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Histopathological Study of Endometrial Biopsies in Perimenopausal and Post Menopausal Women - A Study at Tertiary Care Hospital

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Abstract: ***Introduction: Evaluation of Endometrial biopsies and curettings provides important information regarding structural and functional pathology and identifying causes of bleeding. Other indications include evacuation of conceptus, abortions or retained tissues and also evaluating benign, premalignant and malignant pathological causes. Objectives: To determine clinical features in patients of perimenopausal and postmenopausal age group and to describe their spectrum of histopathological findings. Material and Methods: This study was conducted on endometrial biopsies of total 252 patients; at the pathology department, C U Shah Medical College, Surendranagar, Gujarat; for 3 years period from January 2022 to December 2024. Cases were grouped according to their menstrual status- perimenopausal and post-menopausal period as well as according to their presenting complaints. Results: 252 cases included 72 post-menopausal and 180 perimenopausal women, from which 221 cases presented with bleeding - 158 cases of perimenopausal and 63 cases of post-menopausal bleeding. Other 31 patients without bleeding presented with abdominal pain or whitish discharge. Histopathological findings includes 14.7% benign conditions, 29% pre malignant conditions and 5.2% of malignancy. Rest 48% showed other miscellaneous findings. Conclusion: Most common complaint in these age groups is AUB caused by Endometrial Hyperplasia without atypia and others conditions like hormonal imbalance and disordered endometrium.***

Keywords: perimenopausal bleeding, postmenopausal bleeding, endometrial hyperplasia, metaplasia, malignancy

1. Introduction

Evaluation of Endometrial biopsies and curettings provides important information regarding structural and functional pathology and the status of endometrium in menstrual cycle thus identifying causes of bleeding. The other indications include evacuation of conceptus, abortions or retained tissues. Another important indication is evaluating benign, premalignant and malignant pathological causes.

Abnormal uterine bleeding (AUB) is any type of vaginal bleeding that is irregular, heavy or longer than usual- could be spotting/ bleeding in between the normal menses. It consists of disorders in frequency, predictability duration, rate or amount of flow. Acute AUB require immediate intervention to minimize or prevent further blood loss. [6] For sampling, hysteroscopy and biopsy is best method followed by dilatation and curettage.

In the revised International Federation of Gynecology and Obstetrics-Abnormal Uterine Bleeding (FIGO-AUB) system 1 in 2018, terms such as menorrhagia, metrorrhagia, oligomenorrhoea and dysfunctional uterine bleeding has been removed.[6]

FIGO recommends endometrial sampling as the first line management of perimenopausal women with AUB. Although some studies have indicated that age is not important an independent variable, most suggest that endometrial sampling be considered for all women over a certain age, usually 45 years. [8, 9]

Parameters	Normal	Abnormal (<24 days / >38 days)
Frequency	>24–≤38 days	Infrequent (≥38 days) / Absent (=amenorrhea)
Duration	≤8 days	Prolonged (>8 days)
Regularity	Regular (shortest to longest cycle variation: ≤7-9 days)	Irregular (shortest to longest cycle variation: ≥8-10 days)
Flow volume	Normal	Light / Heavy
Intermenstrual bleeding	None	Random cycle / Cyclic-early cycle / Mid-cycle / Late cycle
Unscheduled bleeding on progestin ± oestrogen gonadal steroids (birth control pills, rings, patches or injections)	Not applicable (not on gonadal steroid medication) / None (on gonadal steroid medication)	Present

Perimenopause is defined as transitional period of two to eight years preceding menopause and one year after the final menses.[7] AUB is the most common presenting complaint of perimenopausal bleeding followed by pain caused by structural and nonstructural causes like- polyp, adenomyosis leiomyoma or any malignancy along with disorders of coagulation, ovulatory/ endometrial function or other iatrogenic causes.

Menopause occurs between 45- 55 years of age in India with mean year of age at 50 years. Bleeding in this age is caused by endometrial hyperplasia, malignancy or benign causes like endometrial polyp.

2. Aims and Objectives

The aim of this study were

1) To describe the clinical features of the patients in perimenopausal and post-menopausal age group whose endometrial biopsies were received
2) To describe their histopathological findings- Benign, premalignant and malignant.

3. Material and Methods

This study was conducted at the pathology department, C U Shah Medical College, Surendranagar, Gujarat. This study included Total 252 specimens of endometrial biopsies which were received over 3 years period from January 2022 to December 2024.

Cases were grouped according to their menstrual status- perimenopausal and postmenopausal period as well as according to their presenting complaints-i.e. with/ without bleeding. Causes of bleeding included complaints of menorrhagia and irregular menses. Other presenting complaints like pain or whitish discharge were also considered. Their histopathological findings were analyzed. This data was analyzed using Microsoft Excel MSO 2016 (version 2502) and graphical representation was done using histograms, bar diagrams and pie charts.

4. Results

252 cases included 72 post-menopausal and 180 perimenopausal women (Figure 2), from which 221 cases presented with bleeding (Table 4) - 158 cases(highest in 40 years or less; n=58) of perimenopausal and 63 cases (highest in 46-50 years of age; n=19)of post-menopausal bleeding.(Figure 1) Highest number of cases with perimenopausal bleeding were seen with hormonal imbalance and cystic glandular hyperplasia in cases of postmenopausal bleeding (Table 5A-B). Patients in age group of 41-45 years presented with highest number of cases with bleeding (Figure 6). Perimenopausal bleeding had highest number of cases falling in miscellaneous category (n=81); followed by premalignant causes (n=46). (Figure 7) Postmenopausal bleeding had highest number of cases falling in premalignant causes (n=24) with 8 cases of malignancy. (Figure 8)

Other 31 patients without bleeding presented with abdominal pain or whitish discharge (3). Spectrum of histopathological findings includes 14.7% benign conditions, 29% pre malignant conditions and 5.2% of malignancy. Rest 48% showed other miscellaneous findings (Table 1).

Cases of malignancy were more on post-menopausal women (n=8) in age group of 50 or more (Figure 4). Total 13 cases (Table 3B) of malignancy were observed out of which most common malignancy were of endometrioid adenocarcinoma in all these cases (n=11), one cases of high- grade stromal sarcoma and one case of carcinosarcoma. (Figure 5)

Premalignant conditions were seen in perimenopausal women with highest number in age group of 41-45 years (n=12.3%) followed by that in age group of 46-50 years (n=9.9%) (TABLE 2) amounting to total 53 of 73 cases. (Figure 4) Majority of the cases showed hyperplasia without atypia in total 58 cases. (Table 3A) This histopathological finding was highest number of all the spectrum of findings.

Benign conditions included endometrial polyp being more in perimenopausal women with highest number in age group of <40 years of age (n-=15) (Table 2) than in postmenopausal women (n=10). There were 4 cases having endometritis. 2 cases of adenomyoma and 1 case each of adenofibroma, adenomyomatous polyp and atypical polypoidal adenomyoma were also found. (Table 3A)

Other miscellaneous findings were also included in this study which comprised of hormonal imbalance (n=37 cases), disordered / biphasic endometrium (n=25). There were 6 cases with retained product of conceptus, 3 cases of anovulatory cycle, and one rare cases of osseous metaplasia of endometrium.

There were 8 cases of these biopsies were no opinion could be given- included inadequate samples. (Table 3A)

Most common presenting complaint of abnormal uterine bleeding was menorrhagia (n=114). (Figure 3) Out of all these biopsies, most common finding was endometrial hyperplasia without atypia (n=28%) followed by hormonal imbalance (9.6%). 7 cases of endometrial polyp presented with menorrhagia. (Table 5C)

Abdominal pain with or without bleeding was the second common complaint (n=62) with maximum number of cases with endometrial hyperplasia without atypia, hormonal imbalance, endometrial polyp. (Table 5D) Osseous metaplasia was an incidental finding in a case presenting with pain and secondary infertility.

13 cases of hormonal imbalance presented with irregular menses. (Table 5E)

5. Discussion

AUB is defined as an episode of heavy bleeding that, in the opinion of the clinician, is of sufficient quantity to require immediate intervention to minimize or prevent further blood loss.[6]

In study done by Kuru et al., histopathologic analysis of endometrial biopsy specimens revealed predominantly benign findings: 137 (40.4%) had proliferative endometrium, 126 (37.2%) had endometrial polyp, 30 (8.8%) had non-atypical hyperplasia, 18 (5.3%) had secretory/iatrogenic endometrium, and 22 (6.5%) had atypical hyperplasia. Only two (0.6%) patients were diagnosed with endometrial cancer and in our study 5 cases (3.2%) based on the biopsy results.[1] In perimenopausal bleeding, 40 (25%) had non-atypical hyperplasia, and 6 (3.8%) had atypical hyperplasia. 19 cases with perimenopausal bleeding had benign findings.

Study done by Nair BL et al had about 29.31% had disordered proliferative endometrium, 4.3% had proliferative endometrium, 5.2% each had polyp or hyperplasia without atypia, 2.58% each had well differentiated adenocarcinoma or

atrophic endometrium. In our study, 12 % cases had biphasic/ disordered endometrium.

In Sreelakshmi et al study proliferative endometrium contributed to 30.3%, secretory endometrium was 27.4% and disordered proliferative endometrium 6.6%.[12]

In the study by Vani et al 30.3% cases were proliferative endometrium, 25.97% were secretory endometrium and 5.62% were disordered proliferative endometrium. [16]

Geethalaxmi et al study showed that among the endometrial causes of pre and postmenopausal bleeding, polyp was the commonest finding, constitute 30.48% of cases, followed by cases of simple hyperplasia, complex hyperplasia and complex hyperplasia with atypia constitutes 13.33% each. The most common endometrial lesions observed in the age group between 36 to 40 years were proliferative endometrium in 4 cases (33.33%) and simple hyperplasia in 3 cases (25%). In the age range between 41 and 45 years, the most prevalent endometrial lesions were polyp in 8 instances (28.57%), followed by simple and complex hyperplasia in similar numbers of cases (14.29%). One case (3.57%) of squamous metaplasia was noted in the age group between 4l-45 years. In the age range 46 to 50 years, the most prevalent lesions were 14 cases (32.56%) of polyp and 9 instances (20.93%) of complicated hyperplasia. Similarly, polyps were prevalent in the 51-55 year old age group, with 5 cases (38.46%) and 4 cases (30.77%) of complicated hyperplasia with atypia. Adenocarcinoma was diagnosed in 3 cases (23.08%). All the 3 cases were seen in the age group above 50 Years. Most common- premenopausal bleeding was menorrhagia. The common endometrial lesions in pre-menopausal age group in the present study were polyp 28.92%, followed by 15.67% of simple and complex hyperplasia each. The common endometrial lesion in post- menopausal age group in the present study was polyp 36.36%. [17]

In the Dhakhwa et al studied 96 cases of endometrial biopsies, only three (3.1%) cases showed histopathologic evidence of endometrial malignancy while our study showed 5.2% cases with malignany. Majority of patients with AUB had a hormone imbalance pattern on endometrial biopsy (41.7%). Our study showed 37 cases with hormonal imbalance i.e. 14.6% of total studied biopsies (n=252). In study by dhakhawa et al, Five (5.2%) cases showed features of endometritis. In four (4.1%) cases AUB was due to endometrial polyp.[19] and Menorrhagia, in 35 (36.4%) cases, was the most common presenting symptom. [19]

We also observed in our study, that the common age of AUB was noted in the 40-45years age group (29%) followed by less than 40 years age group (27%). In our study the commonest histological pattern in perimenopausal women was hormonal imbalance pattern (17.2%).[19] Most of the studies done by various authors showed that menorrhagia is the most common presenting complaint.[2, 11, 12, 14, 15, 19,20,29,30]

Abid, et al. reported a lower incidence of endometritis (9.1%) in perimenopausal age group than in reproductive age group (18%) which they attributed to the fact that the women in reproductive age group had a greater chance of exposure to caesarean sections, spontaneous and therapeutic abortion and intrauterine contraceptive device etc. hence prone to develop chronic endometritis.[23] In our study, 1.58% had endometritis.

Perveen, et al. found chronic endometritis in a larger number of cases (37%).25 This variation may be due to socioeconomic status, hygienic conditions or exposure to surgical intervention.[24]

Azim, et al. demonstrated an increasing frequency of polyp with advancing age.[25] In our study, 10% cases had endometrial polyp.

According to age distribution in a study by Jain et al maximum number of cases between age group of 40 to 44 was 48%, and 38% of cases between age group of 45-49 years, suggesting abnormal uterine bleeding in perimenopausal women is common.[29]

In a study conducted by Chapagain in a tertiary hospital in Nepal, majority of cases of AUB seen in perimenopausal age group was between 40-44 years (45.5%). In the study conducted by Chapagain, menorrhagia was the commonest presenting complaint (40.3%) followed by menometrorrhagia. [20]

6. Conclusion

As women approach menopause, cycles shorten and become intermittently anovulatory due to the decline in the level of ovarian follicles and estradiol level.[21,22]

Abnormal uterine bleeding is a commonly encountered problem in gynecological practice. It accounts for 70% of gynecological pathology. Prevalence of AUB among reproductive aged women is 3%-30%. At least one third of women are affected at some time in their life. [2,5]

AUB is persistent and either unexplained or inadequately treated, endometrial sampling is necessary- if possible- in association with hysteroscopic evaluation of the uterine cavity.[10]

Evaluation of AUB in perimenopausal age is an important step since excessive or continuous bleeding may severely compromise the quality of woman's life and daily activities leading to anemia if left untreated.[11] Endometrial sampling is mandatory in the evaluation of anovulatory bleeding in women older than 45 years or in younger women who are obese, those with a history of prolonged anovulation, or in those who do not respond to medical therapy.[28]

Majority of women presents as menorrhagia with or without pain and/or irregular menses. Most common cause of this condition was hormonal imbalance and endometrial hyperplasia, Thus such cases can be medically managed rather than opting for surgery in in older as well as middle aged group.

In conclusion, the management of perimenopausal and postmenopausal bleeding may be based on hysteroscopy in combination with endometrial biopsy, because it is a reliable tool for precisely evaluating the topography of the uterine cavity and the nature of the endometrium. Early diagnosis by

hysteroscopy followed by endometrial biopsy is the most effective way for postmenopausal women with AUB to rule out malignancy rather than by dilation and curettage.

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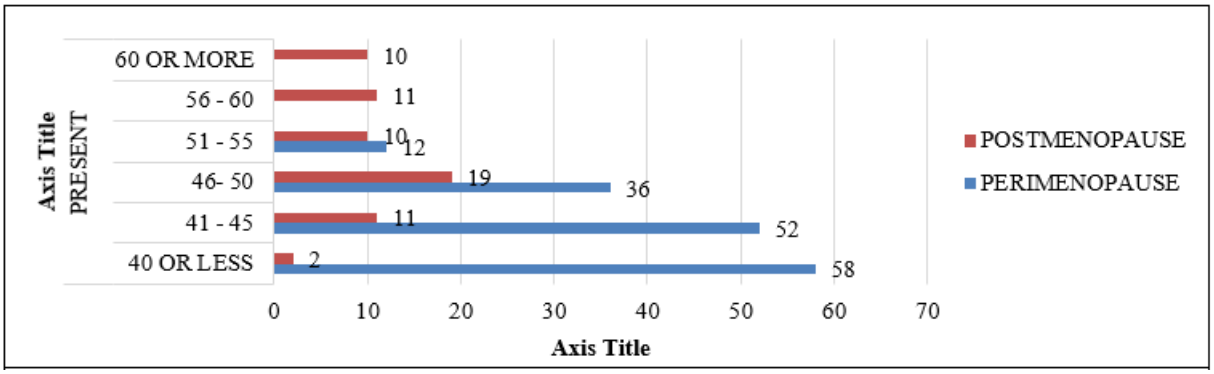


Figure 1: Distribution Of Perimenopausal & Postmenopausal Bleeding in Different Age Groups

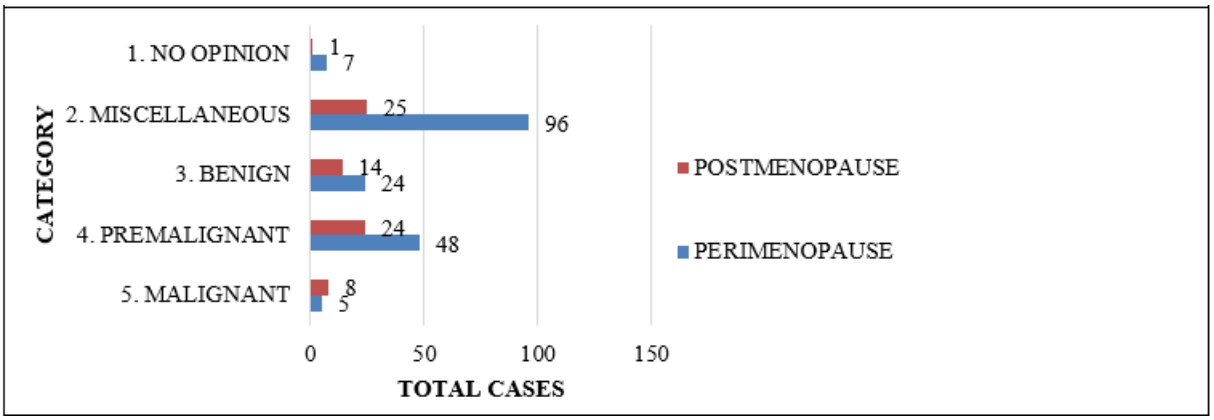


Figure 2: Category Wise Distribution in Perimenopausal & Postmenopausal Women

Table 1: Distribution of Cases According to Menstrual Status

Category	Perimeno Pause	Postmeno Pause	Total
Malignant	2.78%	11.11%	5.16%
Premalignant	26.67%	33.33%	28.57%
Benign	13.33%	19.44%	15.08%
Miscellaneous	53.33%	34.72%	48.02%
No Opinion	3.89%	1.39%	3.17%

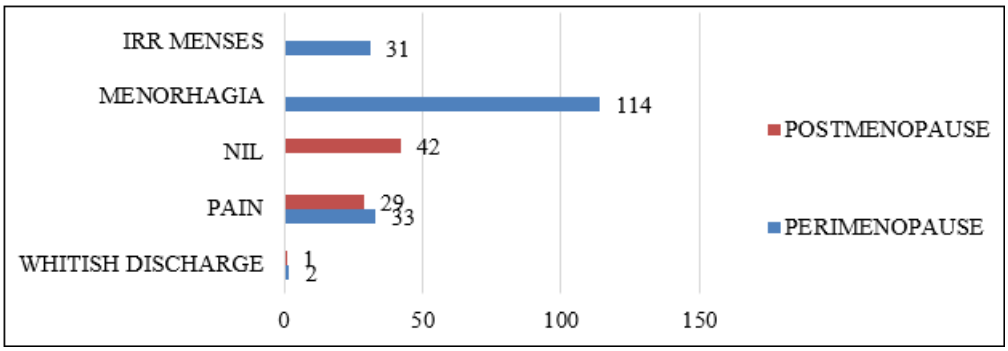


Figure 3: No. of Cases by Complaints

Table 2: Age Wise Distribution of Cases in Different Categories

Diagnosis	No Opinion	Miscelaneous	Benign	Premalignant	Malignant	Grand Total
40 OR LESS	0.8%	20.6%	5.6%	3.6%	0.8%	31.3%
41 - 45	1.2%	11.9%	2.0%	12.3%	0.4%	27.8%
46- 50	0.8%	10.3%	1.6%	9.9%	0.8%	23.4%
51 - 55	0.4%	3.2%	2.4%	2.0%	1.2%	9.1%
56 - 60	0.0%	1.6%	0.8%	0.8%	1.2%	4.4%
60 OR MORE	0.0%	0.4%	2.4%	0.4%	0.8%	4.0%
Grand Total	3.2%	48.0%	14.7%	29.0%	5.2%	100.0%

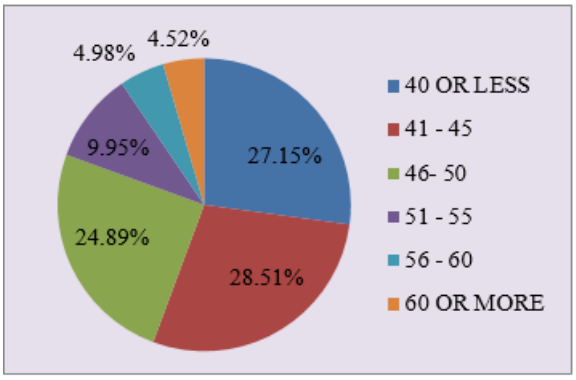


Figure 6: Age Group Wise Distribution of Cases with Bleeding

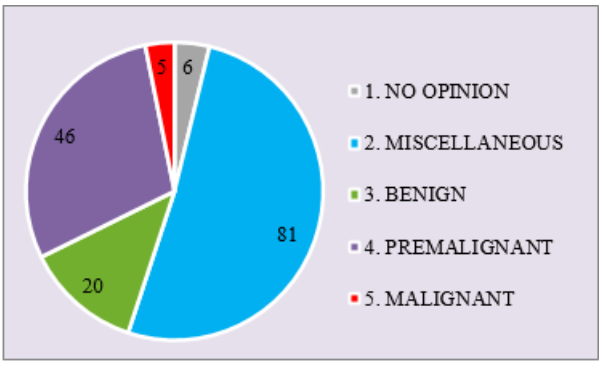


Figure 7: Category Wise Distribution in Cases of Perimenopausal Bleeding

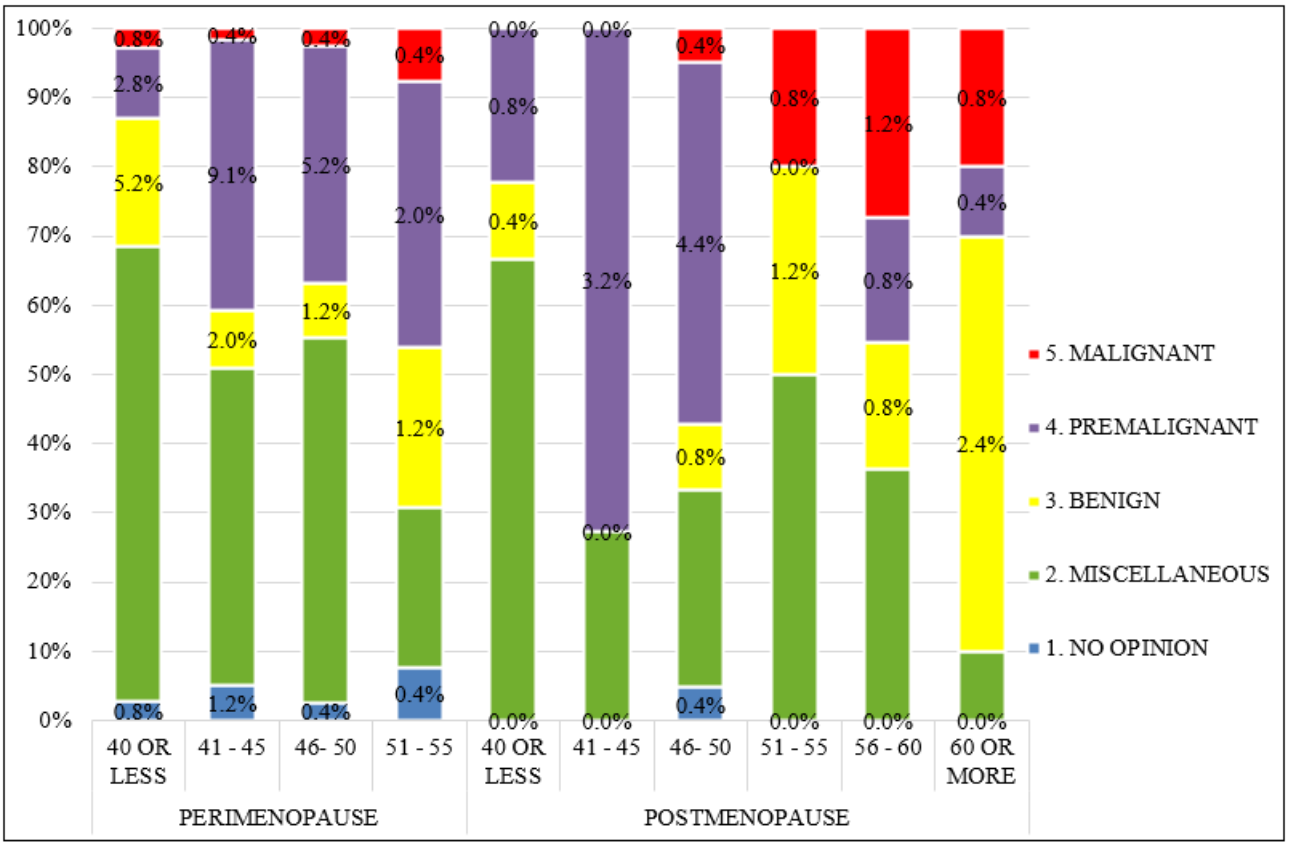
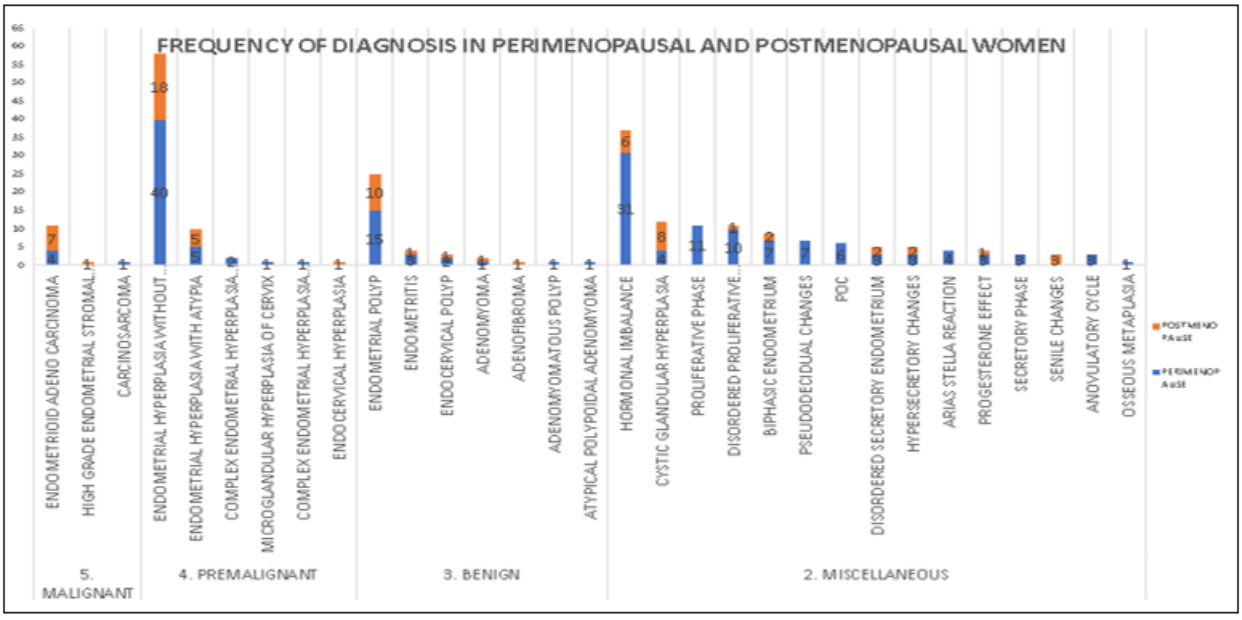


Figure 4: Agewise Distribution of Categories



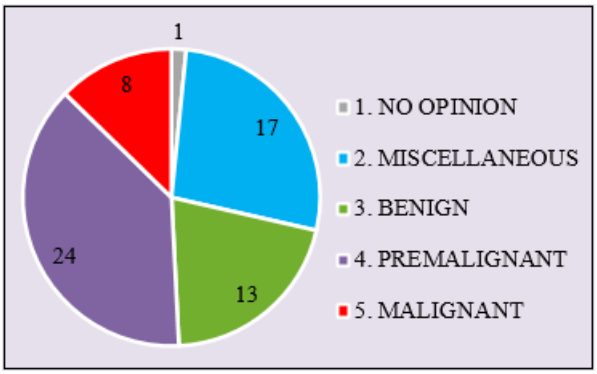


Figure 8: Category Wise Distribution in Cases of Postmenopausal Bleeding

Table 3 (a): Histopathological Spectrum Wise Distribution of Cases

MISCELLANEOUS	**121**	**100.00%**	Benign	38	100.00%
Anovulatory Cycle	3	2.48%	Adenofibroma	1	2.63%
Arias Stella Reaction	4	3.31%	Adenomyoma	2	5.26%
Biphasic Endometrium	9	7.44%	Adenomyomatous POLYP	1	2.63%
Cystic Glandular Hyperplasia	12	9.92%	Atypical Polypoidal Adenomyoma	1	2.63%
Disordered Proliferative Endometrium	11	9.09%	Endocervical POLYP	3	7.89%
Disordered Secretory Endometrium	5	4.13%	Endometrial POLYP	25	65.79%
Hormonal Imbalance	37	30.58%	Endometritis	4	10.53%
Hypersecretory Changes	5	4.13%	Microglandular Hyperplasia Of Cervix	1	2.63%
Osseous Metaplasia	1	0.83%	Total	38	100.00%
POC	6	4.96%	Premalignant	72	100.00%
Progesterone Effect	4	3.31%	Complex Endometrial Hyperplasia With Atypia	1	1.39%
Proliferative Phase	11	9.09%	Complex Endometrial Hyperplasia Without Atypia	2	2.78%
Pseudodecidual Changes	7	5.79%	Endocervical Hyperplasia	1	1.39%
Secretory Phase	3	2.48%	Endometrial Hyperplasia With Atypia	10	13.89%
Senile Changes	3	2.48%	Endometrial Hyperplasia Without Atypia	58	80.56%
Total	**121**	**100.00%**	Total	72	100.00%

Table 3b: Histopathological Spectrum Wise Distribution of Cases

Malignant	**13**	**100.00%**
Carcinosarcoma	1	7.69%
Endometrioid Adeno Carcinoma	11	84.62%
High Grade Endometrial Stromal Sarcoma	1	7.69%
Total	**13**	**100.00%**

Table 4: Age Distribution of Cases with Bleeding

Category	Peri Menopause	Post Menopause	Total
Age Group			
	158	**63**	**221**
40 OR LESS	58	2	60
41 - 45	52	11	63
46- 50	36	19	55
51 - 55	12	10	22
56 - 60		11	11
60 OR MORE		10	10
Total	**158**	**63**	**221**

Table 5e: Distribution of Cases – Irregular Menses

1. NO OPINION	**3.2%**	**1**
NO OPINION	3.2%	1
2. MISCELLANEOUS	**67.7%**	**21**
HORMONAL IMBALANCE	41.9%	13
BIPHASIC ENDOMETRIUM	6.5%	2
PROLIFERATIVE PHASE	6.5%	2
PROGESTERONE EFFECT	3.2%	1
PSEUDODECIDUAL CHANGES	3.2%	1
ARIAS STELLA REACTION	3.2%	1
HYPERSECRETORY CHANGES	3.2%	1
3. BENIGN	**12.9%**	**4**
ENDOMETRIAL POLYP	9.7%	3
ENDOMETRITIS	3.2%	1
4. PREMALIGNANT	**12.9%**	**4**
ENDOMETRIAL HYPERPLASIA WITHOUT ATYPIA	12.9%	4
5. MALIGNANT	**3.2%**	**1**
ENDOMETRIOID ADENO CARCINOMA	3.2%	1
Grand Total	**100.0%**	**31**

DIAGNOSIS WISE DISTRIBUTION IN CASES OF POSTMENOPAUSAL BLEEDING	PERCENTAGE	NO OF CASES
1. NO OPINION	1.6%	1
NO OPINION	1.6%	1
2. MISCELLANEOUS	27.0%	17
CYSTIC GLANDULAR HYPERPLASIA	9.5%	6
SENILE CHANGES	4.8%	3
HORMONAL IMBALANCE	4.8%	3
BIPHASIC ENDOMETRIUM	3.2%	2
PROGESTERONE EFFECT	1.6%	1
DISORDERED SECRETORY ENDOMETRIUM	1.6%	1
HYPERSECRETORY CHANGES	1.6%	1
3. BENIGN	20.6%	13
ENDOMETRIAL POLYP	14.3%	9
ADENOFIBROMA	1.6%	1
ENDOMETRITIS	1.6%	1
ADENOMYOMA	1.6%	1
ENDOCERVICAL POLYP	1.6%	1
4. PREMALIGNANT	38.1%	24
ENDOMETRIAL HYPERPLASIA WITHOUT ATYPIA	28.6%	18
ENDOMETRIAL HYPERPLASIA WITH ATYPIA	7.9%	5
ENDOCERVICAL HYPERPLASIA	1.6%	1
5. MALIGNANT	12.7%	8
ENDOMETRIOID ADENO CARCINOMA	11.1%	7
HIGH GRADE ENDOMETRIAL STROMAL SARCOMA	1.6%	1
Grand Total	100.0%	63

DIAGNOSIS WISE DISTRIBUTION IN CASES OF PERIMENOPAUSAL BLEEDING	PERCENTAGE	NO OF CASES
1. NO OPINION	3.8%	6
NO OPINION	3.8%	6
2. MISCELLANEOUS	51.3%	81
HORMONAL IMBALANCE	18.4%	29
DISORDERED PROLIFERATIVE ENDOMETRIUM	5.7%	9
BIPHASIC ENDOMETRIUM	4.4%	7
PSEUDODECIDUAL CHANGES	4.4%	7
PROLIFERATIVE PHASE	3.2%	5
POC	3.2%	5
CYSTIC GLANDULAR HYPERPLASIA	2.5%	4
PROGESTERONE EFFECT	1.9%	3
HYPERSECRETORY CHANGES	1.9%	3
DISORDERED SECRETORY ENDOMETRIUM	1.9%	3
ARIAS STELLA REACTION	1.9%	3
SECRETORY PHASE	1.3%	2
ANOVULATORY CYCLE	0.6%	1
3. BENIGN	12.0%	19
ENDOMETRIAL POLYP	7.6%	12
ENDOMETRITIS	1.3%	2
ENDOCERVICAL POLYP	1.3%	2
ADENOMYOMATOUS POLYP	0.6%	1
ADENOMYOMA	0.6%	1
ATYPICAL POLYPOIDAL ADENOMYOMA	0.6%	1
4. PREMALIGNANT	29.7%	47
ENDOMETRIAL HYPERPLASIA WITHOUT ATYPIA	24.1%	38
ENDOMETRIAL HYPERPLASIA WITH ATYPIA	3.2%	5
COMPLEX ENDOMETRIAL HYPERPLASIA WITHOUT ATYPIA	1.3%	2
MICROGLANDULAR HYPERPLASIA OF CERVIX	0.6%	1
COMPLEX ENDOMETRIAL HYPERPLASIA WITH ATYPIA	0.6%	1
5. MALIGNANT	3.2%	5
ENDOMETRIOID ADENO CARCINOMA	2.5%	4
CARCINOSARCOMA	0.6%	1
Grand Total	100.0%	158

Table 5c: Distribution of Cases with Complaint of Menorrhagia

1. NO OPINION	**4.4%**	**5**	**3. Benign**	**11.4%**	**13**
No Opinion	4.4%	5	Endometrial Polyp	6.1%	7
2. Miscellaneous	**46.5%**	**53**	Endocervical Polyp	1.8%	2
Hormonal Imbalance	9.6%	11	Microglandular Hyperplasia of Cervix	0.9%	1
Disordered Proliferative Endometrium	7.9%	9	Endometritis	0.9%	1
Pseudodecidual Changes	5.3%	6	Adenomyoma	0.9%	1
POC	4.4%	5	Atypical Polypoidal Adenomyoma	0.9%	1
Biphasic Endometrium	3.5%	4	**4. Premalignant**	**34.2%**	**39**
Cystic Glandular Hyperplasia	3.5%	4	Endometrial Hyperplasia Without Atypia	28.1%	32
Proliferative Phase	2.6%	3	Endometrial Hyperplasia with Atypia	3.5%	4
Disordered Secretory Endometrium	2.6%	3	Complex Endometrial Hyperplasia without Atypia	1.8%	2
Secretory Phase	1.8%	2	Complex Endometrial Hyperplasia with Atypia	0.9%	1
Progesterone Effect	1.8%	2	**5. Malignant**	**3.5%**	**4**
Arias Stella Reaction	1.8%	2	Endometrioid Adeno Carcinoma	2.6%	3
Hypersecretory Changes	0.9%	1	Carcinosarcoma	0.9%	1
Anovulatory Cycle	0.9%	1	**Grand Total**	**100.0%**	**114**