/NEW immune stain was positive in our study in about 23%, while in American study it was only 4%.(15,16)

Regarding the association between breast cancer types and ER immune stain, we found that there is statistical significant association between them which is similar to results found in study conducted in India .(17)

On the other hand, the study showed that there is no statistical significant association between PR and HER2/NEW immune stain and type of breast cancer which is not consistent with the results detected by Sotiriou and Pusztai in their study.(18)

Conclusion:

Our study showed that the most common affected age group was 41-50 years, by about 32% and the most common type of breast cancer was IDC which represent 85%. There was statistical significant association between type of cancer and ER immune stain, while no statistical significant association between type of cancer and PR and HER2/NEW immune stain, and also state of metastasis.

References:

1. Osborne CK, Allred DC ,Harvey JM, Clark GM. Immune stain and breast cancer. J ClinOncol2009:13:1232–40.
2. Fritschi L , Heyworth J, El-Zaemey S, Nagi N: epidemiology of Breast cancer among Yemeni women. Cancer Epidemiol. 2014 Jun;32 (3):255 -60.
3. Liu Y, Nguyen N, Cowlitz GA. Links between alcohol consumption – and breast cancer :a look at evidence. Health of women. 2015;11 : 65-77
4. Yaziji H, Gown AM, Sneige N. Detection of stromal invasion in breast cancer: the my epithelial markers. AdvAnatPathol 2000;7:100–9.
5. Sloane JP. Biopsy pathology of the breast. 2nd ed. Arnold, London, 2001 : 139-40.
6. Berx G, Cleton-Jansen A-M, Strumane K, de Leeuw WJF, Nollet F, van Roy F, et al. E-cadherin is inactivated in a majority of invasive human lobular breast cancers by truncation mutations throughout its extracellular domain. Oncogene 1996;13:1919–25.
7. Bankfalvi A, Terpe HJ, Breukelmann D, Bier B, Rempe D, Pschadka G, et al. Immunophenotypic and prognostic analysis of E-cadherin an beta-catenin expression during breast carcinogenis and tumour progression: a comparative study with CD44. Histopathology. 1999;34:25-34..
8. Harvey JM, Clark GM, Osborne CK, Allred DC. Estrogen receptor status by immune histochemistry is superior to the ligand-binding assay for predicting response to adjuvant docrine therapy in breast cancer. J ClinOncol 1999:17:1474–81.
9. Elledge RM, Green S, Pugh R, Allred DC, Clark GM, Hill J, et al. Estrogen receptor (ER) and progesterone receptor (PgR) by ligand-binding assay compared with ER, PgR and pS2, by immuno-histochemistry in predicting response to tamoxifen in metastatic breast cancer: a Southwest Oncology Group study. Int J Cancer (PredOncol) 2000;89:111– 7.
10. Nicholson RI, Hutcheson IR, Harper ME, Knowlden JM, Barrow D, McClelland RA, et al. Modulation of epidermal growth factor receptor in endocrine-resistant, oestrogen receptor–positive breast cancer. EndocrRelat Cancer 2001;8:175–82.

11. Hussein O, Mosbah M, et al. Breast Cancer: Basic and Clinical Research 2013:7 51–57. available at (http://insights.sagepub.com/breast-cancer-basic-and-clinical-research-journal-j84) accessed 29\7\2017.

12. Alwan NAS. Breast Cancer Among Iraqi Women: Preliminary Findings From a Regional Comparative Breast Cancer Research Project. Journal of global oncology 2016;5:255-258.available at (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5493264/) accessed in 29\7\2017.

13. Lakkis NA, Adib SA et al.Sociological Transition and Breast Cancer in the Arab World: the Experience of Lebanon. Asian Pacific Journal of Cancer Prevention,2017: 18 (5),1375-1364. Available at(http://ascopubs.org/doi/pdfdirect/10.1200/jgo.2015.003087) accessed 29\7\2017.

14. El-Zaemey S, Nagi N, Fritschi L , Heyworth J:Breast cancer among Yemeni women using the National Oncology Centre Registry 2004-2010 . Cancer Epidemiol. 2012;36(3):249-53 .

15. Benjamin O. Anderson :Global Breast Cancer Trends . UICC world Cancer Congress 2014 : www.bhgi.info .

16. Blows FM, Driver KE, Schmidt MK, et al . Subtyping of breast cancer by immune histochemistry to investigate a relationship between subtype and short and long term survival: a collaborative analysis of data for 10,159 cases from 12 studies . PLoS Med. 2010;7(5):e1000279 .

17. Torsten A. ,Heidi L. ,Susan G., et al. Breast Cancer Patients with Progesterone Receptor PR-A-RichTumors Have Poorer Disease-Free Survival Rates. Clinical Cancer Research.2004; 10:2751–2760.

18. Christos Sotiriou and Lajos Pusztai. Gene-Expression Signatures in Breast Cancer. The new England journal of medicine .2018 ;5:318-330.