

Nipple Discharge as Presentation of Underlying Breast Disease at Alkindy Teaching Hospital, Interventional Study

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Abstract: Background:- Nipple discharge is the third most frequent complaint of female patients visiting a breast clinic, it's a common presenting finding that may be caused by an underlying intraductal pathology, hormonal imbalance or a physiologic event. **Aim of the study:-** Is to determine the most common type of nipple discharge and to assess the association between nipple discharge and breast diseases at Al-Kindy teaching hospital Baghdad / Iraq. **Patients & Methods:-**This is a descriptive study of patients who visited the breast clinic at Al-kindy teaching hospital over a period of two years 1st January 2018 to 31st of December 2019, all patients with nipple discharge included in the study. Full history, clinical examination, laboratory investigations and hormonal investigation (S. prolactin, TSH,T3,T4) was done for all patients. Radiological examination including ultrasound was done for all patients, Mammography for patients above 40 years and MRI for the patients presented with suspicious nipple discharge with normal U/S and mammography. Direct cytology from nipple discharge was done for all patients. Fine needle aspiration cytology (FNAC) or TRU-CUT biopsy and histopathological examination was done for patient presented with nipple discharge associated with breast lump. **Results:-**The descriptive study included (120) patients presented with nipple discharge, the age of patients range from (19 years - 70 years) with a mean age(39.3+ 13.5) years. Positive family history of breast cancer found in (7) cases (5.8%) and only (15)cases (12.5%) had previous breast surgery. The most common type of nipple discharge according to the type were the bloody nipple discharge found in (52) patients (43.3%), Breast lump was found in (48) cases (40%), also we had (32) cases(26.7%) with spontaneous nipple discharge. In (34) cases (28.3%) the nipple discharge from uni-ductal orifice. Regarding laterality of nipple discharge, (83)cases (69.2%) presented as unilateral, the abnormal nipple discharge are more common with benign (103) cases (85.8%) than malignant breast disease(17)cases (14.2%). The bloody nipple discharge was associated with malignant disease in (11) cases (21.1%). Regarding the histopathological and cytological results of nipple discharge the most common result was duct papilloma (43)cases (35.9%). **Conclusions:-** Spontaneous bloody, unilateral, single duct discharge needs a work up and thorough evaluation, nipple discharge in most patients is due to benign causes.

Keywords: Breast cancer, Nipple discharge, Duct papilloma.

INTRODUCTION

Nipple discharge is a common symptom women complain of. It is classified as normal or abnormal depending on features such as laterality, cycle variation, quantity, color or presentation (induced vs spontaneous). It can be related to benign conditions such as intraductal papilloma, duct ectasia, plasma cell mastitis, galactorrhoea or malignant such as ductal or papillary carcinoma. [Zervoudis, S. *et al.*, 2008] Nipple discharge is the third most common complaint of patients seeking medical attention for breast disease, accounting for about 5% of all breast symptoms.[Hussain, A.N. *et al.*, 2006; Santen, R.J. *et al.*, 2005] Nipple discharge is regarded as one of the three most common presenting complaints in women attending a breast clinic; the other two complaints being breast pain and the finding of a lump.[Lippa, N. *et al.*, 2015; Chen, L. *et al.*, 2012] Nipple discharge is categorized as normal physiologic nipple discharge as a result of pregnancy, hormonal problem due to high prolactin level (hyperprolactinoma) or pathologic (suspicious) nipple discharge due to an underlying breast disease.[Salzman, B. *et al.*, 2012] Nipple discharge often raises concern for the possibility of two uncommon but serious conditions breast cancer and a pituitary tumor. [Falkenberry, S.S. *et*

al., 2002] Nipple discharge its considered suspicious when it occurs spontaneously and is persistent, unilateral, bloody, or serous, as well as when it occurs in patients who are not pregnant or breastfeeding. [Van Gelder, L. *et al.*, 2015] Nipple discharge has been classified based on its appearance as milky, yellow, watery, pink or bloody.[Zervoudis, S. *et al.*, 2010; Chen, L. *et al.*, 2012] A clear, serous discharge may be "physiological" in parous woman or may be associated with duct papilloma or mammary dysplasia. Multiduct, multicolored discharge is physiological and patient may be reassured. [Zervoudis, S. *et al.*, 2010] A blood stained discharge may be caused by duct ectasia, duct papilloma or carcinoma. A duct papilloma is usually single and situated in one of the larger lactiferous duct; it is sometimes associated with cystic swelling beneath the areola. Black or green discharge is usually the result of duct ectasia and its complications. [Zervoudis, S. *et al.*, 2010]

AIM OF THE STUDY

Is to determine the most common type of nipple discharge and to assess the association between nipple discharge and breast diseases at Al-kindy teaching hospital in Baghdad / Iraq.

PATIENTS AND METHODS

This is a descriptive study of patients who visited the breast clinic at Al-kindy teaching hospital over a period of two years 1st January 2018 to 31th of December 2019, all patients with nipple discharge included in the study. Full history, clinical examination, laboratory investigations and hormonal investigation (S. prolactin, TSH,T3,T4) was done for all patients. Radiological examination including ultrasound was done for all patients, Mammography for patients above 40 years and MRI for the patients presented with suspicious nipple discharge with normal U/S and mammography. Direct cytology from nipple discharge was done for all patients. Fine needle aspiration cytology (FNAC) or TRU-CUT biopsy and histopathological examination was don for patient presented with nipple discharge associated with breast lump.

Inclusion Criteria:

All female after menarche who visited breast clinic complaining of nipple discharge included in the study.

Exclusion Criteria:

- 1-Male
- 2-Congenital retracted nipple
- 3-Lactating female

Statistical Analysis

Statistical analysis was performed by using descriptive of qualitative variables as numbers or percentages.

RESULTS

The descriptive study included 120 patients presented with nipple discharge.

In the present study, the age of patients presented with nipple discharge range from(19 years _ 70 years) with a mean + SD (39.3+ 13.5)years. Where the highest incidence (29.1%) of nipple discharge in the age group (30-39) years. Figure (1).

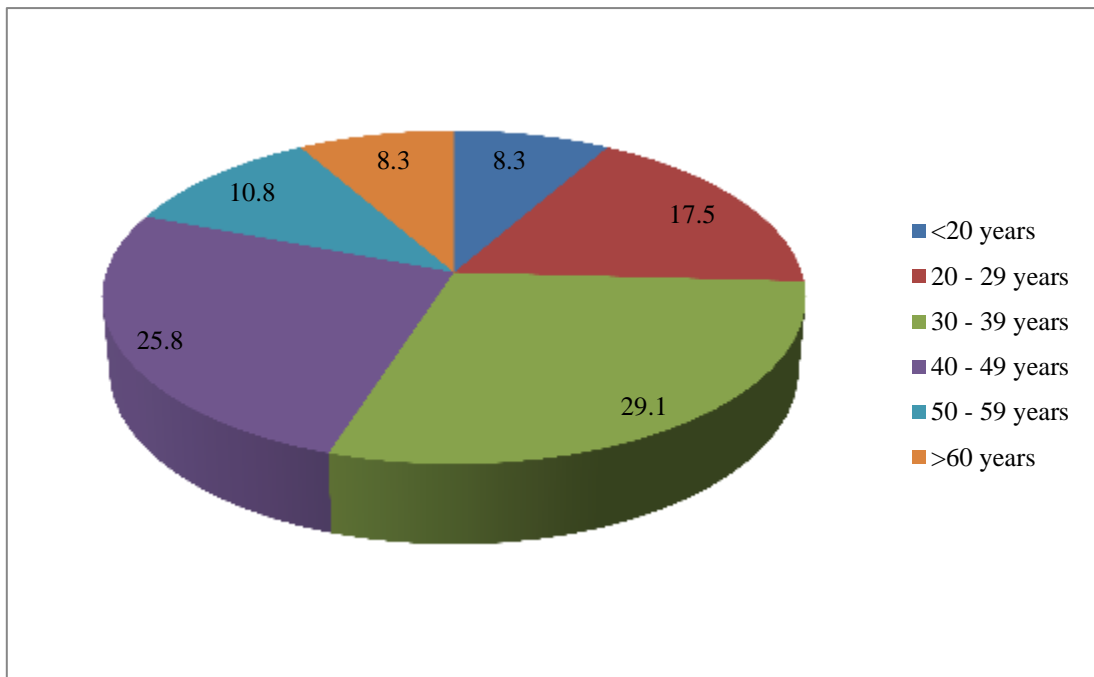


Fig (1): Age distribution of patients with nipple discharge

Regarding the demographic characteristics of the patients with nipple discharge (81.7%) were married, (18.3%) were single. Eighty seven cases were pre-menopausal (72.5%). Post-menopausal female were (27.5%), pre-menopausal were (87) cases (72.5%). The majority of patients (98)

(81.7%) had at least one child, and (22) (18.3%) were nulliparous. Positive family history of breast cancer found in (7) cases(5.8%) and only (15) cases (12.5%) had previous breast surgery. Table (1)

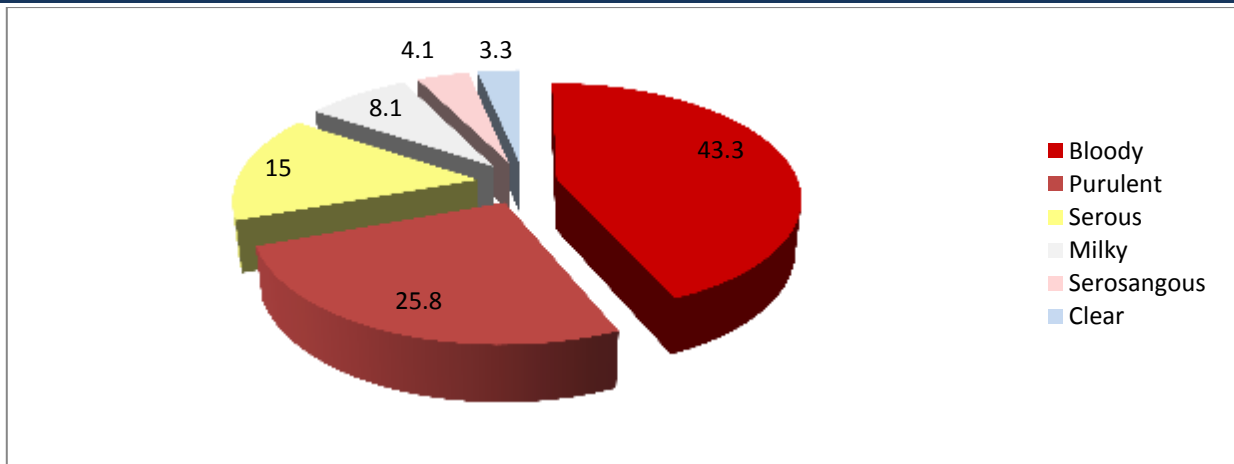


Fig (2): types of nipple discharge according to the color

Table (1): Demographic Characteristics of the patients with nipple discharge

Total (n=120)		
Marital status	No.	%
Single	22	18.3
Married	98	81.7
Menstrual status	No.	%
Pre-Menopausal	87	72.5
Post-Menopausal	33	27.5
Parity status	No.	%
Nulliparous	22	18.3
Parous	98	81.7
Family history	No.	%
Yes	7	5.8
No	113	94.2
History of breast surgery	No.	%
Yes	15	12.5
No	105	87.5

The most common type of nipple discharge according to the color were the bloody nipple discharge found in (52) patients (43.3%), and (31) patients (25.8%) presented with purulent discharge, (10) patients (8.3%) presented with milky discharge, (18) patients (15%) with serous discharge, (5) patients (4.1%) with serosangous discharge and only (4) patients (3.3%) presented with clear discharge. Figure (2). Breast lump was found in (48) cases (40%). We had (32) cases (26.7%) with spontaneous nipple discharge

and (88) cases (73.3%) occurred on areolar and periareolar squeezing. In (34) cases (28.3%) the nipple discharge from uni-ductal orifice. About (86) cases (71.7%) with nipple discharge are multi-orifice presentation. Regarding laterality of nipple discharge, (83) cases (69.2%) presented as unilateral, (37) cases (30.8%) was bilateral. In the majority of patients, the discharge was intermittent (103) cases (85.5%) and it was persistent in (14.2%) of cases. Table (2)

Table (2): Breast Changes and nipple discharge characteristics

Total (n=120)		
Breast lump	No.	%
Absent	72	60
Present	48	40
Discharge release	No.	%
Spontaneous	32	26.7
Squeezed	88	73.3
Orifice	No.	%

Uni-orifice	34	28.3
Multi-orifice	86	71.7
Laterality	No.	%
Unilateral	83	69.2
Bilateral	37	30.8
Persistency	No.	%
Persistent	17	14.2
Intermittent	103	85.8

Regarding the relationship between types of nipple discharge and presence of breast lump. The most common type of nipple discharge associated with mass was bloody (23 cases) (47.9%), purulent (11

cases) (22.9%), serous (10 cases)(20.8%), serosanguous and clear was (2 cases) (4.1%) for both. Fig (3)

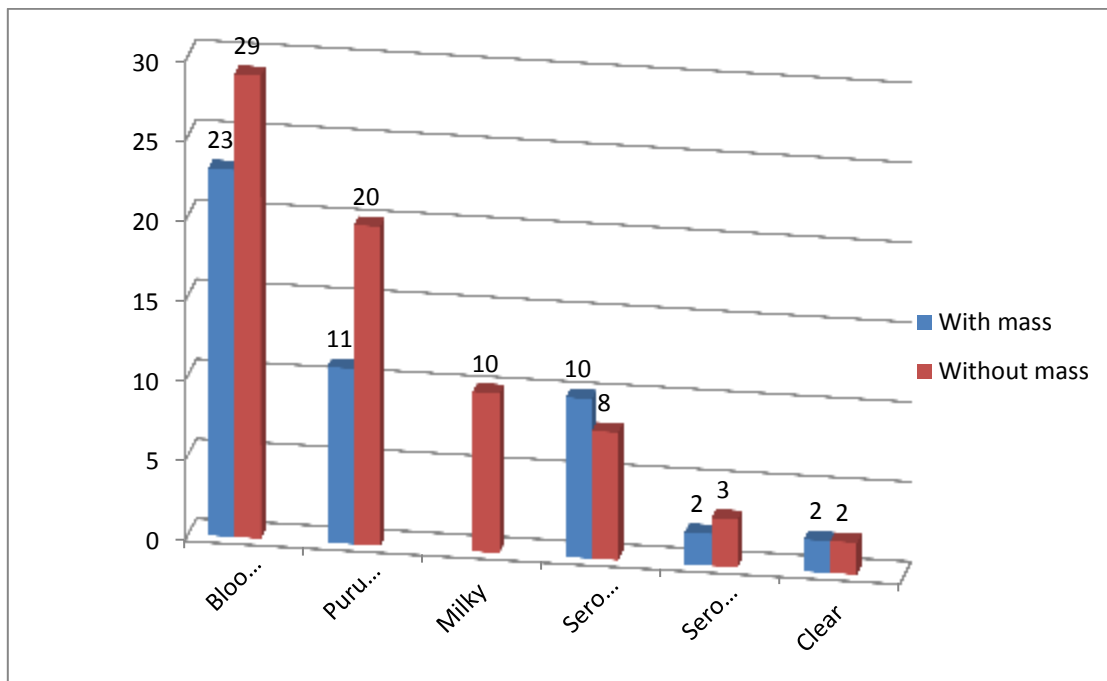


Fig (3): Relationship between types of ND and breast mass

Regarding the relationship between types of nipple discharge and breast diseases (Benign and Malignant), the abnormal nipple discharge are more common with benign (103) cases (85.8) than malignant breast disease (17) cases (14.2%). The bloody nipple discharge was related with

malignant disease in (11) cases (21.15%). The purulent, serous and serosanguous are also associated with malignant breast disease but less common than bloody nipple discharge, Milky and clear nipple discharge had no relation with malignant breast disease. Table (3)

Table (3): Relationship between types of nipple discharge and breast diseases (benign and malignant)

Type of nipple discharge	Benign breast disease No. (%)	Malignant breast disease No. (%)	Total
Bloody	41(78.84)	11 (21.15)	52(43.3%)
Purulent	28 (90.3)	3 (9.6)	31(25.8%)
Milky	10 (100)	—	10(8.3%)
Serous	16 (88.9)	2 (11.1)	18(15%)
Serosanguous	4 (80)	1 (20)	5(4.1%)
Clear	4 (100)	—	4(3.3%)
Total	103 (85.8)	17(14.2)	120

Regarding the effectiveness of diagnostic tests for the diagnoses of the malignant breast disease that

associated with nipple discharge, the best modality for diagnosis was histopathological study, FNAC

and direct cytology, while the least diagnostic tests were the clinical examination and radiological test

including (Breast ultrasound, mammography). Table (5)

Table (4): Effectiveness of diagnostic tests in nipple discharge to diagnose malignant breast disease

Diagnostic test	No. of malignant cases	%
Clinical examination	4:17	17.6
Radiological test (U/S, mammography, MRI)	7:17	41.2
Direct smear cytology from nipple discharge	14:17	82.3
FNAC	15:17	88.2
Histopathological study	17:17	100

Regarding the histopathological and cytological results of nipple discharge the most common result was duct papilloma (43)cases (35.9%), fibrocystic disease (23) cases (19.2%). Ten cases were galactorrhea (8.3%), Inflammatory cells are (12)

cases (10%), and (15) cases (12.5%) were duct ectasia. Most of the cases with nipple discharge are benign (103) cases (85.8%), and seventeen cases are malignant (14.2%).Table (6)

Table (5): Cytological result characteristic of the patients with nipple discharge

Nipple discharge cytological features	Total No. (120)	
	No.	%
Benign	103	85.8
Duct papilloma	43	35.9
Fibrocystic disease	23	19.2
Duct ectasea	15	12.5
Inflammatory cells	12	10
Galactorrhea	10	8.3
Malignant	17	14.2
DCIS	9	52.9
Invasive ductal carcinoma	5	29.4
Papillary carcinoma	2	11.8
DCIS with micro invasion	1	5.9

DISCUSSION

Nipple discharge is a common reason for referral to breast clinic. [Seltzer, M.H, 2004]

The type and character of ND have a good prognostic value and often reflect the type of underlying breast lesion. [Paterok, E.M. et al., 2003] ND of the breast is a common complaint. Between 5% and 10% of women presenting for routine examination will report spontaneous nipple discharge, and as many as 80% of women will experience at least one episode of ND during their reproductive years. [Goodson, W.H. et al., 2004] In the present study the age of patients presented with ND ranged from (19 years to 70 years), with mean + SD of (39.3 + 13.5) These results are agree

with the result of Ahmed, M.A. al., [2018], who had studied 500women with ND, with mean age (39.6+ 11.8) years. In the current study show that(33) patients (27.5%) in the post-menopausal period, pre-menopausal female were 87 (72.5%). A comparable result about the post-menopausal status was found by Cheung, K.L. et al., [1997], they documented that 26 (25%) of their patients with ND in post-menopausal period. In the current study show that (7) cases (5.8%) had positive family history in their relatives, This result agree with Morrogh, et al., [2007], found that the family history of breast cancer among their patients was (4.3%).

Table (6) character of Nipple Discharge

Demographic character of patient with ND	Current study n=120	Study Cheung, K.L. et al., (1997) n=104	Study of Morrogh, et al., (2007) n=376
Menstrual status	Post-menopause (33/120) (27%)	Post-menopause (26/104) (25%)	–
Family history of breast disease	+ve family history (7/120) (5.8%)	–	+ve family history (16/376) (3.8%)

Regarding the types of ND according to the color, bloody nipple discharge found in (52) patients (43.3%), and (31) patients (25.8%) presented with purulent discharge, (10) patients (8.3%) presented with milky discharge, (18) patients (15%) with serous discharge, (5) patients (4.1%) with serosanguous discharge and only (4) patients (3.3%) presented with clear discharge. The same results was obtained by Dolan, *et al.*, [2010], they reported that the discharge was milky in 9%

(27/313) of cases, serous in 42% (130/313) of cases, bloody in 44% (137/313) of cases, and purulent in 6% (19/313) of cases. Another results were observed by Morrogh, *et al.* [2007]. They reported that the nipple discharge was white /milky discharge in 26 patients (6.3%), clear/serous/pink discharge in 125 patients (30%), bloody discharge in 224 patients (53.8%), and green/brown discharge in 41 patients (9.9%).

Table (7) Types of ND according to color

Types of ND according to color	Current study n=120	Study of Morrogh, et al., (2007) n=416	Study of Dolan, et al., (2010) n=313
Bloody	(52/120) 43.3%	(224/416) 53.8%	(137/313) 44%
Purulent	(31/120) 25.8%	(41/416) 10%	(19/313) 9%
Serous	(18/120) 15%	(125/416) 30%	(130/313) 42%
Milky	(10/120) 8.3%	(26/416) 6.3%	(27/313) 9%

In current study breast lump was found in (48) cases (40%), the results agree with Lumachi, F. *et al.*, [2002], in their study of 2,879 patients, 1,663 patients (57.8%) associated with breast lump, 1,173 patients (40.7%) presented with breast mass. In the current study the majority of patients (88) cases (73.3%) the discharge released by areolar and periareolar squeezing. while (32) cases (26.7%) of ND was spontaneous release. In other study Dolan, *et al.*, [2007], found that the minority of their patients had active (spontaneous) nipple discharge (96/313; 31%). This study observed that (34) cases (28.3%) the ND from uni-ductal orifice and (86) cases (71.7%) with ND are multi-orifice presentation This result agree with result of Osama abd allah [Abd Allah, M.D, 2020]. He observed that in (18/50) patients (36%) of the nipple

discharged from uni-orifice and in (32/50) patients (64%) of the nipple discharged from multi-orifice. In the majority of the patients, the discharge was intermittent in (88.8%) and it was persistent in 11.2% of the cases. Regarding laterality of nipple discharge, (83)cases (69.2%) presented as unilateral, (37) cases (30.8%) was bilateral, this results agree with the results of Jeffrey, *et al.*, [2000], the discharge was unilateral in 21 cases (60%), bilateral in 14 cases (40%). In this study the discharge was intermittent (103) cases (85.5%) and it was persistent in (14.2 %) of cases, its similar to the results of Morrogh, M. *et al.*, [2007]. In eight cases (16%) the discharge was persistent and in forty two cases (84%) the discharge was intermittent.

Table (8) Breast changes and ND character

Breast changes and ND character	Current study n=120	Study of Dolan, et al., (2010) n=313	Study of Lumachi, et al (2002) n=2819	Study of Osama abd allah, (2020) n=50	Study of Jeffry, et al., (2000) n=35
Breast lump	(48/120) 40%	–	(1174/2819) 40.7%	–	–
Discharge release	Spontaneous (32/120) 26.7%	Spontaneous (96/313) 31%	–	–	–
Orifice	Uniorifice (34/120) 28.3% Multiorifice (76/120) 71.7%	–	–	Uniorifice(18/50) 36% Multiorifice (32/50) 64%	–
Latrality	Unilateral (83/120) 69.2% Bilateral (37/120) 30.8%	–	–	–	Unilat-(21/35) 60% Bilat-(14/35) 40%

Regarding the relationship between types of nipple discharge and breast disease (Benign and Malignant), the abnormal nipple discharge are more common with benign (103) cases (85.8) than malignant breast disease(17)cases (14.2%). The bloody nipple discharge was related with malignant disease in (11) cases (64.7%). The purulent, serous and serosanguous are also associated with malignant breast disease but less common than bloody nipple discharge, Milky and watery nipple discharge had no relation with malignant breast disease, this results agree with Caleffi, M. *et al.*, [2004], Bloody nipple discharge was most common type in malignant breast disease rather than other type of nipple discharge. Another study by Adepoju, L.J. *et al.*, 2005 and Dinkel, H.P. *et al.*, (2001) concluded that there was no association between bloody discharge and an increased risk of breast cancer was also controversial. Regarding the effectiveness of diagnostic tests for the diagnoses of the malignant breast disease that associated with nipple discharge, the best modality for diagnosis was histopathological study(100%), FNAC(85.7%) and direct cytology(78.5%), while the least diagnostic tests were the radiological test including (Breast ultrasound, mammography) and clinical examination. These results agree with the finding

of Pritt B *et al* and Johnson T.L. *et al* [Pritt, B. *et al.*, 2004; Johnson, T.L. *et al.*, 1991], on 466 case specimens from 395 patients from 1995-2002 presented with nipple discharge. Of the 395 patients, 98 had abnormal cytologic findings (27 cases with intraductal papilloma of which 24 cases with atypia, 9 cases with moderate epithelial hyperplasia, 3 cases with ductectasia, and 18 cases with duct carcinoma) The positive predictive value for cytology was 92% and the negative predictive value was 94% Regarding the histopathological and cytological results of nipple discharge the most common result was duct papilloma (43) cases (35.8%), fibrocystic disease (23) cases (19.2%). Ten cases were galactorrhea (8.3%), Inflammatory cells are (12) cases (10%), and (15) cases (12.5%) were duct ectasia. Most of the cases with nipple discharge are benign (103) cases (85.8%), and seventeen cases are malignant (14.2%). This results agree with Funge *et al* [Johnson, T.L. *et al.*, 1991], (85%) including; duct papilloma in 78 cases (44%), duct ectasia in 31 cases (18%), fibrocystic disease in 25 cases (14%) and other (9%)and malignant (27 cases) (15%). Heinz *et al* [Fung, A. *et al.*, 1990], studied (63 cases), were duct papilloma (28 cases) (44%), duct ectasea (18 cases) (28.3%), fibrocystic disease (9 cases) (14%) and malignant (18 cases) (12%).

Table (9) Histological & cytological results

Histological & cytological results	Current study n=120	Study of Funge et al (25) n=177	Study of Heinz et al (26) n=63
Benign	(103/120) 85.8%	(150/177) 85%	(55/63) 88%
Duct papilloma	(43/120) 35.9%	(78/177) 44%	(28/63) 44%
Fibrocystic disease	(23/120) 19.2%	(25/177) 14%	(9/63) 14%
Duct ectasea	(15/120) 12.5%	(31/177) 18%	(18/63) 28.5%
Inflammatory cells	(12/120) 10%	–	–
Galactorrhea	(10/120) 8.3%	–	–
Malignant	(17/120) 14.2%	(27/177) 15%	(8/63) 12%

List of abbreviation:-

ND	Nipple discharge
TSH	Thyroid stimulating hormone
MRI	Magnetic resonance imaging
FNAC	Fine needle aspiration cytology
DCIS	Ductal carcinoma in situ

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