



ABSTRACT

Background : The aim of this work is to assess the role of breast sonography and ductography in the evaluation of different causes of nipple discharge.

Methods : The study will be carried out on twenty-five female patients referred to the Radiodiagnosis department at Alexandria Main University Hospital presenting with nipple discharge.

They were divided into two groups:

Group I include 10 patients (40%) with surgically significant nipple discharge who were the patients with unilateral, uniorificial surgically significant colour type nipple discharge .They were investigated by mammography, sonography, and ductography.

Group II include 15 patients (60%) with surgically insignificant nipple discharge. They were further subdivided into 9 patients (36%)

with unilateral multiorificial and 6 patients (24%) with bilateral nipple discharge. They were subjected to mammography ,sonography without ductography.

Results Nipple discharge is the release of fluid from the nipple. It is the third most common breast complaint for women seek medical attention, after lumps and breast pain. It is a symptomatic problem that causes many women both discomfort and anxiety.

Conclusion : The current study showed certain diagnostic sonographic features for patients of multiple papillomatosis was agreed with studies carried out

Key words : Breast, Ductography, Nipple

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Introduction

The aim of this work is to assess the role of breast sonography and ductography in the evaluation of different causes of nipple discharge.

A. Age of patients presenting with nipple discharge

The present study has shown that the mean age of patients presenting with nipple discharge was 46.28 years. The age range of the patients presenting with nipple discharge in this study agreed with many reports of similar literature who reported mean ages ranging between 43.5 and 49 years ^(6, 41-44). Our findings did not agree with other reports who reported mean ages ranging between 50 and 59 years ^(45, 46-48).

B. Type of nipple discharge and correlation to pathological results:

The present study included 11patients (44%) with bloody nipple discharge, which was the most common

type of discharge. Serosanguinous discharge constituted the second most common type and was presented by 20% of patients. Serous discharge was encountered in (16 %), watery discharge in (12%), milky discharge was encountered in two patients (8%).

This agreed with previous studies which reported similar results considering the type and incidence of nipple discharge, emphasizing that the most common type of discharge was the bloody discharge followed by other types of discharges. ^(45, 41-44, 49)

This fact could be explained on the grounds of referral of bloody discharge patients by the clinicians for further evaluation more often than other types of discharge. ⁽⁴⁴⁾ This was based on the results of the studies that stated that up to 25% of patients with bloody discharge had carcinoma of the breast as the etiology for bleeding per nipple; the fact that it is the most alarming type of discharge to the patients.

The study carried out by Yamamoto et al ⁽⁴⁶⁾ did not agree with the findings of the current study. They stated that the serous discharge was the most common type of discharge (92.3%) followed by bloody discharge in (7.7%).

On correlating types of nipple discharge to pathological data gathered on discharge cytology, fine needle aspiration cytology and biopsy with or without ultrasound guidance, the present study showed that (63%) of patients had papillary lesion(including benign papillomatosis and solitary papilloma) , (50%)of duct ectasia and (60%) of breast carcinoma (including both IDC and DCIS) were presented with bloody discharge. On the other hand FCDB presented with watery (50%), milky discharge (25%) and serosanguinous (25%), benign cyst presented with milky discharge.

Our findings confirmed that pathological nipple discharge is usually spontaneous, unilateral, and most often contains blood. We also stress that it is important for one to keep the risk of breast cancer in mind when assessing nipple discharge cases at the time of admission.

The most common cause of bloody discharge encountered in the present study was intraductal papilloma 63% followed by breast carcinoma 60%. Similar findings had been reported in studies of Simmons et al ⁽⁶⁾, Rissanen et al ⁽⁴⁵⁾, Hou et al ⁽³⁴⁾, Vargas et al ⁽⁴⁴⁾, and Dawes et al ⁽⁴⁹⁾, Goksel A ⁽⁵⁰⁾ who stated that most of patients presented by bloody discharge caused by papillary lesion. Also Chung et al ⁽⁴²⁾ reported that most common type of discharge encountered was the bloody discharge found in five

of the eight (63%) cases of benign tumors.

The present study showed that (50%) of patients of duct ectasia were presented with bloody discharge particularly in age range between (40-50),this agreed with study carried by Greenall et al ⁽⁵¹⁾ who reported that duct ectasia correlated to frank blood stained discharge particularly in the premenopausal and older age groups .

In spite of the finding of our study that supposed a reliable correlation between the types of nipple discharge and underlying etiological factors, Greenall et al ⁽⁵¹⁾ reported that in general, the type of discharge is not a reliable indicator of the type of lesion.

Breast density and mammographic finding:

In the current study, the density of the breast tissue in those patients with nipple discharge was assessed from the mammographic findings. The breast density was classified into four grades according to ACR Classification. ⁽⁵²⁾

Grade I: Atrophic (Fatty breast) type of breast parenchyma.

Grade II: Fibroglandular type of breast parenchyma.

Grade III: Hetrogenous dense type of breast parenchyma.

GradeVI: Dense breast.

The grade I and II constituted most common type of breast density parenchyma in our studied patients. This agreed with the study carried out by Wang et al ⁽⁵³⁾ who found that grade 1 and II was the commonest breast density in benign and malignant breast lesions correlated with nipple discharge.

In the study carried out by Simmons et al⁽⁶⁾, mammography had a poor positive predictive value (16.7%), indicating that it is not reliable in diagnosing the etiology of a woman's nipple discharge. They stated that the sensitivity of mammography for detecting malignant ductal pathology is 57% and nearly half of the women with underlying malignant pathology who underwent mammography, an accurate diagnosis of ductal pathology could not be made.

Methods:

In the present study, retroareolar fullness, opacity and macrocalcification were the most common abnormalities in mammogram (20% for each abnormalities) followed by Asymmetrical density of breast (16%). Other studies demonstrated that mammography showed abnormal findings only in 8% of patients presenting with nipple discharge. The main abnormal findings encountered on mammography were retroareolar fullness indicating dilated ducts and radio dense nodules and to a lesser extent microcalcification.^(54,55)

Sonomammographic features of lesions causing nipple discharge

The ductal dilation was the most common sonographic finding present in 17 patients (68%) out of 25 studied cases followed by multiple intraductal mass and fibrocystic breast changes present in five patients (20%) for each, this agreed with studies carried out by Mcsweeny et al⁽⁵⁶⁾ and Nani et al⁽⁵⁷⁾ who reported that the common sonomammographic feature was dilatation of the discharging ducts.

Significant debate was encountered regarding judgment of mammary duct caliber normality. Some literature reported <3mm caliber is a sign of dilation.^(40,58) Others reported 0.5-1mm caliber a sign of normal mammary duct caliber and considered dilated when the diameter exceeds 1mm.⁽⁵⁹⁾ Other report considered a 2mm caliber is a sign of normal duct diameter.⁽⁴⁵⁾ In the present study a duct diameter exceeding 2mm caliber was considered dilated.

The sonomammographic features of patients of **duct ectasia** in the present study was agreed with study carried by Mcsweeny et al⁽⁵⁶⁾, Nani et al⁽⁵⁷⁾ and Hari et al⁽⁶⁰⁾ who reported that the Ultrasound of the breast for patient with duct ectasia demonstrated dilated, anechoic, noncompressible tubular structures without any color flow consistent with dilated tortuous ducts. No intraductal mass was seen. Sonomammography was not able to detect the dilatation of the terminal ducts.

In the current study, the **single papilloma** were in agreement with study carried out by Ganesan et al⁽¹⁴⁾ who broadly classified papillomas into central and peripheral types. Central types are usually solitary and subareolar in location within a major duct, while the peripherally located papillomas tend to be multiple within the terminal duct lobular unit. The dilated duct with a papillary lesion may resemble a cyst with an intracystic solid component when there is ductal obstruction, this variant being termed as an intracystic papilloma. Other studies carried out by Cilotti et al⁽⁶¹⁾, Han et al⁽⁶²⁾ and Cilotti et al.⁽⁶³⁾ demonstrated almost similar sonomammographic features to our study and they reported that there are three basic patterns of intraductal papillary neoplasms are recognized on ultrasound ; intraductal mass with or without ductal dilatation, intracystic

mass and a predominantly solid pattern which totally filling the duct. A distinct vascular pedicle is identified within the central core of intraductal papilloma with branching vessels arborising within the mass which can be depicted by Doppler Ultrasound. Also the studies carried out by Rissanen et al⁽⁴⁵⁾, Bern-Serna et al⁽⁴⁰⁾ and Sardanelli et al⁽⁶⁴⁾ demonstrated almost similar sonomammographic features to our study.

The current study showed certain diagnostic sonographic features for patients of **multiple papillomatosis** was agreed with studies carried out by Ganesan et al⁽¹⁴⁾, Kersschot et al⁽⁶⁵⁾, Han et al⁽⁶²⁾ and Bern-Serna et al⁽⁴⁰⁾ who stated that multiple peripheral papillomas are located in the peripheral duct system within the terminal ductal lobular unit with segmental dilatation of the ducts. The ductal dilatation may vary in size from a minimally dilated duct to a large cystically dilated, obstructed duct. Similarly the intraductal soft tissue component may range in size from a very small lesion which may be impossible to image to a large mass completely filling the dilated duct. Colour flow studies are sensitive in identifying even very small Intraductal papillary neoplasms in view of its characteristic vascularity

In current study, the most evident sonomammographic features reported among patients diagnosed as **DCIS** were also reported in 2 previous studies carried out by Cabioglu et al⁽⁶⁶⁾ and Nakahara H⁽⁶⁷⁾ who reported duct dilatation, hypoechoic lesions or intracystic tumors within echogenic glandular tissue in 41% of malignant lesions. Almost similar sonomammographic features were reported by studies carried out by Stavros et al⁽⁶⁸⁾, Skaane P.⁽⁶⁷⁾ and Berg et al.⁽⁶⁹⁾

Takebe K.⁽⁷⁰⁾ classified the ultrasound findings in the 23 cases of DCIS into five groups. (1) Relatively

well-defined small masses were detected with major diameter was 3–10mm. The lesions were too small to evaluate the shape, internal echo, and DW ratio, etc. There was no attenuation in posterior echoes. (2) An irregular mottled pattern within a 10mm area (3) A cluster of ducts with a dilated ductal pattern (4) A poorly defined area with lower echoes than those in the surrounding mammary gland (5) Typical ultrasonographic findings for breast cancer, that is, an irregular mass invading adipose tissue.

In the present study, three patients of **IDC** had the following sonomammographic features; dilatation of the discharging ducts, hypoechogenic masses casting acoustic shadows encountered either within the ducts or extending beyond the ductal walls to the surrounding parenchyma of the breast. The duct wall intactness could not be assessed in 2 out of 3 patients in basis of sonographic assessment. In all of the patients, masses were noted deep within the breast parenchyma. Microcalcification could be detected by US in one case which was previously noted by mammogram.

The finding of the present study still does not consider US as efficient as a mammography in evaluation of breast microcalcification as a primary modality of investigation. The only case identified by US was based on previous evaluation by mammography. This is agreed with study carried out by Kang et al⁽⁷¹⁾ and Moon WK⁽²⁷⁾, who reported the low capability to visualize microcalcifications remains a major limitation of sonography for diagnosing intraductal carcinoma. In their study, sonography could initially detect only 58% of mammographically detected

calcifications without knowledge of the mammographic findings. However, when the scans were performed again with mammographic knowledge of the presence of areas of microcalcifications, they were able to detect calcifications in 81% of cases. Accordingly, with no knowledge of mammographic findings, some microcalcifications or small lesions could be missed by sonography.

The studies carried out by Ohtake et al⁽⁷²⁾ and Kang et al⁽⁷¹⁾ reported that the sonographic findings showed significant differences between pure IDC and IDC with an intraductal component included the lesion boundary, duct dilatation, calcifications and vascularity. Pure IDC showed an abrupt interface and increased vascularity in or immediately adjacent to lesions more frequently, whereas IDC with an intraductal component showed an echogenic halo, duct dilatation, calcifications and increased vascularity in surrounding tissue more frequently. Satellite lesions on sonography were considered suspicious for an intra-ductal component. Other similar Sonomammographic features for patients of IDC were supported by many studies carried out by Rissanen et al⁽⁴⁵⁾, Stavros et al⁽⁶⁸⁾, Nakahara H⁽⁷³⁾, Kamio et al⁽⁷⁴⁾ and Ohuchi et al.⁽⁷⁵⁾

In the current study, all 3 patients with **FCDB** features were in agreement with studies carried by Feig S (1989)⁽⁷⁶⁾, Bassett et al (1991)⁽⁵⁴⁾, and Stephen et al (2002).⁽⁷⁷⁾

For one **normal patient** who was diagnosed sonographically as true negative showed normal breast tissue

parenchyma and no abnormalities could be detected within the ductal system.

Detectability of sonomammography:

Almost similar sonomammographic detectability regarding duct ectasia and FCBD was supported by Nani et al⁽⁵⁷⁾ and Mezi et al⁽⁷⁸⁾ who reported that the pathological diagnosis was benign including duct ectasia and FCBD in (90%). Feig A. S⁽⁷⁶⁾ and showed that the accuracy of sonomammography in the detection of FCDB was 100%.

Unlike some previous studies, Rissanen et al⁽⁴⁵⁾ stated that for the malignant causes of nipple discharge, the yield of sonography was lower (20%), because only an echogenic lesion within a dilated duct was considered a positive sonographic finding.

Skaane P. (1999)⁽⁶⁷⁾ stated that sonomammography was able to identify 57.9% of the non-palpable malignant neoplasms and the most carcinomas missed by ultrasonography were DCIS, which was in agreement with the present study.

The study was carried by kim et al⁽⁷⁹⁾ reported that the detectability for a diagnosis of breast carcinoma by US was 94.4% which was almost similar in their results to our results. Chung et al⁽⁴²⁾ study reported that as a result of recent advancements of US equipment, the parts of the ductal system more than 0.5 mm in diameter can be clearly visualized by US and thus the detectability of sonomammography to lesions had been increased.

While the 2 published reports carried out by Dillon MF⁽⁸⁰⁾ and Vargas HI⁽⁴⁴⁾ in which most of the patients had no clinical or

mammographic abnormalities, the correct cause of nipple discharge was identified with sonography in only 10% to 26% of the cases, and all the malignant lesions remained undetected. One reason for the inferior sensitivity of sonography for malignancy might be that carcinomas originate in the terminal ductal lobular unit, where as papillomas causing nipple discharge are usually located more centrally.

The detectability of sonomammography for intraductal papillary lesions in the current study was agreed with the results reported by Sardanelli et al⁽⁶⁴⁾ and Han et al⁽⁶²⁾ who reported US detectability (50%) for both single and multiple papillomas of the duct.

A study was launched by Cilotti et al⁽⁶³⁾ on the role of sonomammography in studying 12 patients of solitary intraductal papillomas. It was able to correctly diagnose eight patients (a detectability of 66.6%), which were verified by cytology to have solitary intraductal papillomas as the cause of nipple discharge and this does not agree with our result.

In the current study, sonographic diagnosis coincided with the pathological diagnosis in 19 out of 25 patients, 18 of them were considered true positive and one was true negative. The study of Cilotti et al⁽⁸¹⁾ agreed with the present study which reported overall sensitivity of sonomammography to the detection of lesions causing nipple discharge was 84%. While not agreed with study carried out by Vargas et al⁽⁴⁴⁾ who found the overall sensitivity of sonomammography was 26% and the specificity was 97%.

Ductographic diagnosis of patients of nipple :discharge

This agreed with studies carried out by Bern-Serna et al⁽⁴⁰⁾ and Peters et al⁽⁸²⁾ who reported that there are numerous characteristic pathological findings in galactography, the most common finding is papilloma followed by ectatic ducts and a combination of both. The least common finding is carcinoma of the breast. Other studies reported that multiple or solitary papillomas are the most common cause of nipple discharge and the most frequent finding was the presence of one or multiple intraductal filling defects which was found in 60% of patients.^(43, 49, 64, 85-87)

In current study the findings observed in the galactogram using the GICS categories were GICS 0: 2 cases(16.6%), GICS 1: 1 case (8%), GICS 2: 3 cases(25%), GICS 3: 1 case (8%), GICS 4: 4 cases(33.3%), GICS 5: 1 case(8%) which was almost similar to the result of study carried Bern-Serna et al (2010)⁽⁴⁰⁾ who found GICS category 2:16 cases (25.8%); GICS category 3: 19 cases (30.6%); GICS category 4:16 cases (25.8%); and GICS category 5: 11 cases (17.7%). This study reported that the GICS classification was developed to standardize the results of galactography, reduce confusion in interpreting galactograms and facilitate the proper management of patients with pathologic nipple discharge. Galactography is a useful procedure for differentiating benign from malignant lesions, establishing the risk of suspected malignancy, and allowing decisions to be made to optimize early detection of breast cancer⁽⁴⁰⁾.

In our study, the ductographic diagnosis coincided with the pathologic diagnosis of 90% of surgically significant patient, (80%) of them. This agreed with studies carried out by Hou et al⁽⁴³⁾, in which the sensitivity was found to be 86.4%, Cilotti et al⁽⁸¹⁾ found it to be 96%. While not agreed with Ambrogetti et al⁽⁸⁹⁾ who found the sensitivity of ductography was equal to 59.6% The specificity of ductography was found to be equal to 100% in present study which agreed with studies carried out by Simmonset al⁽⁶⁾ and Hou et al⁽⁴³⁾ who reported that ductography had a high (96.6%) specificity.

Peters et al ⁽⁸²⁾ stated that the ductography is the only diagnostic procedure that is able to depict and precisely localize small intraductal pathologic processes and normal galactogram is a specific and sensitive indicator of absence of localized disease. Hou et al ⁽⁴³⁾ and Van Zee ⁽⁸⁴⁾ reported that the galactography is a contrast examination of the discharging ducts that is performed to identify and localized intraductal lesions to allow for conservative excision and without galactography, the surgeons have relied on either mastectomy or excision of the major duct system responsible for the discharge.

The percentage of patients was diagnosed by ductography as DCIS differs among many studies. In the present study, it was (20%). This agreed with Hou et al ⁽⁴³⁾ and who reported that ductography could be detect 15% of carcinoma .On contrary the study carried out by Baker (1994) ⁽⁸³⁾ detected only 3.3% for DCIS that does not agree with current study.

Ductographic features of lesions causing nipple discharge:

Results

In our study an important feature of **single papilloma** was the presence of a single filling defect, oval in shape located at the main ducts. The surface of the filling defect was often irregular or fronded.

These features were supported by studies who reported that the ductography helps define the sites, number, and extent of presumed papillomas. If it is not performed, they may remain invisible. In addition to that papillomas secrete fluid profusely, and the duct downstream from the papilloma

(that is, toward the nipple from the papilloma) is often dilated. Paradoxically, proximal to the papilloma, the normal duct is usually not dilated, In addition to filling defects and downstream ductal dilatation, may also cause ductal obstruction or an "amputated duct" or even alteration in the normally smooth duct wall. ^(12, 13, 40, 55, 87)

In current study, the patients of **multiple papillomatosis** showed moderate to marked dilation of main and the branching ducts to similar extents in 66% (unlike single papillomas) or the main duct dilated more than branching ducts in 33% with normal lobular blush .This agreed with studies who reported that patients of multiple papillomatosis had interrupted course of discharging ducts which were often narrowed at more than one site along the main and branching ducts (unlike duct ectasia and single papillomas). Also dilatation of the downstream duct system more than upstream part was found and multiple intraductal filling defects were detected. ^(12, 13, 40, 51, 87).

The second most common pathology encountered by ductography in the present study was **duct ectasia**. This agreed with many studies which reported similar features regarding ductography finding of duct ectasia. They stated that ductography may demonstrate a dilated ductal system without filling defects, obstruction, extravasation, epithelial irregularity, or architectural distortion. Because the orifices on the nipple can be closely positioned and ducts intercommunicate, cannulation occasionally produces opacification of different ductal systems in sequential examinations. ^(12, 13, 40, 44, 64, 85)

Among patients of **FCDB** were supported by other studies. ^(12, 13, 40, 51)

In our study, the most important feature of **DCIS** These features were in agreement with other studies. ^(12, 40, 51, 72)

Although our cases are not sufficiently large in number and further study is needed for precise evaluation between the ductography and sonomammography, in addition to that the comparison of our results with other studies was somewhat problematic because of differences in patient selection criteria, number of patients, examination techniques, and classification of findings in different studies, the present study revealed the following:

▪ In current study the ductography was superior to sonomammography in detecting certain lesions causing nipple discharge as multiple papillary lesions. Ductography detected 100% of the benign papillomatosis patients, while sonomammography detected 66.67%. On the other hand, ductography had the same detectability to solitary papilloma, duct ectasia and FCDB as sonomammography, which was 100%. This agreed with studies carried by Cabioğlu et al ⁽⁶⁶⁾ Ductography and sonomammography were able to diagnose negative patients. Ductography detected 20% negative patients, 10% of which were false negative and 10% were true negatives. Sonomammography diagnosed 30% negative patients, 20% of which were false negative and 10% were true negative.

▪ Ductography is superior to US in visualization of the entire course of discharging duct and in the detection of microcalcifications. It was also superior in demonstrating the location and multiplicity of lesions along the whole course of the discharging ducts. This was supported by studies carried out by Chung et al ⁽⁴²⁾ and Slawson et al ⁽¹³⁾.

▪ On the other hand, sonomammography was superior in its capability to accurately measure the caliber of the discharging duct and the detected lesion. This agreed with study carried by Chung et al ⁽⁴²⁾ who reported that the ultrasonography is superior to galactography in detecting tumors smaller than 0.5 cm in small series with nipple discharge.

▪ sonomammography was superior in demonstrating intraductal extension of IDC and is able to differentiate the cystic or solid nature of the tumors which is important in predicting benignity or malignancy.

The same evaluation was endorsed by who stated that ductography is the state of art approach to investigate patients with nipple discharge, and that it demonstrated the size, location and extension of intraductal abnormalities. It also stated that modern high-resolution ultrasound techniques are helpful in visualizing intraductal disorders and are complementary to alternative radiologic techniques.

The study carried out by Cilotti et al ⁽⁸¹⁾ stated that the sensitivity of ductography was 96% and that of ultrasonography was 84%. Also the study carried out by Moncrief et al ⁽¹⁰³⁾ stated that sonomammography is more sensitive than ductography in cancer diagnosis and permits guided biopsy as well as preoperative localization of non-palpable ductal lesions and percutaneous diagnostic galactography. Both studies were in agreement with the present study.

Discussion

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A. Age of patients presenting with nipple discharge

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In the current study, the **single papilloma** were in agreement with study carried out by Ganesan et al⁽¹⁴⁾ who broadly classified papillomas into central and peripheral types. Central types are usually solitary and subareolar in location within a major duct, while the peripherally located papillomas tend to be multiple within the terminal duct lobular unit. The dilated duct with a papillary lesion may resemble a cyst with an intracystic solid component when there is ductal obstruction, this variant being termed as an intracystic papilloma. Other studies carried out by Cilotti et al⁽⁶¹⁾, Han et al⁽⁶²⁾ and Cilotti et al.⁽⁶³⁾ demonstrated almost similar sonomammographic features to our study and they reported that there are three basic patterns of intraductal papillary neoplasms are recognized on ultrasound ; intraductal mass with or without ductal dilatation, intracystic mass and a predominantly solid pattern which totally filling the duct. A distinct vascular pedicle is identified within the

central core of intraductal papilloma with branching vessels arborising within the mass which can depicted by Doppler Ultrasound. Also the studies carried out by Rissanen et al⁽⁴⁵⁾, Bern-Serna et al⁽⁴⁰⁾ and Sardanelli et al⁽⁶⁴⁾ demonstrated almost similar sonomammographic features to our study.

The current study showed certain diagnostic sonographic features for patients of **multiple papillomatosis** was agreed with studies carried out by Ganesan et al⁽¹⁴⁾, Keresschot et al⁽⁶⁵⁾, Han et al⁽⁶²⁾ and Bern-Serna et al⁽⁴⁰⁾ who stated that multiple peripheral papillomas are located in the peripheral duct system within the terminal ductal lobular unit with segmental dilatation of the ducts. The ductal dilatation may vary in size from a minimally dilated duct to a large cystically dilated, obstructed duct. Similarly the intraductal soft tissue component may range in size from a very small lesion which may be impossible to image to a large mass completely filling the dilated duct. Colour flow studies are sensitive in identifying even very small Intraductal papillary neoplasms in view of its characteristic vascularity

In current study, the most evident sonomammographic features reported among patients diagnosed as **DCIS** were also reported in 2 previous studies carried out by Cabioglu et al⁽⁶⁶⁾ and Nakahara H⁽⁶⁷⁾ who reported duct dilatation, hypoechoic lesions or intracystic tumors within echogenic glandular tissue in 41% of malignant lesions. Almost similar sonomammographic features were reported by studies carried out by Stavros et al⁽⁶⁸⁾, Skaane P.⁽⁶⁷⁾ and Berg et al.⁽⁶⁹⁾

Takebe K.⁽⁷⁰⁾ classified the ultrasound findings in the 23 cases of

DCIS into five groups. (1) Relatively well-defined small masses were detected with major diameter was 3–10mm. The lesions were too small to evaluate the shape, internal echo, and DW ratio, etc. There was no attenuation in posterior echoes. (2) An irregular mottled pattern within a 10mm area (3) A cluster of ducts with a dilated ductal pattern (4) A poorly defined area with lower echoes than those in the surrounding mammary gland (5) Typical ultrasonographic findings for breast cancer, that is, an irregular mass invading adipose tissue.

In the present study, three patients of **IDC** had the following sonomammographic features; dilatation of the discharging ducts, hypoechogenic masses casting acoustic shadows encountered either within the ducts or extending beyond the ductal walls to the surrounding parenchyma of the breast. The duct wall intactness could not be assessed in 2 out of 3 patients in basis of sonographic assessment. In all of the patients, masses were noted deep within the breast parenchyma. Microcalcification could be detected by US in one case which previously noted by mammogram.

The finding of the present study still does not consider US as efficient as a mammography in evaluation of breast microcalcification as a primary modality of investigation. The only case identified by US was based on previous evaluation by mammography. This agreed with study carried out by Kang et al ⁽⁷¹⁾ and Moon WK ⁽²⁷⁾, who reported the low capability to visualize microcalcifications remains a major limitation of sonography for diagnosing intraductal carcinoma. In their study, sonography could initially detect only 58% of

mammographically detected calcifications without knowledge of the mammographic findings. However, when the scans were performed again with mammographic knowledge of the presence of areas of microcalcifications, they were able to detect calcifications in 81% of cases. Accordingly, with no knowledge of mammographic findings, some microcalcifications or small lesions could be missed by sonography.

The studies carried out by Ohtake et al ⁽⁷²⁾ and Kang et al ⁽⁷¹⁾ reported that the sonographic findings showed significant differences between pure IDC and IDC with an intraductal component included the lesion boundary, duct dilatation, calcifications and vascularity. Pure IDC showed an abrupt interface and increased vascularity in or immediately adjacent to lesions more frequently, whereas IDC with an intraductal component showed an echogenic halo, duct dilatation, calcifications and increased vascularity in surrounding tissue more frequently. Satellite lesions on sonography were considered suspicious for an intra-ductal component. Other similar Sonomammographic features for patients of IDC were supported by many studies carried out by Rissanen et al ⁽⁴⁵⁾, Stavros et al ⁽⁶⁸⁾, Nakahara H ⁽⁷³⁾, Kamio et al ⁽⁷⁴⁾ and Ohuchi et al. ⁽⁷⁵⁾

In the current study, all 3 patients with **FCDB** features were in agreement with studies carried by Feig S (1989) ⁽⁷⁶⁾, Bassett et al (1991) ⁽⁵⁴⁾, and Stephen et al (2002). ⁽⁷⁷⁾

For one **normal patient** who was diagnosed sonographically as true negative showed normal breast tissue parenchyma and no abnormalities could be detected within the ductal system.

Detectability of sonomammography:

Almost similar sonomammographic detectability regarding duct ectasia and FCBD was supported by Nani et al ⁽⁵⁷⁾ and Mezi et al ⁽⁷⁸⁾ who reported that the pathological diagnosis was benign including duct ectasia and FCBD in (90%). Feig A. S ⁽⁷⁶⁾ and showed that the accuracy of sonomammography in the detection of FCDB was 100%.

Unlike some previous studies, Rissanen et al ⁽⁴⁵⁾ stated that for the malignant causes of nipple discharge, the yield of sonography was lower (20%), because only an echogenic lesion within a dilated duct was considered a positive sonographic finding.

Skaane P. (1999) ⁽⁶⁷⁾ stated that sonomammography was able to identify 57.9% of the non-palpable malignant neoplasms and the most carcinomas missed by ultrasonography were DCIS, which was in agreement with the present study.

The study was carried by kim et al ⁽⁷⁹⁾ reported that the detectability for a diagnosis of breast carcinoma by US was 94.4% which was almost similar in their results to our results. Chung et al ⁽⁴²⁾ study reported that as a result of recent advancements of US equipment, the parts of the ductal system more than 0.5 mm in diameter can be clearly visualized by US and thus the detectability of sonomammography to lesions had been increased.

While the 2 published reports carried out by Dillon MF ⁽⁸⁰⁾ and Vargas HI ⁽⁴⁴⁾ in which most of the patients had no clinical or mammographic abnormalities, the correct cause of nipple discharge was identified with sonography in only 10% to 26% of the cases, and all the malignant lesions

remained undetected. One reason for the inferior sensitivity of sonography for malignancy might be that carcinomas originate in the terminal ductal lobular unit, where as papillomas causing nipple discharge are usually located more centrally.

The detectability of sonomammography for intraductal papillary lesions in the current study was agreed with the results reported by Sardanelli et al ⁽⁶⁴⁾ and Han et al ⁽⁶²⁾ who reported US detectability (50%) for both single and multiple papillomas of the duct.

A study was launched by Cilotti et al ⁽⁶³⁾ on the role of sonomammography in studying 12 patients of solitary intraductal papillomas. It was able to correctly diagnose eight patients (a detectability of 66.6%), which were verified by cytology to have solitary intraductal papillomas as the cause of nipple discharge and this does not agree with our result.

In the current study, sonographic diagnosis coincided with the pathological diagnosis in 19 out of 25 patients, 18 of them were considered true positive and one was true negative. The study of Cilotti et al ⁽⁶¹⁾ agreed with the present study which reported overall sensitivity of sonomammography to the detection of lesions causing nipple discharge was 84%. While not agreed with study carried out by vargas et al ⁽⁴⁴⁾ who found the overall sensitivity of sonomammography was 26% and the specificity was 97%.

Ductographic diagnosis of patients of nipple discharge

This agreed with studies carried out by Bern-Serna et al ⁽⁴⁰⁾ and Peters et al ⁽⁸²⁾ who reported that there are numerous characteristic pathological findings in galactography, the most common finding is papilloma followed by ectatic ducts and a combination of both. The least common finding is carcinoma of the breast. Other studies reported that multiple or solitary

papillomas are the most common cause of nipple discharge and the most frequent finding was the presence of one or multiple intraductal filling defects which was found in 60% of patients. ^(43, 49, 64, 85-87)

In current study the findings observed in the galactogram using the GICS categories were GICS 0: 2 cases(16.6%), GICS 1: 1 case (8%), GICS 2: 3 cases(25%), GICS 3: 1 case (8%), GICS 4: 4 cases(33.3%), GICS 5: 1 case(8%) which was almost similar to the result of study carried Bern-Serna et al (2010) ⁽⁴⁰⁾who found GICS category 2:16 cases (25.8%); GICS category 3: 19 cases (30.6%); GICS category 4:16 cases (25.8%); and GICS category 5: 11 cases (17.7%).This study reported that the GICS classification was developed to standardize the results of galactography, reduce confusion in interpreting galactograms and facilitate the proper management of patients with pathologic nipple discharge. Galactography is a useful procedure for differentiating benign from malignant lesions, establishing the risk of suspected malignancy, and allowing decisions to be made to optimize early detection of breast cancer⁽⁴⁰⁾.

In our study, the ductographic diagnosis coincided with the pathologic diagnosis of 90% of surgically significant patient, (80%) of them. This agreed with studies carried out by Hou et al ⁽⁴³⁾, in which the sensitivity was found to be 86.4%, Cilotti et al ⁽⁸¹⁾ found it to be 96%. While not agreed with Ambrogetti et al ⁽⁸⁹⁾ who found the sensitivity of ductography was equal to 59.6%.

The specificity of ductography was found to be equal to 100% in present study which agreed with studies carried out by Simmonset al ⁽⁶⁾ and Hou et al ⁽⁴³⁾ who

reported that ductography had a high (96.6%) specificity.

Peters et al ⁽⁸²⁾ stated that the ductography is the only diagnostic procedure that is able to depict and precisely localize small intraductal pathologic processes and normal galactogram is a specific and sensitive indicator of absence of localized disease. Hou et al ⁽⁴³⁾ and Van Zee ⁽⁸⁴⁾ reported that the galactography is a contrast examination of the discharging ducts that is performed to identify and localized intraductal lesions to allow for conservative excision and without galactography, the surgeons have relied on either mastectomy or excision of the major duct system responsible for the discharge.

The percentage of patients was diagnosed by ductography as DCIS differs among many studies. In the present study, it was (20%). This agreed with Hou et al ⁽⁴³⁾ and who reported that ductography could be detect 15% of carcinoma .On contrary the study carried out by Baker (1994) ⁽⁸³⁾ detected only 3.3% for DCIS that does not agree with current study.

Ductographic features of lesions causing nipple discharge:

In our study an important feature of **single papilloma** was the presence of a single filling defect, oval in shape located at the main ducts. The surface of the filling defect was often irregular or fronded.

These features were supported by studies who reported that the ductography helps define the sites, number, and extent of presumed papillomas. If it is not performed, they may remain invisible. In addition to that papillomas secrete fluid

profusely, and the duct downstream from the papilloma (that is, toward the nipple from the papilloma) is often dilated. Paradoxically, proximal to the papilloma, the normal duct is usually not dilated, In addition to filling defects and downstream ductal dilatation, may also cause ductal obstruction or an "amputated duct" or even alteration in the normally smooth duct wall. ^(12, 13, 40, 55, 87)

In current study, the patients of **multiple papillomatosis** showed moderate to marked dilation of main and the branching ducts to similar extents in 66%(unlike single papillomas) or the main duct dilated more than branching ducts in 33% with normal lobular blush .This agreed with studies who reported that patients of multiple papillomatosis had interrupted course of discharging ducts which were often narrowed at more than one site along the main and branching ducts (unlike duct ectasia and single papillomas). Also dilatation of the downstream duct system more than upstream part was found and multiple intraductal filling defects were detected. ^(12, 13, 40, 51, 87)

The second most common pathology encountered by ductography in the present study was **duct ectasia**. This agreed with many studies which reported similar features regarding ductography finding of duct ectasia. They stated that ductography may demonstrate a dilated ductal system without filling defects, obstruction, extravasation, epithelial irregularity, or architectural distortion. Because the orifices on the nipple can be closely positioned and ducts intercommunicate, cannulation occasionally produces opacification of different ductal systems in sequential examinations. ^(12, 13,40, 44, 64, 85)

Among patients of **FCDB** were supported by other studies. ^(12, 13, 40, 51)

In our study, the most important feature of **DCIS** These features were in agreement with other studies. ^(12, 40, 51, 72)

Although our cases are not sufficiently large in number and further study is needed for precise evaluation between the ductography and sonomammography, in addition to that the comparison of our results with other studies was somewhat problematic because of differences in patient selection criteria, number of patients, examination techniques, and classification of findings in different studies, the present study revealed the following:

- In current study the ductography was superior to sonomammography in detecting certain lesions causing nipple discharge as multiple papillary lesions. Ductography detected 100% of the benign papillomatosis patients, while sonomammography detected 66.67%. On the other hand, ductography had the same detectability to solitary papilloma , duct ectasia and FCDB as sonomammography, which was 100%. This agreed with studies carried by Cabioglu et al ⁽⁶⁶⁾ Ductography and sonomammography were able to diagnose negative patients. Ductography detected 20% negative patients, 10% of which were false negative and 10% were true negatives. Sonomammography diagnosed 30% negative patients, 20% of which were false negative and 10% were true negative.

- Ductography is superior to US in visualization of the entire course of discharging duct and in the detection of microcalcifications. It was also superior in demonstrating the location and

multiplicity of lesions along the whole course of the discharging ducts. This was supported by studies carried out by Chung et al⁽⁴²⁾ and Slawson et al⁽¹³⁾.

▪ On the other hand, sonomammography was superior in its capability to accurately measure the caliber of the discharging duct and the detected lesion. This agreed with study carried by Chung et al⁽⁴²⁾ who reported that the ultrasonography is superior to galactography in detecting tumors smaller than 0.5 cm in small series with nipple discharge.

▪ sonomammography was superior in demonstrating intraductal extension of IDC and is able to differentiate the cystic or solid nature of the tumors which is important in predicting benignity or malignancy.

The same evaluation was endorsed by who stated that ductography is the state of art approach to investigate patients with nipple discharge, and that it demonstrated the size, location and extension of intraductal abnormalities. It also stated that modern high-resolution ultrasound techniques are helpful in visualizing intraductal disorders and are complementary to alternative radiologic techniques.

Conclusion

The study carried out by Cilotti et al⁽⁸¹⁾ stated that the sensitivity of ductography was 96% and that of ultrasonography was 84%. Also the study carried out by Moncrief et al⁽¹⁰³⁾ stated that sonomammography is more sensitive than ductography in cancer diagnosis and permits guided biopsy as well as preoperative localization of non-palpable ductal lesions and percutaneous

diagnostic galactography. Both studies were in agreement with the present study.

Patients were subjected to

I. Full history taking:

1) Personal history included Name, age, marital status, occupation, and residence.

2) Menstrual history included:

- Age of menarche.
- Regularity of the menstrual cycle.
- Duration and amount of blood loss.
- Associated pain or dysmenorrhoea
- Date and nature of last menstrual period.

3) Obstetrical and Gynecological history: previous abortions, ovarian or uterine pathology, history of lactation and any related problems.

4) Complaint and present history included:

▶ Nipple Discharge:

- Date of onset of the nipple discharge, its duration, course whether stationary or intermittent and frequency of repetition.
- Amount of discharge whether minimal, moderate, or profuse
- Color of discharge whether watery, milky, greenish, serous, serosanguinous, or bloody.

▶ Discharging ducts:

- Number of ducts discharging stating the colour of discharge of each duct, among patients with multiple duct discharge.

- **Mode of discharge whether spontaneous or upon pressure stating the site of pressure giving maximum discharge.**

▶ associated symptoms:

General symptoms such as pain whether cyclic or non-cyclic, fever, malaise and loss of weight.

- **Sensation of breast swelling**
- **Mass felt by the patient in the breast and/or axilla.**
- **Nipple erosion, retraction or inversion.**

5) **Past history:**

- **Of breast pathology.**
- **Of milk retention.**

- Of diabetes, inflammation especially staphylococcal or tuberculous, trauma, tumors.
 - Of bleeding tendency or blood disorders.
 - Of endocrinal pathology
- 6) Family history included:

History of similar condition or any other breast pathology with special concern for breast carcinoma.
- 7) Operative history included:
 - History of previous operations in the breast.
 - History of gynecological or endocrinal operations.
- 8) Drug history:
 - Of contraceptive pills, its dose and duration.
 - Of any form of hormonal supplement or therapy.
 - Of corticosteroid intake.

II. Thorough Clinical Examination:

A. General examination: Stressing on signs of hormonal disturbance.

B. Local examination of the breasts:

1. Inspection:

The following points were noted:

- The level and size of the two breasts.
- The condition of the nipple: if there was recent retraction, destruction, discoloration, displacement and spontaneous discharge.
- The condition of the areola: for ulceration, dimpling, vesicle formation, and hyper-pigmentation.
- Skin manifestations: as dimpling, puckering, retraction, peau d" orange,

dilated veins, ulcerations and skin nodules.

2. Palpation:

The following were carried out:

- Confirmation of the presence of an associated mass and determining its:
 - ▶ Site, size, shape, tenderness and local temperature.
 - ▶ Surface: whether smooth, nodular, finely granular or irregular.
 - ▶ Borders whether well defined or irregular.
 - ▶ Consistency: whether soft, firm, cystic or hard.
 - ▶ Attachment to skin, breast tissue, muscles or ribs.
- Examination of ipsilateral and contralateral axillary cervical and supraclavicular lymph nodes.

III. Investigations:

(a) Mammography

All mammograms were obtained using a dedicated X-ray unit (siemens, mammomat nova machine) having 0.5 target focal spot in a molybdenum anode. Technique used for a mammogram is low Kilo-voltage Peak (KvP) about 24 to 30. The milli-Ampere-seconds (mAs) vary depending on breast tissue density, ranging from 30 to 60 mAs. This technique results in mammograms with a high film contrast, making it easier for the radiologist to read.

Views:

Four films were obtained, two views for each breast, the cranio-caudal and the mediolateral oblique views. Mediolateral oblique view was done with an angle 45°. All views were taken while the patients were standing. Compression was applied to all breasts.

Technique:

The patient was standing with her breast placed horizontally on the film cassette and compression was applied to flatten out the breast, to avoid motion and enhance visualization. A craniocaudal film was taken, where the beam was directed 90 degrees from the mediolateral position. Then breast was held vertically, side to side compression was applied and a mediolateral film was taken where the X-ray beam was directed from medial to lateral.

Interpretation and data analysis:

A comparison of both breasts was done. Both the MLO and CC views are mounted back to back, so that the right breast is compared with the left breast. The contour, size of the breasts and its symmetric density are evaluated. Any suspicious area which causes disruption of the normal symmetrical pattern of the breast and architectural distortion was looked for. Interpretation involves careful viewing of the normal mammographic pattern and any abnormalities which present itself as a disruption of the normal pattern.

Viewing the mammogram:

- Was carried out on viewing box, with dim light of the surroundings.
 - The MLO, and CC films of both breasts were put back to back, and both breasts were compared to each other.
 - A magnification lens was used sometimes to confirm subtle findings.
 - Confirming adequate positioning was done, using the following criteria:
- a) The whole breast tissue was included in the mammogram, and in cases of

large

breasts, overlapping films were needed to image the whole breast.

- b) The pectoralis major muscle was seen till the level of the nipple in the MLO view.
 - c) The axilla and inframammary fold were included in the MLO films.
 - d) The nipple should be seen in profile in all projections, although some of the patients have congenitally inverted nipple (by history).
 - e) Any lesion detected in mammography in the CC view, should be detected within 1cm from its depth at the MLO view.
 - f) Fat should be seen posterior to breast parenchyma in all views.
- Identifying the normal breast pattern, and detecting any abnormality.
 - The lesions were evaluated as follows:
- a) Position of the lesion (upper outer, upper inner, lower outer or lower inner quadrants, retro areolar or axillary)
 - b) Regular or irregular outlines.
 - c) The borders were described as circumscribed, obscured, spiculated, lobulated or ill defined.
 - d) The lesions were classified as dense or lucent.
- Calcifications were classified according to size into macro and micro calcifications and according to distribution as regional and segmental.
 - Architectural distortion and tissue oedema were detected. Skin thickening was also reported. Axillary lymph nodes were detected.

(b) Ultrasound:

All the patients were subjected to bilateral breast US using 7.5 MHz linear probe (Phillips machine and siemens).

The transducers were directly applied to the skin surface with the patient in the supine position to examine the inner quadrants of the breasts, and the supine oblique position, to evaluate the outer quadrants. The examined side is elevated and the ipsilateral arm is extended above the head to stabilize the breast and flatten it against the chest wall. Scanning was performed in the radial and antiradial planes in relation to the nipple, and/or saggital and transverse planes were used, where it begins in the upper inner quadrant of the breast and proceeds slowly to the outer quadrant to obtain saggital images. The transducer is then moved lower on the breast and the scanning action is repeated until the whole breast has been examined. At that point the transducer is rotated 90° and transverse scan is taken proceeding from inner to outer. Both axillary regions are then examined by longitudinal scanning. All nodes were examined in the longitudinal and transverse nodal planes that demonstrated the largest and smallest diameters of the node.

The comment on the US was as follows:

- Description of the breast parenchymal pattern.
- Skin thickening was detected.
- Ducts were evaluated for duct ectasia and intraductal soft tissue lesions, or inspissated secretions.
 - Detection of any focal lesions, with evaluation of the lesions as follows:
 - a) The site of the lesion.
 - b) Size of the lesion.
 - c) Echogenicity (hypo, hyper, iso or anechoic).
 - d) Internal echo pattern (homogenous or heterogenous)
 - e) Regular or irregular shape.

f) Borders are well defined, ill defined, angular or microlobulated.

g) Posterior acoustic phenomena (shadowing, enhancement or none).

h) Associated architectural distortion or tissue oedema.

i) Vascularity of the lesion on Doppler US.

j) Effect of compression on the lesion, whether it is flattened, compressed or not.

k) If the lesion is mobile or fixed under the probe.

• The axilla was examined for detection of lymph nodes, which were classified as non specific or suspicious, where the L.N.S with oval shape and preserved echogenic hilum were considered nonspecific, or suspicious. L.N.S with oval shape and preserved echogenic hilum were considered nonspecific, while those with globular or irregular shape, distorted or lost hilum were considered suspicious.

(c)Galactography:

Technique:

The nipple was cleansed with antiseptic solution (povidone-iodine) and the discharging duct was located. A 27 gauge cannula was used freehand to cannulate the mammary duct. Approximately 0.5-2 ml of non ionic contrast media (Iopromide) which commercially named ultravist was injected until the patient felt fullness of tightness in her breast.

After successful cannulation and injection of the contrast medium, two views of the breast; one craniocaudal was taken. The films were processed and viewed immediately to insure proper needle placement and filling of the ducts. Mediolateral oblique views were then taken accordingly.

No sharp or burning pain resulted from the injection; if such pain had occurred, it would have suspect that the needle had penetrated beyond the duct wall with resultant contrast extravasations. In that patient, it would have been best to withdraw the needle and the patient was advised to apply hot compresses to her breast to aide drainage and resorption of the contrast medium left, and the patient was scheduled for another examination.

(d) Histopathology

a) Nipple discharge cytology

The breast is squeezed gently from all areas around the areola to get the patient's discharge, then it is taken on a clean glass slide then it is smeared by flat pressure using a second glass slide, then immediate fixation is done by immersing the slide in 96% alcohol and then the slide is stained for cytological examination.

b) Ultrasound guided fine-needle aspiration biopsy if indicated.

US guided FNAB procedure was done as follows:

- The procedure is explained to the patient.
- Skin is cleaned with alcohol.
- Acoustic coupling between the transducer and the skin is obtained with gel. The patient is placed in a supine position with her ipsilateral side elevated somewhat depending on the position of the lesion. The free hand method is applied. The transducer held in one hand and the needle in the other. The needle (20 to 25 gauge needle was used) inserted and directed towards the target lesion and followed up by the US probe. The needle should pass parallel and lateral to the transducers mid point. The needle tip appears as bright echo.
- Sampling of the lesion is undertaken. The cellular material

obtained expressed into a glass slide where it is smeared, fixed and stained.

- ❖ The medical ethics will be considered; the patient should be aware of the examination, patient approval should be obtained, the economic status of the patient should be considered and the patient has to get benefit from the examination.

Statistics used in the current study:

SE, SP, ACC, PPV and NPV

Sensitivity: The capacity of the test to correctly identify diseased individuals in a population "TRUE POSITIVES". The greater the the sensitivity, the smaller the number of unidentified case "false negatives".

Specificity: The capacity of the test to correctly exclude individuals who are free of the disease "TRUE NEGATIVES". The greater the specificity, the fewer "false positives" will be included.

Positive Predictive Value: The probability of the disease being present, among those with positive diagnostic test results

Negative Predictive Value: The probability that the disease was absent, among those whose diagnostic test results were negative.

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