Expression of pten and p53 in atypical hyperplasia and endometrial malignancy in perimenopausal women presented with AUB: Retrospective analysis study from an institute of central India

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ABSTRACT

Introduction: Although it must have become routine practice, immunohistochemistry for PTEN and p53 is becoming gradually available for population in need in resource limited countries.

Objectives: To explore the PTEN and p53 gene immunoexpression in atypical endometrial hyperplasia and endometrial malignancies in perimenopausal women presenting with abnormal uterine bleeding and to assess their prognostic significance.

Material and method: in this retrospective study patient files were retrieved for relevant informations, histological diagnosis was reviewed and fresh unstained slides from paraffin embedded tissue blocks were prepared for IHC. Immunoexpression of cases against the suitable controls were interpreted, scored and analysed.

Statistical analysis: Summary statistics, Chi-square tests (test of significance) and Kappa values calculation. Differences were assumed to be statistically significant if the *p* value is less than 0.05.

Results: Of 78 premenopausal women, 25 (32.1%) cases were of atypical endometrial hyperplasia and remaining 53 were of malignancies, including 43 endometrioid carcinoma cases. Mean age was 49.87+-7.72 years. Positive PTEN immunoexpression in 80% whereas wild type (normal) immunoexpression of p53 in all cases of atypical hyperplasia was noted. Positive PTEN immunoexpression in majority of grade1 endometrioid carcinoma, whereas negative in grade3 (high grade) was observed. p53 positive immunostaining of mutant type (over expression) was observed in majority of grade3 endometrioid carcinoma.

Conclusion: Loss of PTEN expression reflect progression to endometrial carcinoma. Negative PTEN immunoexpression and p53 positive immunostaining of mutant type (over expression) reflect comparatively poor prognosis and high probability of tumor recurrence.

Key words: Atypical Endometrial Hyperplasia, Carcinoma Endometrioid, Endometrial Neoplasm's, Gene's p53, Immunohistochemistry, PTEN protein human

INTRODUCTION

Endometrial carcinoma being one of the most common gynecological malignancies with 150,000 new cases diagnosed annually worldwide, accounts for 4-8% of all carcinomas. It occupies the forth position after breast, colon and lung cancers in females and approximately 7400 die due to disease.[1] Endometrial carcinoma occurs in premenopausal women (25%) and postmenopausal women (75%) and the most common age group is between 50-59

years.[2]Approximately 90% of endometrial carcinomas are sporadic, and the remaining 10% are hereditary.[3]

Endometrial carcinomabroadlycategorized into two: Estrogen-dependent endometrioid endometrial carcinomas (EECs), or type I, is of low grade, arising in early postmenopausal women and non-endometrioid endometrial carcinomas (NEECs), or type II tumors, occurs in elderly postmenopausal women.[2,4,5] About 70-80% of type I endometrial adenocarcinoma cases occur on a background of endometrial hyperplasia.[3]Endometrioid type being the most common form (2/3rd) of endometrial carcinoma, usually develops from precursor lesion i.e. endometrial hyperplasia.[6]

Perimenopause (40-55yrs) is the interval in which a women's body makes a natural shift from regular cycles of ovulation and menstruation toward permanent infertility or menopause.[7]In premenopausal age, any change in menstrual period frequency, duration, amount of flow, as well as bleeding between cycles, is considered as abnormal. In postmenopausal women, abnormal uterine bleeding is defined as vaginal bleeding for 12 months or more, after the cessation of menstruation or unpredictable bleeding in those who have been receiving therapy for 12 months or more.[8]

Most frequently altered gene in endometrial carcinoma are PTEN (Phosphatase and tensilonhomologue) & p53 tumor suppressor genes, mutated in about 30-50 % of endometrial cases.[9] PTEN gene is normally regulated, in presence of estrogen, it is expressed greatly in physiological endometrial gland. Thus, diminished PTEN tumor suppressor function is directly related to carcinoma risk, particularly in high-estrogenic states.[10]p53 is a tumor suppressor gene and thus its inactivation helps the neoplastic cells to divide and proliferate rapidly.[11] Detection of such genes is important in early diagnosis of endometrial carcinomas and hyperplasias.

Although The Cancer Genome Atlas (TCGA) has published molecular categories of endometrial cancer, it cannot be easily and completely implicated in clinical practice due to high costs and the need to use fresh or frozen tumor tissue[12] thus letting p53 and PTEN immunohistochemistry (IHC) remain as most important adjunct tool in endometrial tumor evaluation.

Because of the complex patterns of expression of many antigens, the use of panels of antibodies is often necessary. [13]

The aim of this study was to investigate the PTEN and p53 gene immunoexpression in cases of endometrial carcinoma, and clarify their prognostic significance by analyzing the correlation between PTEN and p53 expression with tumor grade and disease stage.

Correlation of clinical, radiological and histopathological examination is needed to confirm the diagnosis. The molecular profiling can help in early detection and guiding clinicians for the targeted therapy which will help in early cure and improving the overall prognosis.

MATERIALS AND METHODS

The present study was a retrospective study, conducted in the Department of Pathology, at R.D. Gardi Medical College, Ujjain, during 2017 to 2019. The retrospective data was collected for consecutive past five years. Ethical clearance for the study originally titled as "Expression of PTEN & p53 in atypical hyperplasia and endometrial malignancy in premenopausal women presented with AUB" was obtained from Institutional Ethics Committee.

A total of 78 cases (25 of atypical hyperplasia and 53 of endometrial malignancy) underwent PTEN and P53 IHC staining and were analyzed.

Endometrial biopsy and hysterectomy specimens of histologically diagnosed cases of atypical endometrial hyperplasia & endometrial malignancy in perimenopausal group presented with abnormal uterine bleeding (AUB) were included.

Cases with inadequate biopsy material, AUB due to intra uterine devices, pregnancy and due to non endometrial causes like lesions of myometrium and adnexa were excluded.

METHODOLOGY

Patient files of the cases enrolled as per inclusion criteria were retrieved from the record section, clinical details and investigations done were recorded, histological diagnosis was reviewed and reconfirmed and fresh unstained slides from paraffin embedded tissue blocks were prepared for IHC (PTEN and P53).

Pre diluted and ready to use, lyophilized rabbit monoclonal antibodies of Biogenex and BioGenex Super Sensitive ^{TM} polymer-HRP Detection System technique were used on the air dried and fixed smears to detect PTEN & P53 antigen (table 1).

Section from normal proliferative endometrium was included as positive control where distinct cytoplasm staining in glandular epithelial cells was regarded as positive staining. A negative control (without addition of the primary antibody) was included in every batch of immunostaining.

Interpretation-Stained sections were examined under microscope and were graded empirically as a combination of staining intensity and the percentage of positive cells.

Semi quantitative Scoring System- Kapucuogh et al[14], is claimed to be a reliable scoring system which assess both the proportion of stained cells and intensity of staining on the whole section. Using light microscopy, the relative intensity of the brown oxidized diaminobenzidine in each of a given number of the tumor cells was visually assessed and then recorded for each specific marker. The assessment of the tissues was conducted at a variety of microscopic magnifications. Magnification of 4-40X was commonly used in making a final assessment of IHC staining intensities and percentages of stained cells. At least 10 representative fields with maximum staining under high power magnification (40X) were chosen and 100 cells were counted for each case. If the number of cells was less than 100, then all available cells were counted and the results were expressed as mean percentage. The scoring criteria of the percentage of positive cells are as follows

Based on immunoreactivity-

1. Negative (0) - 10 % of positive cells
2. Score (+ 1) - 10 to 50 % of positive cells
3. Score (+ 2) - >50 % of positive cell

Based on Intensity-

1. Score 0- absent in the cytoplasm
2. Score (+1) - light brown in the cytoplasm
3. Score (+2) - brown to dark brown in the cytoplasm

STATISTICAL ANALYSIS

This has been carried out by using following statistical tools.

1. Summary statistics with given details of the number of cases and mean values.
2. Chi-square tests (test of significance) were used for comparing the quantitative variables &analyzing the association between the various groups. Differences were assumed to be statistically significant if the *p* value is less than 0.05.
3. Kappa values were calculated to analyse the degree of agreement between intensity & immunoreactivity of PTEN & p53 immunoexpression.
4. Data was combined using Microsoft Excel & analysed using SPSS 20 version.

RESULTS

Of all, 78 registered perimenopausal women, 30 were postmenopausal i.e. they had attained menopause; biopsy was performed in 41 cases and hysterectomy was done in 37 cases.

The patient in present study belonged to age range of 40 to 58 years and the mean age of patients were 49.87±7.72 years. Majority of patients (26 i.e. 33.3%) in present study belonged to 56 to 58 year range, followed by 22 patients (28.3%) to 40 to 45 year range, 16 (20.5%) to 51 to 55 years and 14 (17.9%) to 46 to 50 year range (table 2).

In present study, atypical hyperplasia was observed in younger age group with mean age of 45.08 years as compared to endometrial carcinoma (mean age of 52.14 years).

All the patients had abnormal uterine bleeding. Other associated clinical features were noted in some (table 3)

Ultrasonographic (USG) findings are summarised in table 4, having carcinoma suspicion for 31 (39.8%) cases.

Histologically 25 cases (32.1%) were of atypical hyperplasia and remainders were carcinoma as shown in table 5.

Table 6 represents that 6 patients of postmenopausal group were diagnosed with atypical hyperplasia with 50% patients falling in 56 to 58 years of age. Remaining 24 patients of postmenopausal group were diagnosed with malignancy with 58.3% patients of this category also falling in 56-58 years of age. There was statistical significant association of age with type of lesion amongst postmenopausal women (p<0.05).

In present study, grading was done in all the 49 cases of carcinoma, while staging was possible for endometrioid carcinoma in which hysterectomy was done.

Table 7 is displaying PTEN and p53 immunoexpression in atypical hyperplasia and endometrial malignancies. Table 8is displayingPTEN and p53 immunoexpression with staging of Endometrioid carcinoma

There was statistical significant association of expression of PTEN intensity and immunoreactivity for atypical hyperplasia (p<0.05, k=0.69) and endometrioid carcinoma (p<0.01, k=0.71) with good level of agreement.Level of agreement and test of significance could not be applied for serous carcinoma. Excellent level of agreement between PTEN intensity and immunoreactivity was found in ESS which was observed to be statistical insignificant (p>0.5) as shown in table 9.

As shown in table 10,The test of significance & measurement of agreement between p53 intensity and immunoreactivity could not be calculated for atypical hyperplasia, however a high statistical significant association (p<0.01) and good level of agreement (k=0.365) was observed for endometrioid carcinoma Level of agreement was excellent (k=1.00) between p53 intensity and immunoreactivity in serous carcinoma with high statistical significance (p<0.01).There was excellent level of agreement (k=1.00) between p53 intensity and immunoreactivity for endometrial stromal carcinoma (p>0.05) which was observed to be statistically insignificant (p> 0.05)

Table 1: Antibodies used

Antibody	Source	Clone	Protocol	Chromogen
Anti PTEN	Biogenex AN-746	Monoclonal SP 218	Microwave-enhanced epitope retrieval	Diaminobenzidine
Anti p53	Biogenex AN-728	Monoclonal EP-9	Microwave-enhanced epitope retrieval	Diaminobenzidine

Table 2: Distribution of patients according to Age group

Age group (years)	Frequency	Percentage
40-45	22	28.3
46-50	14	17.9

51-55	16	20.5
56-58	26	33.3
Total	78	100

Table 3: Distribution of patients according to clinical features

Clinical features	Frequency	Percentage
AUB	78	100
Abdominal Pain	4	5.1
Backache	3	3.8
White discharge	1	1.3

Table 4: Distribution of patients according to USG findings

USG	Frequency	Percentage
Not done	24	30.8
Fibroid	8	10.3
Endometrial hyperplasia	6	7.7
Suspicious of carcinoma	31	39.8
Uterine polyp	7	9
Cervical polyp	1	1.3
Inflammatory	1	1.3
Total	78	100

Table 5: Type of histology lesions found in patients

Diagnosis	Frequency	Percentage
Atypical hyperplasia	25	32.1
Endometrioid Carcinoma (Type I)	43	55.1
Serous Carcinoma (Type II)	6	7.7
Endometrial stromal sarcoma (ESS)	3	3.8
Carcinosarcoma	1	1.3
Total	78	100

Table 6: Association of age with type of lesions in Postmenopausal women

Type of lesion		Age				Total	Chi square	*p* value
		40-45 (%)	46-50 (%)	51-55 (%)	56-58 (%)			
Atypical hyperplasia		0 (0)	1 (16.7)	2 (33.3)	3 (50)	6	20.67	0.02
Endometrial Malignancy	Endometrioid	0 (0)	1 (4.2)	9 (37.5)	14 (58.3)	24		
	Serous carcinoma	0 (0)	2 (50)	0 (0)	2 (50)	4		
	Endometrial stromal	0 (0)	0 (0)	0 (0)	0 (0)	0		
	Carcino-sarcoma	0 (0)	0 (0)	0 (0)	0 (0)	0		

Table 7: PTEN and p53 immunoexpression in atypical hyperplasia and Endometrial malignancies

Type of lesion		PTEN		p53 expression	
		Positive (%)	Negative (%)	Wild (%)	Mutant (%)
Atypical Hyperplasia (n=25)		20 (80)	5 (20)	25 (100)	0 (0)
Endometrioid (Type 1)	Grade 1 (n=29)	21 (72.4)	8 (27.6)	29 (100)	0 (0)
	Grade 2 (n=6)	4 (66.7)	2 (33.3)	4 (66.7)	2 (33.3)
	Grade 3 (n=8)	0 (0)	8 (100)	3 (37.5)	5 (62.5)
Serous (Type II)	Grade 1 (n=6)	6 (100)	0 (0)	1 (20)	5 (80)
Stromal variant	ESS (n=3)	2 (66.7)	1 (33.3)	2 (66.7)	1 (33.3)
	Carcino-Sarcoma (n=1)	1 (100)	0 (0)	0 (0)	1 (100)

Table 8: PTEN and p53 immunoexpression with staging of Endometrioid carcinoma

Staging	PTEN		p53 expression	
	Positive (%)	Negative (%)	Wild (%)	Mutant (%)
1b(n=10)	5 (50)	5 (50)	8 (80)	2 (20)
1c(n=2)	1 (50)	1 (50)	2 (100)	0 (0)
2a(n=1)	0 (0)	1 (100)	1 (100)	0 (0)
2b(n=1)	0 (0)	1 (100)	1 (100)	0 (0)
chi square	14.81		16.09	
p value	0.07		0.001	

Table 9: PTEN Intensity and Immunoreactivity for various lesions of endometrium

Lesion	PTEN Intensity	Immunoreactivity				Chi square	Kappa	*p* value
		0	1	2	Total			
Atypical Hyperplasia (n=25)	0	5 (100)	0 (0)	0 (0)	5	0.69	0.69	0.001
	1	0 (0)	9 (64.3)	5 (35.7)	14			
	2	0 (0)	0 (0)	6 (100)	6			
Endometrioid Ca(n=43)	0	18 (100)	0 (0)	0 (0)	18	48.10	0.71	0.01
	1	0 (0)	12 (66.7)	6 (33.3)	18			
	2	0 (0)	2 (28.6)	5 (71.4)	7			
Serous Ca(n=6)	0	0 (0)	0 (0)	0 (0)	0	NA	NA	NA
	1	0 (0)	5 (100)	0 (0)	5			
	2	0 (0)	1 (100)	0 (0)	1			
ESS(n=3)	0	1 (100)	0 (0)	0 (0)	1	3.0	1.0	0.08
	1	0 (0)	2 (100)	0 (0)	2			
	2	0 (0)	0 (0)	0 (0)	0			

Table 10: p53 Intensity and Immunoreactivity in various lesions of endometrium

Lesion	p53 Intensity	Immunoreactivity (IR)				Chi square	Kappa	*p* value
		0	1	2	Total			
Atypical Hyperplasia (n=25)	0	0 (0)	0 (0)	0 (0)	0	NA	NA	NA
	1	0 (0)	20 (80)	5 (20)	25			
	2	0 (0)	0 (0)	0 (0)	0			
Endometriod Ca(n=43)	0	0 (0)	0 (0)	0 (0)	0	9.61	0.365	0.002
	1	0 (0)	23 (63.9)	13 (36.1)	36			

	2	0 (0)	0 (0)	7 (100)	7			
Serous Ca(n=6)	0	0 (0)	0 (0)	0 (0)	0	6.0	1.0	0.014
	1	0 (0)	1 (100)	0 (0)	1			
	2	0 (0)	0 (0)	5 (100)	5			
ESS(n=3)	0	0 (0)	0 (0)	0 (0)	0	3.0	1.0	0.08
	1	0 (0)	2 (100)	0 (0)	2			
	2	0 (0)	0 (0)	1 (100)	1			

Table 11: Comparison of age groups of endometrial malignancy in various studies

Study	Year	Mean age (years)
Setiawan VW et al [18]	2013	61.9±9.5
Stavropoulos A et al [19]	2019	64
Stoenescu VE et al[20]	2017	52.29± 8.14
Present study	2019	49.87±7.72

Table 12: Comparison of age group at presentation with hyperplasia and carcinoma

Study	Year	Hyperplasia	Carcinoma
Sobczuk K et al [21]	2017	50-54	>60
Reed SD et al [22]	2009	50-54 years	-
Hernandez E.et al [16]	2006	-	>60
Present study	2019	40 to 45	56 to 58

DISCUSSION

While studying the association of menopausal status with type of lesions of endometrium, we found that 44 (56.4%) patients were in premenopausal age group whereas 34 (43.6%) patients attained menopause in our study. Amongst patients with atypical hyperplasia, majority i.e. 19 (76%) patients were in premenopausal age group whereas 28 (52.8%) patients of endometrial malignancy were attained menopause. We observed a statistical significant association of menopausal status with atypical hyperplasia and endometrial malignancy (p<0.05). **Pennant ME et al (2017)**[15] observed high incidence of atypical hyperplasia in women of premenopausal age group (age less than 40 years) while **Hernandez E.et al (2006)**[16] in their **ACOG group** study concluded that most cases of endometrial carcinoma were diagnosed in women who attained menopause and were in their mid-60s.

Abnormal uterine bleeding is reported to be a cardinal symptom of endometrial carcinoma by **Kimura T et al (2014)**[17] Similarly in our study, all the patients had a chief complaint of abnormal uterine bleeding. Table 11[18, 19, 20] and table 12[21, 22, 16] are showing relevant age related data across various studies and reflecting that present study is having comparatively younger age group for cases.

We studied, majority of patients were diagnosed with endometrioid carcinoma (55.1%), followed by atypical hyperplasia (32.1%). Serous and stromal variants of endometrial malignancy were observed in 7.7% and 5.1% patients respectively. **EL Kholi MA et al[23]** in their study "Endometrial hyperplasia versus carcinoma" in Egypt included 40 cases. Majority of cases in the reference study were endometrial hyperplasia (55%) and remaining were cases of Endometrial carcinoma (45%). Amongst the cases of endometrial hyperplasia (EH), Hyperplasia without atypia was observed in 25%, whereas atypical hyperplasia was documented in 30% cases. **Stoenescu VE et al[20]**, in their study obtained tissue specimens of 106 women which were diagnosed as EH without atypia in 54 cases (50.9%), EH with atypia in 42 cases (39.6%), and 10 cases (9.4%) were diagnosed as endometrioid endometrial carcinoma type I.

In our study, total of 25 cases of atypical hyperplasia, PTEN expression was positive in 80% patients of atypical hyperplasia whereas p53 expression was wild type (focal positive/normal expression) in 100% cases in patients with atypical hyperplasia. **El Kholi MA et al[23] (2018)** observed positive PTEN expression in 68.2% patients of atypical hyperplasia.**Kim YS et al[24] (1997)** observed p53 immunoreactivity in 17.6% cases of simple hyperplasia, 16.6% cases of complex hyperplasia, none in case of atypical hyperplasia.

We studied, PTEN expression was observed to be positive in 72.4% patients amongst the cases diagnosed with grade 1 endometrioid carcinoma, and p53 expression was wild type in 100% patients, whereas in grade 2, PTEN expression was positive in 66.7% patients and p53 expression was mutant in 33.3% patients. Amongst the cases of grade 3 endometrioid carcinoma, PTEN was absent in 100% cases and p53 immunoexpression was mutant in 62.5% cases. Kappa statistics for endometrioid carcinoma showed good and poor level of agreement between intensity and immunoreactivity of PTEN and p53 respectively with highly statistically significant association (p<0.01). **Inaba F et al[25] (2005)** in their study on endometrial carcinoma observed negative PTEN staining in 40% patients which is suggestive of lost or reduced PTEN function. They observed loss of PTEN staining was significantly related to the advanced staging in the grade 1 (G1) and grade 2 (G2) endometrioid adenocarcinoma group (p=0.026).The reference study observed positive staining for p53 in 20% cases which was mainly seen in case of grade 3 (G3) endometrioid adenocarcinoma. In cases of grade 1 and grade 2 endometrioid carcinoma, 29 cases (31.5%) with reduced PTEN staining showed negative p53 immunoexpression (p=0.025). p53-positive staining in reference study was observed to be associated with a high probability of tumor recurrence in the G1 and G2 group (p=0.0234). They concluded both PTEN and p53 staining to be good indicators of clinical stage and probability of tumor recurrence in Endometrioid carcinoma.

We found, PTEN immunoexpression in case of endometrioid carcinoma was observed to be positive in lower stages (stage 1 b and 1 c) and negative with advanced stages. p53 immunoexpression was observed to be wild type in all stages of endometrioid carcinoma except in stage 1b where 20% cases showed p53 mutation. Similarly Athanassiadou **P et al[26] (2007)** observed a negative correlation of PTEN positivity with staging i.e. increased PTEN expression with decreased stage (p = 0.002). Also the reference study documented significant correlation between positive staining of p53 and increased stage (p < 0.0001), lymph node metastases (p = 0.001), and a non endometrioid histology (p = 0.001).

We observed Mutant type of p53 immunoexpression in 80% cases and positive PTEN immunoexpression in 100% patients diagnosed with Serous carcinoma.We observed no statistical significant difference in immunoexpression of PTEN in different type of endometrial carcinoma (p>0.05) but a high statistical significant association of p53 with endometrial carcinomas (grade 3 EEC & SC) was observed (p<0.01) in our study. **Esmaieli HA et al[27] (2017)** in their study on the prognostic value of p53 and PTEN immunomarkers for endometrial carcinoma using immunohistochemistry included 40 women in which endometrioid, serous and clear cell adenocarcinoma constituted 82.5%, 15% and 2.5% cases respectively. They observed PTEN negativity in all the 6 cases of serous carcinoma whereas P53 was positive in all the cases. They observed no statistical significant difference in immunoexpression of PTEN between different type of endometrial carcinomas (p>0.05). However, a highly statistically significant association of p53 with carcinomas were observed (p<0.01). Similar to the findings of present study. **Mao TL et al[28] (2015)** studied the expression p53, PTEN and several other markers in high grade endometrioid carcinomas. They observed PTEN loss and p53 expression in 37% and 47% in high-grade tumors, whereas PTEN loss and P53 expression was observed in 45% and 32% in high-grade tumors with concurrent low-grade components, respectively. They concluded high-grade tumors to

show positive for PTEN and p53 aberrant expression as compared to high-grade tumors with concurrent low-grade components.
In ESS and carcinosarcoma PTEN was positive in 66.7% and 100% cases respectively whereas p53 was mutant in 33.3% cases of ESS and 100% cases of carcinosarcoma. **Soliman N et al[29] (2018),** observed overexpression of p53 in one out of six cases with carcinosarcoma (16%). They observed insignificant association between p53 expression and the histological type (P=0.2).

CONCLUSION

In this study we observed positive PTEN immunoexpression in atypical hyperplasia in 80% patients whereas wild type (normal) of immunoexpression of p53 was observed in all patients of atypical hyperplasia. So we conclude that PTEN is a prognostic marker of atypical hyperplasia because loss of PTEN expression in patients of atypical hyperplasia may be a precursor for developing endometrial carcinoma.
Positive PTEN immunoexpression was observed in majority of grade1 endometrioid carcinoma, indicative of good prognosis, whereas negative PTEN immunoexpression was found in grade3 (high grade) endometrioid carcinoma, suggesting poor prognosis of the patients.
p53 positive immunostaining of mutant type (overexpression) was observed in majority of grade 3 endometrioid carcinoma, associated with a high probability of tumor recurrence. So screening for PTEN & p53 immunoexpression in endometrioid carcinoma is a good indicator of prognosis & survival of the patients correlating with the severity of disease &tumor recurrence.
Staging was only done for endometrioid carcinoma. p53 immunoexpression was significantly associated with staging of carcinoma, as the stage progresses, p53 immunoexpression tends to become negative or overexpressed, indicative of developing into high grade to invasive carcinoma suggesting severity of disease & probability of tumour recurrence.
In serous carcinoma (type II carcinoma) p53 was of diagnostic and prognostic utility as shown mutant type of immunoexpression in 80% cases of serous carcinoma.
In stromal variant of endometrial carcinoma, mutant type of p53 immunoexpression was shown in carcinosarcoma suggestive of prognostic utility.
A strong correlation between the PTEN & p53 immunoexpression with a good level of agreement between the intensity and immunoreactivity of PTEN & p53 genes in endometrial carcinoma. It suggests the development of high-grade tumour in older patients & implies the involvement of different molecular pathways in the progression of low-grade and high-grade endometrial carcinoma.

RECOMMENDATION

Immunohistochemical evaluation (IHC) becoming easily accessible these days and as it can be performed expeditiously and on small samples(biopsy/currettings) too, it is of great utility for diagnostic and prognostic evaluation.
So all perimenopausal women presenting with AUB should undergo endometrial biopsy evaluation for screening of molecular genetic markers expression by performing IHC for better reflection of clinical outcome & prevention of development of high grade tumours.

LIMITATIONS

Sample size of 78 is less, so is the age range included in the study. Most patients belonged to the certain geographical area therefore not the true representative of target population.

FUNDING
None

CONFLICT OF INTEREST
None declared.

ETHICAL CLEARANCE
It was obtained from Institutional Ethics Committee, Ruxmaniben Deepchand Gardi medical college, Ujjain (IEC Ref no- 174).

AUTHORS' CONTRIBUTIONS
Dr Anjali has substantial contributions to the conception, designing and drafting of the work and all the three contributed for the acquisition, analysis and interpretation of data, revision for important intellectual content and final approval of the version to be published.

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