

Results

I clinical data of the studied cases:**Gender of he studied cases:****Table (1)**

Gender	No	%
Males	30	75
Females	10	25
Total	40	100

Stage of the studied cases:**Table (2)**

Stage	No	%
Stage I	0	0
Stage II	13	32.5
Stage III	21	52.5
Stable IV	6	15
Total	40	100.0

Safety margin of the studied cases:**Table (3)**

Safety margin	No	%
Positive	36	90
Negative	4	10
Total	40	100.0

Lymph node metastasis in the studied cases:**Table (4)**

Lymph node metastasis	No	%
Present	6	15
Absent	34	85
Total	40	100

Distant metastasis in the studied cases:**Table (5)**

Distant metastasis	No	%
Present	19	47.5
Absent	21	52.5
Total	40	100.0

Survival of the studied cases:**Table (6)**

Survival	No	%
Alive	27	67.5
Died	13	32.5
Total	40	100.0

Histopathological data of the studied cases:

- Among the studied cases, histopathological type of bladder cancer was transitional cell carcinoma in 20/40 (50%), squamous cell carcinoma in 13/40 (32.5%), adenocarcinoma in 2/40 (4%), adenosquamous in 2/40 (4%) and undifferentiated in 3/40 (6%) (table 7)
- The grades of bladder cancer in the studied cases was: grade 1 in 5/40 (12.5%) , grade 2 in 16/40 (40%) and grade 3 in 19/40 (47.5%) (table 8).
- Among the studied cases, vascular invasion was present in 29/40 (27.5%) of cases, and absent in 11/40 (27.5%) (table 9).
- Muscular invasion was present in 39/40 (97.5%) of cases and absent in 1/40 (2.5%) (table 9).
- Neural invasion was present in 36/40 (96%) of case and absent in 4/40 (10%) of cases (table 9).
- Bilharzial ova was present in specimen of studied cases in 18/40 (45%) and absent in 22/40 (55%) (table 10).

Histopathological types of bladder cancer in the studied cases (table 7)

Histopathological types	No	%
transitional cell carcinoma	20	50
Squamous cell carcinoma	13	32.5
Adenosquamous cell carcinoma	2	4
Adenocarcinoma	2	4
Anaplastic	3	6
Total	40	100.0

Grades of bladder cancer in the studied cases:

(Table 8):

Grade	No	%
Grade 1	5	12.5
Grade 2	16	40
Grade 3	19	47.5
Total	40	100.0

Histopathological invasion parameter of the studied cases

(table 9)

Invasion	No	%
Vascular		
Present	29	72.5
Absent	11	27.5
Muscular		
Present	39	97.5
Absent	1	2.5
Neural		
Present	36	90
Absent	4	10
Total	40	100.0

Bilharziasis in the studied cases:**(Table 10)**

Bilharziasis	No	%
Present	18	45
Absent	22	55
Total	40	100.0

Immunohistochemical result in the studied cases:

- Immunostaining for E-cadherin could be detected in 22/40 (55%) of cases and not detected in 18/40 (45%). Table 11)
- β -catenin was expressed in 24/40 (60%) of cases and not expressed in 16/40 (40%). Table (12)

E-cadherin expression in the studied cases: (table 11).

E-cadherin	No	%
Positive	22	55
Negative	18	45
Total	40	100.0

β -catenin: (table 12)

β -Catenin	No	%
Positive	24	60
Negative	16	40
Total	40	100.0

Correlation between clinicopathological data and immunohistochemical results:

E-cadherin in relation to gender and bilharziasis:

- Among the 40 studied cases of bladder cancer 30 cases (75%) were males and 10 cases (25%) were females. Among the thirty females cases, 7 cases (23.3%) were E-cadherin positive (+1), 7 cases (23.3%) were E-cadherin positive (+2), 3 cases (10%) were E-cadherin positive (+3) and the remaining 13 cases (43.3%) were E-cadherin negative (table 13).
- Among the 10 females cases, one (10%) was E-cadherin positive (+1) , 3 cases (30%) were E-cadherin positive (+2) , one cases (10%) was E-cadherin positive (+3) and the remaining 5 cases (50%) were E-cadherin negative (table 13).
- Among the 40 studied cases of bladder cancer, 18 cases (45%) were positive for schistosomiasis & 22 (55%) were negative. Among the positive cases, 3 cases (16.6%) were E-cadherin positive (+1) , 5 cases (27.7) were E-cadherin positive (+2) and 10 cases (55.5%) were E-cadherin negative.
- Among the negative cases, 4 (18.1%) were E-cadherin positive (+1), 6 cases (27.2%) were E-cadherin positive (+2) , 4 cases (18.1%) were E-cadherin positive (+3) and 8 cases (36.3%) were E-cadherin negative (table 13).

E-cadherin in relation to Gender and Bilharziasis: (table 13)

Variants		E-cadherin (positive)						E-caderin (Negative)		P. value
No	%	+1		+2		+3		No	%	
Gender		No	%	No	%	No	%	No	%	
♂ (30 75%)		7	23.3	7	23.3	3	10	13	43.3	
♀ (10 25%)		1	10	3	30	1	10	5	50	
Bilharziasis										
Present										
(18 45%)		3	16.6	5	27.7	0	0	10	55.5	
Absent										
(22 55%)		4	18.1	6	27.2	4	18.1	8	36.3	

β -Catenin in relation to gender and bilharziasis

- Among the 40 studied cases , 30 cases (75%) were ♀.
- Among the (30) males cases, 11 (36.6%) were β -catenin positive score +1, 6 cases (20%) were β -catenin positive (+2) , one case (3.3%) were β - catenin positive score (+3) and the remaining 12 cases (40%) were negative (table 14).
- Among the 10 females cases, 2 cases (20%) were β -catenin positive score (+1), 3 (30%) were β -catenin. positive score (+2), 1 (20%) were β -catenin positive score (+3) , and the remaining 4 cases (40%) were negative (table 14).
- Among the studied cases 18 cases (45%) were bilharzial positive and 22 (55%) were bilharzial negative (i.e. no bilharzial ova in the specimen studied).
- Among the 18 positive case for bilharziasis , 6 cases (33.3%) were β -catenin positive score (+1), 4 cases (22.2%) were β -catenin positive score (+2), 1 cases (5.5%) were β - catenin positive score (+3) and the remaining 7 cases (38.8%) were negative for β -catenin (Table 14)
- Among the 22 negative cases 6 cases (27.2%) were β -catenin positive score (+1), 5 cases (22.7%) were β -catenin positive (+2), 1 Case (4.5%) were β -catenin positive score (+3) and the remaining 10 cases (45.4%) were negative (table 14).

β -Catenin in relation to gender and Bilharziasis (table 14)

Variants		β -Catenin (positive)			β -Catenin Negative		P. value
No	%	+1	+2	+3	No	%	
Gender		No %	No %	No %	No %		0.007**
♂ (30	75%)	11 36.6	6 20	1 3.3	12 40		
♀ (10	25%)	2 20	3 30	1 10	4 40		
Bilharziasis							0.924
Present							
(18	45%)	6 33.3	4 22.2	1 5.5	7 38.8		
Absent							0.924
(22	55%)	6 27.2	5 22.7	1 4.5	10 45.4		

E-cadherin in relation to stage and grade:

- Among the studied cases, 13/40 (32.5%) had stage I, II and 27/40 (67.5%) had stage III & IV. Among the cases whom had stage I & II 10/13 (76.9%) were negative for E-cadherin and 3 cases (23%) were positive, two of the positive cases had score I and one had score 2 (table 15).
- Among the cases whom had stage III & IV. 9/27 (33.3) were negative, for E-cadherin and 18/27 (66.6%) were positive, among the positive cases 6 had score one, 8 had score 2 and 4 had score 3. The relation was statistically highly significant ($P=0.004$). (table 15).
- Among the studied cases, 5/40 (12.5%) had grade I one of them (20%) were negative for E-cadherin and 4 cases (80%) were positive, the immunostaining score of the positive case was +1 in 2 cases and +2 in 2 cases, (table 15).
- Among the studied cases, 16/40 (40%) had grade 2, 6 of them (37.5%) were negative for E-cadherin and 10 cases (62.5%) were positive. The immunostaining score of the positive cases was +1 in 3 cases, +2 in 4 cases and +3 in 3 cases (table 15).
- Among the studied cases 19/40 (47.5%) had grade 3, 11 of them (57.8%) were negative for E-cadherin and 8 (42.1%) were positive. The immunostaining score in the positive cases was +1 in 3 cases, +2 in 4 cases and +3 in one case. (table 15).
- Among the 5 cases whom had grade 1, 5/5 (100%) were positive for β catenin, all of them had score +1. (table 16).
- Among the 16 cases whom had grade 2, 8/16 (50%) were negative for β catenin and 8/16 (50%) were positive, the immunostaining score was +1 in 2 cases, +2 in 5 cases and +3 in one of the positive cases (table 16).

E-cadherin in relation to stage and grade of bladder cancer : (table 15)

Variants		E-cadherin positive						E-cadherin Negative		P. value
No	%	+1		+2		+3		No	%	
		No	%	No	%	No	%	No	%	
Stage I & II										0.004**
(13	32.5)	2	15.3	1	7.6	0	0	10	76.9	
Stage III & IV										
(27	67.5)	6	22.2	8	29.6	4	14.8	9	33.3	
Grade										
I (5	12.5)	2	40	2	40	0	0	1	20	0.251
II (16	40)	3	18.7	4	25	3	18.7	6	37.5	
III (19	47.5)	3	15.7	4	21	1	5.2	11	57.8	

* = Significant.

**= Highly significant

β -Catenin in relation to stage and grade of bladder cancer:

- Among the 13 cases whom had stage I & II, 8/13 (61.5%) were negative for β -catenin and 5 (38.4%) were positive, the immunostaining score was +1 in 4 cases and +2 in one of the positive case (table 17).
- Among the 27 cases whom had stage III & IV , 8/27 (29.6%) were negative for β -catenin and 19/27 (70.3%) were positive, the immunostaining score was +1 in 9 cases, +2 in 8 cases and +3 in 2 cases.. The relation was proven to be statistically significant ($P=0.036$). Table (17)

β -Catenin in relation to stage and grade of bladder cancer (table 16)

Variants No %	β -catenin positive						β -catenin Negative		P. value
	+1		+2		+3		No	%	
	No	%	No	%	No	%	No	%	
Stage I & II (13 32.5)	4	30.7	1	7.6	0	0	8	61.5	0.036*
Stage III & IV (27 67.5)	9	33.3	8	29.6	2	7.4	8	29.6	
Grade									0.679
1 (5 12.5)	5	100	0	0	0	0	0	0	
2(16 40)	2	12.5	5	31.2	1	6.2	8	50	
3(19 47.5)	6	31.5	4	21	1	5.2	8	42.1	

E-cadherin in relation to safety margin and lymph node metastasis:

- Among the 36 cases whom had safety margin invaded, 15/36 (41.6%) were negative for E-cadherin and 21/36 (58.3%) were positive. The immunostaining score was +1 in 8 cases, +2 in 9 cases and score +3 in 4 of the positive cases. (table 17).
- Among the 4 cases whom had safety margin not invaded, 3/4 (75%) were negative for E-cadherin and 1/4 was, positive score +2 (table 17).
- Among the 6 cases whom had lymph node metastasis, 2/6 (33.3%) were negative for E-cadherin and 4/6 (66.6%) were positive. The immunostaining score was +1 in 3 cases, and was +2 in one of the positive cases. (Table 17).
- Among the 34 cases whom had no lymph node metastasis 16/34 (47%) were negative for E-cadherin and 18/34 (52.9%) were positive. The immunostaining score was +1 in 5 cases, was +2 in 9 cases, the and was +3 in 4 of the positive cases (table 17).

E-cadherin in relation to safety margin and lymph node metastasis:
(table 17)

Variants		E-cadherin positive						E-cadherin Negative		P. value
No	%	+1		+2		+3		No	%	
		No	%	No	%	No	%	No	%	
Safety margin										0.191
Positive										
(36	90%)	8	22.2	9	25	4	11.1	15	41.6	
Negative										
(4	10%)	0	0	1	25	0	0	3	75	
Lymph node metastasis										0.636
Present										
(6	15%)	3	50	1	16.6	0	0	2	33.3	
Absent										
(34	75%)	5	14.7	9	26.4	4	11.7	16	47	

**β -Catinin in relation to safety margin and lymph node metastasis:
(table 18):**

Variants		β-Catenin positive						β-catenin Negative		P. value
No	%	+1		+2		+3		No	%	
		No	%	No	%	No	%	No	%	
Safety margin										0.571
Positive										
(36	90%)	11	30.5	8	22.2	2	5.5	15	41.6	
Negative										
(4	10%)	2	50%	1	25	0		1	25	
Lymph node metastasis										0.840
Present										
(6	15%)	3	50%	1	16.6	0		2	33.3	
Absent										
(34	75%)	10	29.4	8	23.5	2	5.8	14	41.1	

E-cadherin in relation to invasion parameters:

- Among the 29 cases whom had vascular invasion 16/29 (55.1%) were E-cadherin negative and 13/29 (44.8%) were positive, the immunostaining score was +1 in 7 cases, +2 in 4 cases and +3 in 2 of the positive cases. The difference was proven to be statistically highly significant. ($P=0.002$) (table 19).
- Among the 11 cases whom had no vascular invasion 2/11 (18.1%) were negative for E-cadherin and 9 cases (81.8%) were positive. The immunostaining score was +1 in one case, +2 in 6 cases and +3 in 2 of the positive cases (table 19).
- Among the 39 cases whom had muscular invasion positive 18/39 (46.1%) were E-cadherin negative and 21/39 (83.8%) were positive. The immunostaining score was +1 in 8 cases, +2 in 9 cases and +3 in 4 of the positive cases (table 19).
- The only one case whom had no muscular invasion was positive for E-cadherin +2 (table 19).
- Among the 36 cases whom had neural invasion positive 18/36 (50%) were negative for E-cadherin and 18/36 (50%) were positive. The score of immunostaining was +1 in 7 cases, score +2 in 7 cases and +3 in 4 of the positive cases (table 19).
- The 4 cases whom had neural invasion negative were positive for E-cadherin, 3 of them had score +2 and one had score +1. The relation was proven to be statistically significant. ($P=0.037$) (table 19).

β -catenin in relation to invasion parameters:

- Among the 29 cases whom had vascular invasion 15/29 (51.7%) were negative for β -catenin and 14/29 (48.2%) were positive. The immunostaining score was +1 in 8 cases, +2 in 5 cases and +3 in one of the positive cases (table 20).
- Among the 11 cases whom had no vascular invasion 1/11 (90%) was negative for β -catenin and 10/11 (91%) were positive. The immunostaining score was +1 in 5 cases, +2 in 4 cases and +3 in one of the positive cases the difference was proven to be statistically significant. ($P = 0.015$) (table 20).
- Among the 39 cases whom had muscular invasion positive, 16/39 (41%) were negative for β -catenin and 23/39 (59%) were positive the immunostaining score was +1 in 12 cases, +2 in 9 cases and =3 in 2 of the positive cases (table 20).
- The only one case whom had no muscular invasion was positive for β -catenin score =1 (table 20).
- Among the 36 cases whom had neural invasion positive 16/36 (44.4%) were negative for β -catenin and 20/36 (55.5%) were positive. The immunostaining score was +1 in 10 cases, +2 in 8 cases and score +3 in one of the positive cases (table 20).
- Among the 4 cases whom had no neural invasion, they are all positive for β -catenin. The immunostaining score was +1 in 3 cases and +2 in one case (table 20).

β -Cateinin in relation to invasion parameters (table 20):

Variants		β-Cateinin positive						β-Cateinin Negative		P. value
No	%	+1		+2		+3				
		No	%	No	%	No	%	No	%	
Invasion										0.015*
Vascular										
Present (29	72.5)	8	27.5	5	17.2	1	3.4	15	51.7	
Absent (11	27.5)	5	45.4	4	36.3	1	9	1	9	
Muscular										0.334
Present (39	97.5)	12	30.7	9	23	2	5.1	16	41	
Absent (1	2.5%)	1	100	0	0	0	0	0	0	
Neural										0.728
Present (36	90)	10	27.7	8	22.2	1	2.7	16	44.4	
Absent (4	10)	3	75	1	25	0	0	0	0	

Table (21) E-cadherin and Beta catenin expression in Schistosoma-associated (SA) and non-Schistomsoma-Associated (NSA) bladder cancer:

Schistosomiasis: no (%)	E-Cadherin		Beta catenin	
	Positive No (%)	Negative	Positive	Negative
SA Bladder Cancer : 18/40 (45.1%)	8 (44.4%)	10(55.6%)	11(61.1%)	7(38.9%)
NSA Bladder Cancer: 22/40 (55%)	14(63.6%)	36.3%	13(59.1%)	9(40.9%)
Total : 40	22	18	24	16

Correlation between invasion parameters and E-cadherin-catenin expression and grade:

- Among the 22 cases whom had E-cadherin positive, 13 had vascular invasion positive and 9 cases had vascular invasion negative.
- Among the 18 cases whom had E-cadherin. negative 16 cases had vascular invasion positive and 2 cases had vascular invasion negative. The difference was proven to be statistically highly significant. (P =0.002)
- Among the 24 cases whom had β -catenin positive, 14 cases had vascular invasion positive and 10 cases had no vascular invasion. (table 22)
- Among the 16 cases whom had β -catenin negative, 15 cases had vascular invasion positive and only one case had no vascular invasion. The difference was proved to be statistically significant (P = 0.015) (table 22).
- Neural invasion was present in 18/22 (81.8%) of cases whom had E-cadherin. positive compared with 18/18 (100%) whom had E-cadherin negative. The result was proven to be statistically significant (P =0.037) (table 22)
- Among the 5 cases whom had grade 1, 4 cases had no vascular invasion and one cases had vascular invasion positive.
- Among the 16 cases whom had grade 2,11 cases had vascular invasion positive and 5 cases no vascular invasion.
- Among 19 cases whom had grade 3,17 cases had vascular invasion positive and 2 cases had vascular invasion negative . the difference was proven to be statistically significant. (P=0.017) (table 22).
- Among the 5 cases whom had grade 1,2 cases had neural invasion positive and 3 cases were had neural invasion negative. Among he the 16

- Among the 40 studied cases, distant metastasis was absent in 19 (47.4%) and present in 21 case (52.5%). E-Cadherin expression was absent in 6/19 (31.5%) in cases whom had no distant metastasis compared with 12/21 (57.1%) whom had distant metastasis positive. The relation was statistically significant ($P=0.12$) (table 23).
- β -catenin expression was lost in 4/19 (21%) in cases whom had no distant metastasis compared with 12/21 (57.1%) in cases whom had distant metastasis positive. The relation was proved to be highly significant ($P=0.001$). (Table 24).

Variants		E-Cadherin positive						E-cadherin	P. value	
No	%							Negative		
		+1		+2		+3				
		No	%	No	%	No	%	No	%	
Distant metastasis										0.012*
Absent (Mo)										
(19 47.5%)		3	15.7	6	31.5	4	21	6	31.5	
Present (M1& Mx)										0.012*
(21 52.5%)		5	23.8	4	19	0	0	12	57.1	

E-cadherin and Beta catenin in relation to survival:

- 1/22 (45%) of died cases were E-cadherin. positive compared with 13/18 (72.2%) were E-cadherin negative. The difference was proved to be statistically highly significance ($P = <0.0001$) (table 25)
- 5/24 (20.8%) of died cases were β -catenin. positive compared with 9/16 (56.2%) were β -catenin negative. The difference was statistically significant ($P=0.042$) Table (25)

Table 25: E-cahderin and Beta catenin Expression in relation to survival in 40 Bladder Cancer patients.

	Survival		P. value
	Living No (%) 26 (65%)	Dead No (%) 19 (35.3%)	
E-cadherin Expression:			
Positive :22/40 (55%)	21 (95.5%)	1(4.5%)	< 0.0001**
Negative : 18.40 (43.6%)	5 (27.7%)	13 (72.2%)	
Beta catenin Expression:			
Positive: 24/40 (60%)	19(79.2%)	5 (20.8%)	0.042*
Negative : 16(40 (40%)	7(43%)	9(56.2%)	
Total	26(65%)	14(35%)	

* = Significant, ** = Highly significant.