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Positive Predictive Rate of Breast Imaging-Reporting and Data System (BI-RADS) Category 4 Lesions For Breast Cancer Taking Histopathology as Gold Standard

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ABSTRACT

Objective: To determine positive predictive rate of Breast imaging-reporting and data system (BI-RADS) category 4 and its sub-categories for breast cancer taking histopathology as gold standard.

Study Design: Cross sectional validation study.

Place and Duration of Study: Department of Radiology, Pakistan Institute of Medical Sciences, Islamabad Pakistan, from Sep to Nov 2020.

Methodology: 60 female patients who were diagnosed as Breast imaging-reporting and data system (BI-RADS) category 4 lesions on mammography were included in the study and afterwards followed for biopsy report. Data was collected and analyzed using SPSSv25.

Results: Patient's mean age was 50.6±9.7yrs. Among sixty patients with BIRADS 4, 13(21.7%) had BIRADS 4A, 22(36.7%) had BIRADS 4B and 25(41.7%) had 4C. Positive predictive value for BIRADS 4 was 68.33%, 4A was 15.3%, 4B was 72.7% and for 4C was 92%. Sensitivity & Specificity of BIRADS 4A being benign and BIRADS 4B, & 4C being malignant is 91.49% and 69.23% respectively. Overall, diagnostic accuracy of BIRADS 4B & 4C classification was found to be 83.33%.

Conclusion: Sub-categorization of Breast imaging-reporting and data system (BI-RADS) category 4 is not routinely practiced, however results of current study conclude that it helps to stratify the associated risk of malignancy and update the level of concern to referring physician and pathologist.

Keywords: Breast Cancer, Breast Imaging-Reporting and Data System (Bi-Rads), Diagnostic Accuracy, Mammography.

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INTRODUCTION

Breast cancer is the most commonly occurring malignancy among females and is one of the most common 10 causes of death. Around a million new cases are diagnosed each year.[1] Over all, it is the 2nd most prevalent cancer after lung carcinoma.[2] Among Asian countries, Pakistan has highest incidence of breast cancer with every 9th Pakistani female having chance of getting it.[3] According to a research in Pakistan, almost 80% patients are diagnosed at late stage with metastatic disease which is associated with poor survival.[4] Factors responsible for late presentation include lack of awareness, financial problems and lack of screening programs.[5] Breast cancer is one of the few malignancies which can be diagnosed by screening in early stage. Screening mammography decreases mortality by 30% in women aged 40 years or older. Though screening mammography involves use of ionizing radiations, however, it is well documented that benefits from early screening far outweighs the risks. Annual screening mammography is recommended by American College of Radiology (ACR) starting at the age of 40 years for every female while earlier screening at age of 30 years is recommended for high risk group.[6] Interpretation and reporting of mammograms is based on standardized system developed by ACR i.e. Breast imaging-reporting and data system (BI-RADS). According to BIRADS, the lesions are divided in seven categories from BIRADS 0 to BIRADS VI on the basis of imaging features such as breast composition, mass lesions, its margins, associated architectural distortion, asymmetries, calcifications and skin thickening (Table-I).

BIRADS is designed to standardize mammographic findings and communicate the associated likelihood of malignancy to referring clinicians so that further management can be done accordingly. Patients with BIRADS 4 have chances of malignancy ranging from 2 - 95%. Therefore, Fourth edition of BIRADS published in 2003 divides suspicious looking lesions falling in BIRAD 4 into

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further 3 subcategories with mild, intermediate and moderate concern for malignancy respectively. Histopathological verification is necessary for BIRADS 4 and its subcategories to evaluate the diagnostic accuracy. This sub-categorization helps radiologists to communicate the level of concern for malignancy as concluded by Lazarus *et al*.[7] The aim of current study was to determine the positive predictive value of BIRADS 4 lesions on mammography as compared to histopathology in our setup. Furthermore, positive predictive value of BIRADS-IV sub-categories was calculated and will help in developing guidelines of sub categorization of BIRADS 4 lesions in our population.

Table-I. Breast Imaging-Reporting and Data System (BI-RADS) Classification

S.#	Category	Risk of Malignancy
0	Additional imaging or examination is required	N/A
I	Negative	Essentially 0%
II	Benign	Essentially 0%
III	Probably benign	0 – 2%
IV	Suspicious	2% – 95%
V	Features typical for malignancy	>95%
VI	Biopsy proven cases	N/A

METHODOLOGY

This validation study was conducted in Federal Breast Cancer Screening Centre, Department of Radiology, Pakistan Institute of Medical Sciences, Islamabad. Study was conducted for a period of 3 months from September, 2020 to November, 2020. Approval was taken from ethical review committee vide letter no F.1 -1/2015/ERB/SZAMBU/630. Sample size was calculated by using sensitivity and specificity calculator keeping sensitivity of 100%, specificity of 93% and confidence interval of 95%.[8] Non-probability consecutive sampling technique was used. After taking informed consent, patients were recruited.

Inclsuion Criteria: female patients who were diagnosed as BIRADS-IV lesions on mammography were enrolled for study.

Exclusion Criteria: Patients already diagnosed with breast carcinoma or those having residual cancer after surgery were excluded. Pregnant females, males and those who were unwilling to undergo biopsy were also excluded from the study. Mammography performed with two basic projections i.e. craniocaudal & mediolateral oblique views taken. Additional true lateral, axillary and magnification views were taken if required. A radiologist with minimum experience of 5 yrs. in breast imaging did reporting and interpretations of mammograms. Lesions were evaluated on basis of size, morphology, boundary, and associated findings like skin thickening, architectural distortion, types of calcification, and abnormal axillary nodes. According to which final diagnosis was made & BIRADS classification and BIRADS 4 subdivision into 4A, 4B & 4C was given. Histopathology reports of patients were followed and mammographic data was compared with the biopsy report.

Collected data was analyzed through computer software SPSS v23.0. Quantitative variables like age presented as mean and standard deviation. Positive predictive value (prevalence) of malignant lesions was calculated for BIRAD 4 and its sub divisions by taking percentage. 2×2 contingency table was further used to calculate sensitivity, specificity, diagnostic accuracy of BIRADS 4B & 4C lesions, taking histopathology as gold standard. BIRADs 4A were taken benign in calculation of accuracy.

RESULTS

Mean age of the patients was 50.6±9.47. Among sixty patients with BIRADS 4, 13(21.7%) had BIRADS 4A, 22(36.7%) had BIRADS 4B and 25(41.7) had 4C. Positive predictive value for BIRADS 4 was 68.33%, 4A was 15.3%, 4B was 72.7% and for 4C was 92%.

Thirty-one (52.6%) had right sided lesions, all others had left sided lesions. Only one had bilateral mass. Majority (n=24, 40%) of the patients had mass in upper outer quadrant. Majority had indistinct (n=25, 41.7%) and spiculated margins (n=24, 40%), only 8 had lobulated margins. Mostly patients (n=36, 61%) did not have associated calcifications.

Table-II: BI-RADS 4 Sub-Categories versus Histopathology

	Histopathology		Total
	Benign	Malignant	
Birads			
BIRADS 4A	11(84.6%)	2(15.4%)	13
BIRADS 4B	6(27.27%)	16(72.7%)	22
BIRADS 4C	2(8%)	23(92%)	25

Thirty (50%) had architectural distortion, seven (11%) had skin thickening and twenty-one (35%) had enlarged lymph nodes. Among BIRADS 4C patients, majority (n=21, 84%) had spiculated margins and pleomorphic calcifications (n=14, 56%). Twenty-two (88%) had architectural distortion and 14(56%) had enlarged fatty lymph nodes. Among seven cases of

skin thickening, five belonged to BIRADS 4C group. Figure-2 shows the comparison of architectural distortion and spiculated margins with BIRADS categorization. Over all sensitivity & specificity of BIRADS 4 was 82.9% and 57.8% respectively. Overall diagnostic accuracy of BIRADS 4 was found to be 83.33%.

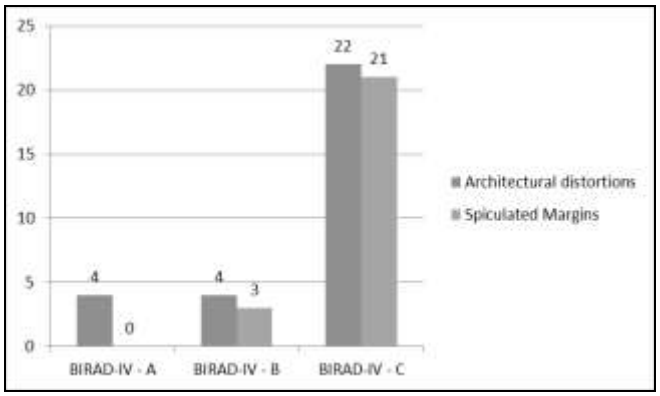

Figure: Comparison between Architectural Distortion, Spiculated Margins & BIRADS 4 Classification

Table-III: Comparison of BI-RADS Category 4 Vs Histopathology

	Histopathology		Total
	Yes	No	
Birads 4			
Yes	39(82.9%)	8(17.1%)	47
No	2(15.3%)	11(84.7%)	13

Table-IV: Diagnostic Parameters of BI-RADS Category 4

Diagnostic Parameters	Values
Sensitivity= True Positive/(True Positive +False Negative)	39/(39+8)* 100=82.9%
Specificity= True Negative /(True Negative +False Positive)	11/(11+8)* 100=57.89%
Positive Predictive Value= True Positive/(True Positive+ False Positive)	39/(39+8)* 100=82.9%
Negative Predictive Value= True Negative/(True Negative +False Negative)	11/(11+8)* 100=84.66%
Diagnostic Accuracy=(True Positive +True Negative)/All Patients	(39+11)/60=83.33%

DISCUSSION

Last few decades demonstrate a rising trend in prevalence of breast cancer in the developing countries associated with higher mortality.[9] Mammography has a vital role in timely diagnosis of breast cancer with sensitivity ranging between 85-95%.Women of all ages are predisposed to breast cancer but in contrast to western population, the peak age of incidence is lower in Asian females. In our study, mean age was 50.6±9.47 years with most of the patients presenting between the age of 40 – 50 years. Leong *et al.*, reported similar peak age group in Asian population.[10]

Upper outer quadrant was found to be the most common site for breast cancer. Andrew *et al.*, proposed that higher amount of breast tissue is the reason behind the higher rates of involvement of upper outer quadrant.[11] Spiculated/indistinct margins, architectural distortion and micro-calcifications are hallmarks for malignancy. In current study spiculated margins were found in 25 i.e. 42% of malignant lesions and indistinct margins were found in 24 i.e. 40% of malignant lesion. Madiha *et al.*, concluded that presence of micro-calcifications was strongly associated with invasive ductal carcinoma and multifocal breast cancer.[12] We found micro-calcifications in that 56% of the malignant lesions. Elverici *et al.*, also reported that features associated with malignant mass lesions were; irregular shape with PPV of 66%, speculated margin with PPV of 80% and non-parallel orientation with positive predictive value of 58.9%.[13] Our results were concordant with it.

Among 60 patients with BIRAD 4, 41 were proven to be malignant on histopathology with PPV of 68.33%. This is comparable to a Brazilian study done by Roveda, who evaluated positive predictive value of mammography in detection of non-palpable breast masses and reported it to be 63%.[14] In another study, Sarangan *et al.*, reported PPV of 56% for BIRADS 4 lesions.[15] Current study is in concordance with another local study by Isani *et al.*, who reported PPV of 68% for BIRADS 4 lesions.[16]

The suspicious lesions falling in BIRADS category 4 displays a wide range of breast cancer risk from 2 – 95%. Thus, ACR recommends subdivision into three categories, 4A having low suspicion of breast cancer, 4B mildly suspicious for malignancy and 4C with moderate suspicion for malignancy. Sub-categorization of BIRADS 4 is not routinely practiced by radiologists in our country; however, we found that it is helpful in predicting the outcome. Among subcategory 4A, 2 out of 13 patients had malignant lesions on histopathology i.e. 15%. In 4B, 16 out of 22 were malignant i.e. 72% and in 4C 23/25 were malignant i.e. 92%. In a study conducted by Anjum at Faisalabad, percentage of subcategories of BIRADS 4 were 20% 4A, 22% 4B and 55% 4C.[17] Elverici *et al.*, reported PPVs of 19% (4A), 41% (4B), and 74% (4C).[13]

Lazarus *et al*., also studied subcategories and noticed the PPV of 6%, 15% and 53% for BI-RADS 4A, B and C respectively.7 In another study conducted by Sanders and Ronald, PPV of BI-RADS 4A was 10%, 4B was 21% and 4C was 70%.[18] Contrary to other studies, current study had higher percentage of malignant lesions in 4B. It may be due to inter-observer variations in assigning the subdivisions of BIRADS 4.Current study showed sensitivity and specificity of 91% and 69% for BIRADS 4B & BIRADS 4C lesions with diagnostic accuracy of 83%. Renato *et al*., compared diagnostic accuracy of ultrasound, mammography and MRI for detection of malignant lesions and reported 72% diagnostic accuracy for mammography.[19]

CONCLUSION

We found PPV of 68.3% for BI-RADS category 4, 15.3% for 4A, 72.7% for 4B and 92% for 4C. Sub-categorization of BIRADS4 in not routinely practiced, however results of current study conclude that it helps to stratify the likelihood of malignancy and update the level of concern to referring physician and pathologist.

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Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

SBZ & ASM: Data acquisition, data analysis, critical review, approval of the final version to be published.

NM: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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