RESEARCH COMMUNICATION

Histopathological Patterns and Risk of Female Breast Lesions at a Secondary Level of Care in Saudi Arabia

Tarek Tawfik Amin[1]*, Abdul Rahman Saleh Al-Mulhim[2], Rajan Chopra[3]

Abstract

Objective: The objective of this study was to characterize the histopathological patterns of female breast lesions encountered at a secondary level of care centre in Al Hassa, Saudi Arabia, with special emphasis on multiplicity of benign lesions, their proliferative nature and level of risk for progression. Methods: In this retrospective, hospital record-based descriptive study, all histopathology records of patients attending King Fahd Hospital in Hofuf, Al Hassa between January 2001 and December 2007, were reviewed using a structured compilation form. Nine hundred and sixty nine histopathology reports were legible and included. Data regarding type of specimens, age, laterality of the lesions and the prominent cellular morphology were analyzed. Results: Out of 969 records reviewed, benign lesions accounted for 60.1%, followed by malignancy (21.4%) and inflammatory lesions (18.5%). Multiple benign lesions were found in 51.1% and more than two lesions in 21.1% of cases. Non-proliferative breast lesions with low risk were reported in 81.4%, intermediate risk lesion without hyperplastic atypia in 14.6%, while high risk lesions with atypia were only 4.0%. Infiltrating ductal carcinoma was the dominant lesion among the latter and 62.1% of cases were diagnosed before the age of 50 years. Conclusion: Benign breast lesion multiplicity is frequent among Saudi female patients; with or without atypia these lesions represent a sizable risk of potential progression to breast cancer. Meticulous follow up with frequent screening may be useful for prevention of cancer development and early intervention in affected patients.

Key Words: Histopathology - breast lesions - benign changes - proliferative lesions - Saudi Arabia

Asian Pacific J Cancer Prev, **10**, 1121-1126

Introduction

Studying disease patterns prepare the medical community and health administrators for the emerging and potential challenges (Cheidozi et al 2003). Globally, breast cancer ranks first among cancers affecting women and worldwide 1 in 10 women is affected by breast cancer during their lifetime (World Health Organization 2007). In Saudi Arabia, breast cancer is most frequent of malignancy, affecting about 14/100,000 Saudi females, and comprises 21.8% of all age and gender specific malignancies as it Saudi women (Cancer Incidence Report Saudi Arabia, 2001).

The pattern of benign tumors reported to be pre-malignant, their multiplicity and the increased risk of developing breast cancer associated with proliferative diseases of the breast are needed to be more elaborated in countries with high incidence of breast cancer (Bodin et al 1993; Worsham et al 2007). Benign breast disease in women encompasses a spectrum of histopathologic lesions. Of the many types of benign entities found in human breast, only a few have been shown to have clinically significant premalignant potential. The best characterized lesions include atypical ductal, lobular hyperplasia and lobular carcinoma in situ (Arpino et al 2005). Histopathological diagnosis of these lesions posed variable degrees of risk to develop cancer, ranging from two to ten fold compared to normal population (Cancer Incidence Report Saudi Arabia, 2001). It is estimated that proliferative breast diseases will turn into invasive lesions in the same breast in less than 10 % of cases over a median duration of 11 years of follow up (Dupont and Page, 1987).

Previous studies from Saudi Arabia have reported the pattern of encountered breast lesions in different areas of KSA with special emphasis on malignancy while lacking information regarding the prevalence of such pre-malignant lesions or the pattern of benign lesions multiplicity (Ibrahim, 1999; Altaf 2001; Jamal 2001; Cheidozi et al., 2003). Portraying of breast lesions among the Saudi females is important in this perspective as although breast cancer is reported to be the most frequent malignancy yet, complete characterization of benign and pre-malignant lesions encountered histopathologically is limited to few local reports (Altaf, 2004). Subsequently, the objective of this study was to characterize the histopathlogical patterns of female breast lesions encountered at secondary level of care in Al Hassa with special emphasis on multiplicity of benign lesions, their proliferative nature and level of risk for progression.

*[1]Family and Community Medicine Department, [2]Department of Surgery, College of Medicine-Al Hassa, King Faisal University, [3]King Fahd Hospital, Al Hofuf, Ministry of Health, Kingdom of Saudi Arabia *For Correspondence: dramin55@gmail.com*

Materials and Methods

General

King Fahd Hospital is located in Al Hassa Governorate, Eastern Saudi Arabia, 350 Km form Riyadh. The hospital provides a major portal to secondary level of care to about one million populations. A retrospective, hospital record-based descriptive study design was adopted to achieve the study's objective. All histopathology records and available histopathology slides from excisional biopsies and mastectomies of female patients attended at King Fahd Hospital from January 2001 to December 2007 were reviewed by pathology consultant using a structured compilation form to collect data regarding macroscopic, microscopic, dominant histopathological features, multiplicity of benign tumors, in addition to patients' data including age, laterality of lesions. Male breast biopsies, those without clear and confirmed diagnoses and those with normal findings were excluded (N=144). Nine hundred-sixty nine pathological reports were complete and eligible and hence included.

Based on criteria reported by Dupont and Page in 1985 (Dupont and Page 1985), the included benign lesions were divided into three risk categories: non-proliferative included eight diagnoses; simple apocrine metaplasia, cysts, fibrosis, periductal mastitis/duct ectasia, mastitis, squameous metaplasia, fibroadenoma and others (with no or low risk). Proliferative hyperplastic without atypia included eight diagnoses (intermediate risk): simple adenosis, sclerosing adenosis, apocrine adenosis without atypia, papilloma, radial scar and fibroadenoma associated with hyperplasia and or adenosis, while proliferative lesions with high risk included hyperplastic-lobular atypia associatd with fibroadenoma, simple, sclerosing adenosis, papilloma and radial scar, the pathology review form was designed to capture the prominent microscopic lesions in benign lesions.

The International classification of diseases for oncology (3rd edition) (International Classification of Diseases for Oncology; ICD-O-3 2000) was used to classified the reviewed malignant breast lesions.

Data management and analysis:

Data regarding type of specimens, age, laterality of the lesions and the prominent cellular morphology were analyzed using SPSS version 13 (SPSS Inc. Chicago, ILL.). Categorical data were expressed using proportions and percentage, while continuous variables were expressed using median, interquartile range, mean and standard deviation. Chi-square for trend and t-test were applied whenever appropriate.

Ethical considerations:

Data confidentiality was maintained all through the study. Permissions were obtained form King Fahd Hospital Administration as well as our institution.

Table 1. Final Pathological Diagnoses of the Encountered Benign and Inflammatory Female Breast Lesions (total=969) Distributed in Relation to Side Affected and Age in Years

Final pathological diagnoses	Right No. (%)	Left No. (%)	Bilateral No. (%)	Total No. (%)	Median	Mean ±SD
Benign lesions (total):	237 (43.0)	256 (46.6)	41 (7.4)	583 (60.2)*	27	28.4± 9.3
Fibroadenoma	49 (39.8)	64 (52.0)	7 (5.7)	123 (21.1)	22	21.9± 6.4
Fibroadenoma + fibrocystic disease	16 (72.7)	8 (36.4)	-	22 (3.8)	28.5	27.8± 7.7
Fibroadenoma + adenosis	18 (39.1)	20 (43.5)	8 (17.4)	46 (7.9)	26.5	26.8± 4.7
Fibroadenmoa + adenosis + IDH*	9 (31.0)	13 (44.8)	7 (24.1)	29 (5.0)	22	24.8± 7.1
Fibroadenoma + chronic mastitis	27 (47.4)	30 (52.6)	-	57 (9.8)	22.5	21.9± 6.9
Fibrocystic disease	9 (34.6)	15 (57.7)	3 (11.5)	26 (4.5)	32.5	33.8± 8.1
Fibrocystic disease+ IDH+ adenosis	23 (53.5)	16 (37.2)	4 (9.3)	43 (7.4)	39	39.2± 5.7
Duct ectasia + fibroadenoma	8 (42.1)	8 (42.1)	1 (5.3)	19 (3.2)	35	36.5± 7.7
Duct ectasia+ IDH+ atypia	19 (63.3)	11(36.7)	-	30 (5.1)	32..0	34.3± 9.3
Duct ectasia + fibrocystic disease	15 (65.2)	8 (34.0)	-	23 (3.9)	35	34.9± 5.9
Lactional adenoma	14 (42.4)	19 (57.6)	-	33 (5.7)	25	25.6± 3.9
Lactional changes + fibroadenoma	3 (33.3)	9 (66.7)	-	12 (2.1)	21.5	22.5± 3.9
Lobular hyperplasia + adenosis	1 (10.0)	9 (90.0)	-	10 (1.7)	24	25.5± 3.1
Adenosis + duct ectasia	9 (31.0)	15 (51.7)	5 (17.3)	29 (5.0)	20	22.6± 6.9
Adenosis +IDH+ atypia	1 (8.3)	11 (91.7)	-	12 (2.1)	35.5	35.5± 6.4
Fibroadenomatosis/apocrine metaplasia	2 (14.3)	4 (28.6)	8 (57.1)	14 (2.4)	46	46.3± 4.7
Other lesions !	22 (48.9)	19 (42.2)	4 (8.9)	45 (7.7)	36	32.8±11.7
Inflammatory lesions (total):	89 (54.6)	64 (39.4)	-	179 (18.5)**	30	31.4± 9.7
Acute breast Abscesses	17 (39.5)	25 (58.1)	-	43 (24.0)	27	29.0± 9.6
Chronic breast Abscesses	13 (56.5)	9 (39.1)	-	23 (12.8)	35	36.0±12.6
Chronic mastitis	38 (70.4)	10 (18.5)	-	54 (30.2)	25	28.6±11.7
Granulomatous mastitis	19 (65.5)	10 (34.5)	-	29 (16.2)	35	33.4± 5.1
Acute mastitis	2 (33.3)	4 (66.7)	-	6 (3.4)	21	23.4± 5.8
Fat necrosis and suppurative infection	1 (10.0)	7 (7.0)	-	10 (5.6)	26	25.0± 6.6
Foreign body inflammatory reaction	1 (25.0)	3 (75.0)	-	4 (2.2)	36	33.0± 6.3

* Those with unspecified site of lesion were 27 cases (17 benign: 8 cases with duct ectasia, 6 cases with fibrocyctic and 3 with fibroadenoma). ** 10 inflammatory lesions with unspecified site included 2 granulomatous mastitis, 6 cases with abscess wall, 2 cases with foreign body reaction). IDH = Intra-ducatal hyperplasia. ! Other lesions include cases with: sebaceous cysts (2 cases), galactocele (6), mammary cysts (3), juvenile papillomatosis (2), epidermoid cyst (3), keloid (2), fibrosis (9) accessory breast (6) and arthropod bite lesions (5), lipoma (3), fibrolipoma (2), soft fibroma (2)

Table 2. Non-proliferative Pathological (low risk) Lesions Encountered According to their Prominent Microscopic Features in Relation to Age Groups

Lesions	<20 No. (%)	20- <30 No. (%)	30-<40 No. (%)	40-<50 No. (%)	≥50 No. (%)	Total No. (%)
Fibroadenoma	88 (67.1)	127 (38.8)	70 (28.1)	26 (19.7)	-	311 (35.6)
Duct ectasia	-	29 (8.9)	41 (16.5)	24 (18.2)	15 (44.1)	109 (12.5)
Fibrocystic disease	3 (2.3)	49 (15.2)	29 (11.6)	39 (29.5)	-	120 (13.7)
Mastitis (chronic/granulomatous)	10 (7.6)	43 (13.1)	42 (16.9)	31 (23.5)	16 (47.1)	142 (16.3)
Fibrosis	-	6 (1.8)	3 (1.2)	-	-	9 (1.0)
Lactational adenoma	-	12 (3.7)	21 (8.4)	-	-	33 (3.8)
Chronic abscesses	3 (2.3)	9 (2.8)	14 (5.6)	3 (2.3)	-	29 (3.3)
Simple apocrine metaplasia	4 (3.1)	7 (2.1)	3 (1.2)	-	-	14 (1.6)
Others*	23 (17.6)	45 (13.8)	26 (10.4)	9 (6.8)	3 (8.8)	106 (12.1)
Total	131 (15.0)	327 (37.5)	249 (28.5)	132 (15.1)	34 (3.9)	873 (100)

Pathological lesions are not mutually exclusive, several benign lesions may be found in a single specimen. *Other lesions included: lipoma, fibrolipoadenoma, soft fibroma, galactocele, mammary cysts, juvenile papillomatosis, acute mastitis, lactational changes with fibroadenoma, epidermoid cyst, fat necrosis, keloid, accessory breast, acute breast abscesses and arthropod bite lesions.

Results

Type of tissue reviewed:

Excised breast lump in 331 (34.2%) cases, excisional biopsies in 221 (22.8%), breast tissue, axillary tissue and lymph nodes in 179(18.5), mastectomies in 56(5.8), excised abscess wall in 79(8.2%), breast tissue including skin and nipple 38(3.9%), and necrotic and suppurative breast tissues in 65(6.7%).

Final pathological diagnoses encountered:

Table 1 demonstrates the final pathological diagnoses reported for cases with benign and inflammatory female breast lesions. Out of a total 969 records included, benign lesions were diagnosed in 583 (60.2%); in 298 (51.1%) of these benign lesion multiple benign lesions were reported, 175 (30.0%) with two hsitopathological distinct lesions and 123 (21.1%) with more than two benign histopathological lesions. Fibroadenoma was the most commonly encountered lesions (solely diagnosed in 21.6% of all benign lesions and with other benign lesions in 31.7%), fibrocystic diseases (22.1%). All cases with duct ectasia were not diagnosed solely but in association with other benign lesions. Benign lesions were more on left breast but without statistical significance (P=0.22), bilateral lesions were found in 7.4% of the reviewed records. The median, mean and standard deviation of age in years were given for each group of benign lesions encountered (Table 1). Fibroadenoma occurred at relatively younger age compared to duct ectasia and fibrocystic lesions, those with two benign lesion had a median age of 26.9 (mean ±SD of 30.3±6.1 years), while those with more than two lesion had a median of 29.5 (32.0±7.6) (P=0.033). Inflammatory breast lesions were found in 179 (18.5%) of cases, more on the right side (54.6% vs. 39.4% on the left side) with a median age of 30.0 years (31.4±9.7). Malignant lesions were recoded in another 207 (21.4%) of the reviewed records.

Benign breast lesions and levels of risk:

Tables 2 and 3 demonstrate the distribution of benign breast lesions in relation to the predominant microscopic features and classified into three levels of risk categories among the different age groups. Non-proliferative lesions (low risk) were diagnosed in 873/1072 cases (81.4%)

Table 3. Proliferative Lesions with Intermediate and High Risk Levels Encountered in Relation to Age

Pathological lesions Age groups (years)	< 20 No. (%)	20-< 30 No. (%)	30-< 40 No. (%)	40-< 50 No. (%)	≥ 50 No. (%)	Total No. (%)
Proliferative without atypia: "Intermediate risk"						
Ductal hyperplasia + fibroadenoma	0	13	15	11	7	46 (15.9)
Ductal hyperplasia+simple adenosis	12	26	23	12	0	73 (40.1)
Ductal hyperplasia+sclerosing adenosis	8	4	3	6	0	21 (13.3)
Ductal hyperplasia+papilloma	0	0	2	4	-	6 (3.8)
Lobular hyperplasia+adenosis	0	4	4	2	0	10 (2.5)
Total (% of proliferative lesions without atypia)	20 (12.8)	47(30.1)	47(30.1)	35(22.4)	7 (4.2)	156(78.4)
Proliferative with atypia: "High risk" (includes lobular*-ductal hyperplasia +):						
Simple adenosis associated	0	1	6	4	2	13 (30.2)
Sclerosing adenosis associated	0	0	2	2	0	4 (9.3)
Apocrine adenosis associated	2	2	0	2	0	6 (14.0)
Fibroadenoma associated	0	6	4	2	0	12 (27.9
Papilloma associated	0	2	2	0	0	4 (9.3)
Radial scar associated	0	0	0	2	2	4 (9.3)
Total (% of proliferative lesions with atypia).	2 (4.7)	11 (25.6)	14 (32.6)	12 (27.9)	4 (9.3)	43 (21.6)
Total (age based %)	22 (11.1)	58 (29.1)	61 (30.7)	47 (23.6)	11 (5.5)	199 (100)

Table 4. Pathological Diagnoses of Malignant Breast Lesions Distributed in Relation to Side Affected and Age

Final pathological diagnoses	Right No. (%)	Left No. (%)	Total No. (%)	Age in years Median	Mean ±SD
Infiltrating ductal carcinoma	64 (39.3)	99 (60.7)	163 (78.7)	45	45.7±9.5
Lobular carcinoma	14 (87.5)	2 (12.5)	16 (7.7)	35	37.4±3.2
Lobular and ductal carcinoma	6 (100)	-	6 (2.9)	44	43.0±3.0
Medullary carcinoma	-	6 (100)	6 (2.9)	38	38.2±1.4
Tubular carcinoma	-	3 (100)	3 (1.4)	35	35.0±3.0
Phylloides tumour	-	3 (100)	3 (1.4)	40	40.0±2.0
Ductal Carcinoma in situ	3 (75.0)	1 (25.0)	4 (1.9)	31	32.8±8.6
Paget's disease of the nipple	2 (100)	-	2 (1.0)	47	45.9±10.3
Metastatic carcinoma	1 (25.0)	3 (75.0)	4 (1.9)	27	28.9±12.7
Total	90 (43.4)	117 (56.5)	207 (100)	42	44.5±8.7

primarily included fibroadenoma, duct ectasia, fibrocystic diseases, chronic mastitis, lactional adenoma and other lesions. Most non-proliferative lesions (37.5%) were clustered in age groups of 20 to < 40 years of age but without significant relation to age (Chi square for trend, P=0.61). Proliferative lesions without atypia (intermediate risk) were encountered in 14.6% (156/1072), these lesions were common among age groups of 20- < 40 years (P=0.093). These lesions included ductal and lobular hyperplasia without atypia associated with fibroadenoma, simple adenosis, and papilloma and sclerosing adenosis. Proliferative benign lesions with atypia (high risk) were encountered in 43 cases (4.0%). These lesions included ductal and/or lobular hyperplasia with atypia associated with simple adenosis, sclerosing adenosis, apocrine adenosis, fibroadenoma, papilloma and radial scar. These lesions were found in all age groups with special predilection among those in the age range of 20 to < 50 years (Table 3).

Malignant breast lesions:

Infiltrating ductal carcinoma represented 78.7% of cases, more on the left side, with a median age of 45.0 years (mean of 45.7±8.7), followed by lobular carcinoma in 7.7% of cases, more on the right side with a median age of 35.0 years (37.4±3.2). Carcinoma in situ was only reported in 1.9% of cases with a relatively younger age compared to other malignant lesions (median =31.0 years) (Table 4).

Out of 207 malignant cases, 21.8% were in the age group of <40 years, while 62.0 % of were diagnosed before the age of 50. All malignant lesions reported in the age group < 40 years were infiltrating duct carcinoma. Only 1.9% of malignant lesions were in situ, 10.1% (21/179) were in grade I, grade II/III (143/179) represented 69.1 % of cases with secondary regional lymph nodes metastasis. Encountered infiltrating duct carcinomas had a median of 3.5 cm (interquartile range 'QR' of 3.1), lobular with a median size of 3 cm (IQR=2.7 cm), while those presented with both lesions showed higher size (median of 4.5 cm, IQR=1.5).

Discussion

Benign breast diseases have been reported to comprise 68.0% to 91.4% of breast lesions histologically diagnosed in previous reports from different regions of Saudi Arabia while inflammatory lesions were in the range of 11.0% to 42.5% (Ibrahim 1999; Jamal, 2001; Altaf, 2001; Cheidozi et al., 2003), results that are consistent with current findings as our study revealed that benign lesions constituted 60.2% of all lesions, followed by malignant (21.3%) and inflammatory lesions (18.5%). In a previous study from the Eastern Province of Saudi Arabia (Ibrahim 1999), inflammatory breast lesions constituted similar figure and this low level may explained on the ground that most of breast abscesses were usually drained without biopsies. Overall, our results are in concordance with other reports regarding the distribution of benign lesions, for example fibroadenoma constituted the most commonly encountered lesion representing 25.0% in Jeddah and 22.0% in Abha region (Gupta and Al-Misiri, 1998).

No previous study reported the state of multiplicity of benign lesions among Saudi female patients. Amongst the benign lesions encountered in our study; 51.1% with evidence of multiplicity and in 30.0% there were two distinct lesions while in 21.1% more than two benign lesions were diagnosed. Furthermore, those with multiple benign lesions were significantly older compared to those with single breast benign tumor.

Worsham et al (2007) found that among their cohort of constituted of 4,465 women among those developed benign breast lesions (N=2,302) 70.0% of them had more than one benign lesion and 36.0% had multiple benign lesions. Also, they found that multiplicity of benign lesion was a significant predictor of breast cancer at univariate analysis. Information with regard to issue of lesion multiplicity is very limited. Wang et al (2004) reported that 38.0% of women with low grade benign breast disease including non-proliferative and proliferative without atypia contained multiple lesions. Women with multiple non-proliferative or proliferative lesions with or without atypia are at increased risk for breast cancer even after adjustment of age (Worsham et al., 2007).

Our study revealed that non-proliferative lesions (low risk) were encountered in 81.4% of lesions, proliferative lesions without atypia (intermediate risk) constituted 14.6% and those with high risk including ductal/lobular atypia were found in 4.0%. High risk lesions were found in all age groups included. One study reported the pattern of benign and pre-invasive lesions in Saudi Arabia (Altaf 2004) had found that benign non-proliferative lesions constituted 85.3%, proliferative lesions in 9.2% and hyperplasia with atypia recorded in 0.5%, close finding

was found in Yemen (Al-Thobhani et al 2006) where hypeplastic atypia was found in 1% of examined breast lesions; the reason for this difference could be explained on the basis that we have included cases with atypical epithelial hyperplasia even when they are associated with adenosis, fibroadenoma and radial scar; as has been done in some recent studies (Worsham et at 2007; Worsham et al 2007).

Nevertheless, our results are much higher than those reported other Saudi and Yemeni studies but close to those reported from a recent cohort study employing similar categorization of benign breast lesions (Worsham et al., 2007) where among the 4,465 women included; 51.6% have had risk 1 (low) level with non-prolierative lesions, 16.5% had risk 2 (intermediate) level with proliferative lesions without atypia and 3.6% had risk level 3 (high) of proliferative lesions with atypia. It was also found that among the previous cohort during an average follow up period of 10.3 years, 4.5% of these women developed breast cancer. Women with multiple nonproliferative lesions showed an increased relative risk (RR=1.8) for cancer development compared to those with only one non-proliferative lesion. Proliferative lesions (single or multiple) in the same biopsy with or without atypia were significant risk factor for breast cancer while women with single proliferative lesion without atypical hyperplasia conferred a RR of 2.06 for breast cancer, those with multiple proliferative lesions without atypia had a 2.87-fold risk, the presence of atypia as the sole lesion had the highest risk (RR=6.26) (Bodin et al., 1993; Worsham et al., 2007) .

The risk difference for progression to malignancy was not significant at 5 years follow up between women with nonproliferative lesions and those with proliferative lesions without atypia, but significantly increased for both women with proliferative lesions with or without atypia (Dupont and Page 1987; Worsham et al., 2007) and the risk was directly related to the degree of atypia (Krieger and Hiatt., 1992; Jacobs et al., 1998; Worsham et al., 2007). Cancer risk in the presence of atypical hyperplasia was reported to imply a risk of 4.4, mounted to 8-10 folds in the patients with positive family history of breast cancer (Worsham et al 2007; Worsham et al 2007). Predominant pathological features and multiplicity of benign lesions may thus provide an indicator for those patients who need further follow-up and specialist evaluation of their biopsy specimens so that the significant proliferative lesions or the atypical proliferative lesions are not missed.

Various studies on pathological lesions of female breast from Saudi Arabia had emphasized the pattern and features of breast cancer (Gupta and Al-Misiri, 1998; Ibrahim 1999; Altaf, 2001; Jamal, 2001; Cheidozi et al 2003), the reported percentage of cancer have ranged from 5.0 to 32.5% in patients' breast biopsies with mean age ranged from 40-49 years. Report of Saudi National Cancer Registry (Cancer Incidence Report, Saudi Arabia 2001) revealed that breast cancers that develop before 40 years age comprised 26.4% of all female breast cancers compared to 6.5% in United States (Morgan et al., 1998). Furthermore, breast cancer affecting those before the age of 40 years tends to be aggressive and present with higher stage in comparison to older age group; in our study such cases comprised 21.1% of total cancer. Mutations in BRCA1 or BRCA2 genes are likely to occur among 15-30% of western breast cancer patients younger than 35 years (Morgan et al., 1998). The genetic profiles have been found to be a significant predictor of the disease development and outcome in the younger patients and thus it is strongly indicated in the workup of the younger Saudi patients.

In conclusion, benign breast lesion multiplicity is highamong Saudi female patients; proliferative lesions with or without atypia represent a sizable risk of potential progression to breast cancer. Meticulous follow up with frequent screening may be useful for prevention of cancer development and early intervention in these patients. Infiltrating ducatl carcinoma were the predominant malignant lesions encountered with early age of affection and late clinical presentation.

References

Altaf FJ (2001). Pattern of breast disease at King Khaled National Guard Hospital experience. *Ann Saudi Med*, **21**, 3-4.

Altaf FJ, Abdullah LS, Jamal AA (2004). Frequency of benign and preinvasive breast diseases. *Saudi Medical J*, **25**, 493-7.

Arpino G, Laucirica R, Elledge RM (2005). Premalignant and in situ breast disease: biology and clinical implications. *Ann Intern Med*, **143**, 446-57.

Al-Thobhani AK, Raja'a YA, Noman TA, Al-Romaimah MA (2006). Profile of breast lesions among women with positive biopsy findings in Yemen. *Eastern Mediter Health J*, **12**, 5.

Bodin CA, Perzin KH, Lattes R, Hoffman P, Abernathy TG (1993). Prognostic significance of benign prolifertaive breast disease. *Cancer*, **71**, 3896-907.

Cheidozi L, El Hag IA, Kollur SM (2003). Breast diseases in the Northern region of Saudi Arabia. *Saudi Medical J*, **24**, 623-7.

Dupont WD, Page DL (1985). Risk factors for breast cancer in women with proliferative breast disease. *N Engl J Med*, **312**, 146-51.

Dupont WD, Page DL (1987). Breast cancer risk associated with proliferative disease, age at first birth and family history of breast cancer. *Am J Epidemiol*, 1225??, 769-78.

Gupta RK, Al-Misiri S (1998). Profile of breast pathology at Asir Central Hospital - Review of 312 breast cases. *Saudi Med J*, **19**, 190-217.

Ibrahim EM (1999). Pattern and prognosis of breast cancer: data from the Eastern province of Saudi Arabia. *Saudi Med J*, **12**, 227-31.

International Classification of Diseases for Oncology (ICD-O-3) (2000), 3rd ed. Geneva, World Health Organization (WHO), Geneva, 2000.

Jamal A (2001). Pattern of breast diseases in a teaching hospital in Jeddah, Saudi Arabia. *Saudi Med J*, **22**, 110-3.

Jacobs TW, Byrne C, Colditz G, Connolly JL, Schnitt SJ (1999). Radical scars in benign breast biopsy specimens and the risk of breast cancer. *N Eng J Med*, **340**, 430-6.

Krieger N, Hiatt RA (1992). Risk of breast cancer after benign breast disease: variation by histologic type, degree of atypia, age at biopsy and length of follow up. *Am J Epidemiol*, **135**, 619-31.

Ministry of Health (2001). Cancer Incidence Report, Saudi Arabia, 1994-1996, Riyadh No. 2632/13.

Morgan JW, Gladson JE, Rau KS (1998). Position paper of the American Council on Science and Health on risk factors for breast cancer: established, speculated, and unsupported. *Breast J*, **4**, 177-97.

Wang J, Costantino JP, Tan-Chiu E, et al (2004). Low category benign breast disease and the risk of invasive breast cancer. *J Natl Cancer Inst*, **96**, 616-20.

World Health Organization (2007). The World Health Organization's Fight Against Cancer: Strategies that Prevent, Cure and Care. NLM Classification QZ 200, WHO 2007:9-27 Geneva, Switzerland. www.who.int/cancer/en

Worsham MJ, Raju U, Kapke A, Cheng J, Wolman SR (2007). Multiplicity of benign breast lesions is a risk factor for progression to breast cancer. *Clin Cancer Res*, **13**, 5474-9.

Worsham MJ, Abrams J, Raju U et al (2007). Breast cancer incidence in a cohort of women with benign breast disease from a multiethnic, primary health care population. *Breast J*, **13**, 115-21.