ORIGINAL RESEARCH PAPER
Volume-9 | Issue-5 | May-2020 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

MORPHOMETRIC STUDY OF ENDOMETRIAL GLANDULAR LESIONS IN THE PERIMENOPAUSAL AND POSTMENOPAUSAL AGE GROUP WITH SPECIAL REFERENCE TO PROLIFERATIVE ACTIVITY

Pathology

Dr. Neeraj Kumar Junior Resident / Department of Pathology /R.I.M.S./ Ranchi University , India
Dr. Lalita Khess Associate Professor / Department of Pathology / R.I.M.S./ Ranchi University , India
Dr. Jalandhar Mehra* Junior Resident / Department of Pathology / R.I.M.S./ Ranchi University , India.
*Corresponding Author

ABSTRACT

Morphology is the keystone in the evaluation of Endometrial Glandular Lesions, but morphometric evaluation and immunohistochemistry can also be helpful in establishing the correct diagnosis. Morphometric measurements using variables like mean nuclear diameter, mean cytoplasmic diameter, mean nuclear area, N/C ratio, nuclear perimeter help in classifying different glandular lesions of endometrium, especially in dilemma in concluding a lesion benign, premalignant or malignant. The present study is to see the frequency of glandular lesions of endometrium with focus on the avoidance of common diagnostic pitfalls from the correlation between histomorphological, morphometrical studies and immunohistochemical marker studies.The present study was doneat the Department of Pathology, Rajendra Institute of medical sciences, Ranchi between July,2018 to September 2019.Highest number of cases (35%) belonged to hormone induced changes (both exogenous and endogenous)of endometrium in this study. Endometrioid adenocarcinoma constituted the major percentage of cases (82.14%) among carcinoma.Mean nuclear diameter >7.339µm indicating probability of malignancy with sensitivity 85.71 and specificity 89.47 was found. We concluded that morphometric study can be used to differentiate various benign, borderline endometrial glandular lesions from malignant endometrial glandular lesions in perimenopausal and postmenopausal age group.

KEYWORDS

I. INTRODUCTION

Disordered proliferative endometrium resembles normal proliferative tissue consisting of glands lined by cytologically bland, pseudostratified, proliferative, mitotically active epithelium and in having a roughly normal ratio of glands to stroma. It differs from the normal proliferative endometrium in the absence of uniform glandular development. The uniform appearance of the normal proliferative endometrium results from synchronous and coordinated growth of the fundal functionalis under the influence of estradiol. In contrast, the absence of pattern uniformity- a principal defining feature of disordered proliferative endometrium- is a result of dyssynchronous growth of the functionalis.[1] Uterine atrophy most commonly seen in postmenopausal women. Premenopausal causes of uterine atrophy include treatment with oral contraceptives or gonadotropin agonists, premature ovarian failure, or following radiation for cervical carcinoma. Endometrial glandular lesions include-(a)Hormone induced changes(exogenous and endogenous),(b)Endometritis-both acute and chronic types,(c)Endometrial atrophy,(d)Endometrial metaplasia,(e)Endometrial polyps,(f)Endometrial hyperplasia(types are-simple hyperplasia without atypia, complex hyperplasia without atypia, simple hyperplasiawith atypia, complex hyperplasiawith atypia),(h)Endometrial carcinoma of uterus.[2] WHO has classified hyperplasia into four categories: 1.simple hyperplasia, 2.complex hyperplasia, 3.simple atypical hyperplasia, 4.complex atypical hyperplasia. [3] Detection of atypical hyperplasia in an endometrial biopsy specimen carries a higher risk of occult or subsequent carcinoma.[4,5]

II. MATERIAL AND METHODS

A total of 100 cases of perimenopausal and postmenopausal age group with complaints of abnormal vaginal bleeding were taken for morphometry analysis and proliferative studies.

Study Design: Prospective & observational study
Study Location: Department of Pathology at Rajendra Institute of Medical Sciences, Ranchi
Study Duration: July 2018 to September 2019
Sample size: 100 patients.

INCLUSION CRITERIA:

(a) Irregular vaginal bleeding and discharge occurring in perimenopausal and postmenopausal women.
(b) Ultrasonography showing increased endometrial thickness in perimenopausal and postmenopausal women

EXCLUSION CRITERIA:

(a) Absence of above clinical parameters,
(b) Patient with above symptoms but due to refusal of subsequent investigations.

III. OBSERVATIONS AND RESULTS

TABLE1:
Distribution of cases according to age in Perimenopausal and Postmenopausal age group

Histopathological Diagnosis	Age in years		
	40-49 yrs	50-60 yrs	61-70 yrs
Endometrial Adeno Carcinoma	3	16	9
Endometrial Hyperplasia	15	5	0
Hormonal effect on endometrium	30	5	0
Chronic Endometritis	5	1	0
Atrophy of endometrium	0	2	4
Endometrial Polyp	2	2	0
Secretory endometrium with focal atypia	1	0	0

Figure 1 showing distribution of cases according to endometrial thickness in perimenopausal and postmenopausal age group

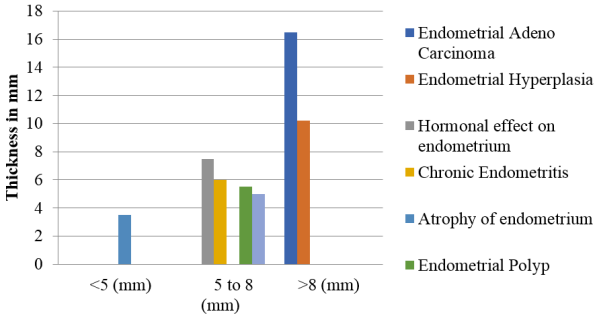

TABLE 2 showing:
Result of Morphometric Study (on H and E stained section)

Histopathological Diagnosis	MMND (µm)	MMCD (µm)	MMNA (µm)	M(N:C)	MNP (µm)
Endometrioid adenocarcinoma of uterus.	8.556	10.295	65.539	0.761	27.396
Serous papillary carcinoma of endometrium	10.059	12.063	84.408	0.695	32.036

Simple hyperplasia without atypia of endometrium.	6.209	11.290	30.282	0.321	20.837
Complex hyperplasia with atypia of endometrium	6.803	12.671	37.134	0.298	21.484
Hormonal effect on endometrium	5.850	11.808	28.245	0.253	18.406
Chronic Endometritis	5.858	15.115	27.398	0.184	18.375
Atrophy of endometrium	5.493	10.388	24.015	0.281	17.374
Endometrial Polyp	6.094	12.223	34.649	0.208	19.944
Secretory endometrium with focal atypia	5.601	13.492	24.652	0.172	17.601

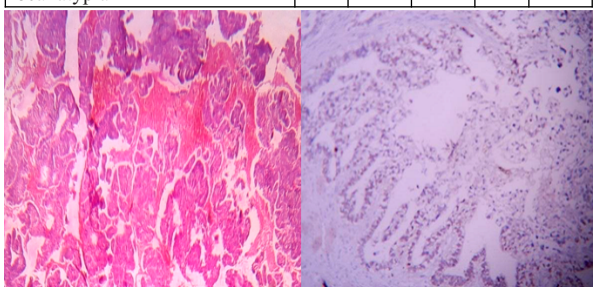

Figure 2: Well differentiated endometrioid adenocarcinoma of uterus involving less than ½ thickness of myometrium: scanner view (H/E,40X).

Figure 3: Endometrioid adenocarcinoma of uterus: IHC for Ki67(100X): showing positive nuclear staining.

Table 3 : showing distribution of cases according to Mean Ki67 index and Mean PCNA index in perimenopausal and postmenopausal age group.

Histopathological Diagnosis	Immunohistochemistry
	Mean Ki67 index (%)
Proliferative Endometrium	28.00
Secretory Endometrium	4.10
Endometrioid adenocarcinoma of uterus	20.17
Serous papillary carcinoma of endometrium	23.00
Simple hyperplasia without atypia of endometrium	11.44
Complex hyperplasia with atypia of endometrium	10.15
Hormonal effect on endometrium	6.50
Chronic Endometritis	6.08
Secretory endometrium with focal atypia	5.10
Endometrial Polyp	5.58
Atrophy of endometrium	2.00

I. DISCUSSION

Highest number of cases (35%) belonged to hormone induced changes (both exogenous and endogenous)of endometrium in this study. Cases of endometroid adenocarcinoma and serous papillary carcinoma of endometrium were 23% and 5% respectively. Among the total 28 cases of endometrial adenocarcinoma of uterus, endometrioid adenocarcinoma were 23 cases and constituted the major percentage of cases (82.14%) followed by serous papillary carcinoma(17.85%). 2 cases of endometrioid adenocarcinoma with squamous differentiation was noted out of 28 cases of endometrial adenocarcinoma of uterus(7.14%).

In this study, we found mean nuclear diameter >7.339µm indicating probability of malignancy with sensitivity 85.71 and specificity 89.47. Mean nuclear area >42.329µm^2 indicating probability of malignancy with sensitivity 85.71 and specificity 89.47. Mean nuclear perimeter >23.065µm indicating probability of malignancy with sensitivity 85.71 and specificity 89.47. Mean N/C ratio >0.552 indicating probability of malignancy with sensitivity 100 and specificity 100.

In this study we found Mean age of endometrial adenocarcinoma of uterus 58.14 years; of which mean age of endometrioid carcinoma of uterus was 57.3 years whereas mean age of serous papillary carcinoma of uterus was 62 yrs. Mean age of endometrial hyperplasia was 46.25 years; mean age of simple hyperplasia without atypia was 45.83 years whereas mean age of complex hyperplasia with atypia was 50 years.

We found Mean Ki67 index was highest in proliferative endometrium (28%) followed by serous papillary carcinoma of endometrium (23%) and endometrioid adenocarcinoma of uterus (20.17%) followed by simple hyperplasia without atypia of endometrium (11.44%) and complex hyperplasia with atypia of endometrium (10.15%). Mean Ki67 index was lowest in atrophic endometrium (2%).

From these observations, we concluded that morphometric study using nuclear parameters like mean nuclear diameter (MND), mean nuclear area (MNA), mean nuclear perimeter (MNP) and N:C ratio can be used to differentiate various benign, borderline endometrial glandular lesions from malignant endometrial glandular lesions in perimenopausal and postmenopausal age group. Proliferative index (Ki67) showed significant difference ($p<0.05$) between benign, borderline and malignant endometrial glandular lesions from each other. Histomorphology is the keystone in the evaluation of endometrial glandular lesions, but morphometric study and immunohistochemistry are helpful adjunct in establishing the correct diagnosis.

V. REFERENCES

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