Primary and Recurrent Breast Abscess in Non Lactational Women, Assessment of Risk Factors and Bacteria Involved. A prospective Cohort Study for Patients and Healthy Control

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Abstract--- Background: Although inflammatory disease of the breast are uncommon in non lactional women, but it poses a diagnostic and therapeutic dilemma with considerable morbidity.Diabetes mellitus, smoking, obesity, low socioeconomic state are blamed to be a risk factors for mastitis with the subsequent sequel of breast abscess in non lactating women. Poly microbial infection, both aerobic and anaerobic bacteria represent up to 40% of isolates in breast abscess predominantly in non nursing women. Methods: From February 2012 to May 2019, eighty nine patients attending the department of surgery at Al Diwaniyha teaching hospital with primary and recurrent non lactational breast abscess were included in a prospective cohort study. Pus specimens were obtained at the time of drainage which is subjected to gram stain, Ziehl Neelsen stain, aerobic and anaerobic cultures. one hundred age matched healthy female enrolled in the study as a control. Results: Breast abscess was more frequent in the age group 35-45 years.Smoking found to be significantly more prevalent in patients than controls as 41.5 % of patients with breast abscess were smokers as compared to 20% of controls.Diabetes found to significantly more prevalent in patients than controls(24.7 % Vs 8%).Forty six percent of women with breast abscess were with moderate to severe obesity. Only smoking and diabetes was found to significantly more prevalent in recurrence(84.6 % and 76.9%) respectively. p value =0.001. Mixed aerobic and anaerobic bacteria were the commonest isolate 58.4 %, followed by pure aerobic bacteria 12.35 %, while pure anaerobic bacterial isolate comes last 10.1 %. Moreover 17 (19.1 %) out of 89 breast abscess were sterile among which one was positive for AFB. Amoxiclav has the greatest activity upon the gram positive aerobic cocci. Gram negative bacteria were mostly sensitive to cephalosporin and Ciprofloxacin. Metronidazol is still the most effective drug against anaerobic cocci and bacteroids. Conclusion: Smoking, diabetes, overweight / obesity and short breast feeding regimen, all have strong association with primary breast abscess. Only smoking and diabetes have significant association with recurrent abscess. Mixed infection by aerobic and anaerobic bacteria predominates. Anaerobic cocciare the commonest isolated bacterium.

Keywords--- Primary, Recurrent, Non Lactational Mastitis, Risk Factors, Bacteriology.

I. INTRODUCTION

Although inflammatory disease of the breast are uncommon in non lactional women, but it poses a diagnostic and therapeutic dilemma with considerable morbidity (Beassler, 2010).Breast abscess develops commonly after mastitis during breast feeding but it can also occur in non lactating usually older premenopausal women (Efrat et al., 1998). The frequency of abscess was reported as 3-11% of patients with mastitis (Dixon, 2013).Mastitis can occur in

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consistence with duct ectasia and less frequent association with foreign aesthetic prosthesis (Ramalingam et al., 2015). Periductal mastitis is a chronic inflammatory disease of the breast characterized by dilatation of the mammary ducts, with plasma cells infiltration and subsequent abscess formation. It is responsible for 5-25% of symptoms related to benign breast disorders. Recently the description of Idiopathic granulomatous lobular mastitis as a possible cause of recurrent breast infection and abscess has expand the spectrum of diagnosis (Versluijs-Ossewaarde et al., 2005).The most accepted pathogenesis of non lactation mastitis is the presence of keratin plug and squamous hyperplasia in the affected lactiferous duct with subsequent blockage stasis and inflammation due to entrapment and proliferation of bacteria in milk sinus (Johnstone, 2017). Whether bacterial infection is the initial event or a subsequent sequel of cytomorphological changes is still illusive, moreover still many cases of duct ectasia and periductal mastitis are sterile (Sandhu et al., 2014). Most patients presents with signs of mastitis and or abscess with increasing breast pain, often confined to the sub areolar area or to one quadrant of the breast with clinically palpable lump which is often tender with variable degree of redness of the overlying skin(Kataria et al., 2017). The majority of non lactational abscess occur in the subareolar area. Corynebacteria is blamed to be a causative agents in many cases of idiopathic granulomatous mastitis. Diabetes mellitus, smoking, obesity, low socioeconomic state are blamed to be a risk factors for mastitis with the subsequent sequel of breast abscess in non lactating women. Infectious mastitis is commonly caused by skin derived bacteria, s*taphylococcus aureus*being the most common isolate and coagulase negative *Staphylococci* comes in the next frequency. Nowadays methicillin-resistant *S. aureus are the most predominant in breast abscess isolates*. Poly microbial infection, both aerobic and anaerobic bacteria represent up to 40% of isolates in breast abscess predominantly in non-nursing women (Zhang et al., 2018). It has been found that anaerobes were predominant in isolates from chronic recurrent non lactational breast abscess specially in smoker women. Unusual pathogens can be detected in breast abscess including tuberculous bacilli and atypical mycobacteria, however their existence is rare even in tuberculosis endemic area (Bouton et al., 2015).

II. PATIENTS AND METHODS

From February 2012 to May 2019, eighty nine patients attending the department of surgery at Al Diwaniyha teaching hospital with primary and recurrent non lactational breast abscess were included in a prospective cohort study. Pus specimens were obtained at the time of drainage which is subjected to gram stain, Ziehl Neelsen stain, aerobic and anaerobic cultures. One hundred age matched healthy female enrolled in the study as a control. A uniform questionnaire were applied to all participants, including detailed information of age, weight, height, parity, smoking, breast feeding, history of smoking diabetes and autoimmune diseases, and recurrent abscess in patients. All participants informed about the study and oral consent was obtained accordingly. Data were analyzed using SPSS software system version 22. Fisher's exact test. was used for categorical variables and P value ≤ 0,05 considered significant.

III. RESULTS

A total of 89 female patients with primary and recurrent non lactational breast abscess were compared with 100 age matched health female. The mean age of patients and control was 45.1 (36-57) year's, figure 1.
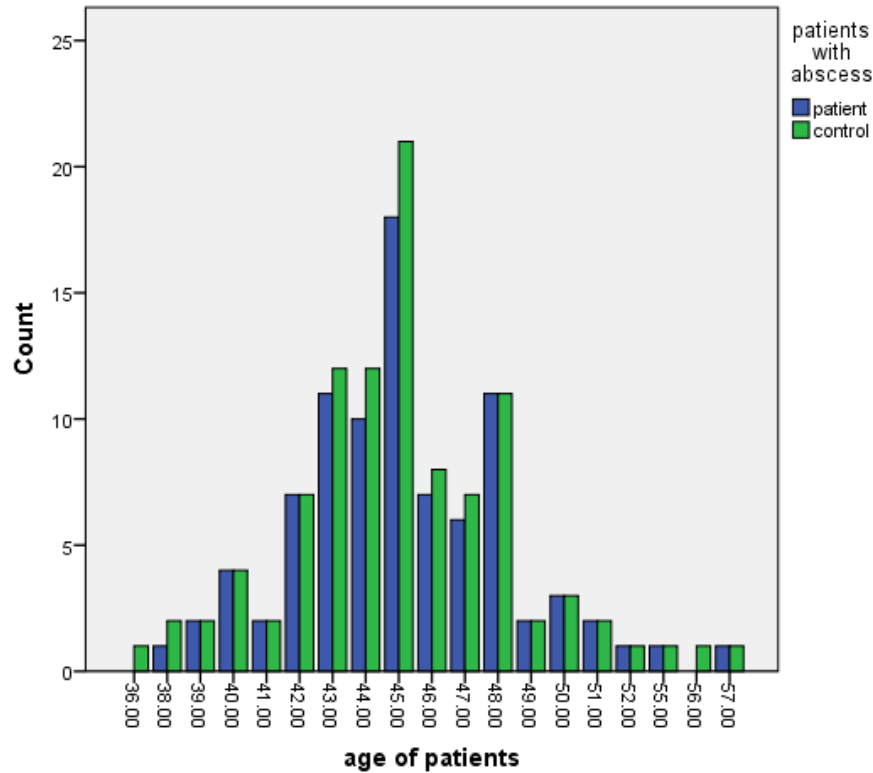
Figure 1: Age of the Study Groups

Breast abscess was more frequent in the age group 35-45 years accounting for 55%, female with more than 45 years of age was the second frequent age group affected. Results showed that non lactational breast abscess is infrequent in females less than 35 years of age and rare in females less than 25 years. Table 1

Table 1: Age Groups Characteristics in Patients and Control

		Age group (year)								Total	
		18-25		25-35		35-45		More than 45			
		No	%	No	%	No	%	No	%	No	%
Patients with abscess	Patient	2	2.3	4	4.5	49	55	34	38.2	89	100
	Control	2	2	3	3	57	57	38	38	100	100
Total		4		7		106		72		189	100

Smoking found to be significantly more prevalent in patients than controls as 41.5 % of patients with breast abscess were smokers as compared to 20% of controls (p value = 0.001) Risk ratio= 2. Among patients with breast abscess, 24.7 % were diabetic as compared to only 8% in the controls. Diabetes found to significantly more prevalent in patients than controls (p value = 0.002) Risk ratio= 3. More than half (53,9) of women with breast abscess breast fed their babies less than 2 months as compared to 25% of controls, the difference found to be highly significant as compared to controls (p value =0.0001) Risk ratio =2. In our cohort No single patients with BMI less than 18 developed breast abscess. In contrast 46% of women with breast abscess were with moderate to severe obesity. The differences were highly significant as compared to control (p value = 0.0001). No significant differences were found between patients and control with the regard to parity and presence of concomitant autoimmune diseases. (table 2)

Table 2: Comparison of Selected Risk Parameters in Study and Control Groups

		Patients with abscess		Total	P value
		Patient	Control		
Smoking	non smoker	52	80	132	0.001
	Smoker	37	20	57	
Total		89	100	189	
Diabetis	non diabetic	67	92	159	0.002
	Diabetic	22	8	30	
Total		89	100	189	
Parity	Nullparous	5	6	11	0.7
	Uniparous	9	7	16	
	Multiparous	75	87	162	
Total		89	100	189	
Breast feeding	Non	5	6	11	0.0001
	Less than 2 months	43	19	62	
	2-12months	38	60	98	
	more than 12 months	3	15	18	
Total		89	100	189	
Autoimmune disease	Negative	83	96	179	0.5
	Positive	6	4	10	
Total		89	100	189	
Body mass index	BMI less than 18	0	1	1	0.0001
	BMI=18-25	7	34	41	
	BMI=25-30	41	54	95	
	BMI=30-35	13	8	21	
	BMI=35-40	19	3	22	
	BMI 40-45	9	0	9	
Total		89	100	189	

Only smoking and diabetes was found to significantly more prevalent in recurrence (84.6 % and 76.9%) respectively. p value =0.001 among the studied parameters table 3.

Table 3: Comparison of Selected Risk Parameters Primary and Recurrent Abscess

Risk factors and recurrence					
		Recurrence		Total	P value
		Negative	Positive		
Smoking in abscess	Non smoker	45	2	52	
	Smoker	31	11	37	0.001
Total		76	13	89	
DM in abscess	Non diabetic	57	3	67	
	Diabetic	19	10	22	0.001
Total		76	13	89	
Parity in abscess	Nulparous	5	0	5	
	Uniparous	6	3	9	0.175
	Multiparous	65	10	75	
Total		76	13	89	
Breast feeding in abscess	Non	5	0	5	
	Less than 2 months	36	7	43	
	2-12 months	32	6	38	0.681
	More than 12 months	3	0	3	
Total		76	13	89	
Autoimmune disease in absceess	Negative	71	12	83	
	Positive	5	1	6	1.000
Total		76	13	89	
BMI in abscess	BMI 18-25	7	0	7	
	BMI25-30	36	5	41	
	BMI 30-35	11	2	13	
	BMI 35-40	15	4	19	0.6
	BMI more than 40	7	2	9	
Total		76	13	89	

Mixed aerobic and anaerobic bacteria were the commonest isolate 58.4 %, followed by pure aerobic bacteria 12.35 %, while pure anaerobic bacterial isolate comes last 10.1 %. Moreover 17 (19.1 %) out of 89 breast abscess were sterile among which one was positive for AFB.

In a decreasing frequency, anaerobic cocci was the most prevalent bacteria isolated in 39.3% of cases, followed by staph aureus 32.5%, staph epidermidis 29%, E coli 25.8%, Bacteriods spp. 19.1%, proteus 10.1%, pseudomonas 5.6%. and lastly Strepto. pyogenes 1.12 table 4

Table 4: Bacterial Growth Involved in Breast Abscess

Growth characteristics	Type of organism	No	%
Aerobic growth	Staph. aureus	3	3.37
	Staph. Epidermidis	5	5.61
	Strepto. pyogenes	1	1.12
	E.coli	1	1.12
	Proteus species	1	1.12
	Pseudomonas aeruginosa	-	0
	Total	11	12.35
Mixed growth	Staph. aureus + Anaerobic cocci	17	19.1
	Staph. Epidermidis +E. coli + Anaerobic cocci	13	14.6
	Pseudomonas aeruginosa + bacteriods	5	5.61
	Staph. epidermidis + Proteus+ bacteriods	8	8.9
	Staph. aureus +E.coli	9	10.1
	Total	52	58.4
Anaerobic growth	Anaerobic sp.	5	5.61
	Bacteroid sp.	4	4.5
	Total	9	10.1
No growth	---------	17	19.1
	Grand total	89	

Table 5: Antibiotics Sensitivity Pattern Presented in Number

Antibiotics	Staph. Aureus no. 29	Staph. Epidermidis no. 26	Strepto. Pyogenes no. 1	E.coli no. 23	Proteus species no. 9	Pseudomonas aeruginosa no. 5	Peptostreptococcus sp. No. 30	Bacteriods no. 17
Co-amoxiclav	25	26	1	19	4	-	5	-
Ampicillin	2	1	1	8	0	-	8	-
Cephalexin	20	18	-	15	2	-	-	3
Cloxacillin	25	22	-	-	-	-	-	-
Erythromycin	24	25	-	-	-	-	27	-
Gentamicin	18	10	-	20	9	4	-	-
Vancomycin	29	26	1	-	-	-	-	-
Amikacin	-	-	-	23	9	5	-	-
Cefotaxime	-	-	-	22	9	-	28	4
Ceftazidime	-	-	-	-	-	5	24	-
Ciprofloxacin	-	-	-	23	9	4	-	2
Imipenem	-	-	-	23	9	5	-	8
Piperacillin	-	-	-	17	8	4	30	16
Clindamycin	23	22	0	-	-	-	30	10
Metronidazole	-	-	-	-	-	-	30	17
Penicillin	3	2	1	-	-	-	-	0

IV. DISCUSSION

All forms of Breast abscess can occur at any time during female life within a frequency of 4.6 -11 %, however breast abscess in non nursing female is less common than lactating women (Gopalakrishnan et al., 2015). The term of non lactational mastitis refers to a spectrum of conditions that cause inflammation and or infection of the breast with or without subsequent abscess, among these periductal mastitis and idiopathic granulomatous mastitis are the most frequent (Bundred, 1992). Breast abscess in non lactating women is more common in perimenoposal women (26). A fact consistent with Our results which showed that Breast abscess was more frequent in the age group 35-45 years. The mean age of patients 45.1 (36-57) year's, these findings were slightly different from findings in other series of fifty patients with mean age of 33 years (27). Among the studied associated risk factors for the development of breast abscess in non lactating women, smoking found to be more frequent in patients than controls, this finding was consistent with other series which confirm the fact that smoking is a risk factor for breast abscess(8,28,29,30,31). Diabetes was extensively studied as a risk factor for non lactational breast abscess, our results declares significantly more frequent occurrence of diabetes in breast abscess as compared to control. Most studies confirms this association(20,30). Liu et al stated that obesity is an independent risk factor for periductal mastitis and abscess, this fact is also confirmed in our study which declared highly significant association of breast abscess with overweight/obesity(32).History of previously adopted breast feeding protocol has been evaluated for the future risk of mastitis in the non lactation state, our results showed significant association between duration of breast feeding in previous pregnancies and the development of breast abscess as more than 50% of patients with breast abscess fed their babies less than 2 months. This finding is confirmed by many literatures(9,33). Our study revealed that parity has no significant association with non lactational breast abscess..Lui et al published a contradictory results of a significant impact of parity and periductal mastitis/ abscess(32). Although immunological response associated with periductal mastitis has been investigated whether a primary local or a consequences of bacterial infection, no available data concerning global immune response in aetiopathogenesis of this condition. Furthermore our data fail to find an association between breast abscess and autoimmune disease(27). It has been stated in most published series that breast abscess in non lactating women is associated with high recurrence rate 35-57% (20,34), However, recurrence rate in our study was only 14.6, this can be explained basically by that most of our patients were primary breast abscess and no follow up was adopted to confirm the real rate of recurrence in those patient group. Moreover among the studied risk factors only smoking and diabetes were significantly more frequent in patients with recurrent than primary breast abscess, unlike the finding of Bharat et al and Gollapalli et al who stated that, smoking is the only risk factor associated with recurrence(20,34). There are a lot of debate and confusing data regarding the infective microorganisms in periductal and granulometous mastitis the two major components of breast abscess in non nursing women. The presence of sterile lesions (negative bacterial growth) were common findings reaching 33% (13,23) And 8 % in other series (35). Sterile abscess represented 17.9% in our study. Unlike other reports, staphylococcus aureus was second most common pathogen accounting for 32.5% of isolated pathogens, and superseded by anaerobic cocci as the commonest isolated bacterium accounting for 39.3% of isolates, however they were commonly found in mixed infection with other pathogens and infrequently as a sole infecting pathogen. The coagulase negative staph epidermidis still has remarkable existence in breast abscess in non

lactating women, commonly in admixture with other bacteria. Most published series reprted higher frequency of staph aureus infection as the most common bacteria involved.AbdelHadi concluded that Staphylococcus Aureus was the commonest pathogen isolated, followed by streptococcus pyogens with no single isolate of staph epidermidis. In contrast, our results declared that the streptococcus pyogens was the least common bacteria isolated acounting only for 1.12 %. Our data declared a substantial frequency of gram negative bacilli in breast abscess41.8% however they were parts of a mixed rather than isolated infection, this finding is contradictory to other series which documented less frequent involvement of these particular kinds if bacteria(Marchant, 2002) Gopalakrishnan et al denied the presence of anaerobic bacteria in cases of non lactational mastitis however, the study was performed for patients not complaining of an abscess, this finding should rise the idea that bacterial infection is a consequences rather than an aetiology. Ramakrishnan et al also found, bacteroids were absent in cultures from an abscess in non lactating women (Ramya et al., 2017). The importance of anaerobic bacteria and especially bacteroids was extensively evaluated in most series concerning breast abscess in non lactating women, both their presence and relationship with recurrence (Bharat et al., 2011). Our data confirmed the presence of bacteroids in 14.6%, of cases as part of mixed infection with aerobic bacteria and 4.5 % as a sole infective organism.Regarding the antibiotics sensitivity, our results showed that amoxiclav has the greatest activity upon the gram positive aerobic cocci and weak activity against gram negative and anaerobic bacteria. Gram negative bacteria were mostly sensitive to cephalosporin and Ciprofloxacin. Metronidazol is still the most effective drug against anaerobic cocci and bacteroids (Al Benwan et al., 2011).

V. CONCLUSION

Non lactational breast abscess is more common in peri menopausal women. Smoking, diabetes, overweight / obesity and short breast feeding regimen, all have strong association with primary breast abscess. Only smoking and diabetes have significant association with recurrent abscess while obesity and breast feeding regimenhave not. Neither parity nor concomitant autoimmune diseases have a significant impact upon the incidence of both primary and recurrent abscess. Mixedinfection by aerobic and anaerobic bacteria predominates. Anaerobic cocciare the commonest isolated bacterium, followed by, staphylococcus aureus.

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