



Endometrial Hyperplasia-Quantification and Morphometry

KEYWORDS

EndometrialHyperplasia,morphometry,D-score,endometrial carcinoma.

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ABSTRACT Endometrial Hyperplasia(EH) is the most common cause of abnormal uterine bleeding. It deserves special attention because of its relationship to Endometrial Carcinoma(EC). A study of endometrial curettings has been taken up in AlluriSitaramaraju Academy of Medical Sciences, ELURU to assess the role of quantitative, objective analysis in the diagnosis of EH.

The average age group of patients in the study was 40.8 years.Commonestclinical presentation is DUB.In all the three classifications i.e., Kurman– Norris, modified classification advocated by M.C. Anderson and Fox & Buckley quantitative morphometry revealed similar findings.

This study implies that quantitative morphometry is more objective in the diagnosis of hyperplasia as the features are assessed basing on a numerical value.Consequently, with the therapeutic decision rule of D score>1, many cases could have been correctly predicted and unnecessary hysterectomies would have been avoided.

INTRODUCTION

Endometrial Hyperplasia(EH) is a non-physiological and non-invasive proliferation at the endometrium level. The term “Endometrial Hyperplasia” refers to an abnormality characterized by the increase of endometrium quantity(volume),alteration of glandular architecture and change of glands/stromal ratio.It deserves special attention because of its relationship to EC^(1,2,3).

There are two forms of hyperplasia : the non-atypical form,which is a self-limiting increase which usually donot seem to progress to cancer and the atypical form, representing a precursor lesion⁽⁴⁾ with certain characteristics found in relation to endometrial adenocarcinoma⁽⁵⁾.

Complete knowledge of the nature of EH is hindered by a confusing multiplicity of descriptive terms and a large variety of unsatisfactory classifications which resulted in low interobserver and intraobserver diagnostic reproducibility. The grades of atypical endometrial hyperplasia(AEH) and well differentiated adenocarcinoma(WDA) differ only in the degree of their cytological and architectural features ^(6,7,8). Objective assessment by quantitative microscopy helps to diagnose EH with accuracy and this method reveal differences and changes which escape subjective observation.

AIMS AND OBJECTIVES:

- Classification of endometrial curettings showing hyperplasia according to three classifications by analysing architectural and cytological features.
- Assessment of the role of quantitative morphometry
 - In the objective study of endometrial curettings.
 - In differentiating hyperplasia from proliferative endometrium.
 - In comparison of different classifications of hyperplasia.
 - Appropriate diagnosis of type of endometrial hyper-

plasia with objective analysis which is better in comparison with subjective analysis.

MATERIALS AND METHODS:

STUDY PLACE:

AlluriSitaramaraju Academy of Medical Sciences, Department of Pathology.

STUDY DURATION:

Study was done from January2013 to July 2015.

STUDY POPULATION:

The study was carried out on 100 patients.

The material was routinely processed, fixed in formalin, embedded in paraffin wax. For morphometry, Eye piece micrometer with 100 divisions was taken.This was calibrated over a Neubauer chamber and fiveparameters were measured.

RESULTS:

The average **age** group of patients in the study was 40.8 years.Commonest**clinical presentation** is DUB.In all the three classifications i.e., Kurman– Norris, modified classification advocated by M.C. Anderson and Fox & Buckley quantitative morphometry revealed similar findings.

Table 1

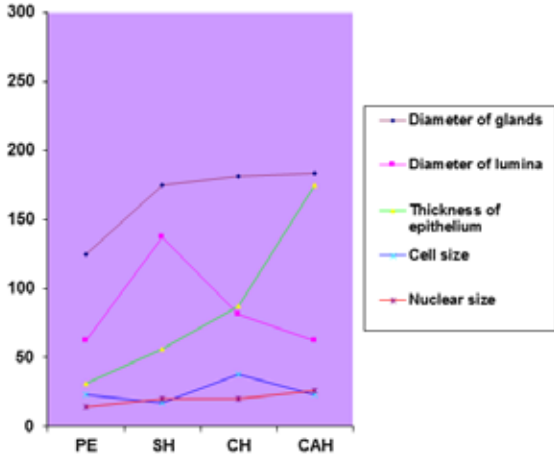
Showing quantitative morphometric features in proliferative phase and different groups of hyperplasias.

Feature	Proliferative endometrium	Simple hyperplasia	Complex hyperplasia	Complex atypical hyperplasia
Diameter of glands	125 μ	175 μ	181.25 μ	183.75 μ
Diameter of lumina	62.5 μ	137.5 μ	81.25 μ	62.5 μ

Thickness of epithelium	31.25 μ	56.25 μ	87.5 μ	175 μ
Cell size	23.2 μ	17.4 μ	37.7 μ	23.2 μ
Nuclear size	14.5 μ	20.3 μ	20.3 μ	26.1 μ

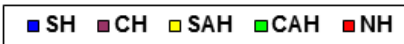
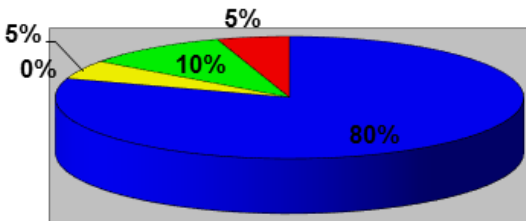
Graphical depiction of quantitative morphological features in proliferative phase and different groups of hyperplasias(Kurman-Norris)

GRAPH - I



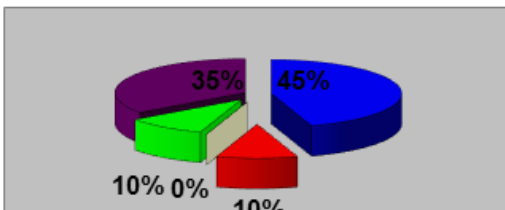
PIE DIAGRAM-I

Showing distribution of cases basing on qualitative features of 20 cases of endometrial hyperplasia (Kurman – Norris).



PIE DIAGRAM-II

Interpretation of twenty curettings basing on qualitative and quantitative features.



On analysing these twenty (20) cases along with quantitative morphometric features 9 (45%) cases showed average diameter of glands as 176.25 μ , diameter of gland lumen as 142.6 μ , thickness of the glandular epithelium as 60 μ , cell-size 20 μ and nuclear size on average 23.2 μ which corresponded with the values of SH. The remaining 7 (35%) cases showed average diameter of glands as 125 μ , diameter of gland lumen 67.5 μ , thickness of the epithelium 31.25 μ , cell size 23.78 μ and nuclear size 14.86 μ which corresponded with the values of proliferative phase endometrium. Two (10%) cases showed average diameter of glands as 200 μ , diameter of gland lumen as 80 μ , thickness of epithelium 90 μ , cell size 35 μ and nuclear size 18 μ which corresponded with the quantitative values of CH. Two (10%) cases showed diameter of glands on average 226.7 μ , diameter of gland lumen 60 μ , thickness of the epithelium 180 μ , cell size 24 μ and nuclear size 26 μ which corresponded with the values of CAH.

Title:ENDOMETRIAL HYPERPLASIA-QUANTIFICATION AND MORPHOMETRY DISCUSSION:

In the present study, a total number of hundred endometrial curettings were studied in the Department of Pathology, AlluriSitaramaraju Academy of Medical Sciences,ELURU.

Out of hundred endometrial curettings(100), fifty curettings (50 prospective) with EH and thirty(30) curettings with proliferative phase endometrium were analysed by quantitative morphometry and classified according to three different classifications. i.e., Kurman – Norris, ⁽¹¹⁾ Fox-Buckley classification ⁽¹²⁾ and Modified classification advocated by M.C. Anderson ⁽¹³⁾.The remaining 20 endometrial curettings with hyperplasia were studied to verify the value of objective analysis in differentiation of hyperplasia from proliferative endometrium:

For quantitative morphometry, five features were measured in each case which included three architectural features i.e., diameter of the glands, diameter of the gland lumina, thickness of the glandular epithelial lining and two cytological features i.e., cell size and nuclear size. The morphometry was done with minimal technical aids i.e., eyepiece micrometer calibrated with modified Neubauer counting chamber and a compound light microscope.

The results of quantitative morphometry on fifty endometrial curettings with hyperplasia and thirty curettings with proliferative phase endometrium of same age group are discussed by comparing with the study of **Baak et al**^(9,10)

In the study done by **Baak et al**^(9,10) with computerized aids, twelve (12) stereological and twelve (12) cytological morphometric features were analysed, in four groups of endometrial proliferations i.e., mild hyperplasia, AH, well differentiated carcinoma and moderately differentiated carcinoma.As in our study, EC were not included, for the quantitative parameters, the observation of **Baak et al**^(9,10) study were taken into consideration for comparison.

The morphometric features observed in our five cases of AH are far away from the features observed by **Baak et al**^(9,10) for well differentiated carcinomaofendometrium. Hence, in the present study, the five cases with atypia were correctly interpreted as AH quantitatively also.

In order to assess the utility of quantitative morphometry in accurate diagnosis of EH, another set of twenty random cases of endometrial curettings were analysed initially bas-

ing on qualitative morphology alone and then followed by quantitative morphometry also.

SUMMARY AND CONCLUSION:

The present study of EH was undertaken in the Department of Pathology, AlluriSitarramaraju Academy of Medical Sciences, ELURU to correlate various histological findings with different classifications and to assess the value of quantitative morphometry in the diagnosis and classification of EH. This study included 50 selected prospective cases of EH already diagnosed, reviewed and confirmed by another independent pathologist.

Another twenty cases of EH were selected at random, not reviewed by any pathologist. The study also included thirty (30) cases of proliferative phase endometrium to find out whether there will be any relation in morphometrical values between normal proliferating endometrium and endometrial hyperplasia. The quantitative morphometric features taken into consideration in our study were three architectural features i.e. diameter of glands, diameter of gland lumen, thickness of the epithelium and two cytological features namely cell size and nuclear size. The following observations were made in our study.

- (1) The quantitative feature, diameter of the glands showed no significant difference in different grades of hyperplasia but increased from proliferative phase to simple hyperplasia.
- (2) The diameter of the gland lumen and thickness of the glandular epithelium were inversely proportional as there was gradual increase in the thickness of the epithelium from simple hyperplasia / low grade to complex atypical hyperplasia / high grade.
- (3) The cell size showed minimal increase from simple / low grade to complex atypical hyperplasia / high grade.
- (4) The nuclear size showed gradual increase from simple / low grade to complex atypical hyperplasia / high grade indicating increased nuclear – cytoplasmic ratio in high grade hyperplasia. The above said observations were in accordance with the study of **Baak et al**^(9,10) and Norris HJ et al.
- (5) In our study, the average thickness of epithelium in proliferative phase endometrium was 31.25 μ , and in SH was 62.5 μ which corresponded with the values of Baak et al study which showed a value of 61.1 μ . These observations showed that when the thickness of glandular epithelium is around 60 μ , the possibility of simple hyperplasia is very strong. The qualitative morphological and quantitative morphometric features in these EH were compared between Kurman & Norris, Modified classification advocated by M.C Anderson and Fox & Buckley classifications. Out of 39 cases of simple hyperplasia, 33 (82%) corresponded with a discrepancy in 6 (18%) cases.
- (6) Out of these six cases, two cases were those categorized as no hyperplasia according to Kurman – Norris because of stromal edema although some architectural changes suggested hyperplasia. These were classified as CGH according to modified classification advocated by M.C. Anderson and as simple hyperplasia according to Fox & Buckley classification as stromal edema does not rule out hyperplasia. When quantitative morphometry was applied, these two cases were confirmed to be proliferative phase endometrium.
- (7) The remaining four (4) cases which showed discrepancy, were categorized as SH according to Kurman – Norris and AH with mild architectural atypia according to

M.C. Anderson basing on presence of glandular outpouchings and focal crowding. These four (4) cases were confirmed as SH on quantitative morphometry.

- (8) There was no difference in morphological features in between Fox & Buckley and modified classification advocated by M.C. Anderson.
- (9) There were no differences in cases with cytological atypia with regard to qualitative morphological and quantitative morphometric features in all the three classifications.
- (10) In the comparative study of twenty (20) random cases of endometrial hyperplasia by qualitative morphological and quantitative morphometric features, discrepancy was observed in seven (35%) cases. These were interpreted as hyperplasia at random but quantitative morphometric values corresponded with the values of proliferative phase of endometrium.
- (11) This study implies that quantitative morphometry is more objective in the diagnosis of hyperplasia as the features are assessed basing on a numerical value.
- (12) Sensitivity of both quantitative and qualitative morphometry is higher when compared to qualitative morphometry.

Consequently, with the therapeutic decision rule $D \text{ score} > 1$, cases could have been correctly predicted as having a very low probability for cancer development. Using this rule, in our present study the D score clearly would have prevented overtreatment in some patients diagnosed as having EH without causing undertreatment in 1 case with cancer progression. $p < 0.05$ was adopted as a level of significance.

TABLE II
Comparison of overall statistical parameter Quantitatively and Qualitatively.

Statistical parameter	Quantitative & Qualitative method	Qualitative method
Sensitivity	100%	75%
Specificity	94%	100%
Positive predictive value	75%	100%
Negative predictive value	100%	94%

Comparison of the WHO classification, clinical outcome and the D score showed that out of 2 patients diagnosed as CAH, only one developed cancer and remaining all patients had a $D \text{ score} > 0$. Likewise of the woman with SAH and a D score > 0 , did not develop cancer. Of the 43 patients with SH who underwent hysterectomy but cancer was not found in the hysterectomy specimen, none had a D score < 0 . This means that many of these patients would not have undergone major surgery if the treatment decision has been made based on D score criteria set out in previous studies.

This study proves that quantitative morphometry is essential for accurate diagnosis of hyperplasia and to avoid false positive and false negative interpretation on endometrial curettings.

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