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Expression of Estrogen and Progesterone Receptor In Perimenopausal and Postmenopausal Endometrium.

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ABSTRACT

Background: Hormonal changes during the menopausal transition significantly influence breast tissue biology. Estrogen receptor (ER) and progesterone receptor (PR) expression are critical markers in breast pathology and significantly impact prognosis and treatment in hormone-responsive breast conditions. This study aimed to evaluate and compare ER and PR expression in perimenopausal and postmenopausal women presenting with breast lesions.

Objective: The aim of the study is to examine the degree of expression of ER and PR in the endometrium of women with perimenopausal and postmenopausal bleeding.

Methods: 50 endometrial biopsy and hysterectomy specimens of perimenopausal and postmenopausal bleeding from the department of obstetrics and gynaecology of RRMCH after routine tissue processing, tissue sections will be stained immunohistochemically for ER and PR receptor expression as per standard procedure with the combination of pathnsitu protocol and pressure cooker antigen retrieval (tris-EDTA buffer- pH 6) and Allred scoring system was used for interpretation.

Results: In the present study, majority of the patients belong to the age group 40 - 45 years (66%). The mean age of the patients was found to be 46.80 + 6.84. All the patients with Proliferative endometrium, disordered proliferative endometrium, cystic atrophy endometrium & lytic endometrium were 100% positive for ER, followed by hyperplasia without atypia 87.5% and secretory endometrium 80%, atypical hyperplasia 66.6% and carcinoma endometrium 50.0%. All the patients with Proliferative endometrium, disordered proliferative endometrium, cystic atrophy endometrium, lytic endometrium were 100% positive for PR, followed by hyperplasia without atypia 87.5% and secretory endometrium 80%, atypical hyperplasia 66.6% and carcinoma endometrium 62.4%. A declining trend in receptor positivity was noted with advancing age and menopausal status, although not statistically significant in all subgroups.

Conclusion: ER and PR expression is more frequently observed in perimenopausal women compared to postmenopausal women. Analysis of steroid hormone receptors plays an important role in patients with perimenopausal and postmenopausal bleeding to predict the response to hormonal therapy

Keywords: *Estrogen receptor, Progesterone receptor, Perimenopause, Immunohistochemistry*

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1. INTRODUCTION

The endometrium is a hormonally responsive tissue that undergoes cyclical changes under the influence of estrogen and progesterone, the two key ovarian steroid hormones. These hormones exert their effects through specific intracellular receptors—estrogen receptors (ER) and progesterone receptors (PR)—which are critical regulators of endometrial growth, differentiation, and function[1]. Alterations in the expression of ER and PR have been implicated in various pathological conditions of the endometrium, including endometrial hyperplasia, infertility, and endometrial carcinoma[2].

Immunohistochemical evaluation of ER and PR in endometrial biopsies provides valuable insights into the hormonal responsiveness of the endometrium and aids in the differential diagnosis of endometrial disorders. Moreover, receptor status can serve as a predictive marker for hormonal therapy responsiveness, particularly in cases of endometrial carcinoma and atypical hyperplasia[3].

This study aims to assess the pattern and intensity of estrogen and progesterone receptor expression in endometrial biopsies across a spectrum of physiological and pathological conditions. Understanding these patterns may enhance diagnostic accuracy and support individualized therapeutic strategies in clinical practice.

2. OBJECTIVES

To study the histopathological changes in endometrium of patients with perimenopausal and postmenopausal bleeding in our institute.
To study the expression of Estrogen and Progesterone receptor status in the endometrium of patients with perimenopausal and postmenopausal bleeding.

3. MATERIALS AND METHODS

Patients presenting with perimenopausal and postmenopausal bleeding are included in the study. The endometrial biopsy and hysterectomy specimen of 50 patients received from the department of obstetrics and gynaecology of RRMCH are fixed in 10% formalin. After routine tissue processing, tissue sections of 4-6 microns will be cut and stained with haematoxylin and eosin stain to study histopathological changes. The representative tissue sections will be stained immunohistochemically for ER and PR receptor expression as per standard procedure with the combination of pathnsitu protocol and pressure cooker antigen retrieval (tris-EDTA buffer- pH 6) and analysed for positivity of receptors in the glandular epithelium and stroma of endometrium. The immunohistochemically stained slides were analysed for the presence of reaction, cellular localization. The percentage of cells stained per 1000 cells counted on 40X power field and the intensity of reaction were analysed. Immunohistochemical scoring for ER and PR receptors were done with Allred scoring system.

INCLUSION CRITERIA:

Patients with abnormal vaginal bleeding aged 40 or > 40 years (perimenopausal and postmenopausal) who presents to the gynaecology department were included in the study.

EXCLUSION CRITERIA:

Patients with insufficient endometrial tissue, treatment with oral contraceptive pills and known case of endometrial carcinoma receiving treatment.

4. RESULTS

TABLE 1: DISTRIBUTION OF PATIENTS ACCORDING TO THEIR AGE GROUP:

AGE	FREQUENCY (N)	PERCENTAGE %
40 - 45 years	33	66.0
46 - 50 years	06	12.0
51-55 years	04	8.0
56-60 years	05	10.0
> 60 years	02	4.0
TOTAL	50	100%
MEAN ± SD	46.80 ± 6.84	

TABLE 2: DISTRIBUTION OF PATIENTS ACCORDING TO THEIR TRANSVAGINAL ULTRASONOGRAPHY FINDINGS OF ENDOMETRIAL THICKNESS:

ENDOMETRIAL THICKNESS	FREQUENCY	PERCENTAGE %
1-5mm	16	32.0
6-10mm	25	50.0
11-15mm	08	16.0
>15mm	01	2.0
Total	**50**	**100%**
MEAN ± SD	7.74 ± 3.19	

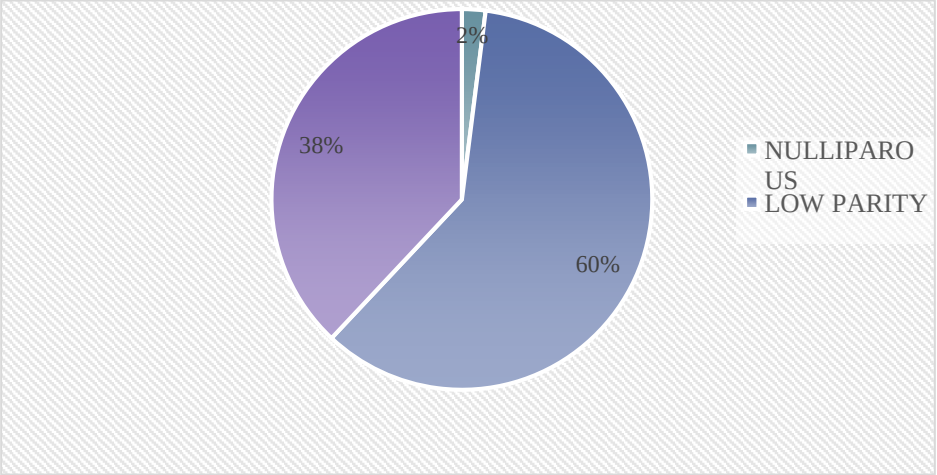

FIGURE 1: DISTRIBUTION OF PATIENTS ACCORDING TO THEIR PARITY:

Among 50 patients, 30 patients (60%) were of low parity (P1 or P2), 16 patients (38%) were multiparous and only 1 patient (2%) was nulliparous.

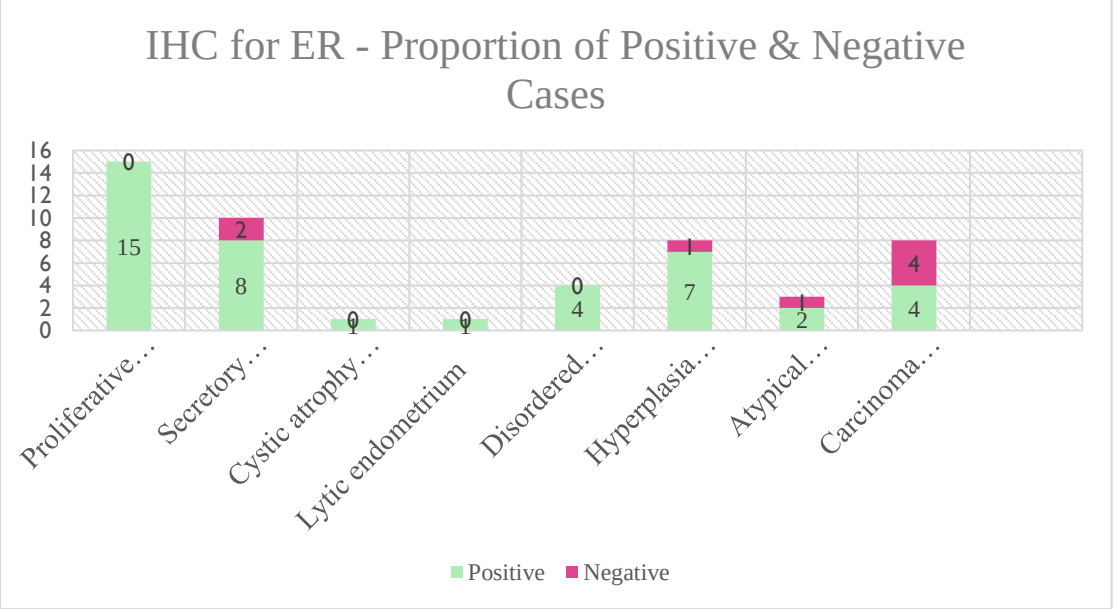

FIGURE 2: DISTRIBUTION OF PATIENTS WITH IHC ON ER ACCORDING TO THEIR HISTOPATHOLOGICAL DIAGNOSIS:

All the patients with Proliferative endometrium, disordered proliferative endometrium, cystic atrophy endometrium & lytic endometrium were 100% positive for ER, followed by hyperplasia without atypia 87.5% and secretory endometrium 80%, atypical hyperplasia 66.6% and carcinoma endometrium 50.0%

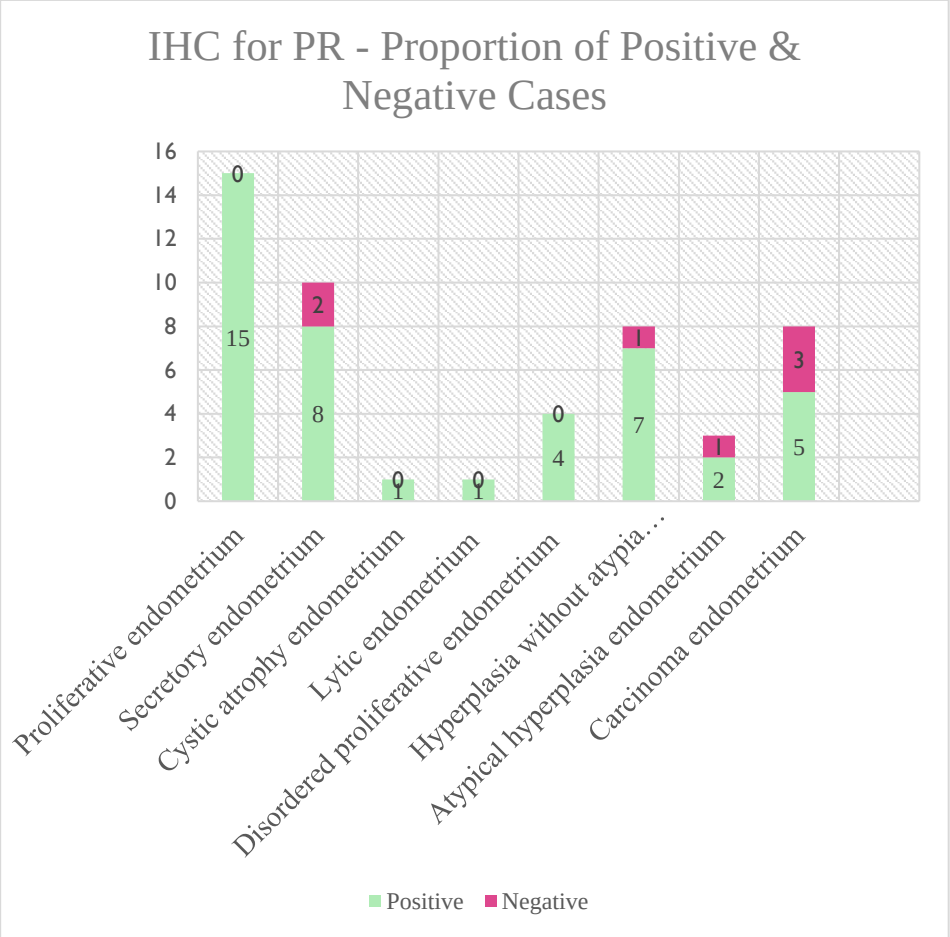

FIGURE 3: DISTRIBUTION OF PATIENTS WITH IHC OF PR ACCORDING TO THEIR HISTOPATHOLOGICAL DIAGNOSIS:

All the patients with Proliferative endometrium, disordered proliferative endometrium, cystic atrophy endometrium, lytic endometrium were 100% positive for ER, followed by hyperplasia without atypia 87.5% and secretory endometrium 80%, atypical hyperplasia 66.6% and carcinoma endometrium 62.4%.

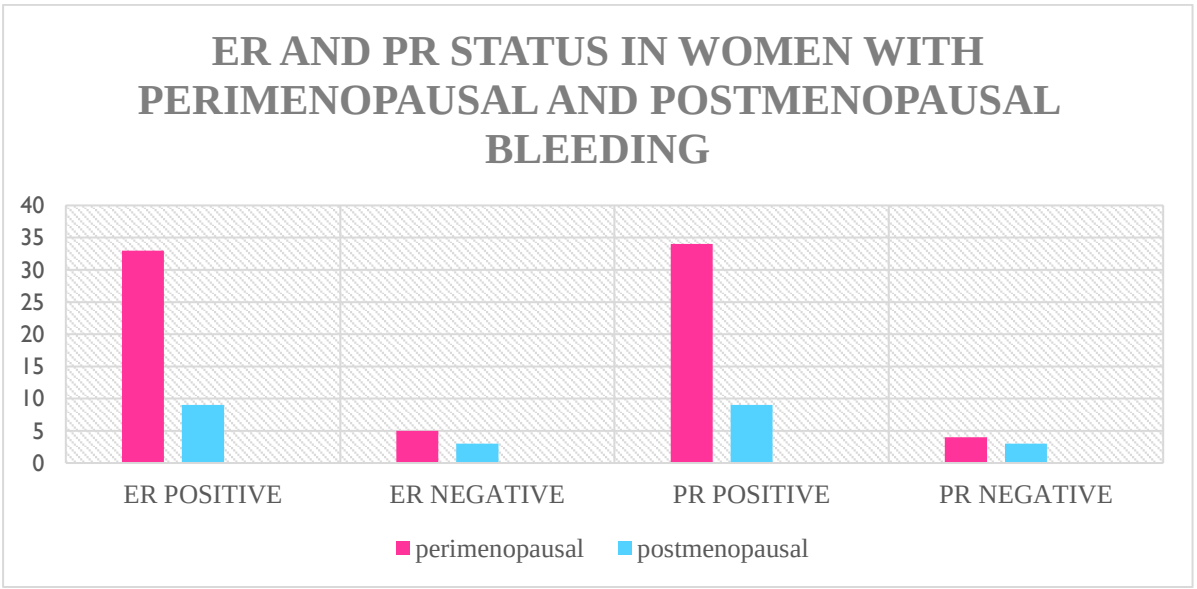

FIGURE 4: ASSOCIATION OF ER AND PR EXPRESSION IN WOMEN WITH THE PERIMENOPAUSAL AND POSTMENOPAUSAL BLEEDING:

TABLE 3: ASSOCIATION OF ER AND PR EXPRESSION IN WOMEN WITH THE PERIMENOPAUSAL AND POSTMENOPAUSAL BLEEDING:

RECEPTOR STATUS		PERI MENOPAUSAL		POST MENOPAUSAL		P value
		N	%	N	%	
ESTROGEN	POSITIVE	33	86.0%	09	75.0%	0.367
	NEGATIVE	05	13.1%	03	25.0%	
PROGESTERONE	POSITIVE	34	89.4%	09	75.0%	0.071
	NEGATIVE	04	10.5%	03	25.0%	

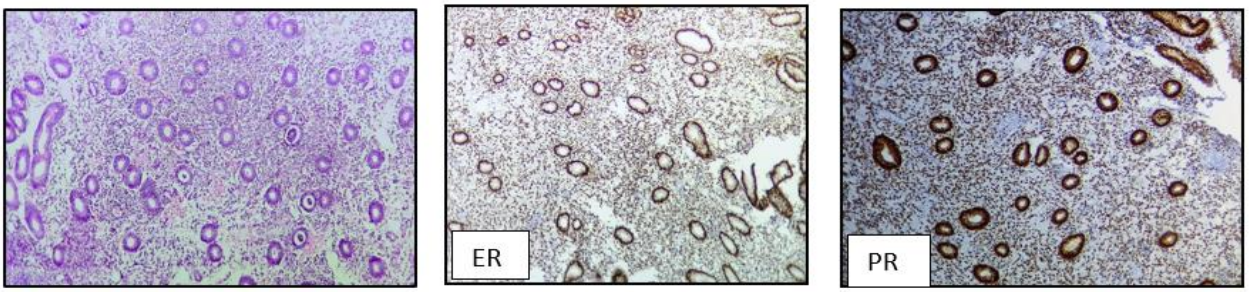

FIGURE 5: Proliferative phase endometrium (H&E,10x) IHC: ER&PR POSITIVE

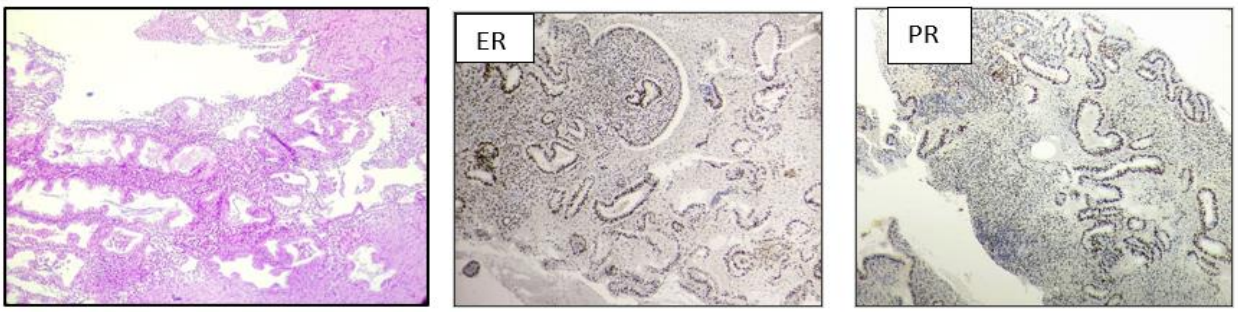

FIGURE 6: Secretory endometrium (H&E,10x) IHC: ER&PR POSITIVE

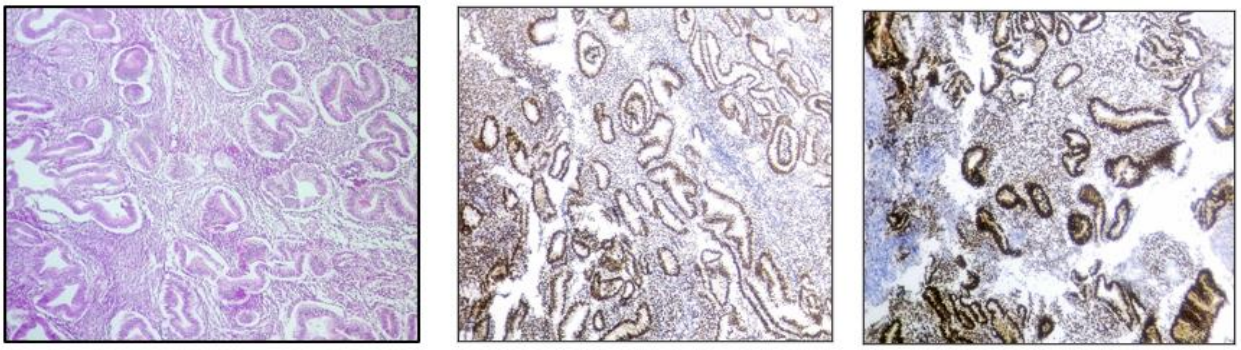

FIGURE 7: Endometrial hyperplasia without atypia (H&E,10x) IHC: ER&PR POSITIVE

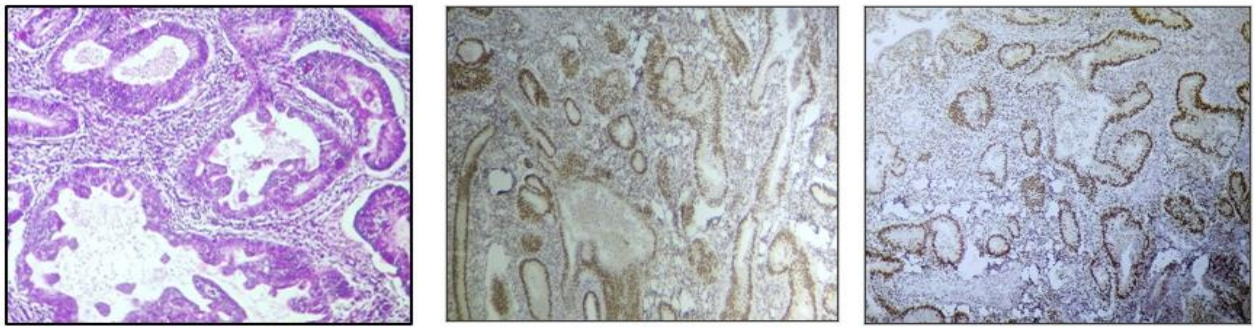

FIGURE 8: Atypical Endometrial hyperplasia/EIN (H&E,40x) IHC: ER&PR POSITIVE

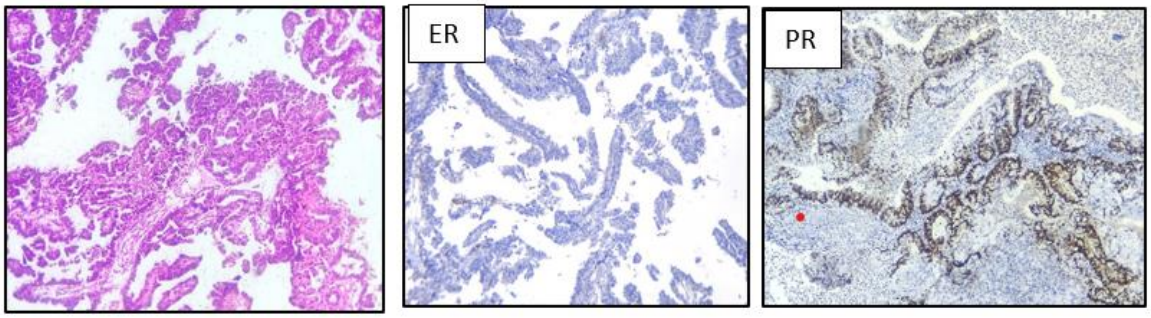

FIGURE 9: Endometrial adenocarcinoma(H&E,10x) IHC: ER NEGATIVE&PR POSITIVE

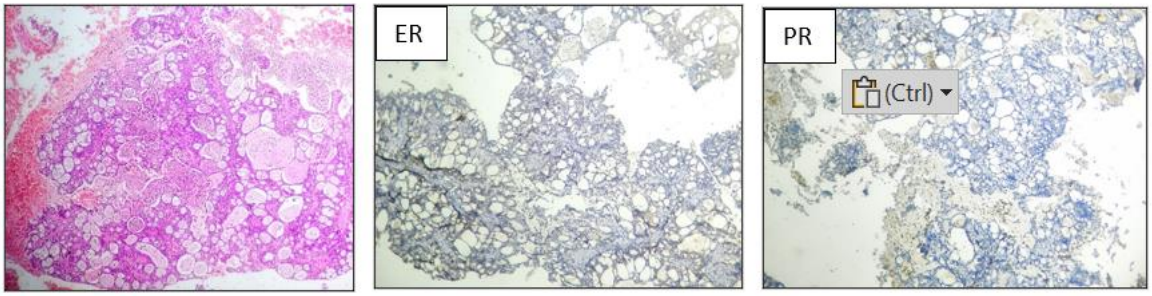

FIGURE 10: Endometrial adenocarcinoma(H&E,10x) IHC: ER NEGATIVE&PR NEGATIVE

5. DISCUSSION

In the present study, Majority of the patients belong to 40 - 50 years (78%) of age. The mean age of the patients was found to be 46.80 ± 6.84. In a study done y Damle et al[7], Maximum numbers of patients were in the age group of 40-49 years (73.94%). These findings correlate with the findings of the present study. In a study done by Talukdar et al[8], 69.97% of the patients were in the age group between 40 and 50 years. In a study done by Sreelakshmi et al[9], Maximum numbers of patients were in the age group of 40-49 years (94.04%). The mean age of the patients was found to be 46.68 ± 2.03 years, which is similar to the findings of the present study. Perimenopause is a period of natural transition to menopause, marking the end of the reproductive years, thereby presenting with menstrual irregularities[9].

In the present study, majority of the women belong to low parity (P1-P2) with 60%. In a study done by Pillai et al[16] 70.5% of women were of low parity, which correlates with the present study. In a study done by Sreelakshmi et al[9] 55.55% of women were of low parity which correlates with the present study and also a study done by Talukdar et al[8] 28.14% of women were of low parity which is not correlated with the present study.

In the present study, 54% of the patients had a clinical diagnosis of AUB and 24% of the patients had a clinical diagnosis of PMB. In a study done by Damle et al[7], 48.86% of the patients had AUB as the clinical diagnosis followed by 26.05% of patients had a clinical diagnosis of PMB. These findings were similar to the findings of the present study.

In the present study, 50% of the patients had endometrial thickness in the range of 6-10mm. 32% of the patients had endometrial thickness in the range of 1-5mm. Only 2% of patients had endometrial thickness more than 15mm. The mean endometrial thickness of the patients was found to be 7.74 ± 3.19. In a study done by Pillai et al[16], 46.7% of the patients had endometrial thickness between 5 and 9.9 mm and 22.7% of the patients had endometrial thickness between 10 and 14.9 mm, which is similar to the findings of the present study.

The histopathological diagnosis of the patients in the present study were seen in the following order: Proliferative endometrium (30%), Secretory endometrium (20%), Hyperplasia without atypia (16%), Carcinoma endometrium (16%), Disordered proliferative endometrium (8%), Atypical hyperplasia endometrium (6%), Cystic atrophy endometrium (2%) and Lytic endometrium (2%). In a study done by Pillai et al[16], 27.2% of the patients had proliferative endometrium and 18.2% of the study participants had secretory endometrium on histopathology.

In a study done by Sreelakshmi et al[9], the most common histopathological findings were proliferative endometrium (30.3%), secretory endometrium (27.4%). In the study done by Damle et al[7] the most common histopathological findings were proliferative endometrium (54.44%) followed by secretory endometrium with 20.9%. These findings were similar to the findings of the present study.

The present study shows the immunohistochemical staining of ER and PR in perimenopausal and postmenopausal women. The non- malignant endometrium studied include proliferative, secretory, disordered proliferative, lytic, atrophic and hyperplasia without atypia. The pre- malignant lesion includes atypical hyperplasia & the malignant lesion includes adenocarcinoma endometrium and its variants. This study shows that most of non-malignant endometrium were positivity for estrogen receptors (92%) and progesterone receptors (96%), followed by atypical hyperplasia with ER & PR showing 66.6% each and were lowest for endometrial adenocarcinoma 50% for ER and 62.8% for PR. The mean values of PI for PR were slightly higher than that for ER.

Mylonas et al[6] compared the expression for ER and PR of normal human endometrium (proliferative and secretory) with that of malignant endometrium. The study revealed that ER and PR expression declined significantly in the glandular epithelium when going from proliferative (high expression) to secretory phase (low expression). The expression of the hormone receptors was lowest with adenocarcinoma endometrium.

In the present study, 84% of the patients were found to be positive for estrogen receptor. The mean estrogen receptor score was found to be 6.14 ± 2.82 and 86% of the patients were found to be positive for progesterone receptor. The mean progesterone receptor score was found to be 6.42 ± 2.90.

Among 50 patients, 33 patients (86.0%) for ER and 34 patients (89.4%) for PR were found to be positive in perimenopausal women, whereas 9 patients (75%) for ER and 9 patients (75%) for PR were found to be positive in postmenopausal women. The association was not found to be statistically significant between the expression of estrogen and progesterone receptors in the perimenopausal and postmenopausal age groups of the patients. In a study done by Jiang et al[3], 95% and 85% of the patients had estrogen and progesterone receptor expression, which is comparable with the findings of the present study[12].

The cyclic change of endometrium is regulated elaborately by hormones. Estrogen promotes hyperplasia of gland and stroma; progesterone promotes gland transformation from proliferating phase to the secretory phase, with stromal decidual change. Estrogen and progesterone specific binding with their receptors are the most important step in their biological effects[12]. Therefore, the quantity and function of ER and PR were the basis to ensure the periodically changes of endometrium.

It is generally known that, along with the growth of age, changes in endometrial ER and PR exist. This correlates with the findings of the present study. The receptor expression in cases with AUB with endometrial dysfunction was comparable in both the perimenopausal and postmenopausal age groups of the study participants. The decreased expressions of estrogen receptor (ER) and progesterone receptor (PR) were observed in women in the postmenopausal age group. Absence of ER and PR expression may be important in the progression of endometrial carcinogenesis.

Estrogen and progesterone receptors belong to the nuclear steroid receptor superfamily. The effect of these steroid hormones is thought to be mediated through these receptors. The ER and PR expression and distribution patterns play an important role in endometrial function and pathogenesis.

6. CONCLUSION

Immunohistochemical analysis of estrogen and progesterone receptors in the endometrium is a very useful adjuvant investigation in the management of perimenopausal and postmenopausal patients who might benefit from the receptor-targeted drugs.

We also identified the role of these receptors in the etiopathogenesis of AUB and consequently the development of simple endometrial hyperplasia, which is a pre-cancerous lesion.

ER and PR expression are used to identify endometrial cancer (EC) patients who can be benefited with hormone therapy, and there are many evidences suggesting that they can be good biomarkers predicting hormone therapy response, but further validation will be required before they are incorporated in routine management of EC patients.

In patients with endometrial cancer, higher level of ER and PR predicted favourable survival and the absence of hormonal receptors was associated with poorer survival.

Conventional histological examination alone may not be enough to guide therapy and to refine outcome prediction. Histopathological examination with hormone receptors ER and PR levels is necessary to evaluate endometrial cancer prognosis.

In endometrial carcinoma, ER and PR are significantly downregulated in both stromal and glandular components compared to non-malignant tissue. Loss of ER in the stroma correlates with diminished epithelial proliferation regulation and increased invasive behavior. PR is also reduced in epithelial cells, possibly compromising anti-proliferative signaling and facilitating disease progression.
We conclude that estrogen and progesterone receptors are a better predictor of disease behaviour than other receptors in these patients.

REFERENCES

[1] Mostafa AM, Elsaid N, Fawzy RA, Elfeky A. Endometrial Estrogen and Progesterone Receptor Expression in Women with Abnormal Uterine Bleeding in the Reproductive Age. Int J Reprod Med Gynecol. 2018;4(2):041-046.

[2] Singh A, Choudhary A. A study of palm-coein classification of abnormal uterine bleeding in perimenopausal women at a tertiary care teaching hospital. jmscr. 2018;6(6);287-292.

[3] Jiang W, Wang Y, Lei F, Zhao L, Zhao W, Zhang J, et al. The putative role of estrogen receptor and progesterone receptor on the pathogenesis of endometrial simple hyperplasia. Int J Clin Exp Pathol. 2016;9(3):3799–804.

[4] Mishra D, & Sultan S. FIGO's PALM–COEIN Classification of Abnormal Uterine Bleeding: A Clinico-histopathological Correlation in Indian Setting. Journal of Obstetrics and Gynaecology of India. 2017; 67(2): 119-125.

[5] Coast E, Lattof SR, Strong J. Puberty and menstruation knowledge among young adolescents in low- and middle-income countries: a scoping review. Int J Public Health. 2019 Mar ;64(2): 293-304. Pillai SS. Sonographic and histopathological correlation and evaluation of endometrium in perimenopausal women with abnormal uterine bleeding. International Journal of Reproduction, Contraception, Obstetrics and Gynecology, 2016, 3(1):113–7.

[6] Mylonas, U. Jeschke, N. Shabani, C. Kuhn, S. Kriegel, M. S. Kupka, et al. Normal and Malignant Human Endometrium Express Immunohistochemically Estrogen Receptor Alpha (ER α), Estrogen Receptor Beta (ER β) and Progesterone Receptor (PR). Anticancer Research. 2005; 25: 1679-1686.

[7] Damle RP. Clinicopathological spectrum of endometrial changes in peri-menopausal and post-menopausal abnormal uterine bleeding: a 2 years study. Journal of clinical and diagnostic research. 2013; 7(12);2774- 2776.

[8] Talukdar B, Mahela S. Abnormal uterine bleeding in perimenopausal women: Correlation with sonographic findings and histopathological examination of hysterectomy specimens. J Midlife Health. 2016;7(2):73–7.

[9] Sreelakshmi U, Tushara B, Subhashini T. Abnormal uterine bleeding in perimenopausal age group women: a study on clinicopathological evaluation and management. International Journal of Reproduction, Contraception, Obstetrics and Gynecology, 2017;7(1):192–7.

[10] Jonathan S, Berek MD, Neville F. Berek & Hacker's Gynecologic Oncology. 6th edition; 2015; 48-52.

[11] Sobczuk K & Sobczuk A. New classification system of endometrial hyperplasia WHO 2014 and its clinical implications. Menopause Review. 2017, 16(3), 107-111.

[12] Gilk B. Uterus: Corpus. Chapter 33. In Rosai and Ackerman's Surgical Pathology. John R Goldblim,Laura W, Lamps, Jesse K, McKenney, Jeffrey L. Myers. 11th edtion. 2011;2; 1322-1347.

[13] Lora Hedrick Ellenson, Edyta C.Pirog. Chapter 22. In Robbins and Cotran pathologic basis of disease. 9th edition. Kumar V. Abbas AK, Fausto N, Astor N, Astor JC Edited. Saunders Elseiver: new Delhi; 2015:1022- 1033.

[14] Munro MG, Malcolm G, Fraser IS. FIGO Menstrual Disorders Committee. The two FIGO systems for normal and abnormal uterine bleeding symptoms and classification of causes of abnormal uterine bleeding in the reproductive years: Int J Gynaecol Obstet. 2018; 143:393–408.
[15] Whitaker L, Critchley HO. Abnormal uterine bleeding. Best Practice and Research Clinical Obstet and Gynaecol. 2016; 34:54–65.
[16] Pillai SS. Sonographic and histopathological correlation and evaluation of endometrium in perimenopausal women with abnormal uterine bleeding. International Journal of Reproduction, Contraception, Obstetrics and Gynecology, 2016, 3(1):113–7.
[17] Laberge P, Leyland N, Murji A, Fortin C, Martyn P & Vilos G. Abnormal Uterine Bleeding in Premenopausal Women. The Canadian Journal of CME, June 2009: 37(4) 362-376.
[18] Lora Hedrick Ellenson, Edyta C.Pirog. Chapter 22. In Robbins and Cotran pathologic basis of disease. 9th edition. Kumar V,Abbas AK, Fausto N, Astor N, Astor JC Editoed. Saunders Elseiver: new Delhi; 2015:1022- 1033.