Cutaneous Manifestations in Breasts among Patients with Breast Tumors Attending Al-Yarmook Teaching Hospital

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Abstract

Breast cancer is the most common cancer in women both in the developed and less developed world. It is the top cancer in women worldwide and is increasing particularly in developing countries where the majority of cases are diagnosed in late stages.

Study Duration: Eight months period, from the first of January to the end of August 2018. Source Population: Patients with skin manifestations in breast who attended study settings during the study period. Sampling Method: A non-random sampling of the attendants at the selected consultation clinics.

Three hundred and ten patients with cutaneous manifestations in their breasts were studied. All patients were female with a mean age of 51.25 ±11.5, the lesions were more common among age group of 50 years and above, most of them were married and were nulliparous, those with 1st degree +ve family history of cancer represent the highest percentage, Most of patients presented with inflammatory skin changes followed by infections. Out of 310 patients only 182 (58.7%) FNA were taken. Patients with +ve result were 86 cases (27.7 %) whereas 96 patients (31.0%) had –ve result. Surprisingly no one of 62 patients with itching had an ultrasound or mammographic indications to do FNA. Out of 86 +ve FNA result, only 24 patients (27.9%) presented with cancer that precede the dermatological manifestations while 62 patients (72.1%) were presented with cutaneous manifestations as first sign of breast cancer. A significant association was seen between having cutaneous manifestations proceeding a positive FNA findings and inflammatory manifestations (inflammation and eczema).

Cutaneous manifestations can be the first clinical indicator of breast cancer. The development of such manifestations if not taken seriously may delay the diagnosis of breast cancer which lead to a poor prognosis. Lesions appearing within the breast may appear harmless to patients, however a dermatologist can be the first person to raise a suspicion of breast cancer or its recurrence.

Keywords: *Cutaneous manifestations, Breast tumor, FNA, Cancer*

Introduction

Breast cancer is the most common cancer in women both in the developed and less developed world .It is the top cancer in women worldwide and is increasing particularly in developing countries where the majority of cases are diagnosed in late stages [3], it is the second cause of cancer death after lung cancer in Asia, although its incidence is more in some developed countries, death is higher in countries with low level of development, therefore, better plans for screening and early detection programs in these countries are suggested [3,4].

Breast cancer typically produces no symptoms when the tumor is small and most easily treated, which is why screening is important for early detection. The most common physical sign is a painless lump, Any persistent change in the breast should be evaluated by a physician as soon as possible, however patients may also seek medical attention because of cutaneous lesions [4,5].

The most frequent cutaneous manifestations include inverted nipple, skin infiltrate, ulceration, satellite nodules or eczema-like changes on the skin, a serous fact is that, breast cancer cells show predilection for pilosebaceous units, causing their complete destruction[6].

Sometimes breast cancer spreads to under arm lymph nodes and causes a lump or swelling, even before the original breast tumor is large enough to be felt, less common signs and symptoms include breast pain or heaviness, persistent changes such as swelling, thickening, or redness of the skin, and nipple abnormalities such as spontaneous discharge (especially if bloody), erosion, or retraction should rise an attentions [5,6].

Macroscopically, the skin of the breast may have an orange peel appearance (peau d'orange) due to the presence of cancer cells blocking the lymphatic vessels in the skin [7].

A specific form of breast cancer is the so-called inflammatory cancer which is a separate clinico-pathological entity characterized by a very rapid development (the period from the onset of symptoms until diagnosis must be shorter than 6 months) and presents as diffuse erythema and oedema involving at least one-third of the breast skin surface [8].

The initial presentation of cutaneous manifestations is frequently subtle and may be overlooked without proper index of suspicion, appearing as multiple or single nodules, plaques, and ulcers, in decreasing order of frequency [9]. Commonly, a painless, mobile, erythematous papule is initially noted, which may enlarge to an inflammatory nodule over time, Such lesions may be misdiagnosed as cysts, lipomas, fibromas, or appendageal tumors [10].

Materials and Methods

Study Setting; The two consultation clinics in AI-Yarmook teaching hospital, dermatological and breast examination clinic.

Study Design: a cross-sectional study has been attempted.

Study Duration: Eight months period, from the first of January to the end of August 2018.

Source Population: Patients with skin manifestations in breast who attended study settings during the study period .

Sampling Method: A non-random sampling of the attendants at the selected consultation clinics.

Sample size: This study trust the following equation to precise the required sample size [1]:

$$n = [\{Z_{(1-\alpha)}^2 \; p\, q / d^2\}] + 10\%$$

Where: n is the estimated sample size

Z=1.96

p= is the proportion of the population possessing the characteristics of interest (23.9%) [2]

q= is (1-p)

d= is the desired level of precision= 0.05

2= is the design effect

5%= is contingency error

$[(1.96)^2 \times 0.23 \times 0.77 / (0.05)^2] + 10\%$

$= [3.84 \times 0.16 / 0.0025] + 10\ \%$

$= [0.6427\backslash 0.0025] + 10\%$

$=272 + 10\%$

$=299 \approx 300$

Data collection: Verbal consent took from the study participants after explanation of the aim and benefit of the study.

Results

Three hundred and ten patients with cutaneous manifestations in their breasts (the inclusion criteria) were studied.

As shown in table (1), all patients were female with a mean age of 51.25 ±11.5, the lesions were more common among age group of 50 years and above (180 patient 58.1%), most of them were married (225patient 72.6%) and were nulliparous (158 patients 51.0%), those with 1st degree +ve family history of cancer represent the highest percentage (116 patients 37.4%).

Table 1: Data of patients under study

		No. of patients	Percent
Age	below 40 yr	55	17.7%
	40- 49yr	75	24.2%
	50yr and above	180	58.15%
MARITAL STATUS	Single	14	4.5%
	Married	225	72.6%
	Others	71	22.9%
PARITY	Nulliparous	158	51.0%
	one para	32	10.3%
	Multipara	120	38.7%
FAMILY HISTORY	negative fhx	92	29.7%
	first degree	116	37.4%
	2nd and more degree	102	32.9%
Total		310	100%

Table 2: illustrate that most of patients presented with inflammatory skin changes (105 patients 33.9%) followed by infections (67 patient 21.3 %) which is somewhat similar to that of itching (62 patient 20.0%), while retracted nipples and ulcerations being the least one (7 patient 2.3%) and (10 patient 3.2%) respectively.

Table 2: Patients' skin manifestation

Skin sign		N0. of patients	Percent
	Itching	62	20.0%
	discharge from nipple	44	14.2%
	Inflammations	105	33.9%
	Ulcer	10	3.2%
	Infections	67	21.6%
	Eczema	15	4.8%
	retracted nipple	7	2.3%
	Total	310	100.0

Figure (1) illustrates that out of 310 patients only 182 (58.7%) Fine needle aspiration (FNA) were taken (had ultrasonic or mammographic indications), the other 128 patients (41.3%) FNA not done (had no indications). Patients with +ve result were 86 cases (27.7 %) whereas 96 patients (31.0%) had –ve result.

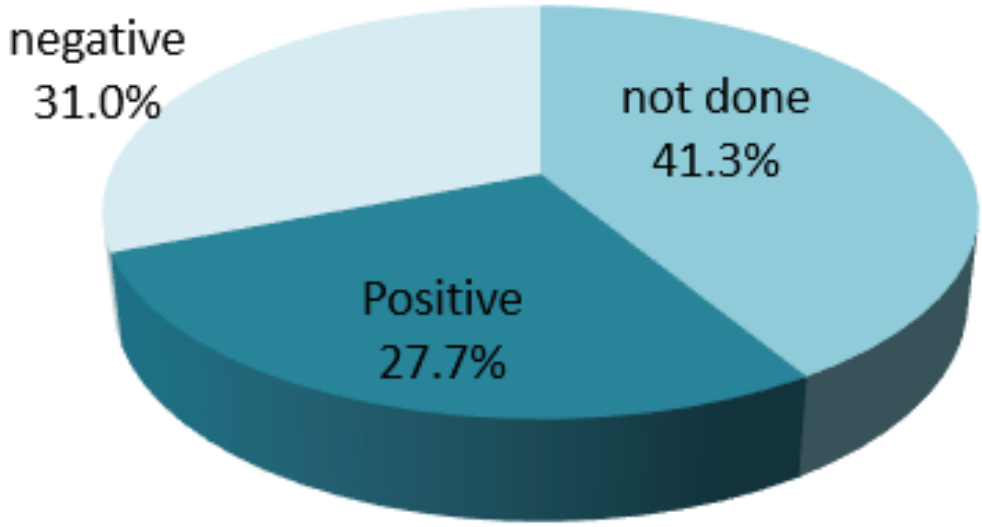

Figure 1: FNA of patients under study

Note: mean age of FNA +ve patients was 50.22±10.5 years.

Table (3) illustrate that most of those 86 patients with +ve FNA results were 55 years age and above (64.0%), had +ve first degree family history of cancer 32 patients (37.7%), were married 49 patients (56.9%) and they were nulliparous 158 patients(51.0%).

Table 3: FNA +ve patients' data

FNA		+ve	Percentage
Age	below 40 yr	12	14.0%
	40- 49yr	19	22.0%
	50yr and above	55	64.0%
Family history	negative fhx	29	33.7%
	first degree	32	37.2%
	2nd and more degree	25	29.1.%
Marital status	Single	7	8.1%
	Married	49	56.9%
	Others	30	35%
parity	Nulliparous	158	51%
One para	32	10.3%	
Multipara	120	38.7%	
Total		86	100%

Table (4) illustrate that out of 310 patients, 105 patients had inflammatory manifestations from which 42 (48.5%) patients had +ve FNA results and out of 10 patients with ulcer, 9 of them had +ve FNA results, 7patients with retracted nipple all had indications to do FNA from which 3 had +ve FNA results while those 67 patients with infections only 9 had +ve results, surprisingly, no one of 62 patients with itching had an ultrasound or mammographic indications to do FNA.

Table 4: FNA for patients under study

not done					
		+ve	-ve	Total	
FEATURES	Itching	62	0	0	62
	discharge from nipple	0	15 (17.5%)	29 (30.2%)	44
	Inflammations	22(20.9%)	42(48.5%)	41(42.5%)	105
	Ulcer	0	9(10.5%)	1(1.4%)	10
	Infections	39(58.2%)	9(10.5%)	19(19.7%)	67
	Eczema	5(33.3%)	8(9.5%)	2(2.1%)	15
	retracted nipple	0	3(3.5%)	4(4.1%)	7
Total		128	86	96	310

Discussion

In the present work, across sectional study design was performed which has the advantages of easy conduction, less time needed and measure the prevalence of an event which highlight the extent of a problem in the community [(11)]. Furthermore, it can determine the relationship between skin manifestations and breast cancer, thus a hypothesis can be created about their association which suggest a further research work to test this hypothesis.

This study showed that the mean age of study sample was (51.25 ±11.5) years, while those with FNA+ve result had mean age of (50.22±10.5) years, this is close to that reported by Molah Karim SA et,al. study (49.42±11.66) years that conducted at North of Iraq in Hewa Hematology and Oncology Hospital during 2011-2013 [(12)], this is expected as Iraqi patients has a premenopausal stage at this age and this is agreed by a preliminary analysis of the relevant database findings belonging to 855 patients diagnosed and treated for breast cancer in a study conducted by Nada A.S. Alwan were it found that 46% of the patients were in their premenopausal age [(13)]. Several factors may accounted for this phenomenon of highest level at premenopausal period (in contrast to the pattern described in west societies), such as early menarche and late menopause which makes the female to be exposed to sex hormones for prolonged period, circulating estrogens and androgens are positively associated with the risk for breast cancer in premenopausal women [(14)].

In our study, patients with FNA +ve result, 56.9% of them were married, 35% either divorced or widow and 8.1% were singles. Interestingly, the total number (married, divorced and widow) represent 91.9% which comes with the result of Nada A.S. Alwan [(13)], where 86.3% of her patients were married (she not took in her account whether patients were divorced or widowed), it is also close to the result of Basim Hussain Bahir et.al,

who conduct his study at Baghdad, Medical City and Al-khadumia Teaching Hospitals during the period between Jan 2009 and Jan 2010, where he found that 68.3% of his cases were married ,22% either divorced or widow and 9.7% were singles [15]. Married females constituted the highest proportion of the sample, which can indicate that married women are more oriented toward breast cancer, one can also expect high risk among married patients due to exposure to stress, life style, obesity, physical inactivity [16], The use of hormonal therapy and long term use of oral contraceptives are other possible explanations for the increased risk [17].

Nulliparous patients and had FNA +ve result represent 51.0% of this study, those had one para were 10.3% while multiparas were 38.7%. Different figures reported by Nada A.S. Alwan study [13], where only 8.5% of her patients were nulliparous, this differences may be due to the fact that 20% of her patients received hormones and **7**% had their first child birth after the age of 35 years, so the risk factors were discussed from different point of view, however the result of our study was come with the result of Usama M. Al-Fadhli et al, that was conducted in Baghdad city during a three months period from January to March 2016 at Al-Amal National Hospital for Cancer Management were 41.6% of his patients were nulliparous [18].

In the present study patients with FNA +ve result and had a first degree family history of cancer represent 37.2%, those with second degree family history represent 29.1%, while negative family history represent 33.7%, this is higher than the result of Molah Karim SA et al. [12] where he found that only 13.49% of cases had a family history, this low fraction in his study could be due to the selection bias as he exclude any Arabic patients or Kurdish patients who lives outside Sulaimanyah government. However our result is close to that of Nada A.S. Alwan [13] where 35% of her patients documented to have a positive family history of malignancy which is similar to the result of Gillian Haber et al (the data source was the National Health Interview Survey), where also 46% of his patients had a positive family history of cancer which support that breast cancer risk perception was associated with the presence of a positive family history of cancer [19].

In this study (27.7%) of sample had cutaneous manifestations with cancer, most common cutaneous manifestations among FNA +ve patients were inflammatory changes (48.5%) followed by discharge from nipple (17.5%), ulcers and infections had same percentage (10.5%) ,whereas eczema and retracted nipples (9.5%) and (3.5%) respectively, this result was higher than Nada A.S. Alwan study [13] (breast cancer among Iraqi women: preliminary findings from a regional comparative breast cancer research project), where cutaneous changes represent only (9.8%) and bloody nipple discharge (4.7%) however our result agree with De Giorgi V. et. al., (work done at department of dermatology, university of Florence, Firenze, Italy) were (23.9%) of his patients had cutaneous manifestations of breast cancer [20].

Conclusions

Cutaneous manifestations can be the first clinical indicator of breast cancer. The development of such manifestations if not taken seriously may delay the diagnosis of breast cancer which lead to a poor prognosis. Lesions appearing within the breast may appear harmless to patients, however a dermatologist can be the first person to raise a suspicion of breast cancer or its recurrence.

Ethical Clearance: The Research Ethical Committee at scientific research by ethical approval of both environmental and health and higher education and scientific research ministries in Iraq

Conflict of Interest: The authors declare that they have no conflict of interest.

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References

1. Wayne W. Daniel. Biostatistics, a foundation for analysis in the health sciences. John Wiley& sons Inc. 2005; p 275-278.
2. Lookingbill DP, Spangler N, Helm KF. Cutaneous metastases in patients with metastatic carcinoma: a retrospective study of 4020 patients. J Am Acad Dermatol. 1993;29:228-36.
3. [https://www.who.int/cancer/detection/breastcancer/en/index1.html. Accessed on 7th Dec. 2018].
4. Mahshid Ghoncheh, Neda Mahdavifar, Efat Darvishi, Hamid Salehiniya. Epidemiology,

Incidence and Mortality of Breast Cancer in Asia. Asian Pac J Cancer Prev, 17, Cancer Control in Western Asia Special Issue,2017, PP 47-52.

5. American Cancer Society. Breast Cancer Facts & Figures 2017-2018. Atlanta: American Cancer Society, Inc. 2017.
6. Agnieszka B. Owczarczyk-Saczonek, Dawid Sigorski, Paweł Różanowski, Agnieszka Markiewicz, Waldemar J. Placek. Cutaneous manifestations of breast cancer. Dermatol Rev/ Przegl Dermatol 2017, 104, 561–569.
7. Rolz-Cruz G., Kim CC.: Tumor invasion of the skin. Dermatol Clin 2008, 26, 89-102.
8. Wollina U., Graefe T., Konrad H., Schönlebe J., Koch A., Hansel G., et al.: Cutaneous metastases of internal cancer. Acta Dermatovenerol Alp Pannonica Adriat 2004, 13, 79-84.
9. Lookingbill DP, Spangler N, Helm KF. Cutaneous metastases in patients with metastatic carcinoma: a retrospective study of 4020 patients. J AmAcadDermatol. 1993;29(2, pt 1):228-236.
10. Karen A. Chernoff, Ashfaq A. Marghoob, Mario E. Lacouture, et al. Dermoscopic Findings in Cutaneous Metastases. JAMA Dermatol. 2014;150(4):429-433.
11. Gordis L: Epidemiology. 3rd edition. Philadelphia. WR saunders company 2004:pp.12_13.
12. Molah Karim SA, Ali Ghalib HH, Mohammed SA, Fattah FH. The incidence, age at diagnosis of breast cancer in the iraqi kurdish population and comparison to some other countries of Middle-East and West. Int J Surg. 2015 Jan;13:71-5.
13. Nada A.S. Alwan. Breast cancer among iraqi women: preliminary findings from a regional comparative breast cancer research project. Journal of Global Oncology. Volume 2, Issue 5, October 2016.
14. Timothy Key. Endogenous hormones and breast cancer collaborative group, sex hormones and risk of breast cancer in premenopausal women: a collaborative reanalysis of individual participant data from seven prospective studies. Lancet Oncol. 14 (2013) 1009-1019.
15. Basim Hussain Bahir, Abdulkhaliq A. Al-Naqeeb, Shatha Mahmood Niazy. Risk factors for breast cancer in a sample of women. Iraqi J. Comm. Med., Jan. 2012 (1).
16. Galobardes B., Shaw M., Lawlor D. A., Lynch J. W., Smith 9. G. D. indicators of socioeconomic position, J Epidemiol Community Health, 2006; 60: 7–12.
17. Anothaisintawee T, Wiratkapun C, Lerdsitthichai P, et al. Risk Factors of Breast Cancer: A Systematic Review and Meta-Analysis; Asia Pac J Public Health, 2013; 25: 368-387.
18. Usama M. Al-Fadhli, Ameel F. Al-Shawi Ahmed S. Al-Nuaimi. Assessment of sociodemographic characteristics in a sample of breast cancer patients in Baghdad. J Fac Med Baghdad Vol.58, No.4, 2016.
19. Gillian Haber, Nasar U. Ahmed, Vukosava Pekovic. Family history of cancer and its association with breast cancer risk perception and repeat mammography. Am J Public Health. 2012 December; 102(12): 2322–2329.
20. De Giorgi V, Grazzini M, Alfaioli B. Cutaneous manifestations of breast carcinoma. Dermatol Ther. 2010 Nov-Dec;23(6):581-9.