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The potential role of villin 1 and estrogen receptor (ER) in differentiation between endocervical adenocarcinoma and endometrial adenocarcinoma

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Abstract
Background: Endocervical adenocarcinoma (ECAC) is the 4th most common cancer in females globally. It has been ranked the 14th most common cancer in Egyptian females. The aim of this work was to study immunohistochemical expression of villin1 in endocervical and endometrial adenocarcinoma, immunohistochemical expression of ER in endocervical and endometrial adenocarcinoma and evaluate the potential role of villin 1 and ER expression in differentiation between endocervical & endometrial adenocarcinoma.
Methods: This retrospective study was carried out on 60 cases of endocervical & endometrial endometroid adenocarcinoma. Patients were classified into two equal groups: Group I: Cases of endocervical adenocarcinomas and Group II: Cases of endometrial endometroid adenocarcinomas.
Results: The positive predictive value of ER as a correlation between ER expression and clinicopathological characteristics has been addressed in our study was 100%. The negative predictive value was 73.1%. The positive predictive value of using panel of villin and ER expression and clinicopathological characteristics has been addressed in our study was 88.8%, the negative predictive value was 66.6%.
Conclusions: Villin1 is good diagnostic tool had high specificity in differentiating endocervical and endometroid adenocarcinoma and has a predictive value in ECAC. ER is good diagnostic tool in differentiating between endocervical and endometroid adenocarcinomas and has predictive value in endometroid adenocarcinoma.

Keywords: Villin 1, estrogen receptor (ER), endocervical adenocarcinoma, endometrial adenocarcinoma

Introduction
The 4th most frequent cancer in women worldwide is endocervical adenocarcinoma (ECAC). Among Egyptian women, it is the 14th most prevalent form of cancer [1].
Endometrial cancer is one of the top-ranking cancers that affect women and is associated with increased death rates [2].
Endometrioid adenocarcinoma (EMAC) is the third leading cause of death from cancer in women and the sixth most frequent malignancy in women worldwide (after cancers of the ovary and cervix) [1].
Both share many of the same histological characteristics, making correct diagnosis and treatment dependent on the originating location of the cancer [3].
Epithelial cells rely on the actin-binding protein villin1 to keep their microvilli in place, as well as to regulate cell shape and cell-specific epithelial anti-apoptotic processes. Villin1 is expressed in intestinal metaplasia, is linked to Barrett's oesophagus and chronic atrophic gastritis, but was not detected in healthy gastric or esophageal tissues [4].
While villin1 is expressed in certain adenocarcinomas, it is not present in normal epithelial tissues, suggesting that it may play a role in epithelial cell hyperplasia, dysplasia, or carcinogenesis [3]. Villin1 in endometrial carcinoma has not been intensively investigated [3]
The reproductive hormones, including estrogen has a mitogenic effect on endometrial tissue, by stimulating the endometrial glands and stromal cells to grow and proliferate during the menstrual cycle.

Unopposed endometrial estrogen exposure, such as estrogen replacement therapy during menopause, is associated with increased risk of developing endometrial cancer [5].

The normal endocervix appears to be controlled by steroid hormones, as the quantity and quality of endocervical mucus varies in response to hormonal alterations throughout the menstrual cycle, and ER has been identified in endocervical columnar epithelium through biochemical and immunohistochemical studies [6].

The aim of this work was to study immunohistochemical expression of villin1 in endocervical and endometrial adenocarcinoma, immunohistochemical expression of ER in endocervical and endometrial adenocarcinoma and evaluate the potential role of villin 1 and ER expression in differentiation between endocervical & endometrial adenocarcinoma.

Patients and Methods

This retrospective study was carried out on 60 cases of endocervical & endometrial endometroid adenocarcinoma. This study was carried out at Pathology Department, Faculty of Medicine, Tanta University, Tanta Cancer Center & private laboratories during the period between December 2019 till May 2021.

The study was done after approval from the Ethical Committee Tanta University. An informed written consent was obtained from the patients.

Patients were classified into two equal groups: Group I: cases of endocervical adenocarcinomas and group II: cases of endometrial endometroid adenocarcinomas.

Gross appearance

The gross picture of each case is obtained from pathology report. Cervical tumors were either exophytic at distal cervix or ulcerative involvement and induration of the wall (barrel shaped cervix). Endometrial endometroid cancer showed diffuse polypoid involvement of the endometrium that is friable and may arise from lower uterine segment.

Microscopic picture

The paraffin wax blocks were collected and cut of 5 µ and subjected to ordinary H&E staining for examination to confirm the histopathological diagnosis and to evaluate varies histological features. Neoplastic endocervical adenocarcinoma are classified into HPV associated adenocarcinoma and non-HPV associated adenocarcinoma according to WHO classification 2019 (5th edition). For confirmation of presence of HPV, P16 immunohistochemistry (the most frequently used surrogate marker for high-risk HPV infection) was done on endocervical adenocarcinom**.** The HPVA ECACs were further substratified into usual-type, villoglandular-type and mucinous**.** NHPVA ECACs were further substratified into gastric-type and clear cell based on their morphological features. As per the IECC (International endocervical adenocarcinoma criteria & classification), endocervical adenocarcinoma (ECAC) was assigned as HPVA based on the presence of apical mitotic features and apoptotic bodies present at scanning magnification. When these features were absent, and the slides were reexamined at × 200. Cases were classified as NHPVA if HPVA features were absent.

Endocervical adenocarcinoma are graded as [7]

Grade I: Well, differentiated, showed more than 50% glands. Grade II: Moderately differentiated, showed 10-50% glands. Grade III: Poorly differentiated, showed less than 10% glands.

Endometrial endometriod adenocarcinoma was classified according to WHO classification 2019 (5th edition)**.** Endometrial endometroid adenocarcinoma tumors were graded according to WHO classification2019 (5th edition).

Endometroid adenocarcinoma

Grade 1: (well differentiated) tumors exhibit ≤5% solid nonglandular, non-squamous growth. Grade II: (moderately differentiated) exhibiting 6% to 50% solid growth. Grade III: (poorly differentiated) exhibiting >50% solid growth.

The presence of marked cytologic atypia increases the grade one level. Pathological staging of studied both tumors were determined according to FIGO staging system 2018 (5th edition).

Immunohistochemical methods

Detection of VIL1 marker using: Rabbit Polyclonal antibodies (Gene Tex, USA, dilution 1:100).

Detection of ER marker using

Mouse Monoclonal Antibody (Ab-1), (Lab vision, USA, dilution 1: 500).

The immunostaining procedure

Histological sections were placed on positively charged glass slides. Then, they were de waxed in xylene and rehydrated by placing them in descending grades of alcohol. Next, we rinsed them in phosphate buffered saline (PBS) for 5 minutes and distilled water for 5 minutes. Endogenous peroxidase activity was blocked by incubating the slides in 3% hydrogen peroxide (H2O2) for 10 minutes, followed by rinse in dH2O for 5-minute and, finally, rinse in PBS for 5-minute. In order to retrieve antigens from the slides, they were heated in the microwave for 10-20 minutes at 100°C in 10mm citrate buffer, pH 6.0, before being cooled for 20 minutes at room temperature.

Tissue was blocked for 30 minutes using a protein blocking reagent to lessen background staining. Two to three drops of VIL1 and ER antibodies were placed on each slide. The slides were then refrigerated at 4 °C overnight in humid closed chamber. The excess reagent was tapped off and the slides were washed with PBS and dried. Tissue sections were treated sequentially with biotin-Labeled secondary antibody. The slides were then incubated at room temperature in humid closed chamber for 30 minutes. The excess reagent was tapped off and the slides were washed with PBS and dried. Two to three drops of streptavidin enzyme label were placed on each slide. The slides were then incubated at room temperature in humid closed chamber for 30 minutes. The excess reagent was tapped off and the slides were washed with PBS and dried. The peroxidase binding sites were detected using diaminobenzidine (DAB) as the substrate. One drop of DAB was added to each 1 ml of buffered substrate. The components were mixed well and kept in a dark place.

The color reagent was applied on the sections for 15 minutes then the slides were rinsed well with distilled water. Finally, the slides were counterstained with Mayer's haematoxylin then dehydrated and cleared and finally mounted. Positive staining is indicated by the presence of a brown colour on the section.

Statistical analysis

Statistical analysis was done by SPSS v20.0 (Armonk, NY: IBM Corp). Quantitative variables were presented as mean and standard deviation (SD) or Median (IQR). Qualitative variables were presented as frequency and percentage (%). Student t-test used for normally distributed quantitative variables, to compare between two studied groups. Chi-square test used for categorical variables, to compare between different groups. F-test (ANOVA) used for normally distributed quantitative variables, to compare between more than two groups. Evaluation of diagnostic performance sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV). A two tailed P value < 0.05 was considered significant.

Results

There was significant relation; the mean age of endometroid adenocarcinoma cases were slightly higher than endocervical adenocarcinoma cases. The size of endometroid adenocarcinoma cases was slightly larger than the size of endocervical adenocarcinoma. Table 1

Table 1: Comparison between the two studied groups according to age and size of tumor, distribution of the studied cases according to cervical stromal invasion in endocervical group and myometrial invasion in endometroid adenocarcinoma group

		Endocervical cases (n = 30)	Endometroid cases (n = 30)	P value
Age (years)		54.37 ± 9.54	62.30 ± 7.15	0.001*
Size of tumor		3.20 ± 1.42	4.90 ± 1.21	<0.001*
Cervical stromal invasion			**No.**	**%**
A			1	3.3
B			8	26.7
C			21	70
Myometrial invasion	< Half		14	46.7
	> Half		16	53.3

Data are presented as mean ± SD or frequency (%), *: Significant p value

The statistical relation between the two studied groups as regarded Lymphovascular invasion, Perineural invasion, Serosal invasion, Adnexal invasion, Distant metastasis, grading, stage was insignificant. Table 2

Table 2: Comparison between the two groups according to different parameters, grading, stage and nodal metastasis

		Endocervical adenocarcinoma (n = 30)		Endometroid adenocarcinoma (n = 30)		P
		No.	%	No.	%	
Lymphovascular invasion		12	40.0	14	46.7	0.602
Perineural invasion		7	23.3	3	10.0	0.166
Serosal invasion		2	6.6	3	10	1.000
Adnexal invasion		3	10	4	13.3	1.000
Distant metastasis		1	3.3	2	6.6	1.000
Grade	I	2	6.7	2	6.7	0.913
	II	19	63.3	17	56.7	
	III	9	30.0	11	36.7	
Stage	I	10	33.3	16	53.3	0.256
	II	5	16.7	5	16.7	
	III	14	36.7	7	23.3	
	IV	1	3.3	2	6.7	
LN metastasis	N0	16	63.3	23	76.7	0.058
	N1	14	36.7	7	23.3	

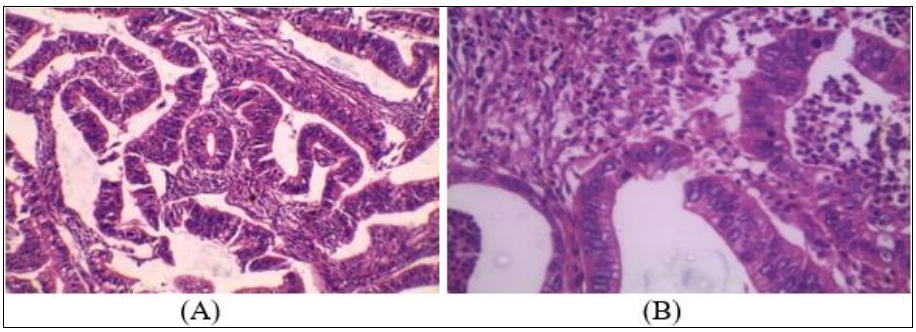

Fig 1: (A) A case of HPV-related endocervical adenocarcinoma (usual type), with numerous mitotic figures and apoptotic bodies favoring a high-risk HPV-related ECA. (H&E, x200) and (B) A case of HPV associated adenocarcinoma showing mitosis (H&E, x 400)

Villin immunostaining showed significant statistical relation with nodal metastasis (p value =0.03), diffuse positivity of villin expression was more statistically significant with presence of nodal metastasis. Also there was significant statistical relation between positivity of villin immunostaining and stromal invasion (p value=0.003), diffuse positivity of villin expression was more significant with pattern C of stromal invasion. No statistical significant relation between villin immunostaining and HPV status, No significant statistical relation between villin and age, size, distant metastasis, lymphovascular, perineural invasion were found. Focal positive villin immunstaining was statistically significant with larger size of tumor (p value= 0.004).Diffuse positive Villin immunostaining was statistically significant with presence of lymphovascular invasion (p value was <0.001) and presence of perineural invasion (p value=0.003). Diffuse positive villin expression was statistically significant with high grade tumors (grade III) (p value <0.001).Also Diffuse villin expression was more statistically significant with presence of nodal metastasis (p value =0.0257). Positive villin immunstaining was statistically significant with myometrial invasion in

endometroid adenocarcinoma cases, as focal positive villin expression was more significant in cases showed myometrial invasion more than half of myometrium (P=.005). Diffuse positive villin immunostaining was more significant with stage III of the tumor (p value= 0.03) and was more statistically significant with presence of adnexal invasion (p value< 0.001). Table 3

Table 3: Relation between villin and different parameters in ECA and in endometroid adenocarcinoma (n = 30)

		Villin						P
		Negative (n = 2)		Focal + (n = 7)		Diffuse+ (n = 21)		
Age (years)		50.0 ± 0.0		59.57 ± 7.35		53.05 ± 10.13		0.241
Size		4.0 ± 0.0		2.43 ± 0.73		3.38 ± 1.56		0.215
		No.	%	No.	%	No.	%	
Lymphovascular invasion		2	100.0	2	28.6	8	38.1	0.254
Perineural invasion		2	100.0	2	28.6	3	14.3	0.234
Sig. bet. Grps		p_1=0.167, p2=0.040*, p_3=0.574						
Grade	I	0	0.0	0	0.0	2	9.5	0.287
	II	0	0.0	5	71.4	14	66.7	
	III	2	100.0	2	28.6	5	23.8	
Stage								
1		2	100.0	0	10.0	8	38.1	0.144
2		0	0.0	1	14.2	4	19	
3		0	0.0	6	85.7	8	38.1	
4		0	0.0	0	0.0	1	4.8	
Nodal metastasis								
N0		2	100.0	6	85.7	13	61.9	0.03*
N1		0	0.0	1	14.2	8	38.1	
Sig.bet.Grps		p_1=0.570, p_2=0.279, p_3=0.242						
HPV status								
-VE		0	0.0	0	0.0	2	9.5	1.000
+VE		2	100.0	7	100.0	19	90.5	
Adnexal invasion		0	0.0	0	0.0	3	28.6	0.489
Serosal invasion		0	0.0	0	0.0	2	28.6	0.313
Distant metastasis		0	0.0	0	0.0	1	9.5	0.634
Cervical stromal invasion								
A		0	0.0	0	0.0	1	4.8	0.003*
B		2	100.0	4	57.1	2	9.5	
C		0	0.0	3	42.9	18	85.7	
Sig. bet. Grps		p_1=0.500, p_2=0.039*, p_3=0.105						
Endometroid adenocarcinoma								
Age (years)		61.91 ± 7.66		64.07 ± 7.65		58.20 ± 1.10		0.291
Size		4.0 ± 0.77		5.64 ± 1.08		4.80 ± 1.10		0.004*
Sig.bet.Grps		p_1=0.001*,p_2=0.226,p_3=0.186						
		No.	%	No.	%	No.	%	
Lymphovascular invasion		0	0.0	9	64.3	5	100.0	<0.001*
		p1=0.001*,p2<0.001*,p3=1.000						
Perineural invasion		0	0.0	0	0.0	3	60.0	0.003*
Sig. bet. Grps		p_1=–, p_2=0.018*, p_3=0.574						
Grade	I	0	0.0	2	14.3	0	0.0	<0.001*
	II	11	100.0	6	42.9	0	0.0	
	III	0	0.0	6	42.9	5	100.0	
Sig. bet. Grps		p_1=0.004*, p_2<0.001*, p_3=1.000						
Stage								
1		10	91.0	5	35.7	1	20.0	0.003*
2		1	9.0	3	21.4	1	20.0	
3		0	0.0	4	28.6	3	60.0	
4		0	00	2	14.2	0	0.0	
Sig. bet. Grps		p1=0.057, p2=0.083, p3=0.420						
Nodal metastasis		0	0.0	4	28.6	3	60.0	0.0257*
Sig. bet. Grps		p1=0.05*, p2= 0.004 *, p3=0.211						
Adnexal invasion		0	0.0	0	0.0	4	80.0	<0.001*
		p1=0.020*, p2=–, p3=0.288						
Serosal invasion		0	0.0	2	14.2	1	0.0	0.364
Distant metastasis		0	0.0	2	14.2	0	0.0	0.293
Myometrial invasion								
< half		9	81.8	5	35.7	0	0.0	0.007*
> half		2	18.2	9	64.3	5	100.0	
Sig. bet. Grps		p1=0.042*, p2=0.005*,p3=0.257						

*: Significant P value

The difference of ER expression in the two groups of gynecological malignancy was statistically significant (P value <0.001). Low expression of ER was more statistically significant with larger size of tumor (p value <0.001) and presence of lymphovascular invasion (p value 0.029).Low expression of ER was more statistically significant with high grade tumors (p value <0.001) and presence of nodal metastasis (p value 0.004).High expression of ER was more statistically significant with low stage of tumor & absence of adnexal and serosal invasion (p value <.001). High expression of ER was more statistically significant with endometroid adenocarcinoma that showed myometrial invasion less than half of myometrium(p value <0.001). No statistical significant relation between ER expression and age, perineural invasion and distant metastasis. Table 4

Table 4: Comparison between the two studied groups according to Villin, relation between ER and different parameters in endometroid adenocarcinoma cases

Villin		Endocervical adenocarcinoma (n = 30)		Endometroid adenocarcinoma (n = 30)		P
		No.	%	No.	%	
Negative		2	6.7	11	36.7	<0.001*
Focal +		7	23.3	14	46.7	
Diffuse+		21	70.0	5	16.7	
Median (IQR)		2.0 (1.0 – 2.0)		1.0 (0.0 – 1.0)		<0.001*
ER		**Low expression (n = 11)**		**High expression (n = 19)**		
Age (years)		60.55 ± 5.77		63.32 ≠ 7.80		0.315
Size		6.27 ± 0.47		4.11 ± 0.66		<0.001*
Lymphovascular invasion		8	72.7	6	31.6	0.029*
Perineural invasion		0	0.0	3	15.8	0.279
Grade	I	0	0.0	2	10.5	0.006*
	II	3	27.3	14	73.7	
	III	8	72.7	3	15.8	
Stage	I	0	0.0	16	84.2	<0.001*
	II	2	18.2	3	15.8	
	III	6	54.5	1	5.2	
	IV	2	18.2	0	0.0	
Nodal metastastis		6	54.5	1	5.3	0.004*
Adnexal invasion		4	36.4	0	0.0	0.01*
Serosal invasion		3	27.2	0	0.0	*0.04
Distant metastasis		2	18.1	0	0.0	0.12
Myometrial invasion	< Half	0	0.0	14	73.7	<0.001*
	> Half	11	100.0	5	26.3	

*: Statistically significant at p ≤ 0.05

ER immunstaining showed high expression in 19 cases out of 30 cases of endometroid adenocarcinoma and it showed low expression in all cases of endocervical adenocarcinoma, so sensitivity was 63.33%and specificity was 100%**.** Cases that show diffuse or focal positivity to villin and low expression of ER were 28 cases of endocervical adenocarcinoma and 14 cases of endometroid adenocarcinoma. Cases that show negative villin expression and\or high expression of ER were 2 cases of endocervical adenocarcinoma and 16 cases of endometroid adenocarcinoma.Sensitivity of the two markers were 53.3%and specificity 93.3%**.** The positive predictive value of villin as a correlation between villin expression and clinicopathological characteristics has been addressed in our study was 84.62%. The negative predictive value was 59.5%**.** The positive predictive value of ER as a correlation between ER expression and clinicopathological characteristics has been addressed in our study was 100%. The negative predictive value was73.1%**.** The positive predictive value of using panel of villin and ER expression and clinicopathological characteristics has been addressed in our study was 88.8%, the negative predictive value was 66.6%. Table 5.

Table 5: Agreement (sensitivity, specificity and accuracy) for Villin, ER

	Cervix (n = 30)		Uterus (n = 30)		Sensitivity	Specificity	PPV	NPV	Accuracy
	No.	%	No.	%					
Villin									
Diffuse+ or Focal +	28	93.3	19	63.3	36.67	93.33	84.62	59.57	65.0
Negative	2	6.7	11	36.7					
ER									
Low expression	30	100.0	11	36.7	63.33	100.0	100.0	73.17	81.67
High expression	0	0.0	19	63.3					
Villin + ER									
Diffuse+ or Focal +and Low expression	28	93.3	14	46.7	53.33	93.33	88.89	66.67	73.33
Negative or High expression	2	6.7	16	53.3					

PPV: Positive predictive value, NPV: Negative predictive value, *: Statistically significant at p ≤ 0.05

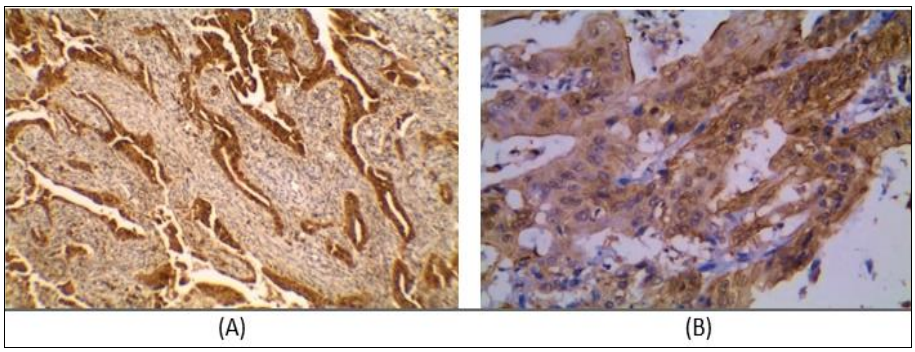

Fig 2: (A) High power view of the previous case showing diffuse cytoplasmic villin staining. (Streptavidin biotin x200) and (B) A case showed diffuse villin cytoplasmic staining. (Streptavidin biotin x400)

Discussion

Cervical cancer is the 4th most common cancer in females globally after (breast, colorectal, lung) and it has been ranked the 14th most common cancer in Egyptian women between fifteen and forty-four years old [8].

In our study, positive villin (VIL1) staining was observed in 93.3% (29 out of 30) of ECA cases.7o% of them showed diffuse villin staining and 23.3% showed focal staining, while in EMC cases the focal positivity of villin staining was found in 14 cases (46.7%) and diffuse villin positivity was found in only 5 cases (16.7%), the difference of villin expression between the two groups of gynecological malignancy was statistically significant (p<0.001). These findings were in agreement with [2].

Nakamura *et al*, 2011 found that VIL1-positive tumors were more frequently identified in cervical adenocarcinoma than in uterine endometroid adenocarcinoma. Immuno histochemical analysis of villin expression showed 13 positive cases out of 23 cases of ECA while positive villin expression was observed in (10 out of 39) cases of endometroid adenocarcinoma.

Also, another study by [3] found that positive staining for villin was observed in 93.3% (14/15) of ECA cases, while in EMC cases, focal postive villin staining was found in only 20%.

The methodology for differentiating ECA and EMA by villin in our results has sensitivity 36.67% and specificity 93.33%.

This was quite similar to [9] that found villin sensitivity was 42% and specificity 100%.This difference could be explained that our study worked on a larger number of cases.

In our present study, the positivity of villin was more statistically significant with presence of nodal metastasis.this was in agree with [3]that found correlation between villin and nodal metastasis,This was different from with [10] that found no relation between villin staining and nodal metastasis in colon cancer cases.

In our present study the expression of positive staining for villin was statistically significant with cervical stromal invasion. Expression of positive diffuse villin was increased in ECA cases that show stromal invasion pattern C, this was in agreement with [3] that found significant correlation between villin and stromal invasion. This could demonstrate the prognostic role of villin in addition to the studied role in differentiation between ECA and EMA in our study.

In our present study, there was no statistical correlation between villin and age, size of tumor, distant metastasis This was the same in [10] study, the result is different from [3] that found a relation between positivity of villin and size of tumor. This may be explained as larger numbers of cases in our study are examined.

In our study,the positivity of villin expression was more statistically significant with grade 3 tumors.[2] study was closely similar to our study as they found villin immunostaininng was found in endometrial endometroid adenocarcinoma with high grade as thy found 3 out of four cases of grade 3 EMA was stained diffusely with villin.

It was found that relation between villin and HPV status was statistically insignificant, this match with [9]. They found that nine out of 14 villin positive cases were HPV negative, and stated that villin positive tumors were more frequently HPV negative. In our study most of villin positive cases were HPV related adenocarcinoma (26 out of 30 cases) and 2 cases were non HPV adenocarcinoma which were stained diffusely with villin.This difference may be due to little number of non HPV cases in our study due to its rarity.

ER immunostaining in our study was highly expressed in (63.3%) of EMA (19 out of 30 cases), and was low expressed in (36.7%) of cases. ECA showed low expression of ER in 100% of cases.

In our study endometriod adenocarcinoma exhibited diffuse, strong nuclear positivity, whereas endocervical adenocarcinoma was generally negative or exhibited focal, weak nuclear immunoreactivity. Staining with ER in endocervical adenocarcinoma was never strong and diffuse This was similar to results of [11] that found ER was not detected in any of the ECA cases. Although in other studies ECA was positive for ER immunostaining as in the study of [12] that found ER stain was positive in 18 out of 24 (75.0%) of EMA and positive in 2 out of 14 (14.3%) of ECA.

In our study ER immunostaining was significantly correlated to the grade of endometroid adenocarcinoma, ER high expression was more statistically correlated with low grade tumors. This result was in line with[13] that higher immunostaining of ER was found in grade 1 or 2 compared with grade 3 endometrial cancer, and also in the study of [14] that found ER was present in 19 cases (86.3%) and absent in three cases (13.4%),the negative cases for ER corresponded to moderate endometrial carcinoma (one case) and poorly differentiated endometrial carcinoma (two cases). This was explained that well-differentiated tumors had a higher number of receptors for estrogen, which is not found in case of poorly differentiated tumors.

In our study ER expression showed statistical correlation with myometrial invasion. ER immunostaining was highly expressed in (73.3%) EMA with myometrial invasion less than half of myometrium and it was stained in (26.3%) of tumors showed myometrial invasion more than half, these result was in line with the results of [14] who found the

endometrial carcinomas that reached the internal half of the myometrium had higher ER values compared with those that have reached the external half.

For the tumors invaded the vascular spaces, in our results ER show statistical correlation with lymphovascular invasion. positivity of ER decreased with presence of vascular invasion,this result was in agree with [14].

Vimentin's apparent insensitivity in EMAC and ECAC has been viewed in contradictory studies. While 1 of 14 (7%) ECAC and 9 of 18 (50%) EMC tested positive for vimentin (Khoury *et al*., 2006), [15] discovered that vimentin was identified in 29 of 30 (96.7%) EMC and 2 of 26 (7.7%) ECAC. Compared to our highly specific marker villin founded in 93.3% of ECA, with sensitivity 36.67.

Conclusions

Villin1 is good diagnostic tool had high specificity in differentiating endocervical and endometroid adenocarcinoma and has a predictive value in ECAC. ER is good diagnostic tool in differentiating between endocervical and endometroid adenocarcinomas and has predictive value in endometroid adenocarcinoma.

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Conflict of Interest: Nil

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