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Histological Analysis and Comparison of Endometrial Sampling and Hysterectomy Specimen in Patients with Abnormal Uterine Bleeding

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ABSTRACT

Objective: To determine the frequency of different causes of Abnormal Uterine Bleeding (AUB) in relation to the age and to determine the degree of concordance in diagnosis on endometrial sampling and hysterectomy specimen with special emphasis on type and FIGO Grade of malignant cases.

Study Design: Cross- sectional study.

Place and Duration of Study: Histopathology Department, Foundation University Medical College Islamabad Pakistan, from July 2022 to July 2023.

Methodology: A total of 321 cases of endometrial sampling were included in the study. Age of the patients along the histological diagnosis was evaluated. Cases that underwent hysterectomy were further compared with the histological outcome.

Results: We found that in the premenopausal age group, among 253 cases, chronic endometritis 102(40.3%) was the most common finding followed by endometrial hyperplasia 66(26%) and disordered proliferative endometrium 38(15%). In the post-menopausal age, the incidence of malignancy was quite high (n=39), with endometrioid carcinoma being the most frequent diagnosis 24(61.5%), followed by endometrial hyperplasia. We observed maximum concordance in the histological diagnosis of malignancy between endometrial and subsequent hysterectomy samples. Strong agreement was also detected between endometrioid carcinomas Grade 1(97.4%) and Grade 2(100%).

Conclusion: chronic endometritis, endometrial hyperplasia, disordered proliferative endometrium and malignancies are the most common causes of abnormal uterine bleeding. Endometrial sampling emerged as a valuable diagnostic tool, particularly in detecting malignancy.

Keywords: Abnormal Uterine Bleeding, Endometrioid Carcinoma, Endometrial Hyperplasia, Hysterectomy.

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INTRODUCTION

Abnormal uterine bleeding (AUB) is one of the most common causes of morbidity among female population especially in the perimenopausal age group. It negatively impacts the quality of life and is responsible for financial damage, health impairment, and enhanced utilization of health care resources.[1] Globally, the prevalence of AUB ranges between 3-30%, with same (2) prevalence among Asian countries.[2,3] In Pakistan, this has been reported at 11%.[4]

Hormonal patterns, endometritis, atrophic endometrium, proliferative lesions like polyps, endometrial hyperplasia and even neoplasms may lead to AUB.[5] Majority of these lesions can be easily detected through histopathological assessment of endometrial sampling which is considered standard practice for the evaluation of AUB. Hysterectomy is considered as the definitive and most effective treatment for cases that do not respond to medical treatment or in cases of suspicion for malignancy.[6]

Endometrial cancer ranks sixth among malignancies worldwide, with the highest rates observed in developed countries.[7] Endometrial carcinoma constitutes a significant proportion of the lesions leading to AUB, especially in the post-menopausal age group.[8] Over the last decade, a significant rise in its occurrence has also been observed especially in females with obesity and diabetes.[9] The diagnosis of both the endometrial hyperplasia and malignancy is primarily based on its histological detection on endometrial sampling.

The aim of this study was to determine the frequency of different causes of AUB in our population in relation to the age of the patient. Furthermore, the present study also determines the degree of concordance in diagnosis on endometrial

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sampling and hysterectomy specimen, with special emphasis on the type, and International Federation of Gynecology and Obstetrics (FIGO) Grade of endometrial carcinoma.

METHODOLOGY

This cross-sectional study was conducted at the Department of Histopathology.at Foundation University Medical College (FUMC) Islamabad from July 2022 till July 2023, after obtaining approval from the Institutional Ethical Review Committee (Ref No. 699/RC/FFH/RWP Dated 16 May 2023).

Inclusion Criteria: Adequate and well-fixed endometrial samples of female patients presenting with AUB were included, along with hysterectomy specimen of patients with pre-operative diagnosis of endometrial hyperplasia and malignancy.

Exclusion Criteria: Poorly fixed and/or inadequate specimens containing no endometrial tissue were excluded.

The sample size was calculated using Raosoft sample size calculator taking confidence interval 95%, margin of error 5%, reported prevalence of AUB 30%.[10] A total of 321 females presenting with AUB were included in the study using non- probability convenience sampling, after obtaining written informed consent.

Tissue specimens fixed in 10% formalin and accompanied with short history were received in the Histopathology Department of Foundation University Medical College (FUMC) for histopathology. The slides prepared were examined by consultant histopathologists at FUMC to give a definite diagnosis. Variables like age, diagnosis on endometrial sampling and hysterectomy specimen were documented. In case of endometrial malignancy, the type and tumour FIGO Grade were assessed on both pre-operative endometrial sampling and subsequent hysterectomy specimens. The endometrioid carcinoma was assigned three Grades according to histological differentiation, including low Grade/well differentiated (G1), moderately differentiated (G2) and high Grade/poorly differentiated (G3). Other tumours including serous carcinoma, clear cell carcinoma and carcinosarcoma are by considered as high Grade.[13]

Data were entered in Statistical Package for Social Sciences (SPSS) version 23. Results were presented as mean ± SD for continuous variables like age, and frequencies and percentages were computed for diagnosis on endometrial sampling and hysterectomy. Degree of agreement and disagreement between endometrial sampling and hysterectomy specimens was calculated with special emphasis on the type and FIGO Grade of malignant cases.

RESULTS

Total number of female patients included in this study was 321, with a mean age of 50.00±8.047 years. Most of these patients 253(78.8%) presenting with AUB were in premenopausal age group while the rest 68(21.2%) were in postmenopausal age. Proportion of different histopathological patterns on endometrial sampling is shown in Figure-1.

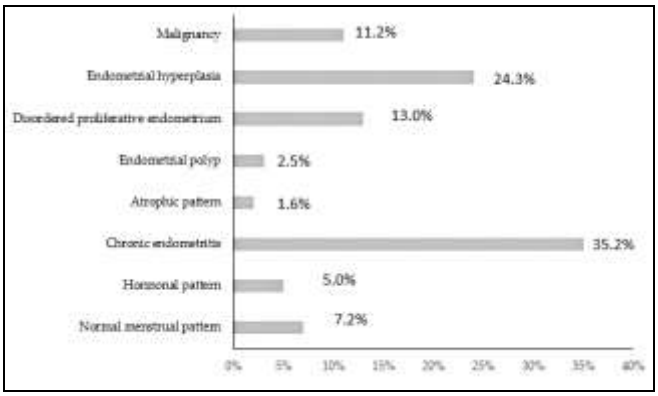

Figure-1: Distribution of Histopathological Patterns on Endometrial Sampling (n=321)

Overall, the most common histopathological pattern on endometrial sampling was chronic endometritis 113(35.2%), followed by endometrial hyperplasia 78(24.3%). Only one out of 113 patients with chronic endometritis was diagnosed as chronic granulomatous inflammation, while the rest of the women had chronic non-specific endometritis. Similarly, 76(23.7%) cases of endometrial hyperplasia were not associated with atypia compared to only two cases of atypical endometrial hyperplasia. In the premenopausal age group, among 253 cases, chronic endometritis 102(40.3%) remained the commonest finding followed by endometrial hyperplasia 66(26%) and disordered proliferative endometrium 38(15%) in third place. However, among 68 cases in post-menopausal age, malignancy 26(38.23%) was the most common cause of abnormal uterine bleeding followed by endometrial hyperplasia 12(17.64%). Normal menstrual pattern was found in only 23(8%) women. Among these patients, the secretory phase was more common 21(6.5%) as compared to only 2 cases of proliferative phase endometrium. The distribution of benign lesions on endometrial sampling is shown in

Table-I. Endometrioid carcinoma was the most frequent diagnosis 24(61%) among 39 cases of malignancies. The distribution of malignant lesions on endometrial sampling is enlisted in Table-I.

After endometrial sampling, 56 out of 321 women underwent subsequent hysterectomy. The histological outcome of findings on endometrial sampling and subsequent hysterectomy specimen in these patients is shown in Table-II. Overall, there was an agreement of 71.4%, and among these cases, there was maximum concordance in the diagnosis of malignancy (92.1%). However, there occurred some disparity in agreement between the type and FIGO Grade of tumours. One out of twenty-three endometrioid carcinomas diagnosed on preoperative endometrial sampling turned out to be serous carcinoma on further hysterectomy and immunohistochemistry (IHC). In addition, 02 cases of atypical endometrial hyperplasia were also found to be endometrioid carcinoma on subsequent hysterectomy. Strong agreement was detected between endometrioid carcinomas Grade 1(97.4%) and Grade 2(100%). Among 38 cases of malignancy in hysterectomy specimen, 24(63.2%) were endometrioid carcinoma, 5(13.2%) were serous carcinoma, 6(15.8%) were carcinosarcoma, 2(0.6%) were clear cell carcinoma, and only one case of low-Grade endometrial stromal sarcoma, which was previously diagnosed as hormonal changes on endometrial sampling.

We found that majority of cases of endometrial hyperplasia were not associated with atypia. Only eleven out of 78 cases under went hysterectomy. There was concordance in 4(36.3%) cases. Among discordant cases, besides the two cases that turned out malignant, 2 cases had the final diagnosis of endometrial polyp, 2 were adenomyosis and only one was leiomyoma.

Table-I: Spectrum of Benign and Malignant Lesions on Endometrial Sampling (n=321)

Benign Lesions (n=282) n (%)		**Malignant Lesions (n=39) n (%)**	
Normal menstrual pattern	23(8.2%)	Atypical endometrial hyperplasia	2(5.1%)
Hormonal pattern	16(5.7%)	Endometrioid carcinoma	24(61.5%)
Senile atrophy	5(1.8%)	Serous carcinoma	2(5.1%)
Chronic endometritis	113(40.0%)	Clear cell carcinoma	3(7.7%)
Endometrial polyp	8(2.8%)	Carcinosarcoma	5(13.0%)
Disordered proliferative endometrium	41(14.5%)	Poorly differentiated carcinoma	1(2.5%)
Non atypical endometrial hyperplasia	76(27.0%)	Metastatic carcinoma	2(5.1%)

Table-II: Histological Outcome of Findings on Endometrial Sampling and Subsequent Hysterectomy Specimen (n=56).

Endometrial Sampling Findings	**Histological outcome on hysterectomy specimen**					
	Leiomyoma n (%)	**Adenomyosis n (%)**	**Endometrial polyp n (%)**	**Non atypical endometrial hyperplasia n (%)**	**Malignancy n (%)**	**n (%)**
Normal menstrual pattern	1(1.78%)	1(1.78%)				2(3.57%)
Hormonal pattern	1(1.78%)				1(1.78%)	2(3.57%)
Chronic endometritis		1(1.78%)				1(1.78%)
Endometrial polyp			1(1.78%)			1(1.78%)
Disordered proliferative endometrium	1(1.78%)	2(3.57%)	1(1.78%)			4(7.14%)
Endometrial hyperplasia	1(1.78%)	2(3.57%)	2(3.57%)	4(7.14%)	2(3.57%)	11(19.6%)
Malignancy					35(62.5%)	35(62.5%)
n (%)	4(7.14%)	6(10.7%)	4(7.14%)	4(7.14%)	38(67.85%)	56(100%)

DISCUSSION

Abnormal uterine bleeding is a well-established cause of morbidity in women. The management of AUB depends on the underlying cause, which can vary according to geographic distribution. The endometrial sampling has become an integral diagnostic tool in these patients.[11]

Overall, in our study, we observed that most of the females presenting with AUB were in the premenopausal age, when compared with post-menopausal cases. Furthermore, majority of these patients were in 40-50 years age group. These findings were quite similar to the findings of other studies that reported maximum incidence of AUB within 40-50 years of age.[12,13]

In our assessment, only 39(11.2%) cases were malignant and the rest of the cases were benign. A similar trend has been documented in other studies.[14,15] According to one study, functional endometrial changes are the most common cause of AUB.[15] A study by Dhakhawa *et al.*, which focused more on females in perimenopausal age, reported disordered proliferative endometrium as the most common cause of AUB followed by hormonal changes.[16] Our findings were in contrast with these previous studies. In our setup, we found that in the premenopausal age group, chronic endometritis was the most common finding, followed by endometrial hyperplasia and disordered proliferative endometrium in third place. These findings are comparable to some extent with a study by Mohanlal *et al.*, who considered endometrial hyperplasia as the second common reason for AUB followed by disordered proliferative endometrium.[17] However, proliferative endometrium was the most frequent finding in perimenopausal age group. The difference could be due to the fact that most of the previous studies were more focused on perimenopausal age. In this age group, AUB is usually a consequence of hormonal imbalances.The higher incidence of chronic endometritis, could be due to low socioeconomic status and poor hygienic conditions in our setup.

In post-menopausal age, the incidence of malignancy was quite high, followed by endometrial hyperplasia, which is considered as a premalignant condition. Thus increasing age is considered an important risk factor in the development of malignancy. Endometrioid carcinoma was the most frequent diagnosis among malignancies. These findings are supported by various other studies.[16-18] Strong agreement was seen in malignant cases when compared with hysterectomy specimens. Only 1 out of 23 endometrioid carcinomas diagnosed on preoperative endometrial sampling turned out to be serous carcinoma on further workup. There was complete agreement in the Grade 2, followed by Grade 1 endometrioid carcinomas. These findings are quite comparable with research by Nithyananda *et al.*, who also found maximum agreement in Grade 2 carcinomas.[19]

LIMITATION OF STUDY

Our main limitation was that we did not follow up the patients to record future outcomes including morbidity and mortality.

CONCLUSION

In conclusion, AUB predominantly affects premenopausal women, with a peak occurrence in the perimenopausal age group. Chronic endometritis is the most frequent histopathological pattern in premenopausal women, while malignancy and endometrial hyperplasia were prevalent among postmenopausal individuals. Endometrial sampling emerged as a valuable diagnostic tool, particularly in detecting endometrial hyperplasia and malignancy.

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Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

RR & TS: Data acquisition, data analysis, critical review, approval of the final version to be published.

SR& SA: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

YW & SF: Conception, data acquisition, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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