Results

Seventy women were enrolled in the present study following histological examination of endometrial samples then dvided into three groups:a group with normal endometrium (23 cases), a group with hyperplastic endometrium (37 cases), and a group with malignant endometrium (10 cases). Particepants were further subgrouped according to histological subgroups into: normal secretory, normal proliferative endometrium, simple hyperplastic endometrium, non-atypical complex hyperplastic endometrium atypical complex hyperplastic endometrium and malignant endometrium.

Comparison of mean value ± SD of bcl-2(unti/mg portein) in cell lysate from endometrial samples was done. Analysis of variance using ANOVA test revealed highly significant difference ($p<0.001$) between mean bcl-2 concentration in cell lysate from normal 45.67±32.71 unite /mg protein), hyperplastic (109.19±64.16 unite/mg protein) and malignant endometrium (64.06±36.24 unite/mg protein) (Table 1) Statistical analysis using unpaired –t test showed that the mean bcl-2 protein concentration in cell lysate from malignant endometrium was significantly higher than that in those from normal secretory ($p<0.01$) and simple hyperplastic endometrium ($p<0.001$). A

statistically non significant difference was observed between mean bcl-2 concentration in cell lysate of h malignant endometrium when compared with those with normal proliferative ($p>0.05$) and atypical complex hyperplastic endometrium ($P>0.05$) (Table 2).

Statistical analysis of mean bcl-2 protin concentration (unite/mg protein) in cell lysate in the different histological subgroups, including normal secretory and proliferative endometrium (SE,PE), simple hyperplastic endometrium (SH), non atypical complex hyperplastic endometrium (NCH), atypical complex hyperplastic endometrium (ACH) and malignant endometrium (EC), was done. Analysis of variance using ANOVA test revealed a statistically significant difference ($p<0.01$) between mean bcl-2 values in cell lysate of those histologic subgroups (Table 3). Further statistical analysis of such different mean values of bcl-2 was done using unpaired –t test (Table 4). A significantly lower mean bcl-2 concentration was observed in cell lysate of secretory endometrium (21.33± 6.99 unite/mg portein) when compaired to mean values of proliferative endometrium (72.41±28.33 unite/mg portein) simple hyperplatic endrometrium (128.08±55.12 unite/mg portein) and non atypical complex hyperplastic endometrium (135.27±68.54 unite /mg portein) ($p<0.01$). Similar finding was observed on comparison

of mean bcl-2 values in secretory endometrium with both atypical complex endometrium (49.56±23.87 unite /mg portein) and endometrial carcinoma (64.06±36.24 unite/mg portein) ($p<0.01$). Proliferative endometrium, on the other hand had a significantly lower bcl-2 mean concentration than the mean values in both simple hyperplasi and non typical complex hypreplastic endometrium ($p<0.01$). However, non significant difference was observed between the mean levels of bcl-2 in cell lysate of proliferative endometrium, and that of atypical complex hyperplastic endometrium, and endometrial carcinoma ($p>0.05$).

Among cases with endometrial hyperplasia only significant difference in bcl-2 mean values was observed on comparison of atypical complex hyperplasia with both simple hyperplastic endometrium and non atypical complex hyperplasia ($p<0.001$). On the other hand, a significantly lower bcl-2 mean protein concentration was detected in cell lysate of endometrial carcinoma when compaired with its mean level in cases with normal secretory endometrium, simple endometrial hyperplasia and non atypical complex hyperplasia ($p<0.01$,<0.001 & <0.01 respectively). However comparison of mean bcl-2 value in cell lysate of proliferative endometrium, atypical complex hyperplasia and endometrial carcinoma revealed non significant difference ($p>0.05$) (Table 4).

A trial was made to define a cut off bcl-2 value to differentiate normal, hyperplastic and malignant endometrium. Three cut off values of bcl-2 (u/mg portein) were tested; 107.35 unite/mg protein which represent the 90 th percentile of the mean bcl-2 values in cell lysate of normal endometrium., 111.18 unit/mg portein which representes the normal endometrial value+2SD and 118.2 unite /mg protein which is the highest recorded value in cell lysate of normal endometrium.

Table (5) demonestrates the frequency of cases above and below these cut off levels of bcl-2 among the 3 studied groups. The distribution of cases of normal, hyperplastic and malignant endometrium above these cut off bcl-2 values were recorded. Statistical analysis of the resultant frequency using chi-square test (x^2) revealed a significant difference in the frequency of cases above and below these cut off value among three groups which was more appearent on using bcl-2 values of 111.18 and 118.20 unite/mg portein. Similarly, the frequenccy of cases above and below such different cut off bcl-2 values were recorded among the different histologic subgroups (Table 6). A significant difference ($p<0.05$) was recorded between the frequency of cases with bcl-2 level above 107.35, 111.18 and 118.20 unite /mg portein and those below such levels in the different histologic subgroups.

Table (1): Analysis of variance (ANOVA) test of mean bcl-2 levels (unit/mg protein) in cell lysate of normal, hyperplastic and malignant endomertium

Group	No.	Bcl-2 protein (U/mg protein)	F test value	P value
Normal endometrium	23	45.67±32.71		
Hyperplastic endometrium	37	109.19±64.16	11.093	P<0.001
Malignant endometrium	10	64.06±36.24		

P < 0.001 = highly significant difference

Table (2) Unpaired "t" test for testing the site of significant variance in the bcl-$_2$ in cell lysate from normal, hyperplastic and malignant endomertrium

Source of variation	bcl-2 protein (unit/mg protein)	Test of significance	P Value
Normal/hyperplastic endomterium	**45.76±32.71/109.19±64.16**	t=5.05	P<0.001
Normal/malignant endomterium	**45.76±32.71/64.06±36.24**	t=1.37	P>0.05
Hyperplastic/malignant endomterium	**109.19±64.16/64.06±36.24**	t_1=2.90	P_1<0.01

P<0.01 & P<0.001 = Highly significant difference

P>0.05 = Non significant difference

Table (3): Analysis of variance (ANOVA) test of mean bcl-2 levels (units/mg protein) in cell lysate of normal (secretory & Proliferative). Hyperplastic (Simple, nonatypical & a typical complex) and malignant endometrial groups.

Histologic Subgroups	**No.**	**Bcl-2 protein llevel in cell lysate (U/mg protein)**	**f test value**	**P value**
Normal secretory endometrium [SE]	12	21.33±6.99		
Normal proliferative Endometrium [PE]	11	72.41±28.33		
Simple hyperplastic Endometrium [SH]	15	128.08±55.12	13.344	<0.01
Non-atypicle complex Hyperplastic endometrium [NCH]	12	135.27±68.54		
Atypical complex hyperplastic Endometrium [ACH]	10	49.56±23.87		
Malignant endometrium [EC]	10	64.06±36.24		

P < 0.01 = highly significant difference

Table (4): Unpaired "t" test for testing the site of significant variance of mean values ± SD of bcl-2 (units/mg protein) in cell lysate of the normal [secretory & proliferative], hyperplastic [simple, non-atypical complex & atypical complex] and malignant endometrium groups

Studied subgroups		Significance	
		t-value	P value
Normal secretary [21.33±6.99]	Normal proliferative [72.41±28.33]	5.82	<0.001
	Simple hyperplastic [128.08±55.12]	7.43	<0.001
	Non-atypical complex hyperplastic [135.27±68.54]	5.73	<0.001
	Atypical complex hyperplastic [49.56±23.87]	3.61	<0.01
	Malignant [64.06±36.24]	3.67	<0.01
Normal proliferative [72.41±28.33]	Simple hyperplastic [128.08±55.12]	3.35	<0.01
	Non-atypical complex hyperplastic [135.27±68.54]	2.92	<0.01
	Atypical complex hyperplastic [49.56±23.87]	2.00	>0.05
	Malignant [64.06±36.24]	0.58	>0.05
Simple hyperplastic [128.08±55.12]	Non-atypical complex hyperplastic [135.27±68.54]	0.29	>0.05
	Atypical complex hyperplastic [49.56±23.87]	4.87	<0.001
	Malignant [64.06±36.24]	3.30	<0.001
Nonatypical complex hyperplastic [135.27±68.54]	Atypical complex hyperplastic [49.56±23.87]	4.05	<0.001
	Malignant [64.06±36.24]	3.11	<0.01
Atypical complex hyperplastic [49.56±23.87]	Malignant [64.06±36.24]	1.06	>0.05

P > 0.05 = Non significant difference

P< 0.01 & P< 0.001 = Highly significant

Table (5): Frequency of normal, hyperplastic and malignant cases using different Bcl-2 cutoff values.

Group / Bcl-2 [U/g protein]	Normal [n=23]	Hyperplastic [n=37]	Malignant [n=10]	X^2 Value	P value
<107.35*	21 [91%]	22 [59%]	8 [80%]	7.54	<0.05
>107.35	2 [9%]	15 [41%]	2 [20%]		
<111.18**	22 [96%]	22 [59%]	8 [80%]	9.54	<0.01
>111.18	1 [4%]	15 [41%]	2 [20%]		
<118.2***	23 [100%]	22 [59%]	8 [80%]	13.4	<0.01
>118.2	0 [0%]	15 [41%]	2 [20%]		

P< 0.05 = Significant difference P<0.01 = HightySignificant difference

* 107.35 u/mg protein = 90% of the mean bcl-2 value in cell lysate of normal endometrium.

** 111.18 u/mg protein = Mean bcl-2 value in cell lysate of normal endometrium + 2SD.

*** 118.2 u/mg protein = The highest recorded value in cell lysate of normal endometrium.

Table (6): Frequency of normal [secretory & proliferative], hyperplastic [simple, non-atypical complex & atypical complex] and malignant endometrium groups using different Bcl-2 cutoff values.

Subgroups / Bcl-2 Unit/ mg pt	Secretory [n=12]	Proliferative [n=11]	Simple [n=15]	Complex [n=12]	Atypia [n=10]	Malignant [n=10]	X^2	P value
<107.35	12 [100%]	10 [91%]	5 [33.3%]	5 [41.7%]	9 [90%]	8 80%]	3.34	<0.05
>107.35	0	1 [9%]	10 [66.7%]	7 [58.3%]	1 [10%]	2 [20%]		
<111.18	12 [100%]	10 [91%]	7 [46.7%]	5 [41.7%]	10 [100%]	8 [80%]	2.07	<0.05
>111.18	0	1 [9%]	8 [53.3%]	7 [58.3%]	0	2 [20%]		
<118.2	12 [100%]	11 [100%]	7 56.7%]	5 [41.7%]	10 [100%]	8 [90%]	4.97	<0.05
>118.2	0	0	8 [53.3%]	7 [58.3%]	0	2 [20%]		

P < 0.05 = significant difference

Table (7): Age, parity, menopausal status, protein level in tissue lysate (mg/ml), bcl-2 level in tissue lysate (U/mg protein) in the normal secretory endometrium (SE) group

No.	Age	Parity	Menopausal status	Cell lysate protein (mg/ml)	Bcl-2 protein in tissue lysate (U/mg protein)
1	28	2	Pre	0.77	**31.5**
2	32	0	Pre	0.39	**21.2**
3	41	3	Pre	1.05	**18.3**
4	38	2	Pre	0.94	**29.0**
5	40	4	Pre	1.12	**9.7**
6	29	4	Pre	1.63	**17.3**
7	30	0	Pre	0.85	**24.6**
8	34	3	Pre	1.02	**15.9**
9	40	2	Pre	0.95	**30.4**
10	31	4	Pre	1.33	**26.1**
11	35	2	Pre	0.67	**13.4**
12	42	2	Pre	0.89	**18.6**

Pre= premenopausal

U= units

Table (8): Age, parity, menopausal status, protein level in tissue lysate (mg/ml), bcl-2 level in tissue lysate U/mg protein) in the normal proliferative endometrium (PE) group

No.	Age	Parity	Menopausal status	Cell lysate protein (mg/ml)	Bcl-2 protein (U/mg protein)
1	31	3	Pre	0.38	**94.8**
2	37	2	Pre	0.79	**50.3**
3	45	4	Pre	1.52	**58.9**
4	43	4	Pre	1.27	**86.5**
5	40	3	Pre	1.66	**109.4**
6	37	5	Pre	1.34	**39.5**
7	35	3	Pre	1.45	**62.3**
8	32	0	Pre	2.21	**27.8**
9	38	4	Pre	1.25	**76.4**
10	42	5	Pre	2.59	**72.4**
11	34	3	Pre	1.87	**118.2**

Pre = Premenopasual

Table (9): Age, parity, menopausal status, protein level in tissue lysate (mg/ml), bcl-2 level in tissue lysate (U/mg protein) in the Simple hyperplastic endometrium (SH) group.

No.	Age	Parity	Menopausal status	Cell lysate protein (mg/ml)	Bcl-2 protein in tissue lysate (U/mg protein)
1	44	5	Pre	1.18	**128.0**
2	45	6	Pre	0.83	**206.0**
3	39	4	Pre	1.06	**127.6**
4	32	2	Pre	0.35	**93.1**
5	47	7	Pre	1.30	**217.2**
6	36	3	Pre	0.62	**84.6**
7	35	0	Pre	0.75	**44.6**
8	48	4	Post	1.42	**224.9**
9	41	2	Pre	0.99	**137.8**
10	37	4	Pre	1.08	**75.3**
11	40	2	Pre	0.97	**171.6**
12	42	5	Pre	1.73	**92.7**
13	41	2	Pre	0.88	**96.1**
14	37	3	Pre	0.73	**86.4**
15	44	5	Pre	1.43	**135.3**

Pre = Premenopasual

Post = Postmenopausal

Table (10): Age, parity, menopausal status, protein level in tissue lysate (mg/ml), bcl-2 level in tissue lysate (U/mg protein) in the non- atypical complex hyperplastic endometrium (NCH) group.

No.	Age	Parity	Menopausal status	Cell lysate protein (mg/ml)	Bcl-2 protein in tissue lysate (U/mg protein)
1	43	6	Pre	2.03	**70.7**
2	46	5	Pre	1.82	**234.0**
3	42	2	Pre	2.31	**82.2**
4	43	7	Pre	0.57	**204.1**
5	41	2	Pre	1.63	**133.9**
6	47	2	Post	0.73	**172.4**
7	38	5	Pre	3.16	**41.8**
8	40	3	Post	0.98	**130.7**
9	42	3	Pre	2.06	**82.2**
10	38	4	Pre	1.53	**230.9**
11	45	6	Pre	0.85	**58.3**
12	43	4	Pre	1.44	**182.0**

Pre = Premenopasual

Post = Postmenopausal

Table (11): Age, parity, menopausal status, protein level in tissue lysate (mg/ml), bcl-2 level in tissue lysate (U/mg protein) in the atypical complex hyperplastic endometrium (ACH) group

No.	Age	Parity	Menopausal status	Cell lysate protein (mg/ml)	Bel-2 protein in tissue lysate (U/mg protein)
1	51	5	Pre	0.85	**62.6**
2	60	4	Post	0.63	**35.2**
3	46	3	Pre	1.17	**22.6**
4	42	3	Pre	0.70	**41.5**
5	52	4	Post	0.58	**52.2**
6	45	2	Pre	0.86	**29.6**
7	46	2	Pre	1.05	**102.1**
8	57	5	Post	0.78	**53.4**
9	59	7	Post	0.93	**28.5**
10	48	6	Pre	1.23	**67.9**

Pre = Premenopasual

Post = Postmenopausal

Table (12): Age, parity, menopausal status, grade (FIGO),protein level in tissue lysate (mg/ml), bcl-2 level in tissue lysate (U/mg protein) in the malignant endometrium (EC) group.

No.	Age	Parity	Menopausal status	Tumor grade	Cell lysate protein (mg/ml)	Bcl-2 protein in tissue lysate (U/mg protein)
1	52	4	Post	G3	2.58	**47.8**
2	50	3	Post	G3	0.84	**59.9**
3	47	6	Pre	G2	0.78	**43.5**
4	56	3	Post	G2	1.05	**42.8**
5	49	4	Post	G3	3.25	**34.1**
6	53	2	Post	G3	1.23	**31.7**
7	59	5	Post	G3	1.70	**52.6**

Pre = Premenopasual

Post = Postmenopausal

Tumor grade according to FIGO.