

RESULTS

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This study was performed on selected 101 thyroid neoplasms, 84 were follicular neoplasms and 17 cases parafollicular C-cell neoplasms (16.8%) that were diagnosed as medullary carcinomas (MC). Follicular neoplasms are subclassified into 23 papillary carcinomas (22.7% PC), 21 follicular carcinomas (20.7% FC), 10 Hurthle cell carcinomas (9.9% HC), 10 anaplastic carcinomas (9.9% AC) and 20 cases of thyroid adenomas (19.8% AD). Seven cases of apparently normal thyroid tissue adjacent to benign tumor area were taken as control.

1 Clinical data:

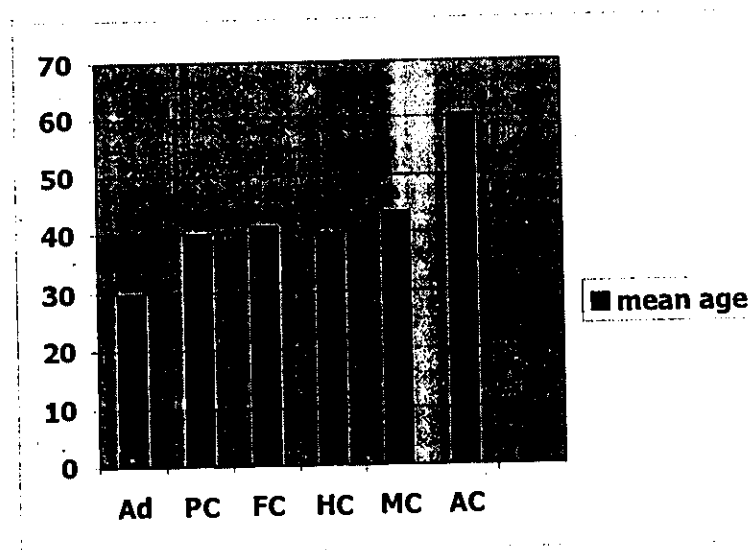
I. Age distribution: Table (8), Graph(1)

- In cases of thyroid adenomas mean age was 29.7 years (range 19-42y). Adenoma with atypia (3 cases) showed mean age 26.7 years (Range 20-35 y).
- PC cases showed mean age 39.8y (range 18-53y).
- The mean age for patients with FC was 41.1year (range 26-73y).
- The mean age for patients with HC was 39.7y (range 28-51y).
- The age of patient with anaplastic carcinoma ranged from 47 years up to 80 years with a mean value 60.4 years.
- The mean age for patients with MC showed mean age 43.5y (range 23-59y).

Table (8): Different age groups in the examined thyroid cases in relation to the histopathological type:

Age group	AD.	PC	FC	HC	MC	AC
10-19y	-	1 (4.4%)	-	-	-	-
20-29y	12 (60%)	4 (17.4%)	3 (14.4%)	1 (10%)	3 (17.7%)	-
30-39y	5 (25%)	6 (26.1%)	7 (33.3%)	4 (40%)	2 (11.7%)	-
40-49y	3 (15%)	5 (21.7%)	7 (33.3%)	4 (40%)	6 (35.3%)	1 (10%)
50-59y	-	4 (17.4%)	2 (9.5%)	1 (10%)	6 (35.3%)	3 (30%)
60-69y	-	3 (13%)	2 (9.5%)	-	-	4 (40%)
70-79y	-	-	-	-	-	1 (10%)
80-89y	-	-	-	-	-	1 (10%)
Mean age	29.7y	39.8y	41.1y	39.7y	43.5y	60.4y
Total	20	23	21	10	17	10

- NB. Cases of adenomas showed the lowest mean age group followed by HC, PC and FC.
- Cases of AC and MC showed the highest mean age respectively.



Graph(1): mean age in relation to the histopathological type.



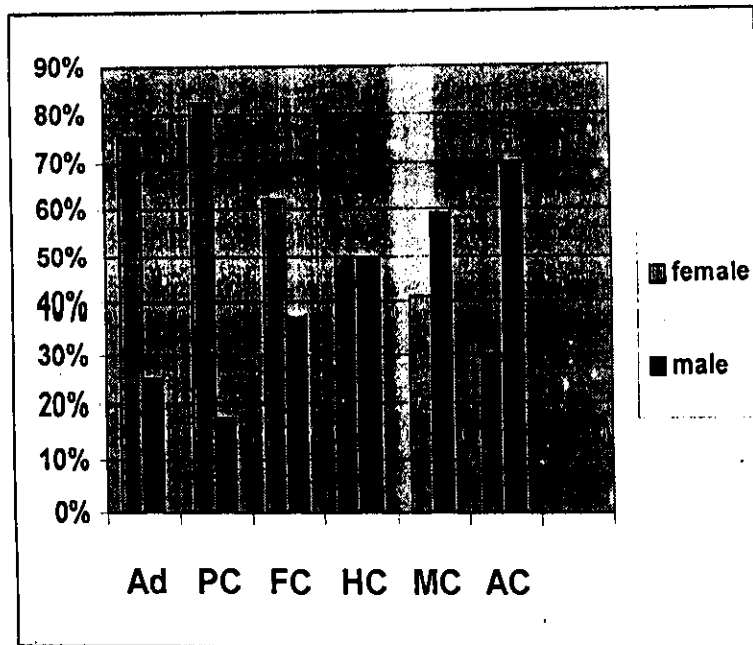
II. The gender of the examined cases: table (9) graph (2).

- Adenomas (20 cases) showed [15 cases (75%) of female gender and five cases (25%) of male gender] with male to female ratio 1:3. Adenomas with atypia (3 cases) [2 cases (66.7%) of female gender and 1 case (33.3%) of male gender] with male to female ratio 1:2.
- PC (23 cases) [19 cases (82.6%) of female gender and 4 cases (17.4%) of male gender] with male to female ratio 1:4.5.
- FC (21 cases) [13 cases (61.9%) of female gender and 8 cases (38.1%) of male gender] with male to female ratio 1 : 1.7
- HC (10 cases) [5 cases (50%) of females and 5 cases (50%) of males] with male to female ratio 1:1.
- MC (17 cases) [10 cases (58.8%) of male gender and 7 cases (41.2%) of female gender] with male to female ratio 1.4 : 1
- AC (10 cases) [7 cases (70%) of male gender and 3 cases (30%) of female gender] with male to female ratio 2.3 : 1.

Table (9): Female and male distribution in relation to the histopathological type of the examined cases :

Hist. Type	Female	Male	Male : Female ratio	Total
AD.	15 (75%)	5(25%)	1 : 3	20
PC	19 (82.6%)	4(17.4%)	1 : 4.5	23
FC	13(61.9%)	8(38.1%)	1 : 1.7	21
HC	5(50%)	5(50%)	1 : 1	10
MC	7(41.2%)	10(58.8%)	1.4 : 1	17
AC	3(30%)	7(70%)	2.3 : 1	10
Total	62 (61.4%)	39(38.6%)	1: 1.5	101

- NB. Low male to female ratio was found In PC followed by AD then FC.
- Equal male to female ratio was present in HC (1 : 1).
- Higher male to female ratio was present in MC and AC.



Graph(2):Female and male distribution in relation to the histological type

III-The tumor size & location for the examined cases:

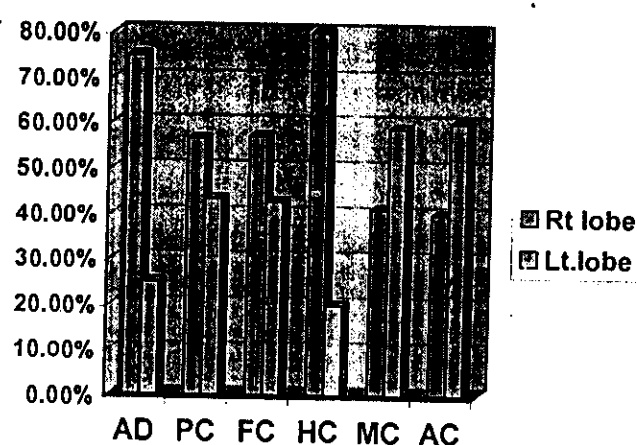
table (10), graph (3).

- All cases of AD including atypical cases showed mean size 2.9cm (range 0.8-6cm) and right lobe location in 15 out of 20 cases (75%).
- Cases of PC showed mean tumor size 3.8cm (range 1.5-7cm) and right lobe location in 13 out of 23 cases (56.5%).
- The mean tumor size for FC was 3.5 cm (range 1.7-7.5cm) and right lobe location in 12 out of 21 cases (57.2%).
- Both HC & MC showed fairly equal mean tumor size (4.7 & 4.8cm) respectively, right lobe location was present in 8 out of 10 HC (80%) and in 7 out of 17 MC (41.2%).
- Cases of AC showed mean tumor size 8.2 cm (range 3-13cm) and right lobe location in 4 out of 10 (40%) of cases examined

**Table (10): Tumor size and location in the histological types examined:**

Histologic type	No. of cases	Tumor size (cm)		Tumor location	
		Range	Mean	Rt. Lobe	Lt. lobe
AD	20	0.8-6	2.9	15 (75%)	5 (25%)
PC	23	1.5-7	3.8	13(56.5%)	10(43.5%)
FC	21	1.7-7.5	3.5	12(57.2%)	9 (42.8%)
HC	10	2-9.5	4.7	8 (80%)	2 (20%)
MC	17	2-9	4.8	7 (41.2%)	10(58.8%)
AC	10	3-13	8.2	4 (40%)	6 (60%)
Total	101	0.8-13	4.7	59(58.5%)	42(41.5%)

- N.B: The mean tumor size was 3.4 cm in AD, 4.3 cm in PC, 4.6 cm in FC, 5.8 cm in HC, 5.5cm in MC, and 8cm in AC.
- Smallest mean tumor size was present in adenomas (2.9cm) and the largest mean size was in AC (8.2cm).
- Tumors in the Rt. thyroid lobe were more frequent (59 cases 58.4%) than left lobe location (41.5%).
- Rt side of the gland was the target side mainly for HC while Lt side was the target for AC and MC respectively.
- MC & AC had the following features in common:
 - Male predominance (male: female ratio 1.4 : 1 & 2.3 : 1 respectively).
 - Older mean age group (43.5 y and 60.4 y) respectively.
 - Affection of the left thyroid lobe more than the right lobe (58.8% and 60% respectively).
 - Larger size of the lesion especially in AC (mean size 8.2cm).

**Graph(3): Tumor side in relation to the histopathological type.**



IV-The lymph node status according to the different malignant groups examined: table (11).

- Studied cases of PC showed lymph node metastases in 20 out of 23 cases (87%).
- FC showed lymph node metastases in 15 out of 21 cases (71.4%).
- Cases of HC showed lymph node metastases in (50%) of cases.
- MC with lymph node metastases were 14 out of 17 cases (82.4%).
- All studied cases of AC showed lymph node metastases (100%).

Table (11): Lymph node status in the different malignant cases examined:

Histo. Type	+ve L.N	-ve L.N	Total
PC	20 (87%)	3 (13%)	23
FC	15 (71.4%)	6 (28.6%)	21
HC	5 (50%)	5(50%)	10
MC	14 (82.4%)	3(17.6%)	17
AC	10 (10%)	0 (0%)	10
Total	64 (79%)	17 (21.9%)	81

- NB. Studied malignant cases showed lymph node metastases in (79%) of cases.
- AC showed the highest percentage of lymph node metastases (100%) of cases.
- HC showed the lowest percentage of lymph node metastases (50%) of cases.



V- The distant metastases in the examined malignant cases in relation to the histopathological type:
table (12)

- Studied cases of PC showed bone metastases in 2 out of 23 cases (8.7%), lung metastases in 5 out of 23 (21.7%) of cases.
- FC showed bone metastases in 10 out of 21 cases (47.6%), lung metastases in 3 out of 21 cases examined (14.3%), simultaneous bone, lung metastases in 2 out of 21 cases (9.5%).
- HC cases showed only lung metastases in 1 out of 10 cases (10%).
- MC showed lung metastases in 4 out of 17 cases (23.5%).
- AC showed bone metastases in 1 out of 10 cases examined (10%) and lung metastases in 4 out of 10 (40%).

Table (12) distant metastases in the examined malignant cases:

Hist. Type	No Met.	Bone met.	Lung met.	Bone, lung met	Total
PC	16(69.6%)	2(8.7%)	5(21.7%)	0(0%)	23
FC	6(28.6%)	10(47.6%)	3(14.3%)	2(9.5%)	21
HC	9(90%)	0 (0%)	1 (10%)	0 (0%)	10
MC	13(76.5%)	0 (0%)	4(23.5%)	0 (0%)	17
AC	5 (50%)	1 (10%)	4 (40%)	0 (0%)	10
Total	49(60.5%)	13(16%)	17(21%)	2 (2.5%)	81

- NB. In the examined cases patients with no metastases(60.5) were more frequent than those showing metastases (39.5%).
- Lung metastases was more frequent (21%) than bone metastases (16%).
- Lung metastases was mostly frequent in AC (40%) of cases and least frequent in HC (10%) of cases.
- Bone metastases was mostly frequent in FC (47.6%).
- FC cases were the only type showed both bone, lung metastases.



VI- The TNM stage according to the different tumors studied: table (13).

- Studied cases of PC were SI in 11 cases (47.8%), SII in 6 cases (26.1%), SIII in 4 cases (17.4%) and SIV in 2 cases (8.7%).
- FC patients (21 cases) were SI in 3 cases (14.3%), SII in 14 cases (66.7%), SIII and SIV in 2 cases (9.5%) for each.
- Examined patients of HC (10 cases) were SI in 5 cases (50%), SII in 4 cases (40%), SIII in 1 case (10%).
- Patients of MC (17 cases) were SI and SII in 2 cases (11.8%) for each, SIII in 9 cases (52.9%) and SIV in 4 cases (23.5%) studied.
- AC (10 cases) were SIV in all (100%) cases studied.

Table (13) TNM stage for the examined malignant cases:

Histo. Type	SI	SII	SIII	SIV	Total
PC	11(47.8%)	6 (26.1%)	4 (17.4%)	2 (8.7%)	23
FC	3 (14.3%)	14(66.7%)	2(9.5%)	2 (9.5%)	21
HC	5 (50%)	4(40%)	1(10%)	0 (0%)	10
MC	2 (11.8%)	2(11.8%)	9 (52.9%)	4 (23.5%)	17
AC	0 (0%)	0(0%)	0(0%)	10 (100%)	10
Total	21(25.9%)	26(32.1%)	16(19.8%)	18(22.2%)	81

VII: Local recurrence in the different tumors examined: table (14)

- Studied adenomas (20 cases) showed local recurrence in 4 cases (20%).
- PC (23 cases) showed local recurrence in 7 cases (30.4%).
- FC (21 cases) showed local recurrence in 9 cases (42.9%).
- HC (10 cases) showed local recurrence in 3 cases (30%).
- MC (17 cases) showed local recurrence in 5 cases (29.4%).



- AC (10 cases) showed local recurrence in 4 cases (40%).

Table (14): Local recurrence in different tumors examined:

Type	No.	Recurrent	No. Rec.
AD	20	4 (20%)	16 (80%)
PC	23	7 (30.4%)	16 (69.6%)
FC	21	9 (42.9%)	12 (57.1%)
HC	10	3 (30%)	7 (70%)
MC	17	5 (29.4%)	12 (70.6%)
AC	10	4 (40%)	6 (60%)
Total	101	32 (31.7%)	69 (68.3%)

- NB. Highest local recurrence rate was present in FC (42.9%) cases.
- Lowest local recurrence rate was present in AD (20%) of cases.

VIII- Patient's overall survival in the malignant tumors: Table (15).

- Alive cases of PC were 14 out of 23 cases (60.9%).
- Alive cases of FC were 8 out of 21 cases (38.2%).
- Alive cases of HC were 7 out of 10 cases (70%).
- Alive cases of MC were 12 out of 17 cases (70.6%).
- Alive cases of AC were 0 out of 10 cases (0%).

Table (15): Patient's overall survival (calculated during 50 month duration) in malignant tumors examined:

Type	No.	Alive	Died
PC	23	14 (60.9%)	9 (39.1%)
FC	21	8 (38.2%)	13 (61.9%)
HC	10	7 (70%)	3 (30%)
MC	17	12 (70.6%)	5 (29.4%)
AC	10	0 (0%)	10 (100%)
Total	81	41 (50.6%)	40 (49.4%)

- N.B: MC showed the highest percentage of alive cases (70.6%) while all cases of AC were died (100%).



2 The histopathological findings:

A-Histopathological analysis for the examined 20 adenomas (AD): Table (16), Fig. (13, 14)

- Studied adenomas were of follicular type, showed atypical features in 3 out of 20 cases (15%).
- All atypical adenoma (100%) showed:
 - Mixed follicle formation and trabecular pattern.
 - Hemorrhage only.
 - Mild colloid secretion.
 - Mild lymphocytic infiltration.
- Adenomas without atypia (17 out of 20 cases) showed colloid secretion in all cases (100%) [++ in 13 cases (76.5%) and +++ in 4 cases (23.5%)] and mild lymphocytic infiltration (+1) in 5 cases (29.4%).

B-Histopathological analysis for the examined 23 papillary carcinomas (Pc) cases: Table (16)

- The subtypes identified in 23 PC studied were 16 (69.9%) of the conventional subtype Fig. (19,20), 1 (4.3%) of the columnar cell variant (CVPC) Fig. (23), 1 (4.3%) of the follicular variant (FVPC), 1 (4.3%) case was papillary microcarcinoma Fig. (22), and 4 (17.3%) cases were of trabecular/solid variant.
- Capsular invasion was present in 19 cases (82.6%).
- Psammoma body formation was present in 11 cases (47.8%) Fig. (21).
- Colloid secretion was mild (+) in 6 cases (26%), moderate (++) in 13 cases (56.5%) and severe (+++) in 4 cases (17.3%).



- Fibrosis was mild in 10 cases (43.4%), moderate in 10 cases (43.4%) and severe (+++) in 3 cases (13.1%).
- Lymphocytic infiltration was mild (+) in 10 cases (43.4%) moderate (++) in 3 cases (13.1%).
- Six cases (26.1%), showed both hemorrhage necrosis, 9 cases (39.1%) showed only hemorrhage.
- Vascular invasion was present in 16 cases (69.5%).
- GI PC were 8 cases (34.7%), GII PC were 11 cases (47.8%) and GIII were 4 cases (71.3%).

C-Histopathological findings in the examined 21 FC cases:
Table (16).

- All the studied cases of FC were widely invasive subtype (100%) of cases, Fig. (30).
- Capsular invasion was present in 19 cases (90.4%), colloid secretion was mild (+) in 7 cases (33.3%), moderate (++) in 9 cases (42.8%) and severe (+++) in 5 cases (23.8%).
- Fibrosis was mild in 11 cases (52.3%), moderate in 8 cases (38.1%) and sever in 1 case (4.7%), while lymphocytic infiltration was mild in 3 cases (14.2%).
- Hemorrhage, necrosis were present simultaneously in 11 cases (52.3%), hemorrhage only was present in 10 cases (47.6%).
- Vascular invasion was seen in 19 cases (90.5%), Fig. (19).
- The examined FC showed GII in 12 cases (57.1%) and GIII in 9 cases examined (4.8%), Fig. (31).

**D-Histopathological findings in the examined 17 MC cases:**

Table (16)

- Fifteen cases were MC with amyloid (88.8%), Fig. (43) while 2 cases were MC with follicle-formation (11.7%).
- Capsular invasion was present in 11 cases (64.7%).
- Colloid secretion was mild in 3 cases (17.6%), moderate in 2 cases (11.7%) and severe in 1 case examined (5.8%).
- Fibrosis was present only in 4 cases examined (mild+) (23.5%), lymphocytic infiltration was seen in 3 cases examined (17.6%) (mild).
- Hemorrhage was present in 12 cases (29.4%).
- Vascular invasion was present in 10 cases examined (37.8%), Fig. (44).
- Five cases out of 17 MC where in GI (29.4%), 9 cases GII (52.9%) and 3 cases were GIII (17.6%), Fig. (45).

E-Histopathological findings in the examined HC (10 cases): Table (16)

- The examined HC showed 8 cases without follicle formation Fig. (38). (80%) and 2 cases were HC with follicle formation (20%), Fig. (39).
- Capsular invasion was present in 9 cases (90%), colloid secretion was mild in 3 cases (30%) and severe in 2 cases (20%).
- Fibrosis was mild in 7 cases (70%) and moderate in 3 cases (30%). Lymphocytic infiltration was seen only in 2 cases (20%).
- Hemorrhage and necrosis were present in 6 cases (60%), hemorrhage only in 2 cases (20%) (moderate ++).



- Vascular invasion was present in 7 cases (70%).
- GI HC were 2 cases (20%), GII were 2 cases (20%) and GIII were 6 cases (60%).

F-Histopathological findings in the examined 10 AC cases:

Table (16)

- Studied Ac showed 5 cases (50%) of giant cell subtype, and 5 cases of mixed round, spindle cell subtype (50%), Fig. (49).
- Capsular invasion was present in 8 cases (80%), mild colloid secretion in 2 cases (20%), mild fibrosis in 8 cases (80%), hemorrhage and necrosis and vascular invasion in all cases (100%).

Table (16) : Histopathological criteria in the examined cases:

Histopathological criteria																										
Subtype	N o.	Caps.		P ^s ammoma		Colloid				Fibrosis				Lymphocytic Infiltration		Hge, Nec.				Vas. Inv.		Gr				
		Pres.	Abs.	P ^s res.	Abs.	-	+	++	+++	-	+	++	+++	-	+	++	-	H	N	HN	Pres	Abs.	I	II		
Ad	20	-	20	-	20	-	3	13	4	20	-	-	-	15	5	-	17	3	-	-	-	20	-	-		
Pc	23	19	4	11	12	-	6	13	4	-	10	10	3	10	10	3	8	9	-	6	16	7	8	11		
Fc	21	19	2	-	21	-	7	9	5	1	11	8	1	18	3	-	-	10	-	11	19	2	-	12		
Hc	10	9	1	-	10	5	3	-	2	-	7	3	-	8	-	2	4	-	6	-	7	3	2	2		
*Mc	17	11	6	-	17	11	3	2	1	13	4	-	-	14	3	-	5	12	-	-	10	7	5	9		
Ac	10	10	-	-	10	8	2	-	-	2	8	-	-	10	-	-	-	-	-	10	10	-	-	-		
Total	101	68	33	11	90	24	24	37	16	36	40	21	4	75	21	5	34	34	6	27	62	39	15	34		

* Amyloid was present in 13 out of 17 cases (76.5%) of the examined Mc.

Key words:

Pres. = Present
 Abs. = Absent
 H = Hemorrhage
 N = Necrosis
 - = Negative
 + = Mild
 ++ = Moderate
 +++ = Severe

**3****Immunohistochemical result:****A. In the control group:**

The apparently normal thyroid tissue adjacent to benign tumor area (control) didn't express cyclin D1 or Bcl-x in the follicular epithelium or the parafollicular c-cells. CD44 was expressed in 7 cases (100%) of the examined 7 control cases.

B. In Adenomas (20 Cases):

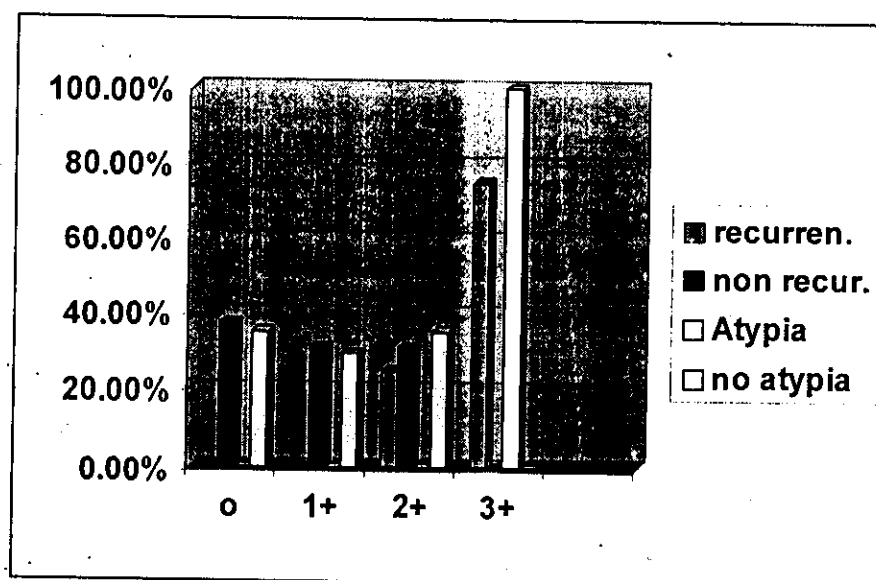
I. Cyclin D1 expression: Table (17), Graph (4), Fig. (16).

- Examined 20 cases of adenoma showed 13 cases (56%) without atypia or local tumor recurrence 3 cases (15%) with atypia and 4 cases (20%) locally recurrent.
- Cases of adenoma showed positive Cyclin D₁ expression in 14 out of 20 cases (70%) [5 cases (25%) were +1, 6 cases (30%) +2, 3 cases +3 expression (5%)].
- Atypical cases of adenomas with atypia showed Cyclin D₁ expression in 3 out of 3 cases (100%) with +3 score.
- All locally recurrent adenomas 4 out of 4 cases (100%) showed positive Cyclin D1 expression [+2 in 1 (2.5%) case and +3 expression in 3 (75%) cases] in relation to 10 out of 16 (62.5%) non recurrent cases showed Cyclin D1 expression [+2 in 5 (31.3%) cases and +1 in 5 (31.3%) cases].

Table(17):Correlation between different clinicopathological entities of adenomas in relation to cyclin D1 expression :

Cl. Path.	Cyclin D ₁ exp.					Total	X2	PV
	0	+1	+2	+3	+4			
Age group								
≤ 40	6(30%)	5(25%)	6(30%)	3(15%)	-	20		
> 40	-	-	-	-	-	-		
Gender								
Female	4(26.7)	3(20%)	6(40%)	2(13.3)	-	15		
Male	2(40%)	2(40%)	-	1(20%)	-	5	3.93	>0.05
Recurrence								
Present	-	-	1(25%)	3(75%)	-	4		
Absent	-	5(31.3)	5(31.2)	-	-	16	14.79	<0.001
Atypia								
+	6(37.5)	-	-	3(100%)	-	3		
-	-	-	-	-	-	-		
Total	6(35.3)	5(29.4)	6(35.3)	-	-	17	20	<0.001
	6 (30%)	5 (25%)	6 (30%)	3 (15%)	-	20		

- NB. Gender was non significantly correlated with Cyclin D₁ expression although females showed high expression (73.3%) than males (60%) ($P>0.01$).
- Locally recurrent adenomas (4 cases) showed highly significant D₁ expression (100%) than non recurrent adenomas (62.5%).
- (Adenomas with atypia showed the highest D₁ expression (+3) with 100% expression in relation to cases without atypia that showed (64.7%) (very highly significant correlation) ($P<0.001$).



Graph(4): Cyclin D1 expression in AD in relation to tumor atypia and local recurrence.

II-Bcl-x expression in adenomas: Table (18), Graph (5), Fig. (17).

- Cases of adenomas showed Bcl-x expression in 18 out of 20 (90%) cases [5 cases (25%) weak (+) intensity, 10 cases (50%) moderate stain (++) Bcl X and 3 cases (15%) strong Bcl-x stain (+++)].
- The 3 cases of adenomas with atypia showed Bcl-x expression (100%) [++ in 1 (33.3%) case and strong Bcl-x (+++) in 2 (66.7%) cases].
- Adenomas without atypia showed Bcl-x expression in 15 out of 17 (88.2%) cases [+ in 5 cases (29.4%) and ++ in 9 cases (52.9%) and +++ was seen in 1 case (5.9%)].
- Locally recurrent adenomas showed Bcl-x expression in 4 out of 4 cases (100%) [++ in 1 case (25%) and strong intensity (+++) in 3 cases (75%)].

III-CD44 expression in adenomas: Table (19), Fig. (18)

- Examined cases of adenomas showed high percentage CD₄₄ expression in 13 out of 20 cases (65%).
- Adenomas with atypia (3 cases) showed high percentage CD₄₄ expression in 2 cases (66.7%). Adenoma without atypia showed high CD44 expression in 11 out of 17 cases (64.7%).
- Locally recurrent adenomas showed high expression in 2 out of 4 cases (50%).

Table(19): Correlation between different clinicopathological variants in adenomas in relation to CD₄₄ expression :

Cl. Path.	CD ₄₄ expression		Total	X2	PV
	Low (1-66%)	High (67-110%)			
<u>Age group</u>					
≤ 40	7 (35%)	13 (65%)	20	-	-
> 40	-	-			
<u>Gender</u>					
Female	6 (40%)	9 (60%)	15	0.66	>0.05
Male	1 (20%)	4 (80%)	5		
<u>Local R.</u>					
+	2 (50%)	2 (50%)	4	0.49	>0.05
-	5 (31.2%)	11 (68.7%)	16		
<u>Atypical</u>					
+	1 (33.3%)	2 (66.7%)	3	0.004	>0.05
-	6 (35.3%)	11 (64.7%)	17		
Total	7 (35%)	13 (65%)	20		

- NB. Non significant correlation was present with CD44 expression in relation to patient's age, gender, local recurrence and atypia.

C. In papillary carcinoma (PC):**I-Cyclin D1 expression in PC: Table(20), Graph(6), Fig. (24,25)**

- **In relation to patients age:** cases of PC ≤ 40 years showed Cyclin D1 expression in 11 out of 17 (64.7%) cases [4 cases (23.5%) +2, 5 cases (29.4%) + 3 score and 2 cases (11.7%) showed + 4 cyclin D₁ expression]. Cases of PC > 40 years showed Cyclin D1 expression in 5 out of 6 patients (83.3%)



[+1 in 1 cases (16.7%) case, + 3 in 2 cases (33.3%) and +4 in 2 cases (33.3%) cases].

- **In relation to patient's gender:** females showed Cyclin D₁ expression in 14 out of 19 cases (73.6%) [1 case (5.3%) + 1, 4 cases (21.1%) + 2, 6 cases (31.6%)+3, and 3 (15.7%) cases + 4]. Males showed Cyclin D₁ expression in 2 out of 4 cases (50%) [1 case (25%) + 3 and 1 case (25%) + 4].
- **In relation to tumor grade:** **GI** PC showed Cyclin D₁ expression in 4 out of 8 cases (50%) [1 case (12.5%) was + 1, 2 cases (25%) were + 2, 1 case (12.5%) was + 3].

GII PC showed Cyclin D₁ expression in 8 out of 11 (72.7%) [2 cases (18.2%) were + 2, 5 cases (45.5%) were + 3 and 1 case (9.1%) was + 4]. All **GIII** PC showed Cyclin D₁ expression in 4 out of 4 (100%) cases [+ 3 in 1 case (25%) and +4 in 3 cases (75%)].

- **In relation to patient's TNM stage:** **SI** PC showed Cyclin D₁ expression in 8 out of 11 cases (72.7%), [1 (9.1%) cases + 2 expression, 4 cases (36.3%) + 3 expression and 3 cases (27.3%) + 4 expression].

SII PC showed Cyclin D₁ expression in 3 out of 6 cases (50%) [+1 in 1 case (16.7%) and 2 cases (33.3%) showed + 2 Cyclin D₁ expression].

SIII PC showed Cyclin D₁ expression in 3 out of 4 cases (75%), [1 case (25%) + 2, 2 cases (50%) showed + 3].

SIV PC showed Cyclin D₁ expression in 2 out of 2 (100%) of cases [1 case (50%) showed + 3 and 1 case (50%) showed + 4].



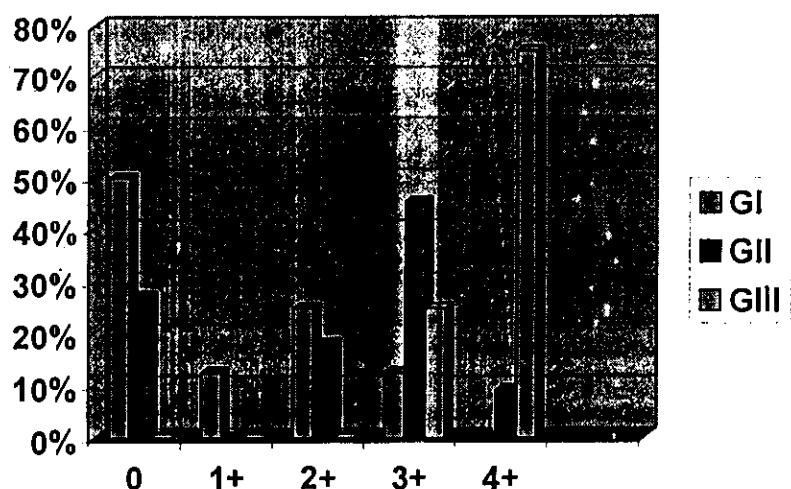
- **In relation to local tumor recurrence:** locally recurrent PC showed Cyclin D₁ expression in 5 out of 7 cases (71.4%), [2 cases (28.5%) were + 2 and 3 cases (42.8%) were + 3]. Non recurrent cases showed Cyclin D₁ expression in 11 out of 16 (68.7%) cases. [1 case (6.2%) was + 1, 2 cases (12.5%) were +2, 4 cases (25%) were + 3 and 4 cases (25%) were + 4 D₁ expression].

- **In relation to patients survival:** alive cases of PC showed Cyclin D₁ expression in 8 out of 14 cases (57.1%) [+ 1 in 1 case (7.1%), + 2 in 2 cases (14.2%), + 3 in 4 cases (28.5%) and + 4 Cyclin D₁ expression in 1 case (7.1%)]. Died cases of PC showed D₁ expression in 8 out of 9 cases (88.8%) [+ 2 in 2 cases (22.3%), +3 and +4 in 3 cases (33.3%) for each].

Table(20):Correlation between different clinicopathological entitles of PC in relation to cyclin D₁ expression :

Cl. Path.	Cyclin D ₁ exp.					Total	X2	PV
	0	+1	+2	+3	+4			
Age group								
<40	6(35.3%)	-	4 (23.5%)	5(29.4%)	2(11.8%)	17	5.96	>0.05
≥40	1(16.7%)	1(16.7%)	-	2 (33.3%)	2(33.3%)	6		
Gender								
Female	5(26.3%)	1(5.3%)	4(21.1%)	6(31.6%)	3(15.7%)	19	1.87	>0.05
Male	2(50%)	-	-	1(25%)	1(25%)	4		
Grade								
I	4(50%)	1(12.5%)	2(25%)	1(12.5%)	-	8	16.26	<0.05
II	3(27.3%)	-	2(18.2%)	5(45.5%)	1(9.1%)	11		
III	-	-	-	1(25%)	3(75%)	4		
IV	-	-	-	-	-	-		
Recurrence								
Present	3(27.2%)	-	1(9.1%)	4(36.3%)	3(27.3%)	11	12.35	>0.05
Absent	3(50%)	1(16.7%)	2(33.3%)	-	-	6		
Survival								
Alive	1(25%)	-	1(25%)	2(50%)	-	4		
Died	-	-	-	1(50%)	1(50%)	2		
Total	7	1	4	7	4	23		

- NB. Both age, gender, stage, local recurrence and overall survival showed non significant correlation with Cyclin D₁ expression. (P<0.005).
- GIII PC₁ showed higher expression D₁ (100%) in relation to GII PC (72.7%) and GI PC (50%) (Significant positive correlation).(P<0.05).



Graph(6): Cyclin D1 expression in PC in relation to tumor grade.

**II-Bcl-x expression in PC:** Table (21), Graph (7), Fig. (26).

- **In relation to the patients age:** cases of PC \leq 40 years showed Bcl-x expression in 15 out of 17 cases (88.2%) [weak Bcl-x expression in 3 cases (42.8%), moderate expression in 7 cases (41.3%) and strong Bcl-x expression in 5 cases examined (29.4%)]. PC > 40 years showed Bcl-x expression in 5 out of 6 cases (83.8%) [+ Bcl-x expression in 1 case (16.6%), ++ in 3 cases (50%) and +++ in 1 case (16.6%)].
- **In relation to the patients gender:** female gender of PC showed Bcl-x expression in 16 out of 19 cases (84.2%) [weak + in 3 females (15.7%), moderate ++ in 8 cases (42.3%) and strong +++ in 5 cases (26.3%)]. Males showed Bcl-x expression in 4 out of 4 cases (100%) [1 case (25%) was +1, 2 cases (50%) were ++ and 1 case (25%) was +++].
- **In relation to tumor grade: GI** PC cases showed Bcl-x expression in 6 out of 8 cases (75%) [weak (+) expression in 2 cases (25%), moderate expression (++) in 3 cases (37.5%) and strong +++ expression in 1 case (12.5%)].
GII PC showed Bcl-x expression in 10 out of 11 cases (90.9%), [weak expression + in 1 case (9.1%), moderate expression ++ in 6 cases (54.5%) and strong expression +++ in 3 cases (27.2%)].
GIII PC showed Bcl-x expression in 4 out of 4 cases (100%) [weak expression + in 1 case (25%), moderate expression ++ in 1 case (25%) and strong expression +++ in 2 cases (50%)].
- **In relation to the patients TNM stage:** Bcl-x expression was seen in 9 out of 11 cases (81.8%) **SI** PC [weak + in 2

**II-Bcl-x expression in PC:** Table (21), Graph (7), Fig. (26).

- **In relation to the patients age:** cases of PC ≤ 40 years showed Bcl-x expression in 15 out of 17 cases (88.2%) [weak Bcl-x expression in 3 cases (42.8%), moderate expression in 7 cases (41.3%) and strong Bcl-x expression in 5 cases (29.4%)]. PC > 40 years showed Bcl-x expression in 5 out of 6 cases (83.8%) [+ Bcl-x expression in 1 case (16.6%), ++ in 3 cases (50%) and +++ in 1 case (16.6%)].
- **In relation to the patients gender:** female gender of PC showed Bcl-x expression in 16 out of 19 cases (84.2%) [weak + in 3 females (15.7%), moderate ++ in 8 cases (42.3%) and strong +++ in 5 cases (26.3%)]. Males showed Bcl-x expression in 4 out of 4 cases (100%) [1 case (25%) was +, 2 cases (50%) were ++ and 1 case (25%) was +++].
- **In relation to tumor grade: GI** PC cases showed Bcl-x expression in 6 out of 8 cases (75%) [weak (+) expression in 2 cases (25%), moderate expression (++) in 3 cases (37.5%) and strong +++ expression in 1 case (12.5%)].
GII PC showed Bcl-x expression in 10 out of 11 cases (90.9%), [weak expression + in 1 case (9.1%), moderate expression ++ in 6 cases (54.5%) and strong expression +++ in 3 cases (27.2%)].
GIII PC showed Bcl-x expression in 4 out of 4 cases (100%) [weak expression + in 1 case (25%), moderate expression ++ in 1 case (25%) and strong expression +++ in 2 cases (50%)].
- **In relation to the patients TNM stage:** Bcl-x expression was seen in 9 out of 11 cases (81.8%) **SI** PC [weak + in 2



cases (18.1%), ++ in 4 cases (36.4%) and strong +++ in 3 (27.2%).

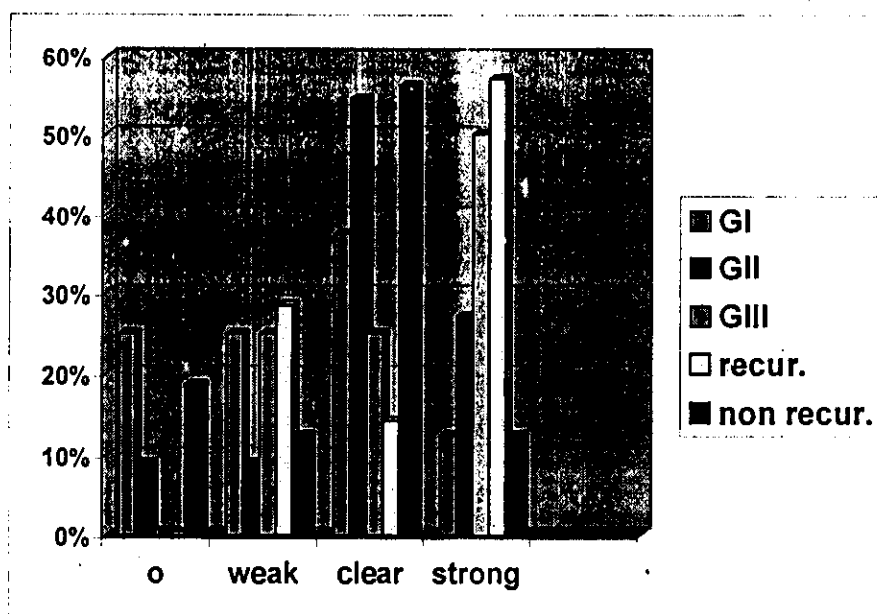
SII PC showed Bcl-x expression in 5 out of 6 cases (83.3%) [+ in 1 case (16.7%), ++ in 2 cases (33.3%) and +++ in 2 cases (33.3%).

SIII PC showed Bcl-x expression in 4 out of 4 cases (100%) [+ in 1 case (25%), ++ in 2 (50%) cases and +++ in 1 case (25%).

SIV PC showed Bcl-x expression in 2 out of 2 cases (100%) with ++ intensity.

- **As regard relation to local recurrence:** locally recurrent cases of PC showed positive Bcl-x expression, in 7 out of 7 cases (100%) [+ expression in 2 cases (28.5%), 1 case (14.3%) showed moderate Bcl-x strain ++ and 4 cases (57.1%) showed strong +++ strain]. Non recurrent PC showed Bcl-x expression in 13 out of 16 cases (81.3%). [+ expression in 2 cases (12.5%), moderate expression ++ in 9 cases (56.2%) and strong expression in 2 cases (12.5%).

- **In relation to patients survival:** alive PC showed Bcl-x expression in 11 out of 14 cases (78.5%) [+ Bcl-x expression in 3 cases (21.4%), moderate ++ expression in 6 cases (42.9%) and strong +++ expression in 2 cases (14.2%)]. Died cases showed Bcl-x expression in 9 cases (100%) [+ Bcl-x expression in 1 case (11.2%), moderate Bcl-x ++ in 4 cases (44.4%) and strong (+++) Bcl-x in 4 cases (44.4%)].



Graph(7): Bcl-x expression in PC in relation to tumor grade and local recurrence.

III-CD44 Expression in PC: Table(22), Graph(8), Fig.(27,28, 29).

- **Concerning the CD₄₄ expression in relation to age:** PC, patients ≤ 40 years showed high expression in 14 out of 17 cases (82.4%). Patients of PC > 40 years showed high expression in 1 out of 6 cases (16.7%).
- **In relation to gender:** high CD₄₄ expression was present in 12 out of 19 females (63.1%) and in 3 of 4 males (75%).
- **As regard tumor grade:** **GI** PC showed high CD₄₄ expression in 7 out of 8 cases (87.5%). **GII** showed high CD₄₄ expression in 7 out of 11 cases (63.6%) while **GIII** showed high CD₄₄ expression in 1 out of 4 cases (25%).
- **As regard relation between CD₄₄ and TNM stage in PC:**
 - SI** PC showed high CD₄₄ expression in 11 out of 11 cases (100%).
 - SII** PC showed high expression in 3 out of 6 cases (50%).
 - SIII** PC showed high expression in 1 out of 4 cases (25%).
 - SIV** PC didn't show high CD₄₄ expression.



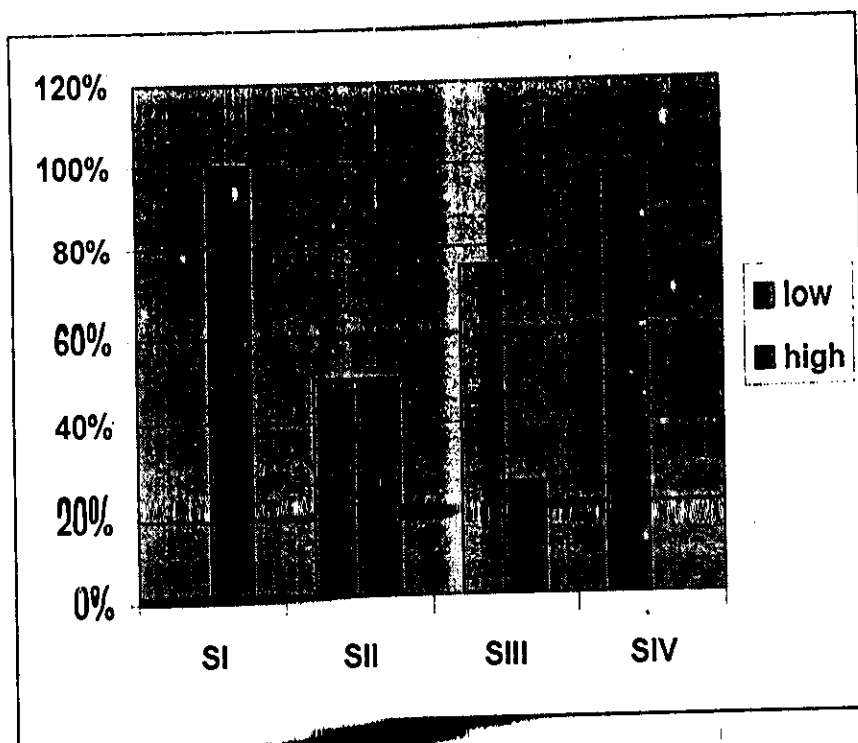
- **In relation to local tumor recurrence:** locally recurrent PC showed high CD44 expression in 3 out of 7 cases (42.9%) while non recurrent cases showed high expression in 12 out of 16 cases (75%).
- **As regard patients survival:** alive cases of PC showed high CD44 expression in 11 out of 14 cases (78.6%) while died cases showed high CD44 expression in 4 out of 9 cases (44.4%).



Table(22): Correlation between different clinicopathological entities of PC in relation to CD₄₄ expression :

Cl. Path.	CD ₄₄ expression		Total	X ²	PV
	Low (1-66%)	High (67-110%)			
Age group					
≤ 40	3(17.6%)	14(82.4%)	17	8.44	<0.05
> 40	5(83.3%)	1(16.7%)	6		
Gender					
Female	7(36.8%)	12(63.2%)	19	0.20	>0.05
Male	1(25%)	3(75%)	4		
Grade					
I	1(12.5%)	7(87.5%)	8	4.61	>0.05
II	4(36.4%)	7(63.6%)	11		
III	3(75%)	1(25%)	4		
Stage :					
I	-	11(100%)	11	13.08	<0.05
II	3(50%)	3(50%)	6		
III	3(75%)	1(25%)	4		
IV	2(100%)	-	2		
Recurrence					
Present	4(57.1%)	3(42.9%)	7	2.22	>0.05
Absent	4(25%)	12(75%)	16		
survival					
alive	3(21.4%)	11(78.6%)	14	2.81	>0.05
dead	5(55.6%)	4(44.4%)	9		
Total	8(34.8%)	15(65.2%)	23		

- NB. PC ≤40 years showed higher expression of CD₄₄ (82.3%) than patients > 40 years (non significant correlation).
- Males of PC showed 75% high CD₄₄ expression while females showed 63.1% CD₄₄ expression. This revealed higher expression in males but it was non significant.
- Non significant inversely proportionate relationship was present between CD44 expression and tumor grade in PC.
- High CD44 expression was present in 100% SI PC, in 50% SII PC, in 25% SIII PC, and not seen in SIV case this revealed significant inverse correlation between tumor TNM stage and high CD₄₄ expression (PV < 0.05).
- Non significant higher CD₄₄ expression in non recurrent PC and alive cases in relation to locally recurrent cases and died cases.



Graph(8): CD44 expression in PC in relation to tumor stage.

D-In follicular carcinoma (FC)

I-Cyclin D1 expression in (FC): Table(23),Graph(9),Fig. (33, 34).

- **In relation to patients age:** FC cases ≤ 40 years showed positive Cyclin D₁ expression in 11 out of 17 (64.7%) cases [+ 1 in 2 cases (11.8%), + 2 in 4 cases (23.5%), + 3 in 3 cases (17.7%) and +4 expression in 2 cases (11.7%)]. FC cases > 40 years were positive for Cyclin D₁ expression in 3 out of 4 cases (75%) [+ 2 in 1 case (25%), + 3 in 1 case (25%) and + 4 in 1 case (25%)].

- **As regard patients gender:** positive Cyclin D₁ expression was present in 8 out of 13 females (69.2%) [+ 1 in 2 cases (15.4%), +2 in 3 cases (23.1%), + 3 expression in 1 case (7.6%), +4 in 2 cases (15.4%)]. Positive Cyclin D1 expression was present in 6 out of 8 males (75%) [+2 in 2 cases (25%), +3 in 3 cases (37.5%) and + 4 in 1 case (12.5%) examined].



- As regard relation between D₁ expression and grade of

FC : GII FC were positive for D₁ expression in 5 out of 12 cases (41.7%) [+ 1 in 2 cases (16.7%), + 2 in 2 cases (16.7%), + 3 in 1 case (8.3%)]. **GIII** FC showed positive Cyclin D₁ expression in 9 out of 9 cases (100%) [+ 2 in 3 cases (33.3%), + 3 in 3 cases (33.3%) and + 4 in 3 cases (33.3%)].

- In relation to patients TNM stage in FC: SI FC showed positive Cyclin D₁ expression in 2 out of 3 cases (66.6%) [+ 1 expression in 1 case (33.3%) and + 2 in 1 case (33.3%)].

SII FC showed positive Cyclin D₁ expression in 9 out of 14 cases (64.3%) [+ 1 in 1 case (7.1%), + 2 in 4 cases (28.6%), + 3 in 2 cases (14.3%) and + 4 in 2 cases (14.3%)].

SIII FC showed positive Cyclin D₁ expression in 2 out of 2 cases (100%) [+ 3 D₁ expression in 1 case (50%) and + 4 in 1 case (50%)].

SIV FC showed positive Cyclin D₁ expression in 1 out of 2 cases (50%) with + 3 expression.

- Concerning the relation between Cyclin D₁ expression and local recurrence in FC: locally recurrent cases showed positive Cyclin D₁ expression in 7 out of 9 cases (77.8%) [+ 1 in 1 case (11.1%), + 2 D₁ in 4 cases (44.5%), + 3 and + 4 in 1 case for each (11.1%)]. Non locally recurrent cases showed positive Cyclin D₁ expression in 7 cases (58.4%) [+ 1 and +2 in 1 case (8.3%) for each, + 3 in 3 cases (25%) and + 4 in 2 cases (16.7%)].

- In relation to patients survival: alive cases of FC showed positive Cyclin D₁ expression in 5 out of 8 cases (62.5%) [+ 1

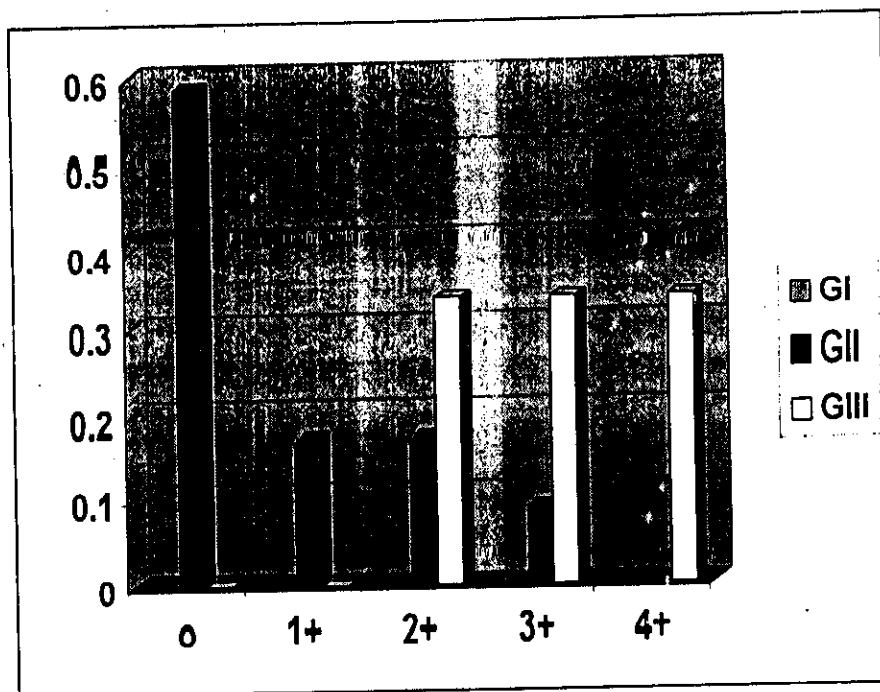


in 1 case (12.5%), + 2 in 2 cases (25%), + 3 and + 4 in 1 case for each (12.5%)). Died FC showed positive D₁ expression in 9 cases (69.2%) [+ 1 in 1 case (7.7%), + 2 and + 3 in 3 cases (23.1%) for each and + 4 in 2 cases (15.4%)].

Table(23):Correlation between different clinicopathological entities of FC in relation to cyclin D₁ expression.

Cl. Path. variants	Cyclin D ₁ exp.					Total	X2	PV
	0	+1	+2	+3	+4			
Age								
<40	6(35.3%)	2(11.8%)	4(23.5%)	3(17.7%)	2(11.7%)	17	1.66	>0.05
>40	1(25%)	-	1(25%)	1(25%)	1(25%)	4		
Gender								
Female	5(38.5%)	2(15.4%)	3(23.1%)	1(7.6%)	2(15.4%)	13	3.85	>0.05
Male	2(25%)	-	2(25%)	3(37.5%)	1(12.5%)	8		
Grade								
I	-	-	-	-	-	-	13.0	<0.05
II	7(58.3%)	2(16.7%)	2(16.7%)	1(8.3%)	-	12	4	
III	-	-	3(33.3%)	3(33.3%)	3(33.3%)	9		
Stage :								
I	1(33.3%)	1(33.3%)	1(33.3%)	-	-	3		>0.05
II	5(35.7%)	1(7.1%)	4(28.6%)	2(14.3%)	2(14.3%)	14	9.56	
III	-	-	-	1(50%)	1(50%)	2		
IV	1(50%)	-	-	1(50%)	-	2		
Recurrence								
Present	2(22.2%)	1(11.1%)	4(44.5%)	1(11.1%)	1(11.1%)	9		>0.05
Absent	5(41.7%)	1(8.3%)	1(8.3%)	3(25%)	2(16.7%)	12	4.7	
Survival								
alive	3(37.5%)	1(12.5%)	2(25%)	1(12.5%)	1(12.5%)	8		>0.05
dead	4(30.7%)	1(7.7%)	3(23.1%)	3(23.1%)	2(15.4%)	13	0.52	
Total	7 (33.3%)	2 (9.5%)	5 (23.3%)	4 (19%)	3 (14.2%)	21		

- NB. FC ≤ 40 years showed 64.7% Cyclin D₁ expression in relation to higher cyclin D₁ expression (75%) in patients < 40years (non significant correlation).
- Males showed non significant higher Cyclin D₁ expression (75%) in relation to females (61.5%).
- Cases with GII FC showed 58.3% Cyclin D₁ expression in relation to GIII FC showed 77.7% D₁ expression. This revealed significant direct proportionate correlation with tumor grade (PV < 0.05).
- Cases with positive local recurrence revealed non significant higher cyclin D₁ expression (77.7%) than non recurrent cases (58.3%).
- Alive cases showed non significant lower D₁ expression (62.5%) than died cases (69.2%).



Graph(9): Cyclin D1 expression in FC in relation to tumor grade.

II-Bcl-x expression in FC: Table (24), Graph (10), Fig. (35).

- **In relation to patients age :** FC ≤ 40 years showed positive Bcl-x expression in 16 out of 17 cases (94.1%) [+in 8 cases (47.1%), ++ in 4 cases (23.5%), +++ in 4 cases (23.5%)]. FC cases > 40 years showed Bcl-x expression in 3 out of 4 cases (75%) with ++ stain.
- **As regard relation to gender:** females of FC cases showed positive Bcl-x expression in 11 out of 13 cases (84.6%) [+in 4 (30.8%) cases, ++ in 5 cases (38.4%) and +++ in 2 cases (15.4%)]. Males FC cases showed Bcl-x expression in 8 out of 8 (100%) cases [+in 4 cases (50%), ++ and +++ expression in 2 cases (25%)].
- **Relation between Bcl-x expression and grade of FC :** Positive Bcl-x expression was present in 10 out of 12 cases (83.3%) **GII** FC [+in 6 cases (50%) and moderate ++ in 4 cases (33.3%)]. **GIII** FC showed Bcl-x expression in 9 out of 9 (100%) cases [+in 2 cases (22.2%), ++ in 3 (33.3%) and +++ Bcl-x expression in 4 cases (44.5%)].



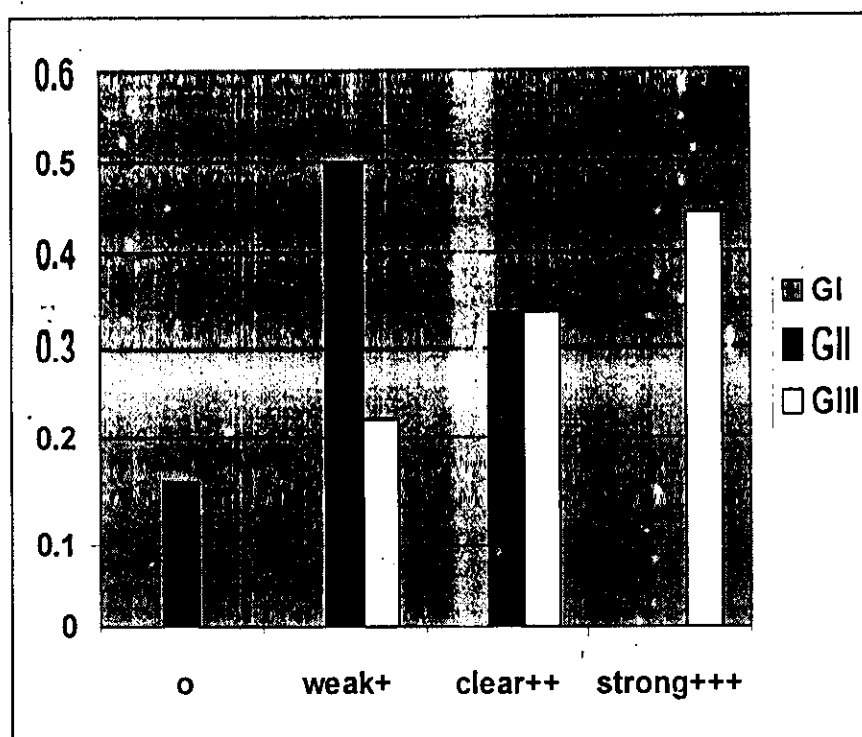
- **Bcl-x expression and stage of FC:** Positive Bcl-x expression was present in 2 out of 3 (66.7%) **SI** FC [+in 1 (33.3%) case and ++ in 1 case (33.3%)].
SII FC showed Bcl-x expression in 13 out of 14 cases (92.9%) [+ weak in 6 cases (42.9%), moderate in 3 cases (21.4%) and strong in 4 cases (28.6%)].
SIII FC showed Bcl-x expression in 2 out of 2 cases (100%) with moderate intensity.
SIV FC showed Bcl-x expression in 2 out of 2 (100%) cases [+ in 1 case (50%) and ++ in 1 case (50%)].
- **In relation to local recurrence:** FC with local recurrence showed positive Bcl-x expression in 9 out of 9 cases (100%) [+ , ++ and +++ Bcl-x expression in 3 cases (33.3%) for each of them]. Non recurrent cases showed positive Bcl-x expression in 10 out of 12 cases (83.3%) [weak in 5 cases (41.7%), moderate in 4 cases (33.3%) and strong in 1 case (8.3%)].
- **In relation to patients survival:** positive Bcl-x expression was present in 6 out of 8 cases (75%) of alive FC [+in 3 cases (37.5%) and ++ in 3 cases (37.5%)]. Died FC showed positive Bcl-x expression in 13 out of 13 cases (100%) [weak in 5 cases (38.5%), moderate and strong in 4 cases (30.8%) for each].



Table(24): Correlation between different clinicopathological variables of FC in relation to Bcl-x expression :

Clinico/ Pathological	Bcl-X				Total	X2	PV
	0	Weak +	Moderate ++	Strong +++			
Age							
≤ 40	1(5.9%)	8(47.1%)	4(23.5%)	4(23.5%)	17	6.64	> 0.05
> 40	1(25%)	-	3(75%)	-	4		
Gender							
Female	2(15.4%)	4(30.8%)	5(38.4%)	2(15.4%)	13	2.22	> 0.05
Male	-	4(50%)	2(25%)	2(25%)	8		
Grade							
I	-	-	-	-	-	7.87	< 0.05
II	2(16.7%)	6(50%)	4(33.3%)	-	12		
III	-	2(22.2%)	3(33.3%)	4(44.5%)	9		
Stage							
I	1(33.3%)	1(33.3%)	1(33.3%)	-	3	6.62	> 0.05
II	1(7.1%)	6(42.9%)	3(21.4%)	4(28.6%)	14		
III	-	-	2(100%)	-	2		
IV	-	1(50%)	1(50%)	-	2		
Recurrence							
Present	-	3(33.3%)	3(33.3%)	3(33.3%)	9	3.28	> 0.05
Absent	2(16.7%)	5(41.7%)	4(33.3%)	1(8.3%)	12		
survival							
alive	2(25%)	3(37.5%)	3(37.5%)	-	8	5.78	> 0.05
died	-	5(38.5%)	4(30.8%)	4(30.8%)	13		
Total	2 (9.5%)	8 (38.1%)	7 (33.3%)	4 (19.1%)	21		

- N.B. Patients of FC ≤ 40 years showed non significant higher Bcl-x expression (94.1%) in relation to patients > 40 years (75%).
- Males showed 100% Bcl-x expression in relation to 84.6% in females (non significant correlation).
- GII FC showed 83.3% Bcl-x expression in relation to 100% expression in GIII tumors this revealed significant direct proportionate relationship ($P < 0.05$).
- SI FC showed 66.6% Bcl-x expression in relation to 92.8% Bcl-x expression in SII tumors. SIII, SIV showed 100% Bcl-x expression. This correlation revealed non significant direct proportional relationship.
- Locally recurrent cases showed non significant higher expression (100%) than non recurrent cases (83.3%)
- Alive cases showed 75% Bcl-x expression while died cases showed higher Bcl-x expression (100%) (non significant correlation).



Graph(10): Bcl x expression in FC in relation to tumor grade.

III-CD44 expression in FC: table (25), Graph (11), Fig.(36,37),

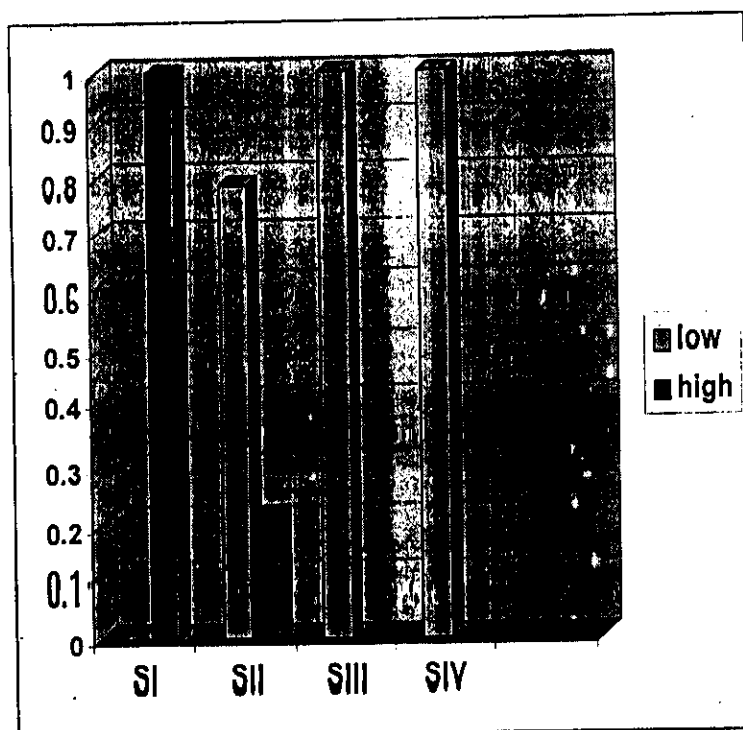
- **In relation to patients age:** high CD₄₄ expression was present in 4 out of 17 cases (23.5%), FC ≤ 40 years and in 2 out of 4 (50%) FC > 40 years.
- **In relation to gender:** high CD₄₄ expression was present in 3 out of 13 females (23%) and in 3 out of 8 males (37.5%).
- **As regard tumor grade:** high CD₄₄ expression was present in 4 out of 12 cases (33.3%) **GII** FC and in 2 out of 9 (22.2%) **GIII** FC.
- **CD₄₄ expression and stage of FC :** High CD₄₄ expression was present in 3 out of 3 (100%) **SIFC**, in 3 out of 14 (21.4%) **SII** cases.
- **In relation to local tumor recurrence:** locally recurrent FC showed high expression in 2 out of 9 (22.2%) cases while non recurrent FC showed high expression in 4 out of 12 cases (33.3%).
- **In relation to patients survival:** alive FC showed high CD₄₄ expression 4 out of 8 (50%) cases. Died FC showed high CD₄₄ expression in 2 out of 13 (15.4%) cases examined.



Table(25): Correlation between different clinicopathological variables of FC in relation to CD₄₄ expression:

Cl. Path. variable	CD ₄₄ expression		Total	X2	PV
	Low (1-66%)	High (67-100%)			
Age					
≤ 40	13 (76.5%)	4(23.5%)	17	1.1	>0.05
> 40	2 (50%)	2(50%)	4		
Gender					
Female	10 (76.9%)	3(23.1%)	13	0.51	>0.05
Male	5 (62.5%)	3(37.5%)	8		
Grade					
I	-	-	-	0.31	>0.05
II	8(66.7%)	4(33.3%)	12		
III	7(77.8%)	2(22.2%)	9		
Stage					
I	-	3(100%)	3	9.45	<0.05
II	11(78.6%)	3(21.4%)	14		
III	2(100%)	-	2		
IV	2(100%)	-	2		
Recurrence					
present	7(77.8%)	2(22.2%)	9	0.31	>0.05
absent	8(66.7%)	4(33.3%)	12		
survival					
alive	4(50%)	4(50%)	8	2.91	>0.05
dead	11(84.6%)	2(15.4%)	13		
Total	15(71.4%)	6(28.6%)	21		

- N.B. Patients > 40 years of FC showed non significant higher CD₄₄ expression (50%) than FC > 40 years (29.5%).
- Males showed higher CD₄₄ expression (37.5%) than females (23%) (non significant).
- Cases with GII FC showed higher CD₄₄ expression (33.3%) followed by GIII FC that showed less CD₄₄ expression (22.2%) this revealed non significant inverse proportionate relationship.
- Cases with SI FC showed 100% high CD₄₄ expression in relation to 21.4% high CD₄₄ expression in SII FC and 0% high CD₄₄ expression in SIII tumors. This revealed inversely proportionate relationship which is significant (P< 0.05).
- Cases with local recurrence showed lower CD₄₄ expression (22.2%) than non recurrent cases (33.3%) but this is non significant.
- Alive Cases showed higher CD₄₄ expression (50%) than died cases (15.3%) (non significant).



Graph(11): CD44 expression in FC in relation to tumor stage

E-In Hurthle cell carcinoma (HC):

I-Cyclin D1 expression in (HC): Table(26), Graph(12), Fig. (40).

- **In relation to patients age:** positive Cyclin D₁ expression was present in 6 out of 8 (75%) HC ≤ 40 years [+1 in 3 cases (37.5%) and +2 in 3 cases (37.5%)]. HC > 40 years showed Cyclin D1 expression in 1 out of 2 cases (50%) with + 1 score.
- **In relation to gender:** females of HC showed positive D₁ expression in 4 out of 5 (80%). [+ 1 in 1 case (20%) HC and + 2 in 3 cases (60%)]. Males showed positive Cyclin D₁ expression in 3 out of 5 cases (60%). [+ 1 in 2 cases (40%), and +2 in 1 case (20%)].
- **In relation to tumor grade:** **GII** HC showed positive D₁ expression in 2 and of 3 cases (66.7%) with + 1 score.
GIII HC showed positive D₁ expression in 5 out of 5 (100%) of cases examined [+ 1 in 1 case (20%) and + 2 in 4 cases (80%)].

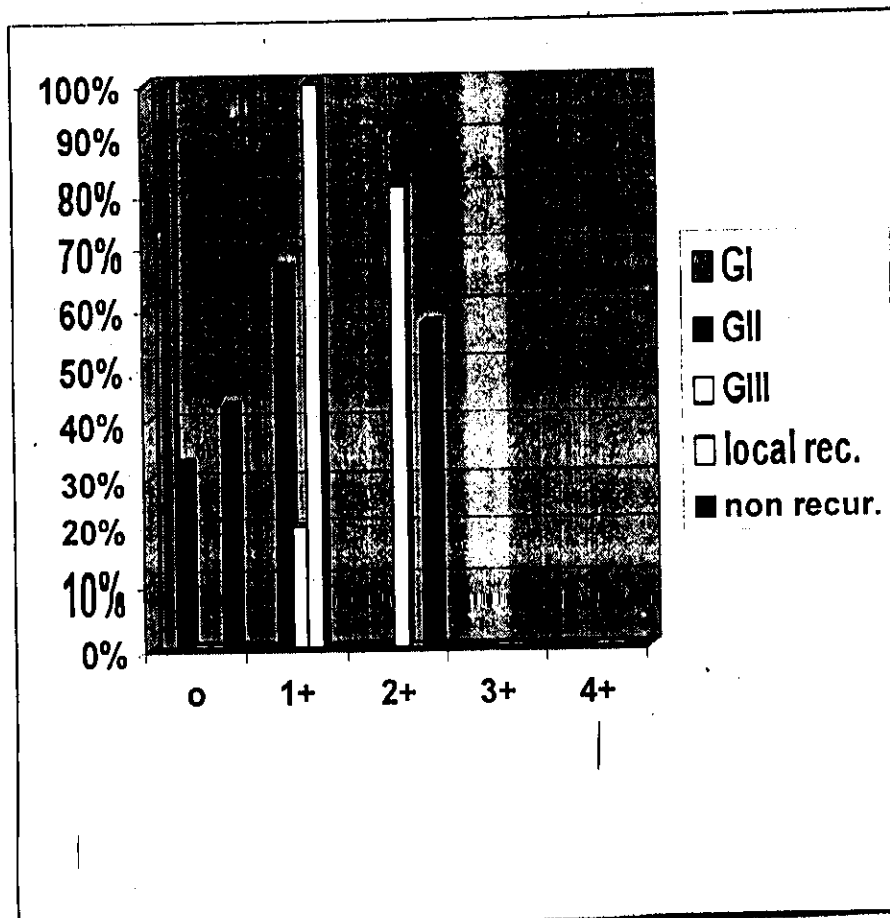


- **As regard TMN stage: SI** HC showed positive Cyclin D₁ expression in 4 out of 5 cases (80%) [+ 1 expression in 2 cases (40%) and + 2 expression in 2 cases (40%)].
SII HC showed positive Cyclin D₁ expression in 3 cases (75%), [+ 1 in 1 case (25%), + 2 in 2 cases (50%)].
- **In relation to local tumor recurrence:** locally recurrent HC showed positive CyclinD₁ expression in 3 out of 3 (100%) cases with + 1 score while non recurrent cases were positive for Cyclin D₁ expression in 4 out of 7 cases (57.1%), with + 2 score.
- **In relation to patients survival:** alive HC showed positive Cyclin D₁ expression in 4 out of 7 cases examined (57.2%) [+1 and + 2 in 2 case (28.5%) for each]. Died HC showed positive CyclinD₁ expression in 3 out of 3 (100%) of cases, [+ 1 in 1 case (33.3%) and +2 in 2 cases (66.7%)].

Table(26):Correlation between different clinicopathological entities of HC in relation to cyclin D₁ expression.

Cl. Path. variable	Cyclin D ₁ exp. in HC					Total	X ²	PV
	0	+1	+2	+3	+4			
Age								
≤ 40	2(25%)	3(37.5%)	3(37.5%)	-	-	8	1.15	>0.05
> 40	1(50%)	-	1(50%)	-	-	2		
Gender								
Female	1(20%)	1(20%)	3(60%)	-	-	5	1.81	>0.005
Male	2(40%)	2(40%)	1(20%)	-	-	5		
Grade								
I	2(100%)	-	-	-	-	2	10.89	<0.05
II	1(33.3%)	2(66.7%)	-	-	-	3		
III	-	1(20%)	4(80%)	-	-	5		
Stage								
I	1(20%)	2(40%)	2(40%)	-	-	5	2.83	>0.05
II	1(25%)	1(25%)	2(50%)	-	-	4		
III	1(100%)	-	-	-	-	1		
IV	-	-	-	-	-	-		
Recurrence								
+	-	3(100%)	-	-	-	3	10	<0.05
-	3(42.9%)	-	4(57.1%)	-	-	7		
survival								
alive	3(42.8%)	2(28.6%)	2(28.6%)	-	-	7	2.6	>0.05
dead	-	1(33.3%)	2(66.6%)	-	-	3		
Total	3(30%)	3(30%)	4(40%)	-	-	10		

- NB. HC patients ≤ 40 years showed non significant higher cyclin D₁ expression (75%) than HC > 40 years (50%).
- Females of HC showed non significant higher D₁ expression (80%) in relation to males (60%).
- Grade I HC did not express D₁, grade II tumors showed D₁ expression in (66.7%) of cases while grade III tumors showed 100% expression (significant direct proportional correlation with tumor grade) (P < 0.05).
- SI HC showed Cyclin D₁ expression in 80% of cases in relation to (75%) expression in SII cases. SIII, SIV cases were negative for Cyclin D₁ expression (non significant inverse relationship with tumor TNM stage).
- Locally recurrent HC showed significant higher Cyclin D₁ expression (100%) in non recurrent cases. (P < 0.05).
- Alive cases showed 57.1% Cyclin D₁ expression in relation to (100%) expression in died cases (non significant correlation).



Graph(12)CyclinD1 expression in HC in relation to tumor grade & local recurrence.

II-Bcl-x expression in HC: Table (27), Graph (13), Fig. (41).

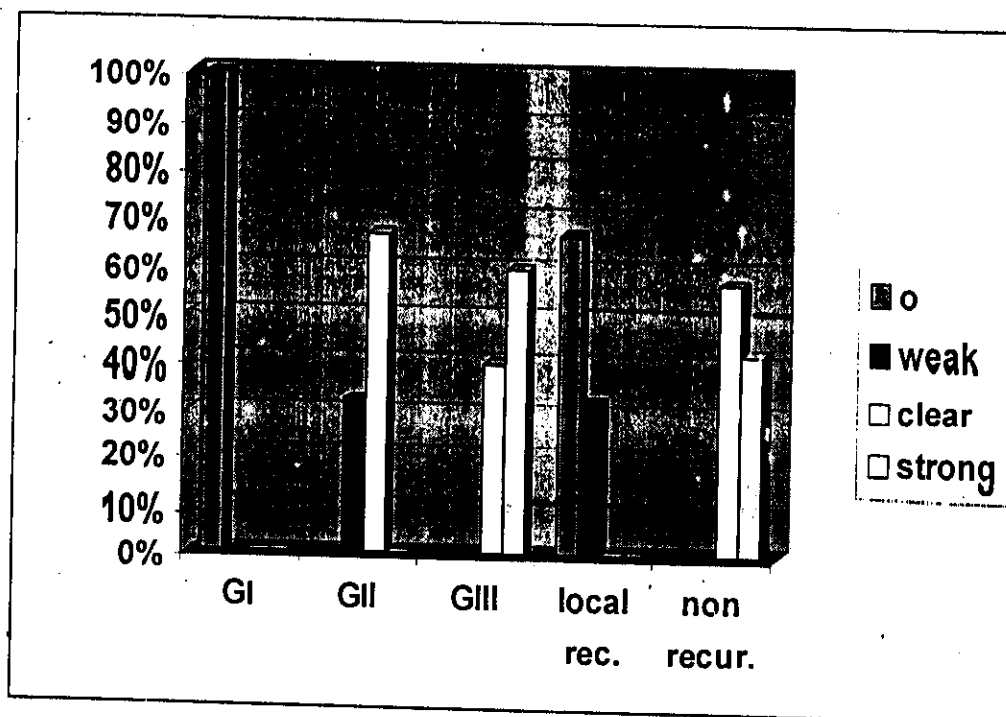
- **In relation to patients age:** positive Bcl-x expression was present in 6 out of 8 (75%) HC ≤ 40 years [+in 1 case (12.5%), ++ in 3 cases (37.5%) and +++ expression in 2 cases (25%)]. HC cases > 40 years showed positive Bcl-x expression in 2 out of 2 (100%) of cases [++ in 1 (50%) case and +++ in 1 case (50%)].
- **As regard patients gender:** females and males of HC were equally positive for Bcl-x expression in 4 out of 5 cases (80%) for each. [Weak (+) expression in 1 female (20%), moderate (++) Bcl-x expression equally in 2 cases (40%) for each and strong (+++) expression in 1 female (20%) and in 2 males (40%)].



Table(27): Correlation between different clinicopathological entities of HC in relation to Bcl X expression :

Cl. Path.	Bcl-X				Total	X2	PV
	0	Weak +	Moderate ++	Strong +++			
Age							
≤ 40	2(25%)	1(12.5%)	3(37.5%)	2(25%)	8	1.14	>0.05
> 40	-	-	1(50%)	1(50%)	2		
Gender							
Female	1(20%)	1(20%)	2(40%)	1(20%)	5	1.33	>0.05
Male	1(20%)	-	2(40%)	2(40%)	5		
Grade							
I	2(100%)	-	-	-	2	14.66	<0.05
II	-	1(33.3%)	2(66.7%)	-	3		
III	-	-	2(40%)	3(60%)	5		
IV	-	-	-	-	-		
Stage							
I	2(40%)	1(20%)	1(20%)	1(20%)	5	5.5	>0.05
II	-	-	2(50%)	2(50%)	4		
III	-	-	1(100%)	-	1		
IV	-	-	-	-	-		
Recurrence							
Present	2(66.7%)	1(33.3%)	-	-	3	10	<0.05
Absent	-	-	4(57.1%)	3(42.9%)	7		
survival							
alive	2(28.5%)	1(14.3%)	2(28.5%)	2(28.5%)	7	2.06	>0.05
dead.	-	-	2(66.6%)	1(33.3%)	3		
Total	2(20%)	1(10%)	4(40%)	3(30%)	10		

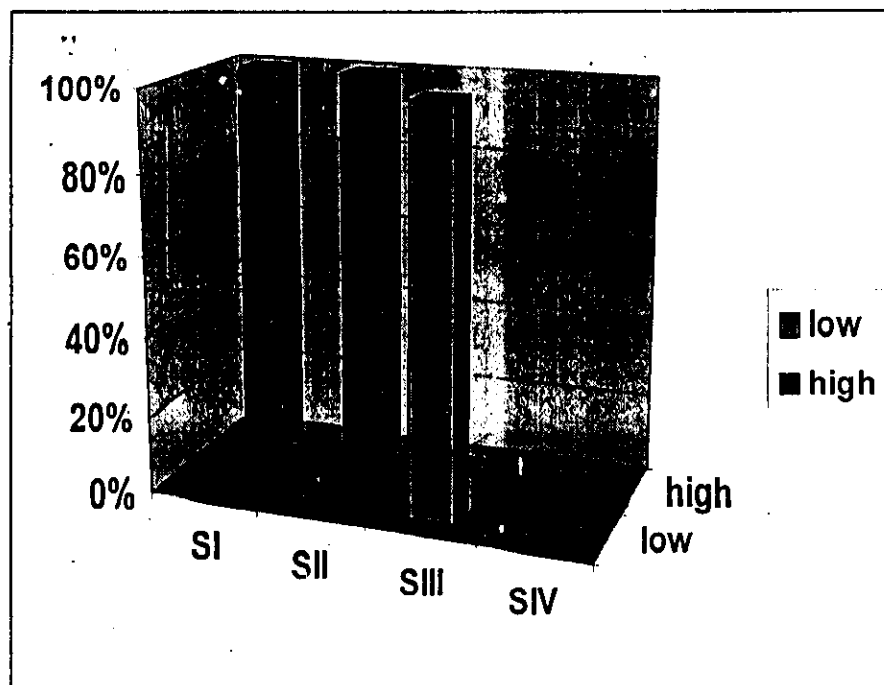
- NB. GI HC didn't show Bcl-x expression while GII and GIII tumors showed 100% expression. This revealed significant direct proportionate relationship ($P < 0.05$).
- SI HC showed Bcl-x expression in 60% of cases while SII & SIII showed 100% expression (non significant direct correlation). ($P > 0.05$)
- Locally recurrent cases of HC showed 33.3% Bcl-x expression while non recurrent cases showed 100% Bcl-x expression (significant higher expression with tumor non recurrence ($P < 0.05$)).



Graph(13): Bcl x expression in HC in relation to tumor grade and local recurrence.

II-CD44 expression in HC: Table (28), Graph (14), Fig.(42).

- **In relation to patients age:** high CD₄₄ expression was present in 7 out of 8 (87.5%) cases ≤ 40 years and in 2 out of 2 (100%) cases > 40 years.
- **As regard relation to patients gender:** females of HC showed high CD₄₄ expression in 5 out of 5 (100%) of cases. Males showed high CD₄₄ expression in 4 out of 5 (80%) of cases.
- **In relation to tumor grade:** high CD₄₄ expression was present in 2 out of 2 (100%) **GI** HC, in 3 out of 3 (100%) **GII** HC, and in 4 out of 5 (80%) **GIII** HC.
- **In relation to patients TNM stage:** high CD₄₄ expression was present in 5 out of 5 (100%) **SI** HC, in 4 out of 4 (100%) **SII** HC.
- **As regard local tumor recurrence:** locally recurrent HC showed high CD₄₄ expression in 2 out of 3 (66.7%) HC while non recurrent HC showed high CD₄₄ expression in 7 out of 7 (100%) cases.
- **In relation to patients survival:** high CD₄₄ expression was present in 7 out of 7 (100%) alive HC and in 2 out of 3 (66.7%) died cases.



Graph(14): CD44 expression in HC in relation to tumor stage.

F-In medullary carcinoma (MC):

I-Cyclin D1 expression in MC: Table (29), Graph (15), Fig. (46).

- **In relation to patients age:** MC cases ≤ 40 years showed positive Cyclin D₁ expression in 8 out of 9 cases (88.9%) [+ 1 expression in 2 cases (22.2%), + 3 and + 4 in 3 cases (33.3%) for each]. MC cases > 40 years showed positive Cyclin D₁ expression in 8 out of 8 (100%) of cases [+ 1 in 1 case (12.5%), + 2 2 cases (25%), + 3 expression in 3 cases (37.5%) and + 4 expression in 2 cases (25%) examined].
- **In relation to patients gender:** positive Cyclin D₁ expression was present in 6 out of 7 females of MC (85.7%) [+ 2 in 1 case (14.3%), + 3 in 3 cases (42.8%) and + 4 in 2 cases (28.6%)]. MC of male gender showed positive Cyclin D₁ expression in 10 out of 10 cases (100%) [+ 1, +3 and + 4 in 3 cases (30%) for each score and + 2 expression in 1 case (10%)].
- **As regard tumor grade:** **GI** MC showed positive D₁ expression in 4 out of 5 cases (80%), with + 3 score.
- GII** MC showed positive Cyclin D₁ expression in 9 out of 9 (100%) cases, [+ 1 and +2 in 1 case for each (11.1%), + 3 expression in 2 cases (22.2%) and + 4 in 5 cases (55.6%)].



GIII MC showed positive, Cyclin D₁ expression in 3 out of 3 (100%) cases [+ 1 in 2 cases (66.7%) and + 2 in 1 case (33.3%)].

- **In relation to patients TNM stage:** **SI** MC showed Cyclin D₁ expression in 2 out of 2 (100%) cases [+1 in 1 case (50%) and + 3 in 1 case (50%)].

SII MC showed Cyclin D₁ expression in 2 out of 2 cases examined (100%) with + 1 score.

SIII MC showed positive Cyclin D₁ expression in 9 out of 9 (100%) of cases [+ 3 in 5 cases (55.6) and + 4 in 4 cases (44.4%)].

SIV MC showed Cyclin D₁ expression in 3 out of 4 cases (75%), [+2 in 2 cases (50%) and + 4 in 1 case (25%)].

- **In relation to local tumor recurrence:** locally recurrent MC showed positive Cyclin D₁ expression in 5 out of 5 (100%) cases, [+ 1 in 1 case (20%), + 3 in 1 case (20%) and + 4 in 3 case (60%)]. Non recurrent MC showed positive Cyclin D₁ expression in 11 out of 12 cases (91.7%), [+1, +2 and + 4 in 2 cases examined (16.7%) for each and + 3 expression in 5 cases (41.6%)].

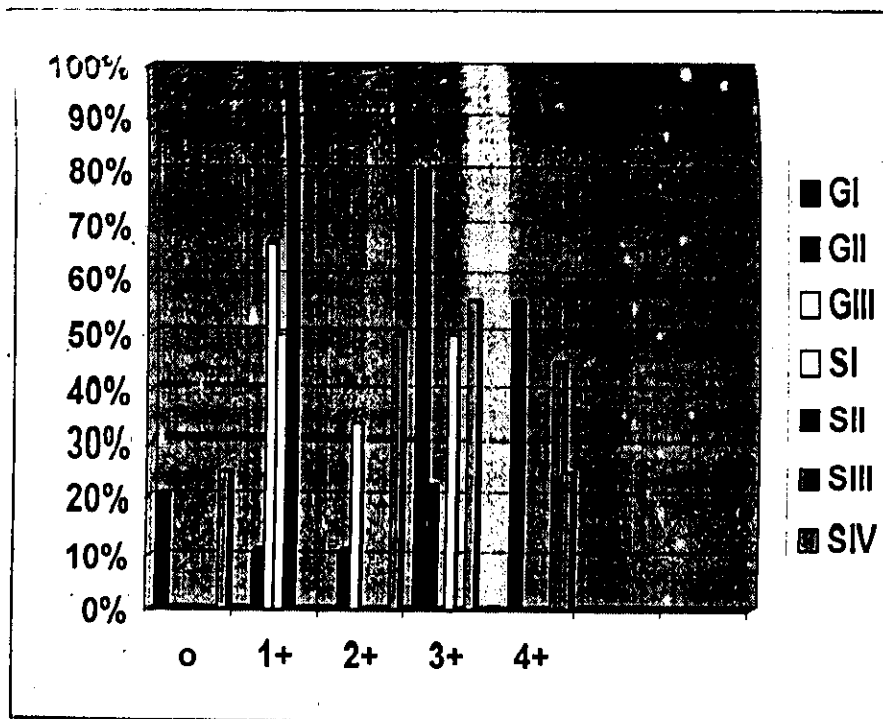
- **In relation to patients survival:** alive MC showed positive Cyclin D₁ expression in 11 out of 12 cases (91.7%), [+1 in 2 cases (16.7%) cases, + 2 in 1 case (8.3%), +3 in 5 cases (41.6%) and + 4 expression in 3 cases (25%)]. Died MC showed positive Cyclin D₁ expression in 5 out of 5 (100%) of cases, [+ 1, +2 and + 3 equally in 1 case (20%) for each while + 4 expression was present in 2 cases (40%)].



Table(29): Correlation between different clinicopathological entities of medullary carcinoma in relation to cyclin D₁ expression:

Path. entities	Cyclin D ₁ exp. in MC					Total	X ²	PV
	0	+1	+2	+3	+4			
≤40	1(11.1%)	2(22.2%)	-	3(33.3%)	3(33.3%)	9	3.49	>0.05
>40	-	1(12.5%)	2(25%)	3(37.5%)	2(25%)	8		
Gender								
Female	1(14.3%)	-	1(14.3%)	3(42.8%)	2(28.6%)	7	3.79	>0.05
Male	-	3(30%)	1(10%)	3(30%)	3(30%)	10		
Grade								
I	1(20%)	-	-	4(80%)	-	5	18.13	<0.05
II	-	1(11.1%)	1(11.1%)	2(22.2%)	5(55.6%)	9		
III	-	2(66.7%)	1(33.3%)	-	-	3		
IV	-	1(50%)	-	1(50%)	-	2	26.1	<0.05
V	-	2(100%)	-	-	-	2		
Recurrence	1(25%)	-	-	5(55.6%)	4(44.4%)	9		
Present	-	-	2(50%)	-	1(25%)	4		
Absent	1(8.3%)	-	-	-	-	-		>0.05
Survival								
Alive	1(8.3%)	1(20%)	-	1(20%)	3(60%)	5	4	
Died	-	2(16.7%)	2(16.7%)	5(41.6%)	2(16.7%)	12		
		2(16.7%)	1(8.3%)	5(41.7%)	3(25%)	12		>0.05
		1(20%)	1(20%)	1(20%)	2(40%)	5	1.59	
	1	3	2	6	5	17		

- NB. MC > 40 years showed non significant higher D₁ expression (100%) than MC ≤40years(88.8%).
- Males were highly expressing Cyclin D₁ (100%) than females (85.7%) (non significant).
- GI MC showed cyclin D₁ expression in 80% of cases in relation to GII, III MC that showed cyclin D₁ expression in 100% of cases (significant direct proportionate correlation with tumor grade (P < 0.05).
- SI, SII, SIII MC showed cyclin D₁ expression in 100% of cases while SIV showed its expression in 75% of cases (significantly inverse correlation with TNM stage (P < 0.05).
- Locally recurrent cases of MC showed non significant higher D₁ expression (100%) than non recurrent cases (91.6%).
- Died cases of MC showed non significant higher cyclin D₁ expression (100%).



Graph(15): Cyclin D1 expression in MC in relation to tumor grade & stage.

II-Bcl-x expression in MC: Table (30), Graph (16), Fig. (47).

- **In relation to patients age:** Bcl-x expression was present in 7 out of 9 (77.8%) MC cases ≤ 40 years [+ in 3 cases (33.4%), ++ in 2 cases (22.2%), +++ in 2 cases (22.2%)]. MC cases > 40 years showed positive Bcl-x expression in 4 out of 8 cases (50%) [+ , +++ intensity in 1 case (12.5%) for each and ++ in 2 cases (25%)]. Mc>40years showed Bcl-x expression in 4 out of 8 (50%) [+ and +++ intensity in 1 case (12.5%) for each; ++ in 2 cases (25%)].
- **In relation to patients gender:** females of MC showed positive Bcl-x expression in 5 out of 7 cases (71.4%) [+ in 2 cases (28.6%) and ++ in 3 cases (42.8%)]. Males of MC showed positive Bcl-x expression in 6 out of 10 cases (60%), [+ in 2 cases (20%), ++ expression in 1 case (10%) and expression in 3 cases (30%)].
- **Bcl-x expression in relation to grade of MC:** Bcl-x expression was present in 1 out of 5 (20%) **GI** MC with weak intensity.



GII MC showed positive Bcl-x expression in 7 out of 9 (77.8%) [+ in 3 cases (33.3%), ++ in 3 cases (33.3%) and +++ in 1 case (11.1%)].

GIII MC showed Bcl-x expression in 3 out of 3 (100%) of cases [++ in 1 case (33.3%) and +++ in 2 cases (66.7%)].

- **In relation to patients TNM stage: SI, SII** MC showed positive Bcl-x expression in 2 out of 2 cases (100%) for each [+ and ++ equally in 1 case for each (50%)].

SIII MC showed positive Bcl-x expression in 6 out of 9 cases (66.7%), [weak in 1 case (11.1%), moderate in 2 cases (22.2%) and strong expression in 3 cases (33.3%)].

SIV MC showed positive Bcl-x expression in 1 out of 4 cases (25%) with weak intensity.

- **As regard relation to local tumor recurrence:** locally recurrent MC showed positive Bcl-x expression in 4 out of 5 cases examined (80%), [+ in 3 cases (60%), ++ in 1 case (20%)]. Non recurrent cases of MC showed positive Bcl-x expression in 7 out of 12 cases (58.3%) [weak in 1 case (8.3%), moderate and strong equally in 3 cases (25%) of them].

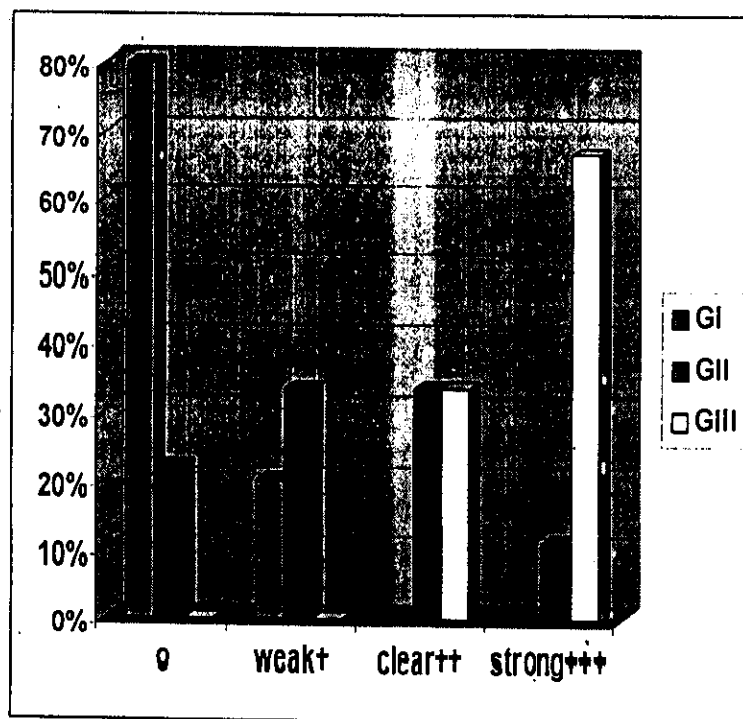
- **In relation to survival:** alive MC showed positive Bcl-x expression in 7 out of 12 cases examined (58.3%), [+ in 4 cases (33.3%), ++ in 2 cases (16.7%) and +++ in 1 case (8.3%)]. Died MC showed positive Bcl-x expression in 4 out of 5 cases (80%), [both moderate ++ and strong (+++) expression equally in 2 cases (40%) for each].



Table(30):Correlation between different clinicopathological entities of MC in relation to Bcl-X expression:

Clinico/ Pathologic.	Bcl-X				Total	X2	PV
	0	Weak +	Moderate ++	Strong +++			
Age							
< 40	2(22.2%)	3(33.4%)	2(22.2%)	2(22.2%)	9	1.95	>0.05
> 40	4(50%)	1(12.5%)	2(25%)	1(12.5%)	8		
Gender							
Female	2(28.6%)	2(28.6%)	3(42.8%)	-	7	4.27	>0.05
Male	4(40%)	2(20%)	1(10%)	3(30%)	10		
Grade							
I	4(80%)	1(20%)	-	-		12.28	<0.05
II	2(22.2%)	3(33.3%)	3(33.3%)	1(11.1%)	5		
III	-	-	1(33.3%)	2(66.7%)	3		
Stage							
I	-	1(50%)	1(50%)	-		9.8	
II	-	1(50%)	1(50%)	-	2		>0.05
III	3(33.3%)	1(11.1%)	2(22.2%)	3(33.3%)	2		
IV	3(75%)	1(25%)	-	-	4		
Recurrence							
Present			1(20%)	-		5.16	
Absent	1(20%)	3(60%)	3(25%)	3(25%)	5		>0.05
Survival							
Alive	5(41.7%)	1(8.3%)			12		
Died	5(41.6%)	4(38.3%)	2(16.7%)	1(8.3%)	12	4.96	>0.05
	1(20%)	-	2(40%)	2(40%)	5		
Total	6	4	4	3	17		

- NB. Cases of MC ≤ 40 years showed non significant higher Bcl X expression (77.7%).
- Females of MC showed non significant higher Bcl-x expression (71.4%).
- Significant direct proportionate relationship between Bcl-x over-expression and tumor grade in MC ($P < 0.05$).
- SI, SII cases of MC showed 100% Bcl X expression in relation to (66.7%) Bcl X expression in SIII tumors and 25% Bcl X expression in SIV tumors. This revealed non significant inverse proportionate relationship.
- Locally recurrent cases of MC showed non significant higher Bcl X expression (80%) than non recurrent cases (58.3%).
- Died MC showed non significant higher Bcl-x expression (80%) than alive cases (58.3%).



Graph(16): Bcl x expression in MC in relation to tumor grade

III-CD 44 expression in MC: Table(31), Graph(17), Fig. (48).

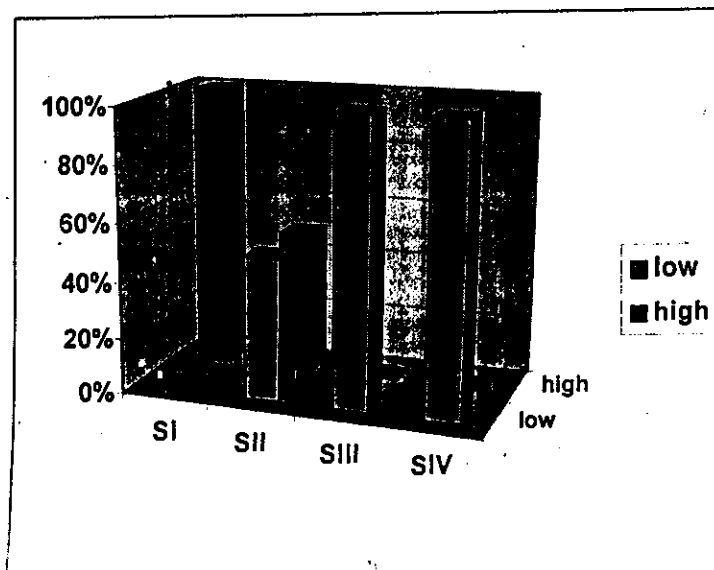
- **As regard patients age:** high CD₄₄ expression was present in 1 out of 9 (11.1%) MC ≤ 40 years and in 2 out of 8 (25%) cases ≤ 40 years.
- **As regard patients gender:** females showed high expression in 1 out of 7 (14.3%). Males of MC showed high CD44 expression in 2 out of 10 cases (20%).
- **In relation to tumor grade:** high CD₄₄ expression was present in 1 out of 5 (20%) **GI** MC, in 1 out of 9 (11.1%) **GII** MC, and in 1 out of 3 (33.3%) **GIII** MC.
- **In relation to patients TNM stage:** **SI** MC showed high CD44 expression in 2 out of 2 cases examined (100%). **SII** MC showed high CD44 expression in 1 out of 2 cases (50%).
- **In relation to local tumor recurrence:** locally recurrent MC didn't show high CD44 expression. Non recurrent MC showed high expression in 3 out of 12 cases (25%).
- **In relation to patients survival:** alive MC showed high expression in 3 out of 12 cases (25%).



Table(31): Correlation between different clinicopathological entities of MC in relation to CD₄₄ expression:

Cl. Path. variable	CD ₄₄ expression		Total	X2	PV
	Low (1-66%)	High (67-110%)			
Age					
< 40	8(88.9%)	1(11.1%)	9	0.56	>0.05
> 40	6(75%)	2(25%)	8		
Gender					
Female	6(85.7%)	1(14.3%)	7	0.56	>0.05
Male	8(80%)	2(20%)	10		
Grade					
I	4(80%)	1(20%)	5	0.67	>0.05
II	8(88.9%)	1(11.1%)	9		
III	2(66.7%)	1(33.3%)	3		
Stage					
I	-	2(100%)	2	13.5	<0.05
II	1(50%)	1(50%)	2		
III	9(100%)	-	9		
IV	4(100%)	-	4		
Recurrence					
Present	5(100%)	-	5	1.51	>0.05
Absent	9(75%)	3(25%)	12		
Survival					
Alive	9(75%)	3(25%)	12	1.51	>0.05
Died	5(100%)	-	5		
Total	14(82.4%)	3(17.6%)	17		

- NB. Significant inverse proportionate correlation between tumor TNM stage and CD₄₄ expression ($P < 0.05$).
- Non significant correlation between CD₄₄ expression and tumor grade (PV > 0.05).



Graph(17): CD44 expression in MC in relation to tumor stage.

**G-In Anaplastic carcinoma:****I-Clinico pathological results: Table (32)****Table(32): The difference between clinicopathological entities of anaplastic carcinoma in relation to the differentiated cases :**

Cl. Path. Var.	Differentiated carcinoma	Anaplastic carcinoma	X2	PV
Age				
Lowest	19y	47y	6.78	<0.05
Highest	73y	80y		
Mean	41y	60.4y		
Gender				
Male:Female	1: 1.6	2.3 : 1	6.58	>0.05
Size				
Lowest	1.5 cm	3 cm	0.12	>0.05
Mean	3.9 cm	8.2 cm		
Highest	9.5 cm	13 cm		
Grade				
GI	15 (21.1%)	-	200	<0.001
GII	35 (49.2%)	-		
GIII	21 (29.5%)	-		
GIV	-	10 (100%)		
Stage				
SI	21 (29.5%)	-	160.36	<0.001
SII	26 (36.6%)	-		
SIII	16 (22.5%)	-		
SIV	8 (11.2%)	10 (100%)		
Recurrence				
Present	24 (33.8%)	4 (40%)	0.77	>0.05
Absent	47 (66.1%)	6 (60%)		
Survival				
Alive	41 (57.7%)	- (0%)	11.7	<0.001
Died	30 (42.2%)	10 (100%)		
Total	71	10		

- NB. Cases of anaplastic carcinomas showed significant higher mean age distribution (60.4 y) in relation to the differentiated malignant tumors that showed mean age (41.y) ($P < 0.05$).
- All cases (100%) of anaplastic carcinoma were GIV and SIV in relation to 0% GIV and 11.2% SIV in differentiated carcinomas this revealed highest grade & stage for anaplastic carcinoma (highly significant correlation) ($P < 0.01$).
- Very highly significant increase in alive cases in differentiated carcinoma (57.7%) in relation to 0% in anaplastic carcinoma cases ($P < 0.001$).



II-Results of Cyclin D1, Bcl-x and CD44 expression in anaplastic carcinoma: Table (33).

- Cyclin D₁ expression in anaplastic compared to differentiated cases: Fig. (50, 51).

Positive Cyclin D₁ expression was present in all cases examined of anaplastic carcinoma (100%) [+2 in 1 case (10%), + 3 in 3 cases (30%) and + 4 D₁ in 6 out of 10 cases (60%)].

Differentiated cases showed Cyclin D1 expression in 53 out of 71 cases (74.7%) [+1 in 9 cases (12.6%), + 2 in 15 cases (21.1%), +3 in 17 cases (23.9%) and +4 in 12 cases (16.9%)].

- Bcl-x expression in anaplastic carcinoma compared to differentiated tumors: Fig. (52).

Bcl-x expression was present in 10 out of 10 cases (100%) of anaplastic carcinoma [weak + in 1 case (10%), moderate (++) in 2 cases (20%) and strong in 7 cases (70%)]. Bcl-x expression was present in 58 out of 71 (81.7%) differentiated cases [+ in 17 cases (23.9%), ++ in 25 cases (35.2%) and +++ in 16 cases (22.5%).

- CD₄₄ expression in anaplastic compared to differentiated cases: Fig. (53) High CD₄₄ expression was present in 2 out of 10 (20%) cases of anaplastic carcinoma in relation to 33 out of 71 (46.4%) of differentiated cases.

Table(33):Correlation between differentiated, anaplastic carcinomas in relation to Cyclin D₁, Bcl X and CD₄₄ expression

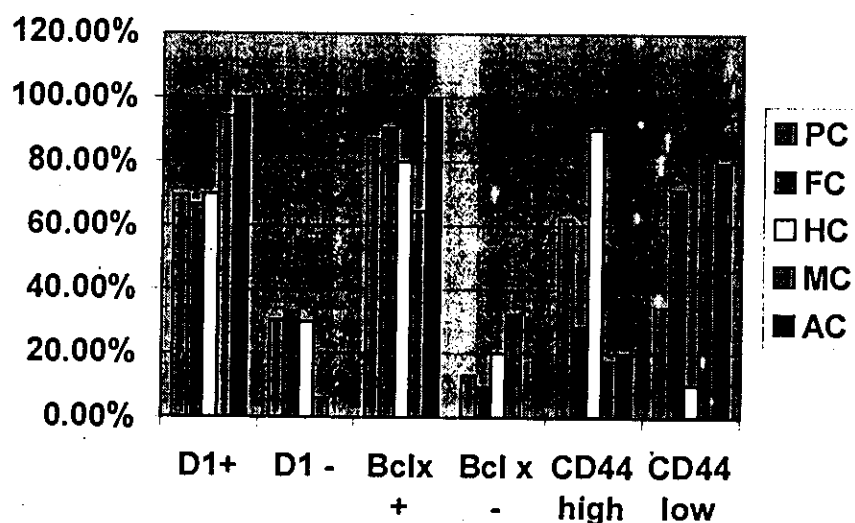
Clinico/ Pathologic.	Differentiated carcinoma	Anaplastic carcinoma	X2	PV
Cyclin D₁				
0	18 (25.3%)	0 (0%)	11.81	<0.05
+1	9 (12.6%)	0 (0%)		
+2	15 (21.1%)	1 (10%)		
+3	17 (23.9%)	3 (30%)		
+4	12 (16.9%)	6 (60%)		
Bcl X				
0	13 (18.3%)	0 (0%)	11.1	<0.05
+	17 (23.9%)	1 (10%)		
++	25 (35.2%)	2 (20%)		
+++	16 (22.5%)	7 (70%)		
CD44				
Low	38 (53.5%)	8 (80%)	3.32	>0.05
High	33 (46.4%)	2 (20%)		
Total	71	10		

- NB. Significant higher positive Cyclin D₁ and Bcl-x expression in anaplastic carcinoma in relation to differentiated cases (P < 0.05).
- Non significant difference in CD₄₄ correlation between differentiated cases and anaplastic carcinoma (PV > 0.05).



Table(34):Cyclin D₁,Bcl-x and CD44 positivity in relation to the histological type and clinic-pathological enteties for the examined cases.

Clinico/ Pathol.	Cyclin D ₁		Bcl-X		CD44		Total
Type:	+	-	+	-	High	Low	No.
Pc	16(69.5%)	7(30.4%)	20(86.9%)	3(13%)	15(62.2%)	8 (39.7)	23
Fc	14(66.6%)	7(33.3%)	19(90.4%)	2(9.5%)	6(28.5%)	15 (71.4)	21
Hc	7(70%)	3(30%)	8(80%)	2(20%)	9 (90%)	1 10%	10
Mc	16(94.1%)	1(5.8%)	11(64.7%)	6(35.2%)	3 (17.6%)	14 (82.3)	17
Ac	10(100%)	-	10(100%)	-	2(20%)	8(80%)	10
	PV < 0.05		PV < 0.05		PV < 0.01		
Grade							
I	8(53.3%)	7(46.6%)	7(46.6%)	8(53.3%)	10(66.6%)	5(33.3%)	15
II	24(68.5)	11(31.4%)	30(85.7%)	5(14.2%)	15(42.8%)	20(57.1%)	35
III	21(100%)	-	21(100%)	-	8(38.1%)	13(5.8%)	21
IV	10(100%)	-	10(100%)	-	2(20%)	8(80%)	10
	PV < 0.01		PV < 0.01		PV > 0.05		
Stage							
I	16(76.1%)	5(23.8%)	16(76.1%)	5(23.8%)	21(100%)	-	21
II	17(65.3%)	9(34.6%)	24(92.3%)	2(7.6%)	11(42.3%)	15(57.6%)	26
III	14(87.5%)	2(12.5%)	13(81.2%)	3(18.7%)	1(6.2%)	15(31.2%)	16
IV	16(88.8%)	2(11.1%)	15(83.3%)	3(16.6%)	2(11.1%)	16(88.8%)	18
	PV > 0.05		PV > 0.05		PV < 0.01		
Recurrence							
Present	24(85.7%)	4(14.2%)	25(89.2%)	3(10.7%)	9(32.1%)	19(67.8%)	28
Absent	39(73.5%)	14(26.4%)	43(81.1%)	10(18.8%)	26(99.1%)	27(50.9%)	53
	PV > 0.05		PV > 0.05		PV > 0.05		



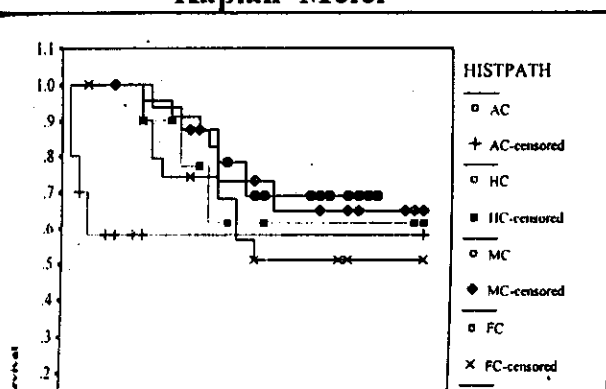
Survival analysis:

A-The histopathological tumor type in relation to local tumor recurrence (6 months from the primary surgery) & overall survival (50 months follow up). table (35) & curves (1,2).

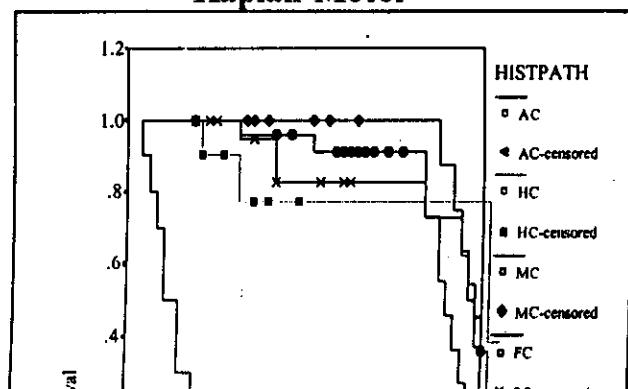
Hist. Type	No. of Cases	Local rec.	Non rec.	Overall survival	Non survival
PC	23	7(30.4%)	16 (69.6%)	14(60.9%)	9(39.1%)
FC	21	9(42.9%)	12(57.1%)	8(38.2%)	13(61.9%)
MC	17	5(29.4%)	12(70.6%)	12(70.6%)	5(29.4%)
HC	10	3 (30%)	7(70%)	7(70%)	3(30%)
AC	10	4(40%)	6(60%)	0(0%)	10(100%)
Total	81	28(34.6%)	53(65.4%)	41(50.7%)	40(49.3%)

- NB. Studied cases of FC showed the highest percentage of local recurrence (42.9%) while MC showed the lowest (29.4%). (significant correlation) ($P= 0.02$).
- MC cases showed the highest percentage for overall survival (70.6%) while AC showed the lowest (0.%) (Very highly significant correlation). ($P= 0.000$)

Kaplan-Meier



Kaplan-Meier



B- Tumor grade with local recurrence and overall survival

table (36) & curves (3,4).

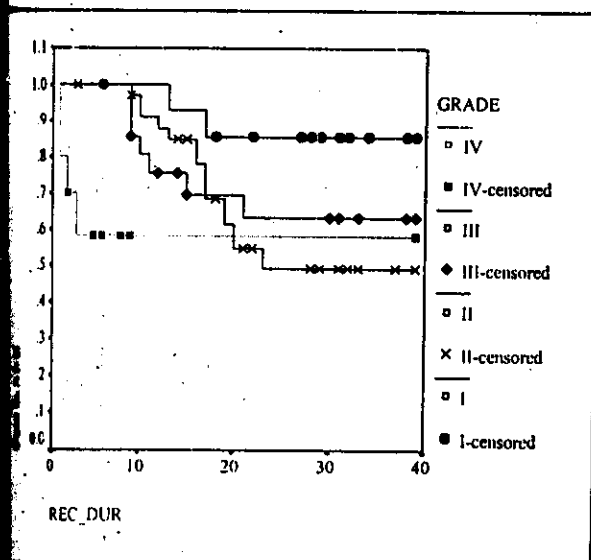
Grade	Rec.	No. Rec.	OS	Non. Survival	Total
GI	2(13.3%)	13(86.7%)	10(66.7%)	5(33.3%) ¹	15
GII	15(42.9%)	20 (57.1%)	26(74.3%)	9(25.7%) ²	35
GIII	7(33.3%)	14(66.7%)	5(23.8%)	16(76.1%)	21
GIV	4(40%)	6(60%)	0(0%)	10(100%)	10
Total	28(34.6%)	53(65.4%)	41(50.6%)	40(49.4%)	81

- NB. Lowest local recurrence rate was present in GI tumors (13.3%).while the highest rate was found for GII tumor (42.9%) (highly significant) ($P = 0.003$).

- Lowest overall survival was for GIV tumors (0%) and the highest

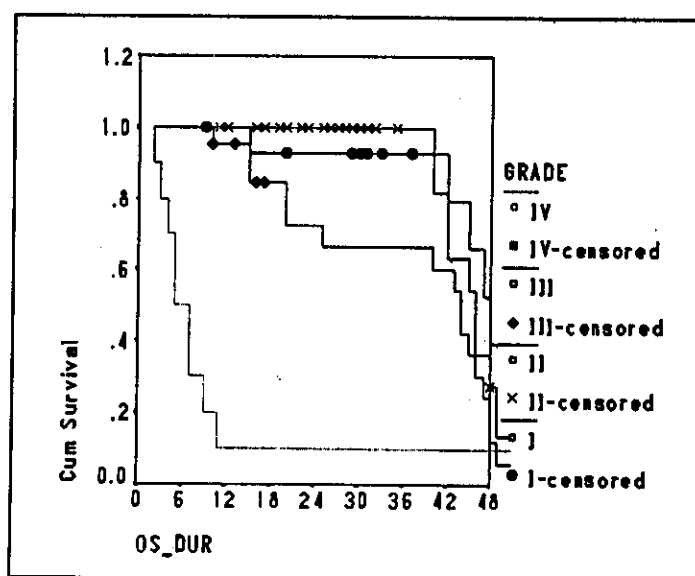
overall survival was for GI tumors (66.7%) (very highly significant) ($P = 0.000$).

Kaplan-Meier



Highly significant tumor grade with local recurrence. Log. Rank ($P=0.003$).

Kaplan-Meier



4) Very highly significant tumor grade with overall survival. Log. Rank ($P=0.000$).



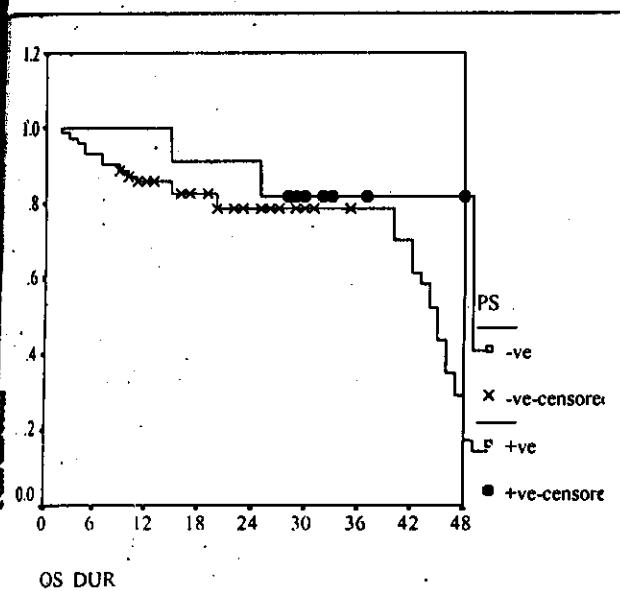
C-Psammoma body formation and hemorrhage & necrosis in relation to local tumor recurrence and overall survival.

Table(37) & curves (5,6).

Variable	+ve Psamma	-ve Psamma	+ve Hge.N	- ve Heg.N	total
Rec.	2(7.1%)	26(92.9%)	26(92.9%)	2(7.1%)	28
Non. Rec.	9(16.9%)	44(83.1%)	40(75.5%)	13(24.5%)	53
OS	8(19.5%)	32(80.5%)	35(87.5%)	5(12.5%)	40
Non OS	3(7.5%)	38 (92.5%)	31(75.6%)	10(24.4%)	41
Total	11	70	66	15	81

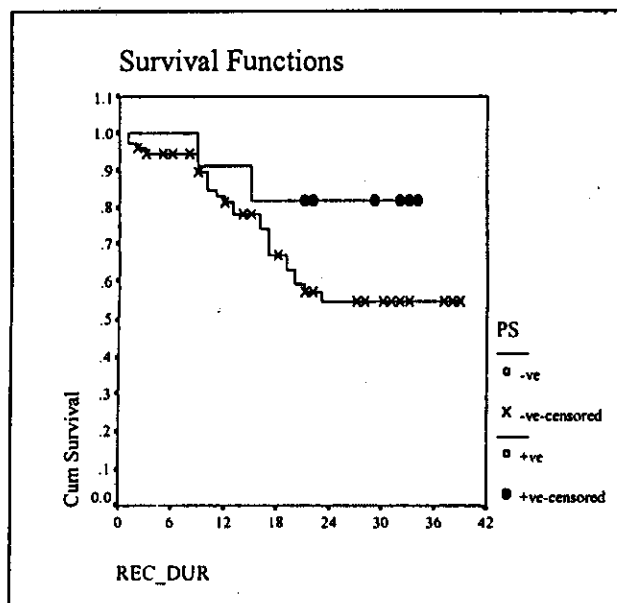
- NB. Examined cases showing Psammoma body formation showed lower recurrence rate (7.1%) which was non significant and higher overall survival (19.5%) which was highly significant. ($P = 0.01$)
- Malignant cases with hemorrhage and necrosis showed higher local recurrence rate (92.9%) (border line significant) ($P = 0.05$) and non significant higher overall survival (87.5%).

Kaplan Meier



Highly significant psammoma body formation overall survival. Log. Rank ($P=0.01$).

Kaplan Meier



6) Non significant psammoma body formation with local tumor recurrence. Log. Rank ($P=0.013$).

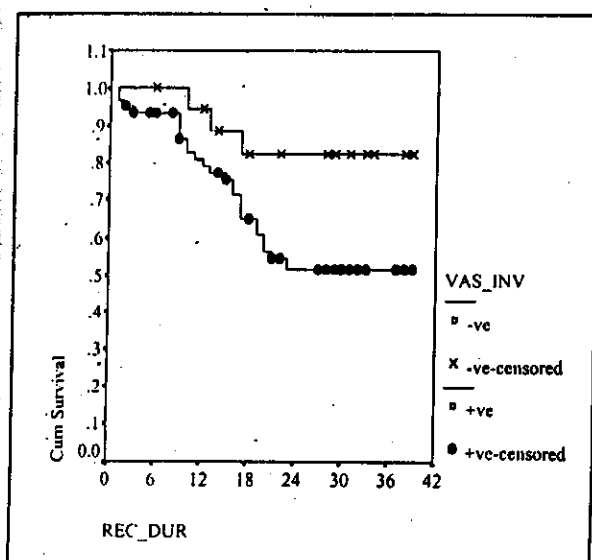


D-Direct capsular invasion, vascular invasion in relation to local tumor recurrence and overall survival, table(38), Curves (7,8,9).

Variable	Cap. Inv.	Non. Cap. Inv.	Vasc. Inv.	Non. Vasc. Inv.	Total
Non Rec.	25(89.3%)	3(10.7%)	25(89.3%)	3(10.7%)	28
Rec.	48(90.5%)	5(9.5%)	37(69.8%)	16(30.2%)	53
Non OS	35(87.5%)	5(12.5%)	35(87.5%)	5(12.5%)	40
OS	38(92.6%)	3(7.4%)	27(65.8%)	14(34.2%)	41
Total	73	8	62	19	81

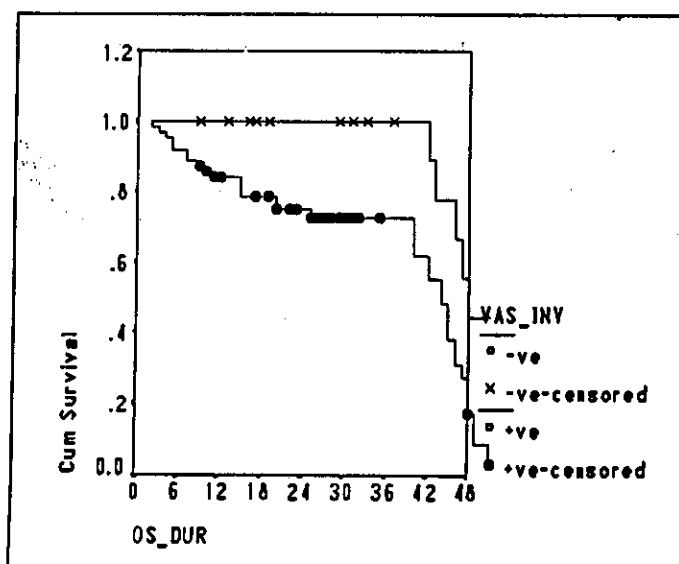
- NB.Studied cases with direct capsular invasion showed lower local recurrence (89.3%) (non significant) and higher overall survival (92.6%) (significant) ($P = 0.02$) in relation to cases without capsular invasion.
- Studied cases with vascular invasion showed higher incidence of local recurrence (69.8%) (significant) ($P = 0.04$) and lower overall survival (65.8%) which was very highly significant. ($P = 0.001$).

Kaplan-Meier



7) Significant vascular invasion with local tumor recurrence. Log. Rank ($P=0.04$).

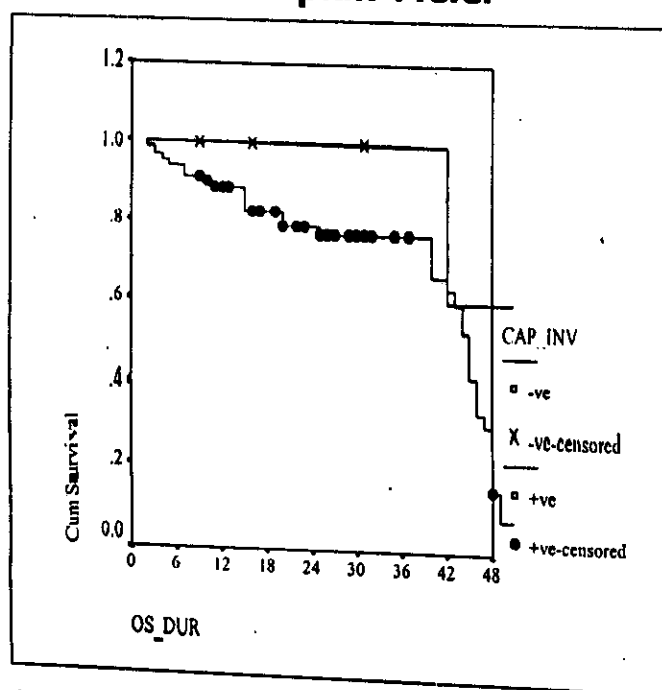
Kaplan-Meier



8) Very highly significant vascular invasion with overall survival. Log. Rank ($P=0.001$).



Kaplan-Meier



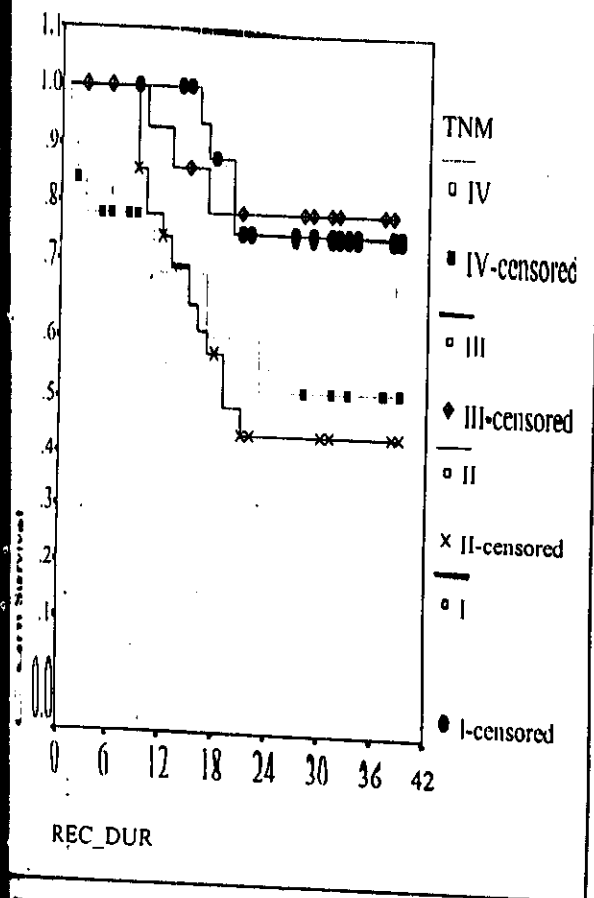
9) Significant capsular invasion with overall survival. Log. Rank ($P=0.02$).

E- Tumor TNM stage with local recurrence & overall survival. table (39) & curve (10,11).

TNM stage	Rec.	No. Rec.	Died	Alive	Total
SI	4(20%)	17(80%)	4(15%)	17(85%)	21
SII	14(53.8%)	12(46.2%)	14(55.6%)	12(44.4%)	26
SIII	3(18.7%)	13(81.3%)	6(37.5%)	10(62.5%)	16
SIV	7(38.9%)	11(61.1%)	16(88.9%)	2(11.1%)	18
Total	28	53	40	41	81

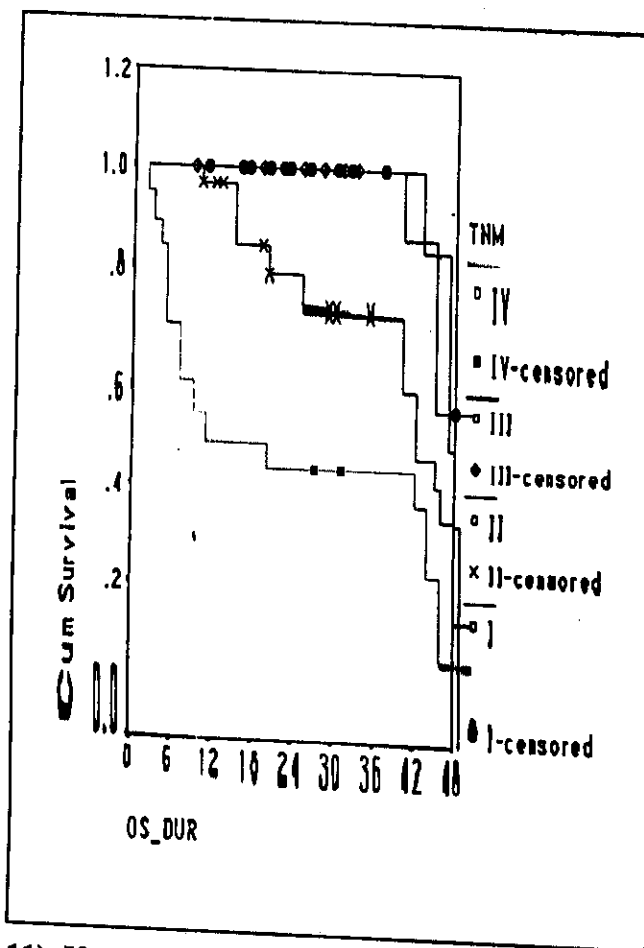
- NB. SI tumors showed significant higher non-recurrence (80%) ($P<0.05$) and very highly significant number of alive cases ($P<0.001$) than SII, SIII, and SIV tumors.

Kaplan-Meier



Significant TNM stage with local tumor recurrence. Log. Rank ($P < 0.05$).

Kaplan-Meier



11) Very highly significant TNM stage with patients overall survival. Log. Rank ($P < 0.001$).

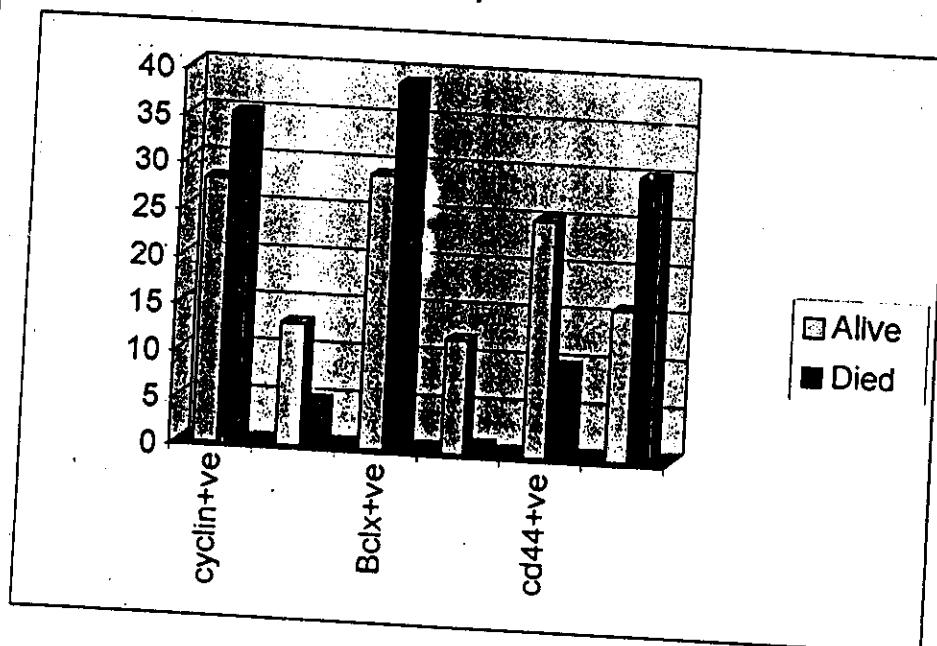
F-Cyclin D1, Bcl-x and CD44 posotivity in relation to overall survival in the examined malignant cases: Table (40), Graph(19).

Survival	Cyclin D1		Bcl-x		CD44		Total
	+	-	+	-	+	-	No.
Alive	28(68.2%)	13(31.7%)	29(70.7%)	12(29.3%)	25(60.9%)	16(39%)	41
Died	35(87.5%)	5(12.5%)	39(97.5%)	1(2.5%)	10(25%)	30(75%)	40
	PV < 0.05		PV < 0.01		PV < 0.01		
Total	63	18	68	13	35	46	81

- NB. Died cases showed significantly higher Cyclin D1 posotivity (87.5%) than alive cases (68.2%) ($P > 0.05$).

- Died cases showed highly significant Bcl-x posotivity (97.5%) (than alive cases (70.7%) ($P < 0.01$).

- Alive cases showed highly significant CD44 posotivity (60.9%) than died cases (25%) ($P < 0.01$).



Graph (19): Cyclin D1, Bcl-x, and CD44 positivity



5 Correlation between different clinico/pathological variable in relation to the studied markers

A- Cyclin D1:

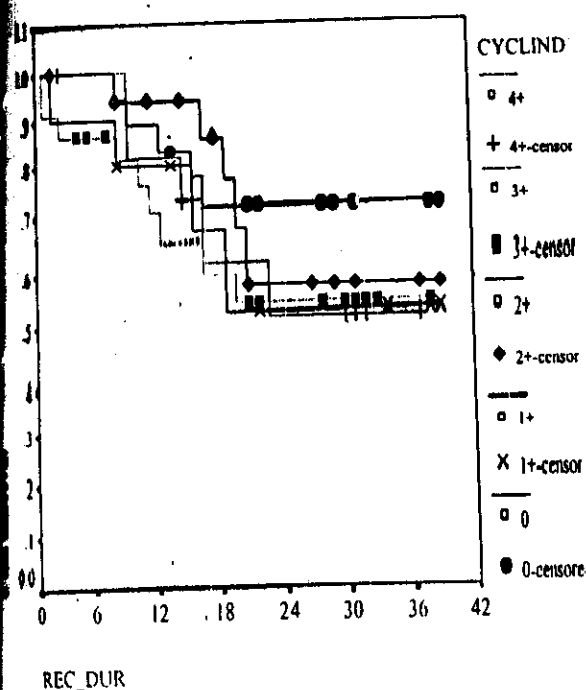
I-Cyclin D1 expression in relation to the studied clinical variables: Table (41), Curves (12,13).

Table (41) Cyclin D1 and clinical variables:

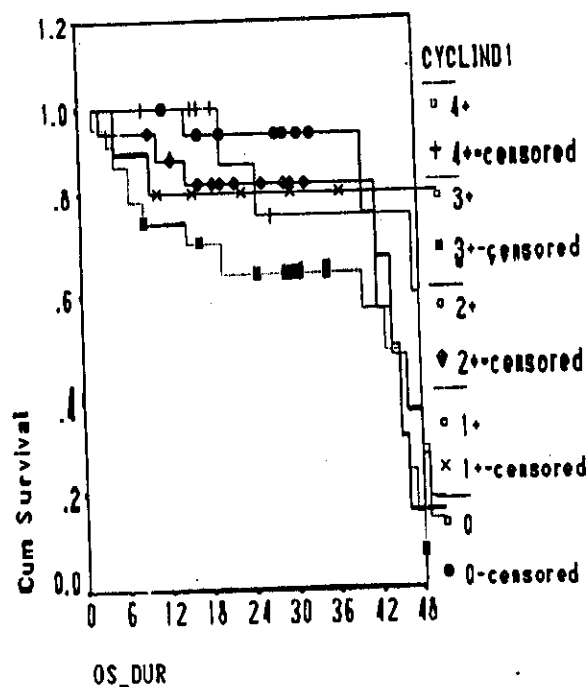
0		+1		+2		+3		+4		Chi2	P value	Total
Freq	%	Freq	%	Freq	%	Freq	%	Freq	%			
3	20	0	17.4	2	13.3	5	33.3	5	33.3	10.75	0.03*	15
21	24.4	15	17.4	22	25.6	21	24.4	7	8.2			
7	18	7	18	8	21	13	33.3	4	10.3	3.16	0.53	39
17	27.4	8	12.8	16	25.8	13	21	8	13			
6	23.1	6	23.1	9	34.6	3	11.5	2	7.7	6.60	0.16	26
18	75	9	12	15	20	23	30.7	10	13.3			
13	22	9	15.3	17	28.8	15	25.4	5	8.5	3.11	0.54	59
11	26.2	6	14.3	7	16.7	11	26.2	7	16.7			
13	20.6	5	7.9	12	19.1	21	33.3	12	19.1	11.94	0.02*	63
5	27.8	5	27.8	6	33.3	2	11.1	0	0			
10	31.3	3	9.4	6	18.8	9	28.1	4	12.5	2.80	0.59	32
8	16.3	7	14.3	12	24.5	14	28.6	8	16.3			
3	15	5	25	6	30	5	25	1	5	27.77	0.06**	20
9	33.3	4	14.8	7	25.9	4	14.8	3	11.1			
3	18.8	0	0	0	0	6	37.5	7	43.8			
3	16.6	1	5.5	5	27.7	8	44.4	1	5.5			
5	17.8	4	14.2	5	17.8	9	32.1	5	17.8	1.34	0.85	28
13	24.5	6	11.3	13	24.5	14	26.4	7	13.2			
9	21.9	8	19.5	10	24.3	8	19.5	6	14.6	5.94	0.20	41
9	22.5	2	5	8	20	15	37.5	6	15			

- NB. Studied cases ≤ 40 years showed significant higher Cyclin D1 over expression than cases >40 years ($P = 0.03$).
- Studied cases with lymph node metastases showed significant higher Cyclin D1 expression than cases without lymph node metastases ($P = 0.02$).
- Highly significant positive correlation was present with Cyclin D1 expression and patients TNM stage ($P = 0.001$).
- Cyclin D1 scoring showed non significant correlation with patient's gender, tumor size, location, local recurrence, OS and distance metastases.

Kaplan-Meier



Kaplan-Meier



Non significant CyclinD1 scoring with local recurrence. Log. Rank ($P < 0.05$).

13) Non significant CyclinD1 scoring with overall survival. Log. Rank ($P < 0.05$).

II-Cyclin D1 expression in relation to histopathological variables: table (42)

Table (42): Cyclin D1 and histopathological variables:

	0		+1		+2		+3		+4		Chi2	P value	Total
	Freq	%	Freq	%	Freq	%	Freq	%	Freq	%			
biology	7	30.4	1	4.3	4	17.3	7	30.4	4	17.3	33.74	0.03*	23
	7	33.3	2	9.5	5	23.9	4	19	3	14.2			21
	1	5.9	3	18	2	9.5	6	35.2	5	29.4			17
	3	30	3	30	4	40	0	0	0	0			10
	0	0	1	10	3	30	6	60	0	0			10
capsular invasion	16	21.9	7	9.6	17	23.3	22	30.1	11	15.1	5.08	0.28	73
	2	25	3	7.3	1	12.5	1	12.5	1	12.5			8
necrosis	15	22.7	9	13.6	14	21.2	18	27.2	10	15.1	0.87	0.93	66
	3	20	1	6.6	4	26.6	5	33.3	2	13.3			15
vascular invasion	13	21	6	10	15	24.1	18	39	10	16.1	2.52	0.64	62
	5	26.3	4	21	3	16	5	26.3	2	10.5			19
tumor grade	7	46.7	1	6.7	2	13.3	4	26.7	1	6.7	15.84	0.20	15
	8	22.9	5	14.3	7	20	8	22.9	7	20			35
	3	14.3	3	14.3	6	28.6	5	23.8	4	19.1			21
	0	0	1	10	3	30	6	60	0	0			10

- NB. Cyclin D1 showed significant correlation with histopathological type (highest positivity was for AC followed by MC, HC, PC lastly for FC) ($P = 0.03$).

- Non significant correlation was found with cyclin D1 in relation to capsular invasion, hemorrhage, necrosis, vascular invasion and tumor grade.

III-Cyclin D1 expression in relation to the other markers:

Table (43).

Table (43): Cyclin D1 & Bcl-x and CD44

0		+1		+2		+3		+4		Chi2	P value	Total
Freq	%	Freq	%	Freq	%	Freq	%	Freq	%			
3	23.1	5	38.5	3	23.1	1	7.7	1	7.7	25.81	0.011*	13
6	33.3	3	16.7	3	16.7	5	27.8	1	5.6			18
8	29.6	1	3.7	8	29.6	7	25.9	3	11.1			27
1	4.4	1	4.4	4	17.4	10	43.5	7	30.4			23
12	25.5	3	6.4	7	14.9	15	31.9	10	21.3	10.13	0.04*	47
6	17.7	7	20.6	11	32.4	8	23.5	2	5.9			34

- NB. Cyclin D1 showed significant positive correlation with BCLX expression ($P = 0.01$).
- Using bivariate analysis correlation coefficient followed by **cox regression test**: Cyclin D1 showed independent significance for BCLX ($P \text{ value} < 0.01$).
- Significant positive correlation was present between Cyclin D1 and CD44 over expression. ($P = 0.04$).

B- Bcl-x

I- Bcl-x expression in relation to the clinical variables:
table(44), curves (14, 15).

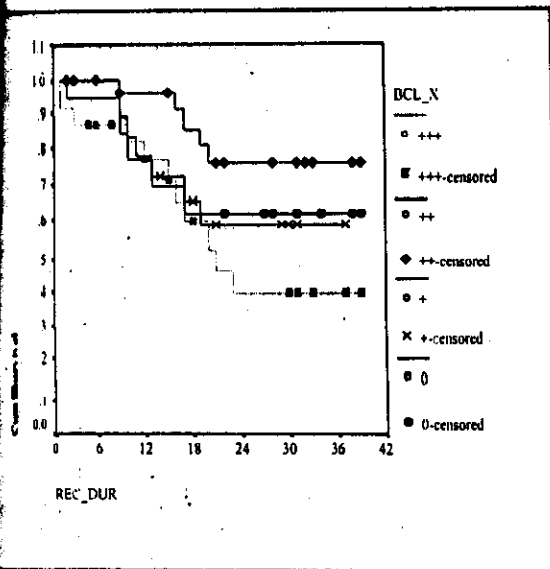
Table (44): Bcl-x and clinical variables:

	0		+		++		+++		Chi2	P value	Total
	Freq	%	Freq	%	Freq	%	Freq	%			
Age											
≤40 years	4	26.7	3	20	2	13.3	6	40	5.72	0.13	15
>40 years	11	12.8	20	23.3	35	40.7	20	23.3			86
Gender											
Male	7	18	10	25.6	11	28.2	11	28.2	2.02	0.57	39
Female	8	12.9	13	21	26	41.9	15	24.2			62
Size											
≤2cm	3	11.5	6	23.1	15	57.7	2	7.7	8.93	0.03*	26
>2cm	12	16	17	22.7	22	29.3	24	32			75
Location											
Rt	7	11.9	15	25.4	25	42.4	12	20.3	4.18	0.24	59
Lt	8	19.1	8	19.1	12	28.6	14	33.3			42
Lymph nodes											
+ve	11	17.5	14	22.2	17	27	21	33.3	6.22	0.10	63
-ve	2	11.1	4	22.2	10	55.6	2	11.1			18
Metastasis											
+ve	6	18.8	10	31.3	5	15.6	11	34.4	7.82	0.05*	32
-ve	7	14.3	8	16.3	22	44.9	12	24.5			49
TNM											
I	3	15	4	20	9	45	4	20	8.40	0.49	20
II	4	14.8	8	29.6	7	25.9	8	29.6			27
III	2	12.5	3	18.8	8	50	3	18.8			16
IV	4	22.2	3	16.7	3	16.7	8	44.4			18
Local recurrence											
+ve	5	17.9	7	25	5	17.9	11	39.3	5.10	0.17	28
-ve	8	15.1	11	20.8	22	41.5	12	22.6			53
Os											
Alive	8	19.5	10	24.4	16	39	7	17.1	5.35	0.15	41
Dead	5	12.5	8	20	11	27.5	16	40			40

- NB. cases with tumor size ≤ 2 cm showed significant higher Bcl-x expression ($P = 0.03$).
- Cases examined without distance metastases showed significant higher Bcl-x expression ($P = 0.05$).
- Non significant correlation was found with Bcl-x intensity in relation to patient's age, gender, tumor location, lymph node status, TNM stage, local recurrence and OS.

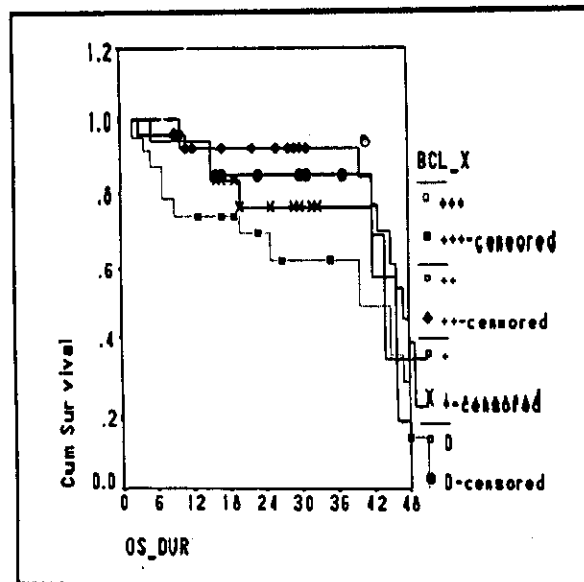


Kaplan-Meier



Non significant Bcl-x intensity with local tumor recurrence. Log. Rank ($P < 0.05$).

Kaplan-Meier



15) Non significant Bcl-x intensity with overall survival. Log. Rank ($P < 0.05$).

II-Bcl-x expression in relation to the histopathological variables: table (45).

Table (45): BCLX and histopathological variables:

	0		+		++		+++		Chi2	P value	Total
	Freq	%	Freq	%	Freq	%	Freq	%			
Pathology											
CPC	3	13	4	17.4	10	43.5	6	26.1	23.45	0.08	23
FC	2	9.5	8	38.1	7	33.3	4	19.1			
MC	6	35.3	4	23.5	4	23.5	3	17.7			
HC	2	20	1	10	4	40	3	30			
AC	0	0	1	10	2	20	7	70			10
Capsular invasion											
+ve	10	13.7	17	23.3	23	31.5	23	31.5	5.84	0.12	73
-ve	3	37.5	1	12.5	4	50	0	0			
H&Nec											
+ve	11	16.7	16	24.2	20	30.3	19	28.8	1.74	0.63	66
-ve	2	13.3	2	13.3	7	46.7	4	26.7			
Ar invasion											
+ve	8	12.9	16	25.8	18	29	20	32.3	6.01	0.11	62
-ve	5	26.3	2	10.5	9	47.4	3	15.8			
Grade											
I	3	20	3	20	9	60	0	0	19.00	0.03*	15
II	5	14.3	10	28.6	11	31.4	9	25.7			
III	5	23.8	4	91.1	5	23.8	7	33.3			
IV	0	0	1	10	2	20	7	70			

- NB. Bcl-x showed highly significant positive correlation with tumor grade ($P = 0.03$).

- Non significant correlation was seen with Bcl-x expression in relation to histopathological type, capsular invasion, hemorrhage & necrosis and vascular invasion.



III-BCLX expression in relation to Cyclin D1 & CD44 markers: table (46).

Table (46): Bcl-x and cyclin D1 & CD44:

	0		+		++		+++		Chi2	P value	Total
	Freq	%	Freq	%	Freq	%	Freq	%			
D1											
0	4	16.7	8	33.3	11	45.8	1	4.2	31.90	0.001**	24
+	6	40	3	20	5	33.3	1	66.7			15
++	3	12.5	6	25	11	44	4	16.7			24
+++	1	3.9	5	19.2	7	26.9	13	50			26
4	1	8.3	1	8.3	3	25	7	58.3			12
CD44											
1-67%	8	15.1	14	26.4	18	34	13	24.5	93	.82	53
100%	7	14.6	9	18.8	19	39.6	13	27.1			48

- NB. BCLX showed highly significant positive correlation with Cyclin D1 scoring while showed non significant correlation with CD44 expression (P = 0.001).

- Using **cox regression test**: Bcl-x showed independent significance for Cyclin D1 (P value = 0.01).

C- CD44:

I- CD44 expression in relation to clinical variables: table (47)

Table (47): CD 44 and Clinical variables:

	1-67%		68-100%		Chi2	P value	Total
	Freq	%	Freq	%			
Age							
≤40 years	15	100	0	0	15.95#	0.001**	15
>40 years	38	44.2	48	55.8			
Gender							
Male	23	59	16	41	1.08#	0.32	39
Female	30	48.4	32	51.6			
Size							
≤2cm	9	43.6	17	65.4	4.48#	0.04*	26
>2cm	44	58.7	31	41.3			
Location							
Rt	26	44.1	33	55.9	4.02	0.07	59
Lt	27	64.3	15	35.7			
Lymph nodes							
+ve	40	63.5	23	36.5	3.48#	0.10	63
-ve	7	38.9	11	61.1			
Metastasis							
+ve	25	78.1	7	21.9	8.78#	0.005**	32
-ve	22	44.9	27	55.1			

- NB. CD44 showed very highly significant negative correlation with the patient's age group (P = 0.001).

- Cases with tumor size ≤ 2 cm showed significant higher CD44 expression (P = 0.04)

- Presence of distant metastasis showed significant negative correlation with CD44 expression (P = 0.005).

- Non significant correlation was present with CD44 in relation to



II- CD44 expression in relation to histopathological variables: table (48).

Table (48): CD44 and histopathological variables:

	1-67%		68-100%		Chi2	P value	Total
	Freq	%	Freq	%			
Histopathology							
PC	8	34.8	15	65.2	28.03	0.001**	23
FC	16	76.2	5	23.8			21
MC	14	82.4	3	17.6			17
HC	1	10	9	90			10
AC	8	80	2	20			10
Capsular invasion							
+ve	42	75.6	31	42.4	0.09#	1	73
-ve	5	62.5	3	37.5			8
He&nec							
+ve	41	62.1	25	37.9	2.46#	0.15	66
-ve	6	40	9	60			15
Vascular invasion							
+ve	36	85.1	26	41.9	2.48	0.11	62
-ve	11	57.9	8	42.1			19
Grade							
I	6	40	9	60	4.05	0.26	15
II	21	60	14	40			35
III	12	75.1	9	42.9			21
IV	8	80	2	20			10

- NB. Very highly significant CD44 expression was present in relation to histopathological type (HC showed the highest CD44 expression while lowest expression was present in MC) ($P = 0.001$).
- Non significant correlation was present between CD44 expression and capsular invasion, hemorrhage & necrosis, vascular invasion and tumor grade.
- **Cox Regression test** for CD44 showed independent significance for: Age (P value = 0.02).
histopathological type (P value = 0.03).
TMN stage (P value = 0.01).



D- Correlation between adenomas versus carcinoma:

table (49)

Table (49) adenoma versus carcinoma:

	Carcinoma		Adenoma		Chi2	P value	Total
	Freq	%	Freq	%			
Age							
≤40 years	15	18.	0	0	4.35#	0.04*	15
>40 years	66	81.5	20	100			86
Gender							
Male	34	42.0	5	25	1.95#	0.21	39
Female	47	58.0	15	75			62
Size							
≤2cm	17	21.0	9	45.0	4.84#	0.04*	26
>2cm	64	79.0	11	55			75
Location							
Rt	44	54.3	15	75.0	2.82#	0.13	59
Lt	37	45.7	5	25.0			42
Psmmoma							
+ve	11	13.6	0	0			11
-ve	70	86.4	20	100			90
CyclinD1							
0	18	22.2	6	30.0	6.63	0.16	24
+1	10	12.3	5	25.0			15
+2	18	22.2	6	30.0			24
+3	23	28.4	3	15.0			26
+4	12	14.8	0	0			12
BCLX							
0	13	16.0	2	10.0	2.78	0.43	15
+	18	22.2	5	25.0			23
++	27	33.3	10	50.0			37
+++	23	28.4	3	15.0			26
Cd44							
1-67%	47	58.0	6	30.0	5.05#	0.04*	53
68-100%	34	42.0	14	70.0			48

- NB. Adenomas showed higher incidence in older age group (>40years) than malignant cases (significant correlation) ($P = 0.04$).
- Malignant cases showed significant higher incidence in tumors >2cm than adenomas ($P = 0.04$).
- Significant higher CD44 expression was present in adenoma than in carcinoma ($P = 0.04$).
- Non significant correlation between benign and malignant cases was present as regard gender, location, BCLX and Cyclin D1 expression.



**Fig. (14): Follicular adenoma showing intact thick fibrous capsule.
No capsular or vascular invasion was seen (H & E x40).**

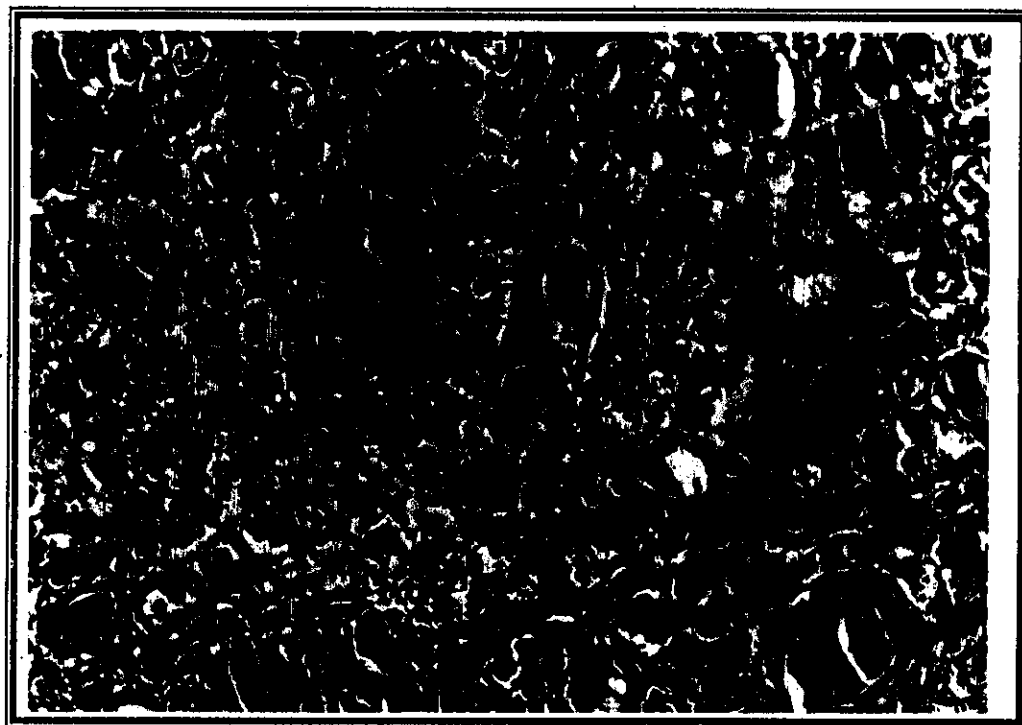


Fig. (15): Atypical adenoma showing hypercellularity, variable-sized & shape follicles, distorted architecture, but no capsular or vascular invasion was seen (H & E x100).



Fig. (16): Follicular thyroid adenoma showing positive brown nuclear staining for Cyclin D1, Score (+2) (streptavidin/Biotin, DAB x400).

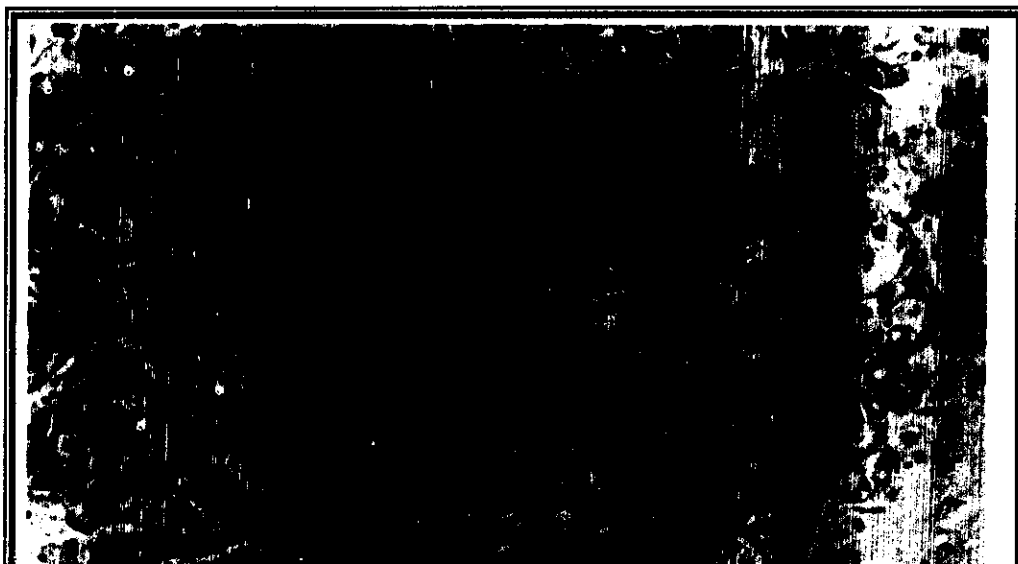




Fig. (18): Follicular thyroid adenoma showing positive brown membranous staining for CD44 high score (80%) (streptavidin/Biotin, DAB x200).





Fig. (20): Papillary thyroid carcinoma showing ground-glass nuclei with often-appearing pattern and intranuclear cytoplasmic invaginations (H & E x400).



Fig. (21): Papillary thyroid carcinoma showing psammomatous calcification with early sclerosis (H & E x100).



Fig. (22): Papillary microcarcinoma of the thyroid showing well-capsulated papillary growth surrounded by adjacent thyroid tissue (H & E x40).



Fig. (23): Papillary thyroid carcinoma showing papillary structure lined by tall columnar cells.



Fig. (24): Papillary thyroid carcinoma showing positive brown nuclear staining for Cyclin D1 score (+3) (streptavidin/Biotin, DAB x200).

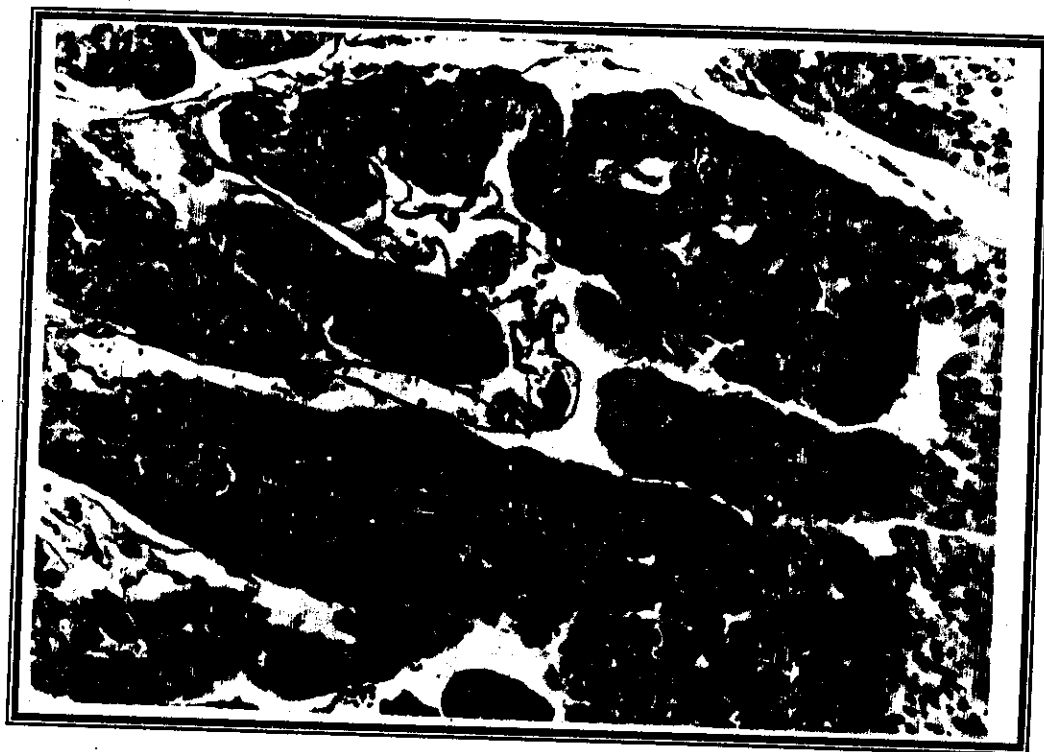


Fig. (25): Papillary thyroid carcinoma grade III, showing positive brown nuclear staining for Cyclin D1 score (+4) (streptavidin/Biotin, DAB x200).



Fig. (26): Papillary thyroid carcinoma showing positive brown cytoplasmic staining for Bcl-x intensity (+++) (streptavidin/Biotin, DAB x200).



Fig. (27): Papillary thyroid carcinoma, positive membranous brown staining for CD44, high score (90%) (streptavidin/Biotin, DAB x200).



Fig. (28): Papillary thyroid carcinoma, positive membranous brown staining for CD44, high score (80%) (streptavidin/Biotin, DAB x200).



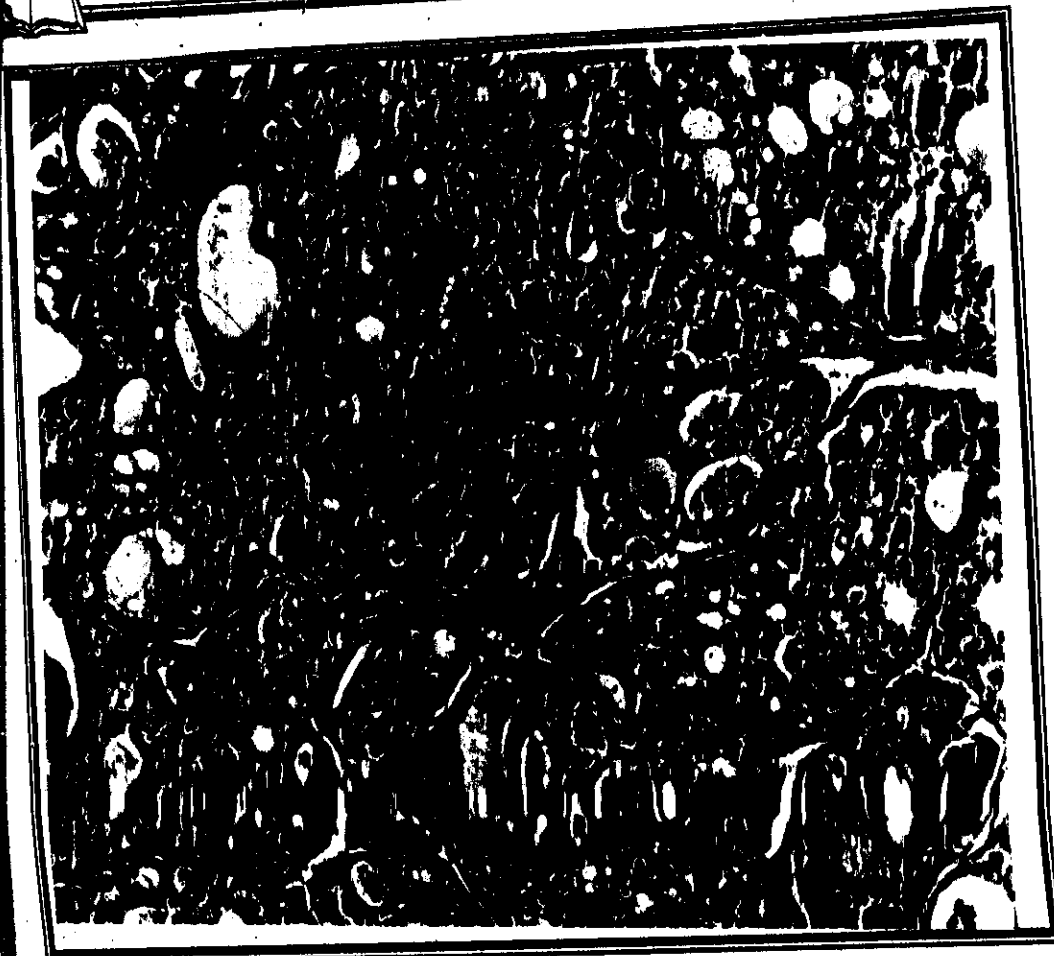


Fig.(30): Follicular thyroid carcinoma grade II, showing pleomorphic follicular growth (H & E x100).



Fig. (31): Follicular thyroid carcinoma grade III, showing insular pattern (H & E x100).

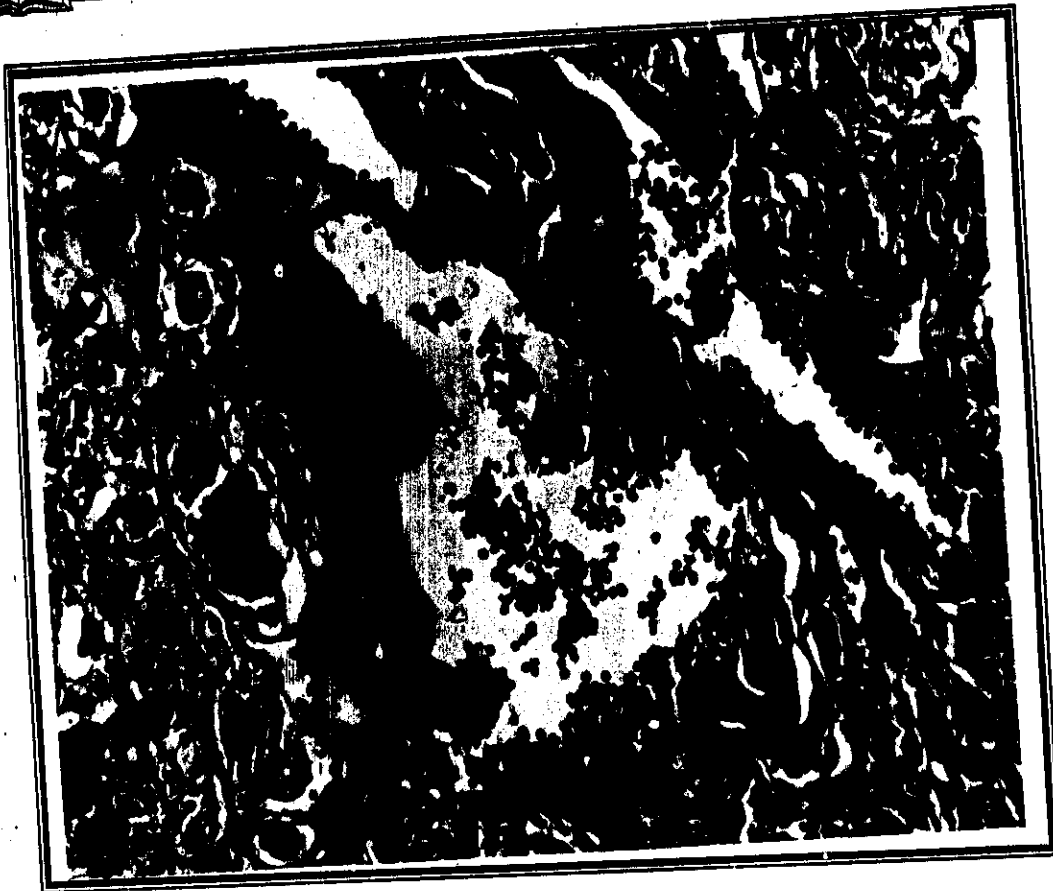


Fig. (32): Follicular thyroid carcinoma showing distorted follicular pattern and vascular invasion (H & E x200).

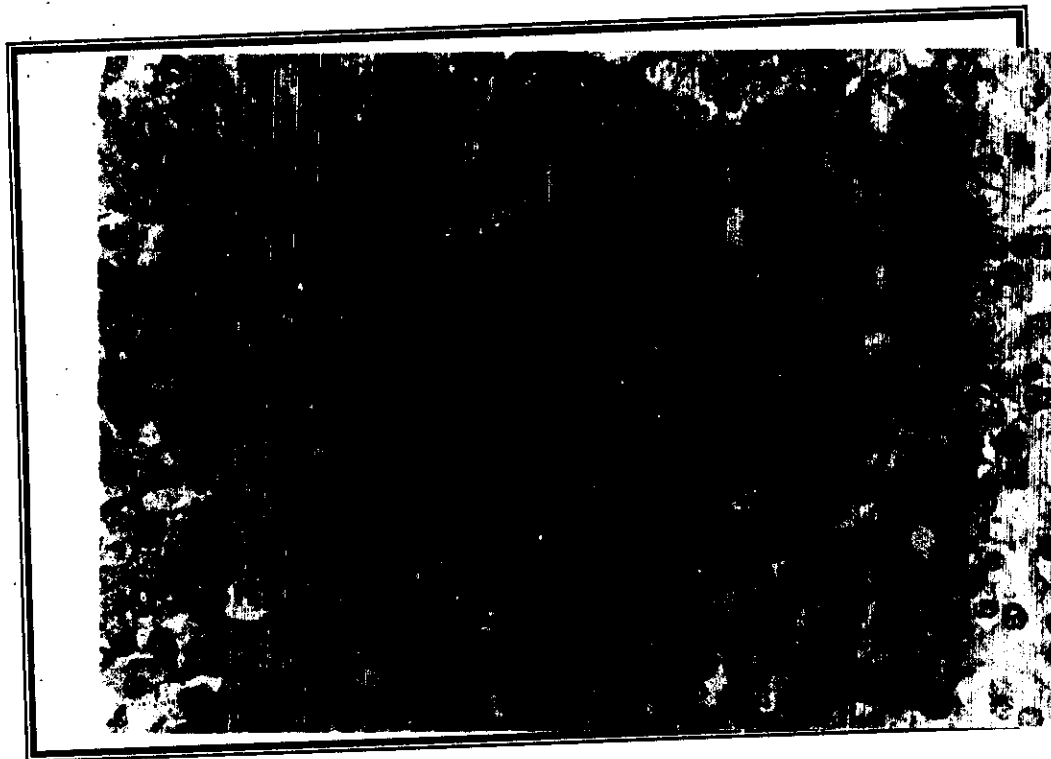


Fig. (33): Follicular thyroid carcinoma showing positive brown nuclear staining for Cyclin D1, score (+4) (Streptavidin/Biotin, DAB x400).



Fig. (34): Follicular thyroid carcinoma grade III, showing positive brown nuclear staining for Cyclin D1, score (+4) (Streptavidin/Biotin, DAB x200).



Fig.(35): Follicular thyroid carcinoma showing positive brown cytoplasmic staining for Bcl-x intensity (+++) (Streptavidin/Biotin, DAB x200).



Fig.(36): Follicular thyroid carcinoma showing positive brown membranous staining for CD44 high score (80%) (Streptavidin/Biotin, DAB x400).



Fig. (37): Follicular thyroid carcinoma showing positive brown membranous staining for CD44 low score (4%) (Streptavidin/Biotin, DAB x400).



Fig. (40): Hurthle cell carcinoma showing positive brown nuclear staining for Cyclin D1, score (+2) (Streptavidin/Biotin, DAB x400).



Fig. (41): Hurthle cell carcinoma showing positive brown cytoplasmic

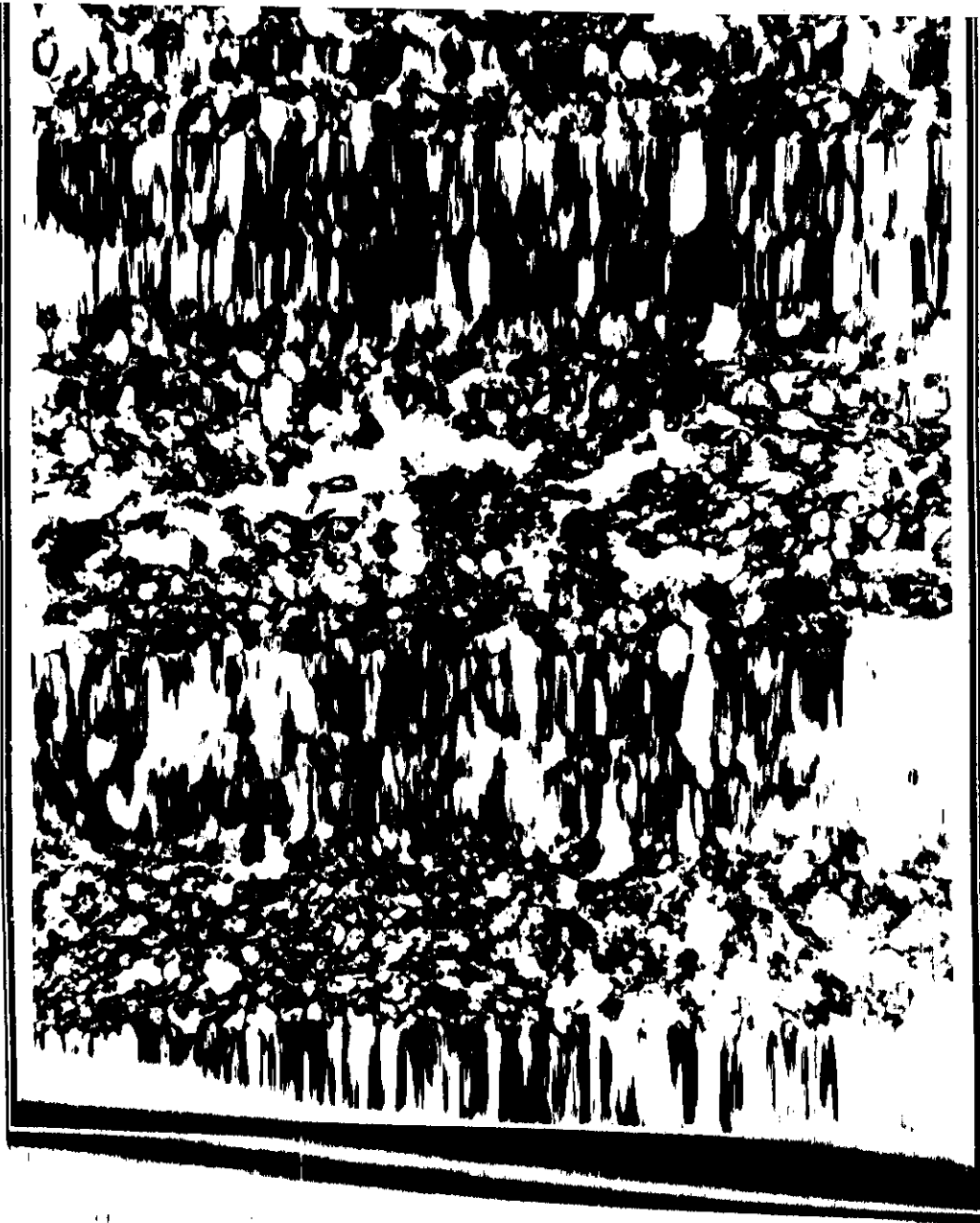


Fig. (42): Hurthle cell carcinoma showing positive brown membranous staining for CD44, high score (95%) (Streptavidin/Biotin, DAB x200).





Fig. (44): Medullary thyroid carcinoma showing nodular pattern of growth and vascular invasion (H & E x100).

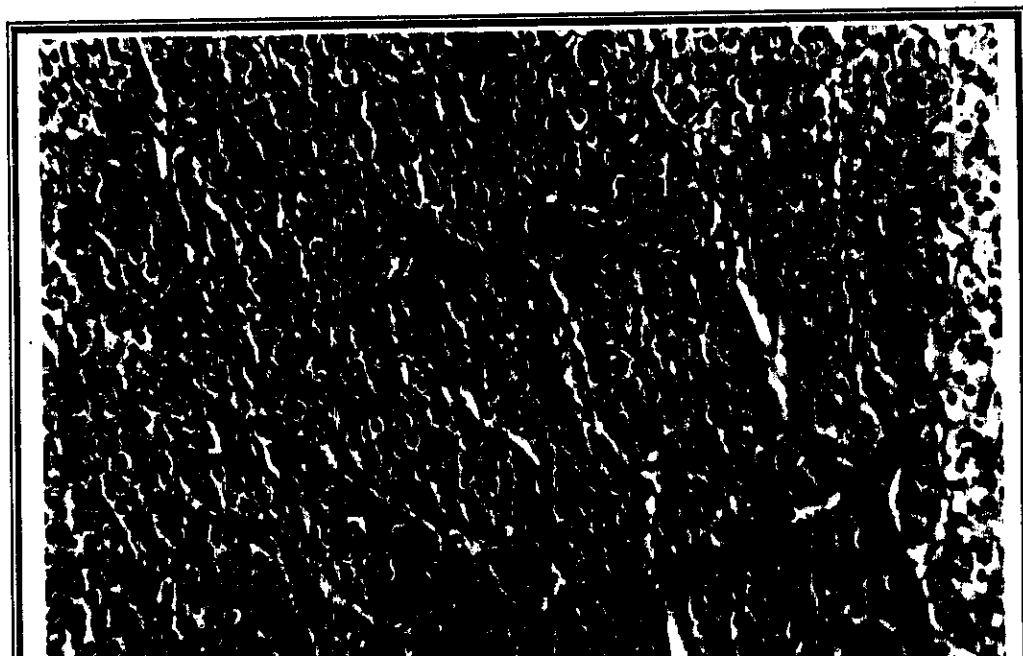




Fig. (46): Medullary thyroid carcinoma showing positive brown nuclear staining for Cyclin D1 in nuclei of tumors cells and negative staining in the adjacent thyroid parenchyma, score (+4) (Streptavidin/Biotin, DAB x200).

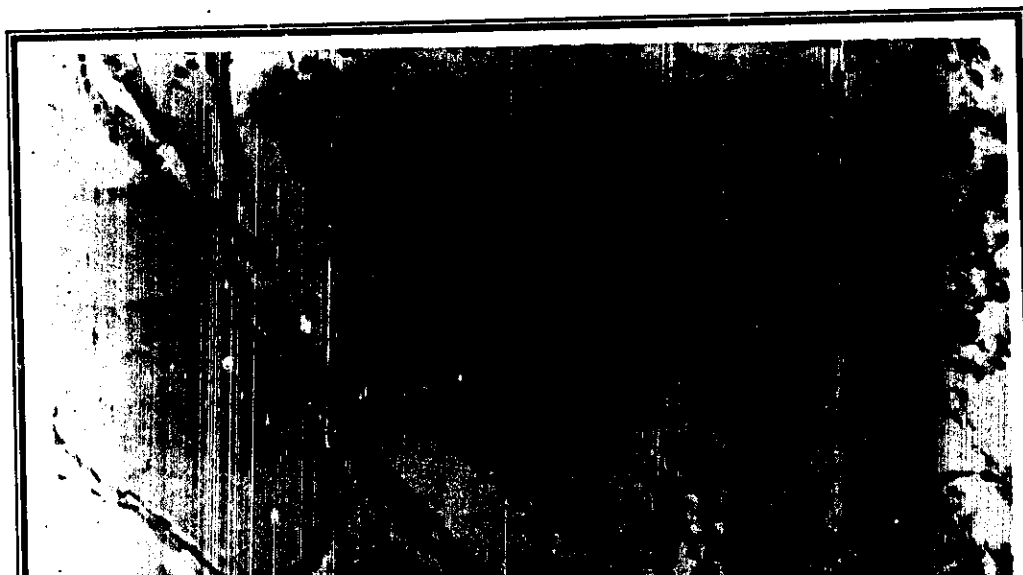
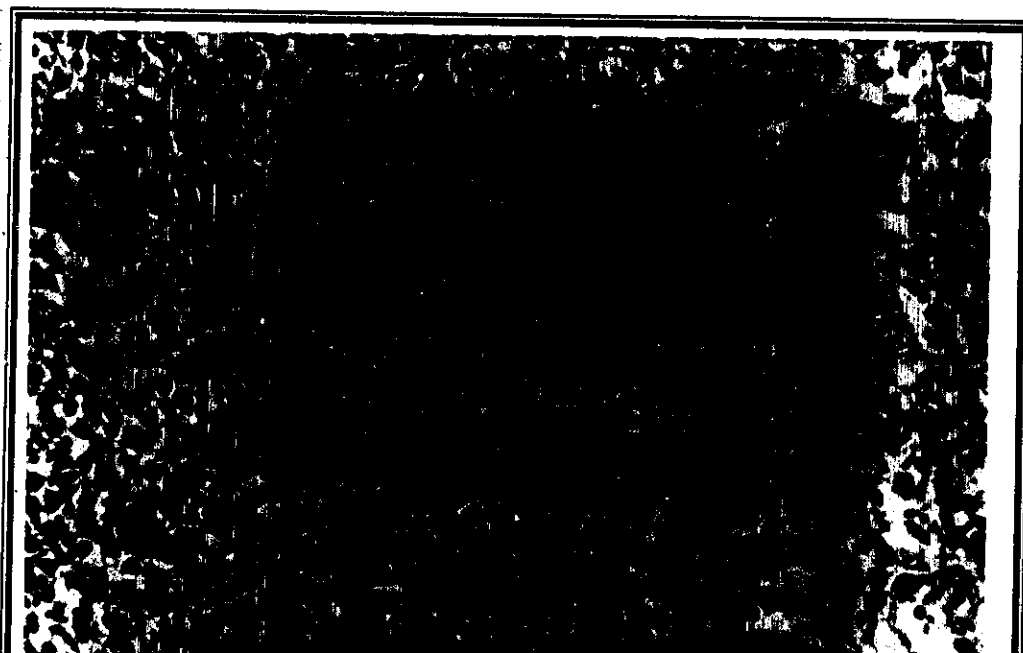




Fig. (48): Medullary thyroid carcinoma showing positive brown membranous staining for CD44, high score (90%) (Streptavidin/Biotin, DAB x400).



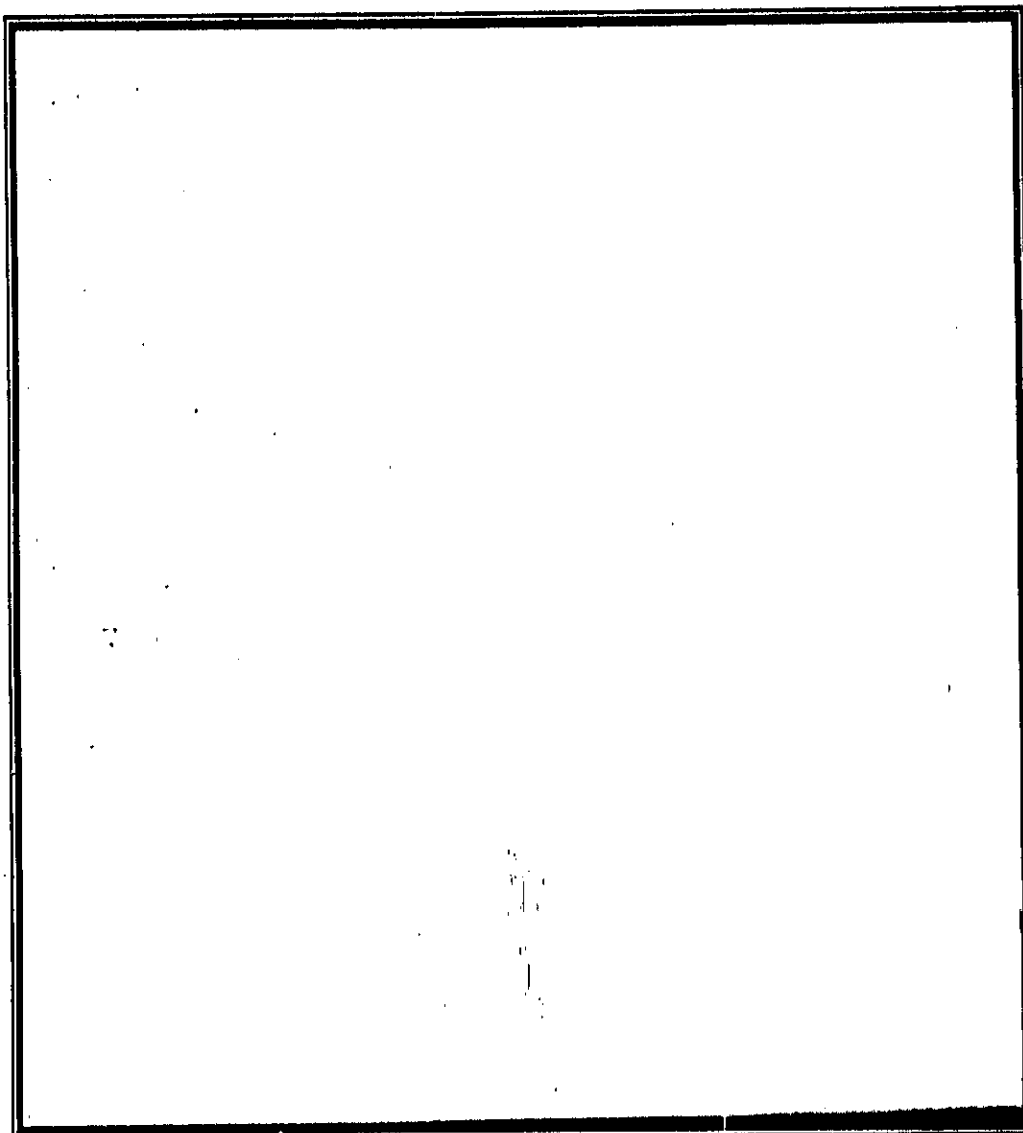
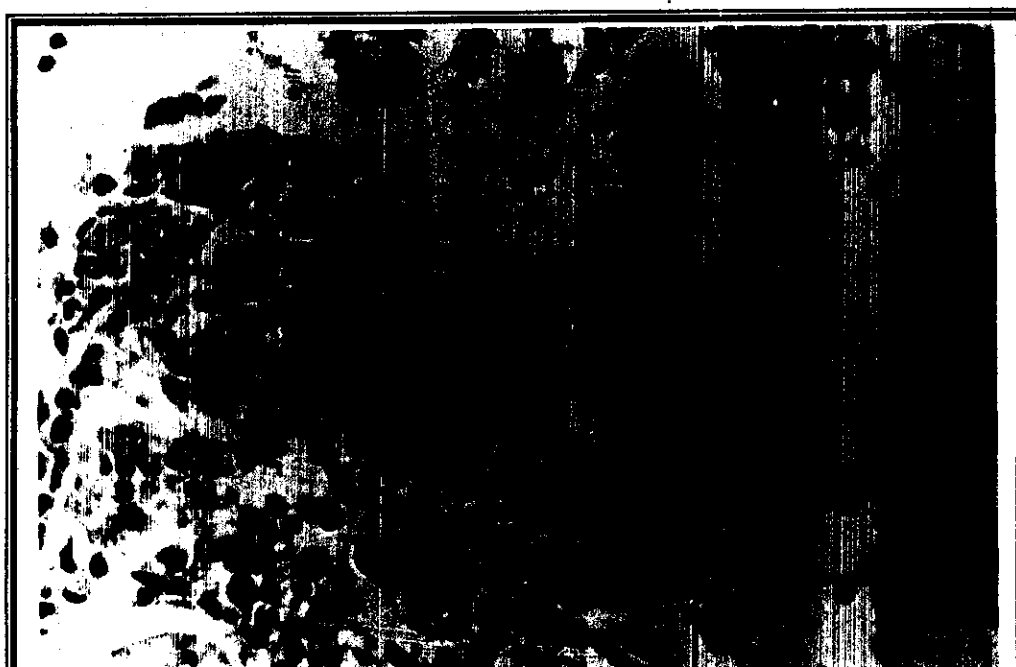


Fig. (50): Anaplastic thyroid carcinoma showing positive brown nuclear staining for Cyclin D1 score (+1) (Streptavidin/Biotin, DAB x200).



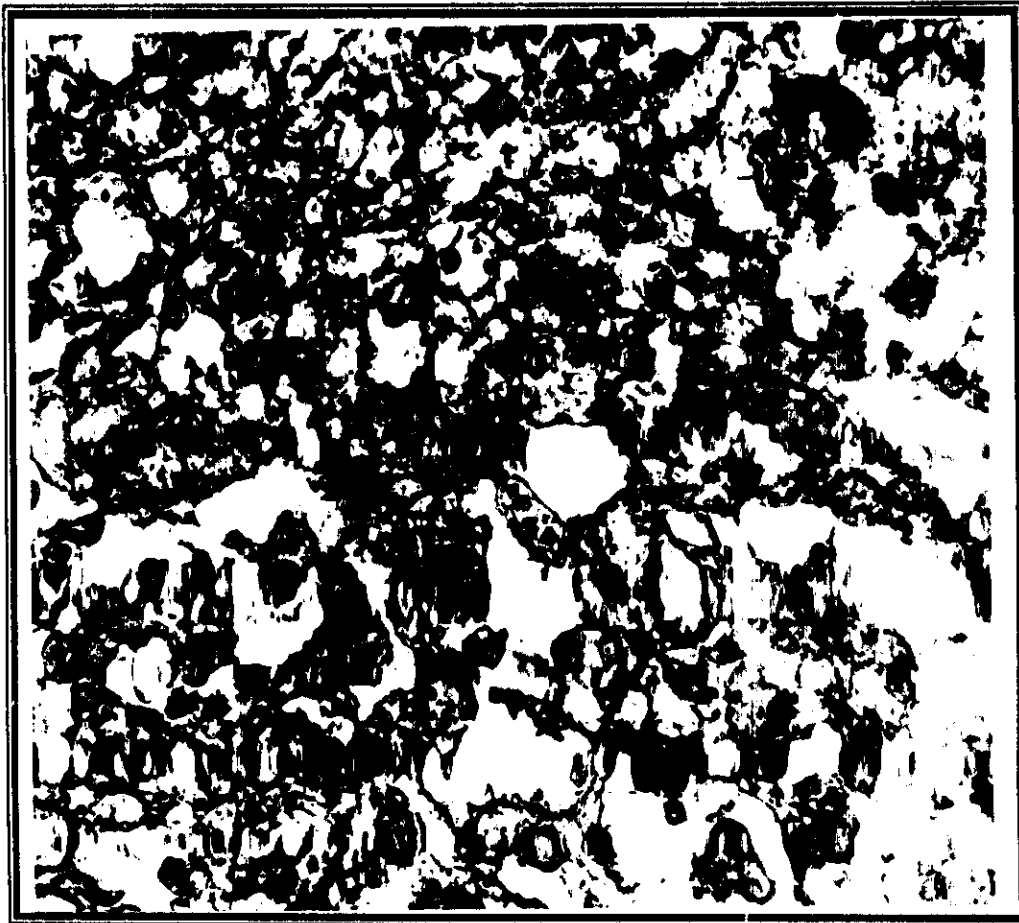


Fig. (48): Medullary thyroid carcinoma showing positive brown membranous staining for CD44, high score (90%) (Streptavidin/Biotin, DAB x400).

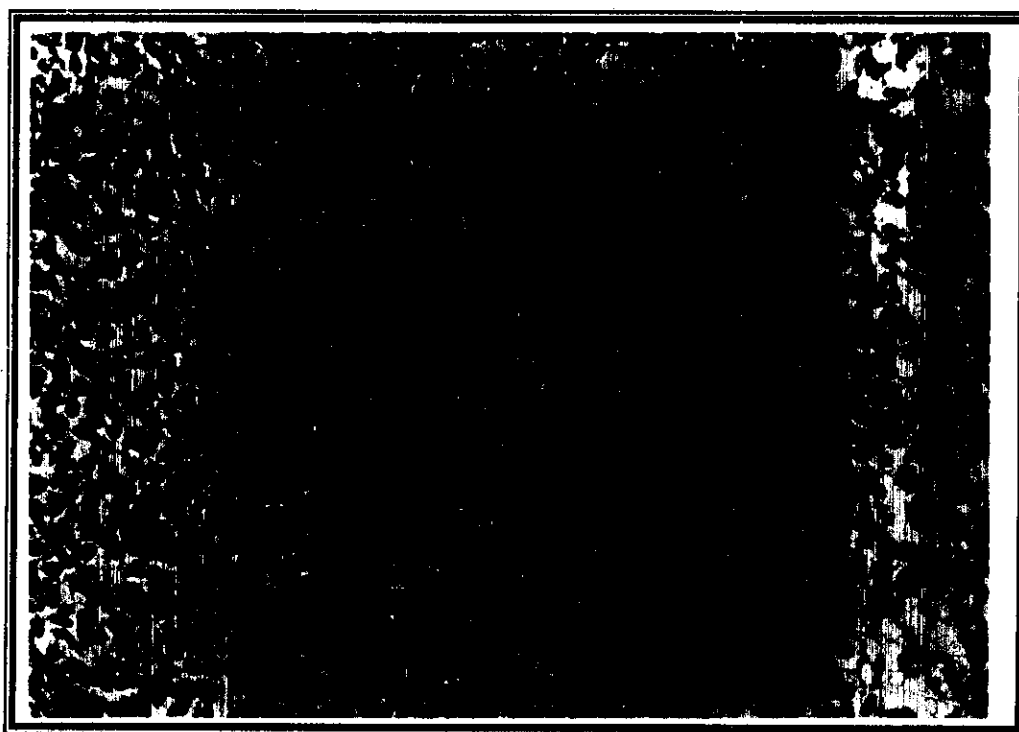


Fig. (49): Anaplastic thyroid carcinoma showing mixed round, spindle-shaped malignant cells (H & E x200).

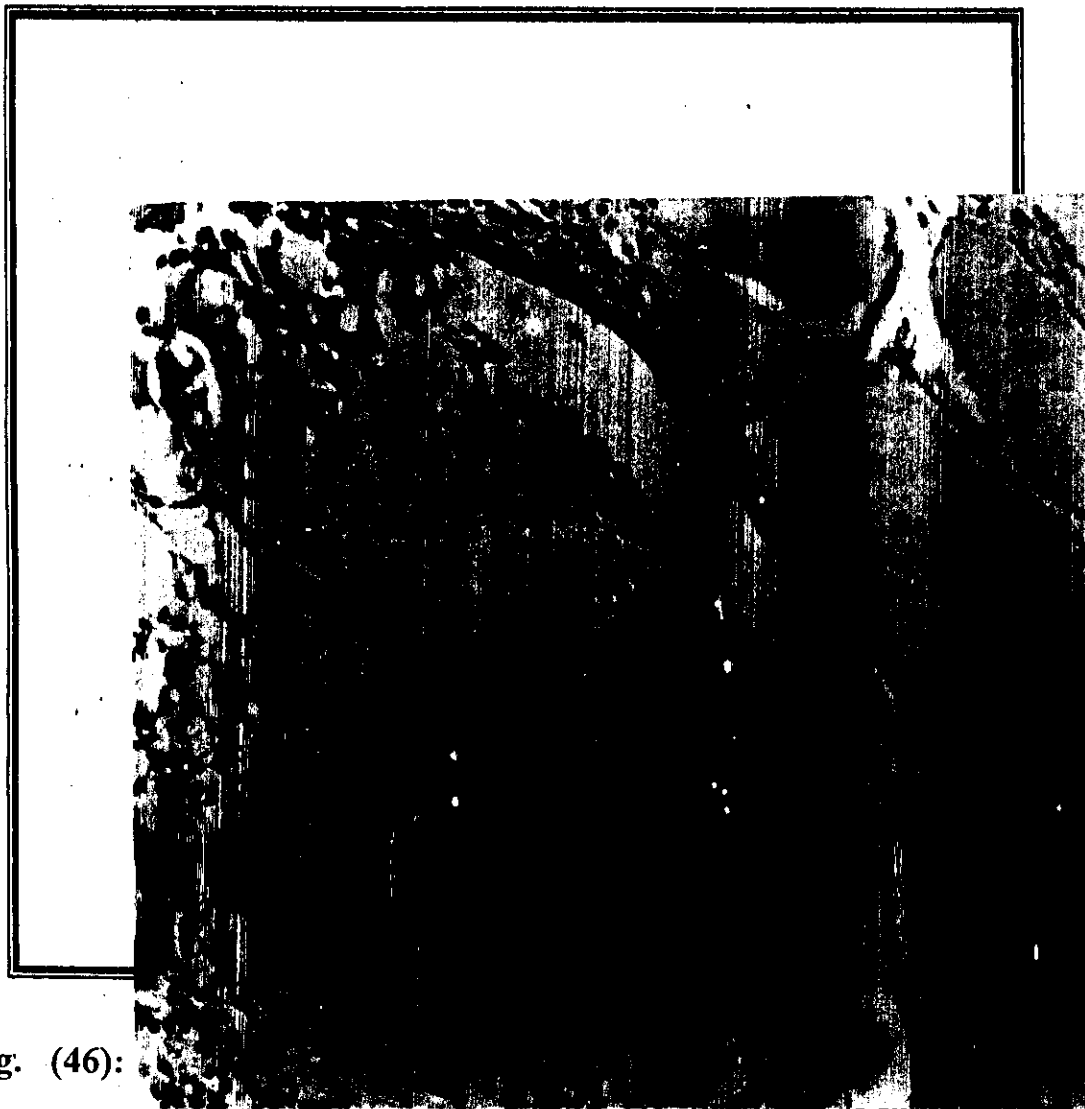


Fig. (46): Nuclear staining for Cyclin D1 in nuclei of tumors cells and negative staining in the adjacent thyroid parenchyma, score (+4) (Streptavidin/Biotin, DAB x200).



Fig. (47): Medullary thyroid carcinoma showing positive brown cytoplasmic staining for Papanicolaou stain (x400).

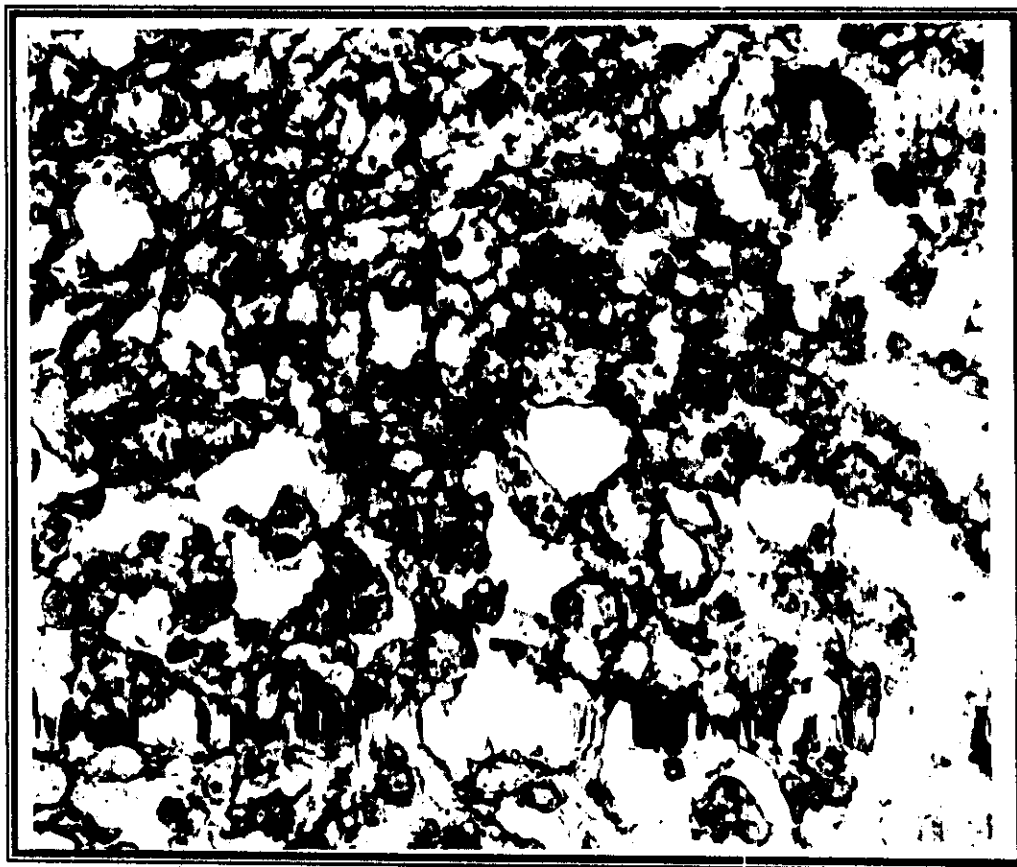


Fig. (48): Medullary thyroid carcinoma showing positive brown membranous staining for CD44, high score (90%) (Streptavidin/Biotin, DAB x400).

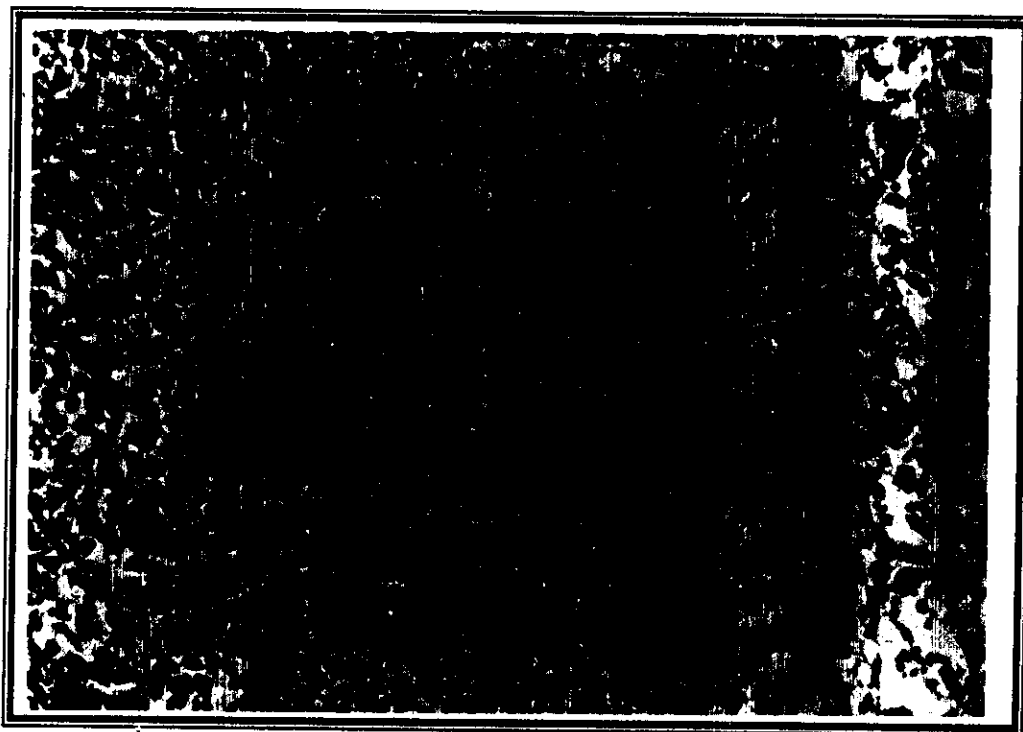


Fig. (49): Anaplastic thyroid carcinoma showing mixed round, spindle-shaped malignant cells (H & E x200).

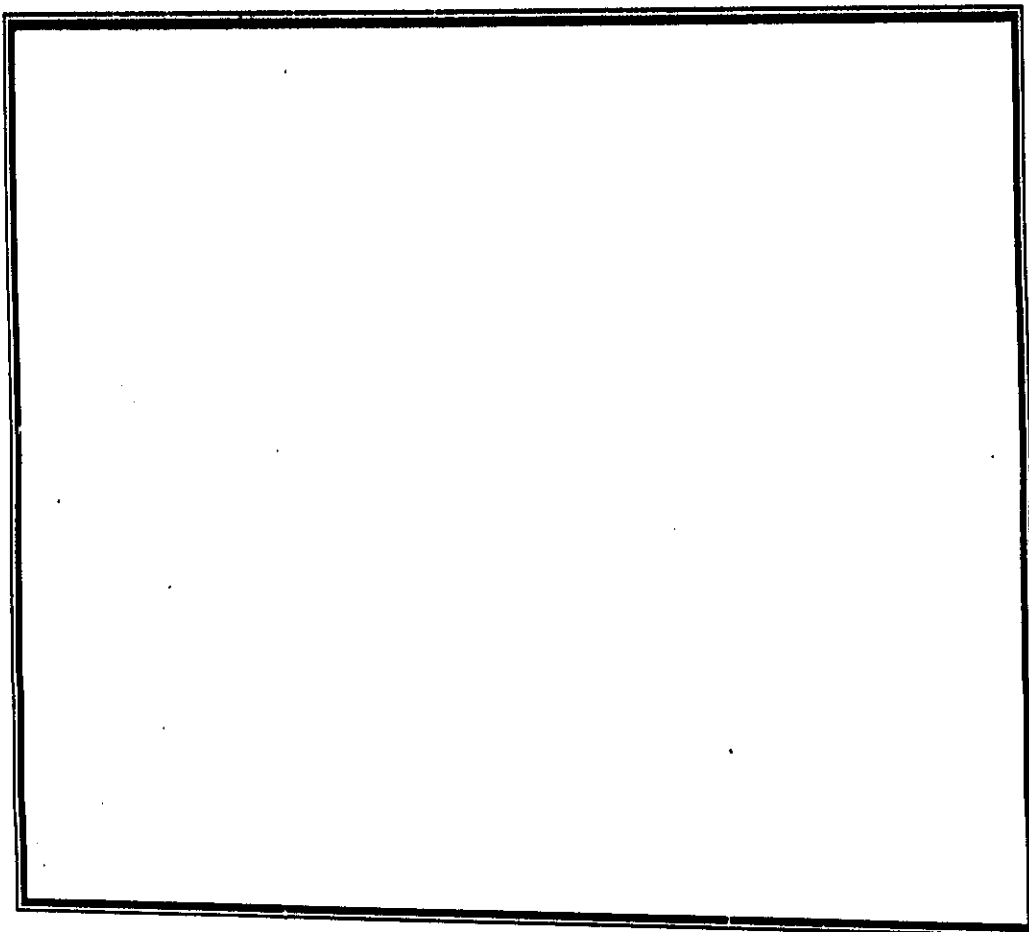


Fig. (50): Anaplastic thyroid carcinoma showing positive brown nuclear staining for Cyclin D1 score (+1) (Streptavidin/Biotin, DAB x200).

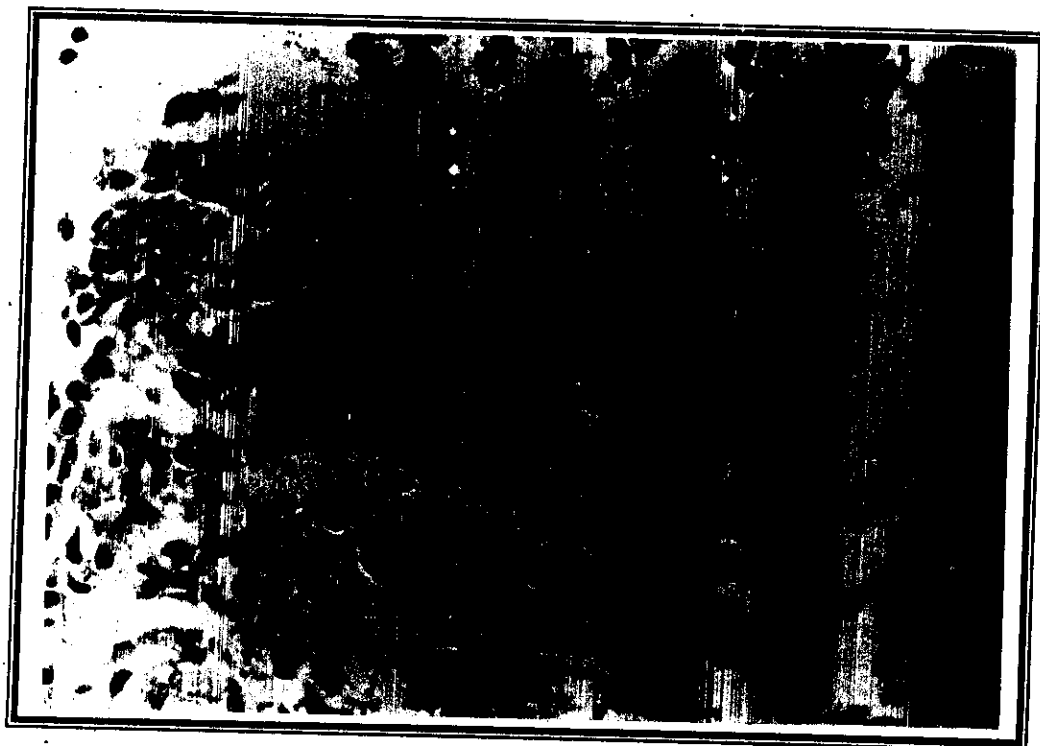


Fig. (51): Anaplastic thyroid carcinoma showing positive brown nuclear staining for Cyclin D1 score (+4) (Streptavidin/Biotin, DAB x200).



Fig. (52): Anaplastic thyroid carcinoma showing positive brown cytoplasmic staining for Bcl-x, intensity (++) (Streptavidin/Biotin, DAB x400).



Fig. (53): Anaplastic thyroid carcinoma showing positive brown membranous staining for CD44 high score (80%) (Streptavidin/Biotin, DAB x200).