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Research Paper

Clinicopathological Assessment of Postmenopausal Bleeding in a Sample of Iraqi Patients

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ABSTRACT:

BACKGROUND:

Bleeding that occurs 12 months or more following the last menstrual period is known as postmenopausal bleeding.

OBJECTIVE:

Is to assess the frequency and pattern of uterine lesions in women with post-menopausal bleeding and to correlate the histopathological changes with clinical variable i.e. the age, associated illness, parity and ultrasonography finding.

MATERIALS AND METHODS:

A retrospective study, which include analysis of 110 cases of women presented with post-menopausal bleeding, the samples were collected from the Teaching Laboratories of Al-Imamain Al-Kadhumain, and Baghdad Medical City from January 2020 to June 2021. For each case the histopathological reports, slides and Paraffin block (if needed) were collected, in addition the clinical parameters such as age, parity, history of previous Dilatation &Curettage, diabetes mellitus and/or hypertension, and ultrasound findings such as (endometrial thickness, uterine size) were also obtained.

RESULTS:

The age range of 110 cases was (45-90 years) with a mean age of 58 years ± 6.6 years. Hypertension was the most common associated illness as it was present in (42.7%) cases. Diabetes mellitus was present in (33.6%) patients. The parity distribution was (4.5%) cases recognized as nulliparous, and (95.4%) were multiparous. The endometrial thickness obtained from ultrasonography ranged from (3-25) mm and distributed as following: ٢٢ (٢٠%) cases were equal to or less than 4 mm, and (80%) were more than 4mm.The most common histopathological diagnosis was endometrial hyperplasia with frequency of (28.5%) of cases and (10.9%) cases were diagnosed as carcinoma.

CONCLUSION:

The most common etiology for postmenopausal bleeding was endometrial hyperplasia. While, the lowest one was chronic endometritis. There is significant correlation between the clinical parameters with endometrial hyperplasia and malignancy.

KEYWORDS: postmenopausal bleeding; retrospective, endometrial carcinoma; endometrial hyperplasia, histopathology

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INTRODUCTION:

Menopause is defined as the end of ovulation and menstrual periods, naturally occurs for most women at the age of 40–55 years[(1)]. Postmenopausal bleeding (PMB) is bleeding that occurs 12 or more months after the last menstrual period and are responsible for 5% of all gynecologic office visits [(2)]. Approximately one in 10 women will experience some bleeding after the menopause.[(3)] Postmenopausal bleeding should always be taken seriously and be investigated, no matter how minimal or non-persistent.

Causes may be nongenital, genital (extrauterine or uterine). The Possible uterine conditions associated with PMB include endometrial atrophy, estrogen therapy, polyps, foreign bodies, trauma, infection, endometrial hyperplasia, and carcinoma.[(4)] The most common presenting symptom of endometrial cancer is postmenopausal bleeding. The primary concern in the evaluation of patients with abnormal uterine bleeding is to rule out endometrial hyperplasia and cancer[(5)].

In patients with atypical uterine bleeding, transvaginal ultrasonography evaluation of endometrial thickness has become a standard procedure and a first line of investigation. Outpatient endometrial biopsy, as well as dilatation and curettage (D&C), is considered to be the gold standard for obtaining endometrial samples[6]. Hypertension (HTN), diabetes mellitus (DM), obesity, polycystic ovarian disease, tamoxifen therapy, and colon or breast cancer are risk factors in addition to age[7]. The risk of developing endometrial cancer increases with age, so endometrial carcinoma is most common in the postmenopausal age group and is most prevalent in women over 50 years of age, Thus, the American College of Obstetricians and Gynecologists recommends endometrial evaluation in women with abnormal uterine bleeding and aged 35 years and older[8].

PATIENTS AND METHOD:

Study design

A retrospective study was intended which include analysis of 110 cases of women presented with post-menopausal bleeding. The type of specimens obtained include 59 cases were hysterectomy specimen and 51 cases were D& C specimen, for each case the histopathological reports ,slides and Paraffin block (if needed) were collected from the Teaching Laboratory of Al-Imamain Al-Kadhumain, and Baghdad Medical City, from January 2020 to June2012 and reexamined ,and retrospectively reviewed. In addition the clinical parameters such as age, parity, history of previous D&C, concomitant medical condition such as diabetes and/or hypertension, and ultrasound findings such as (endometrial thickness, uterine size) were gathere. The data were statistically analyzed and the association relationships were investigated using CHI square test at a significance level of 0.05.

RESULTS:

Age distribution:

The age of sampled cases ranged from (45-90) years with mean value of (58) year ± (6.6 years). The median of the sample was also 58 year which in other words implies that the distribution of the age is almost normal .The commonest age group among women presented with PMB was in age group (51-55). The distribution of age is shown in Figure 1.

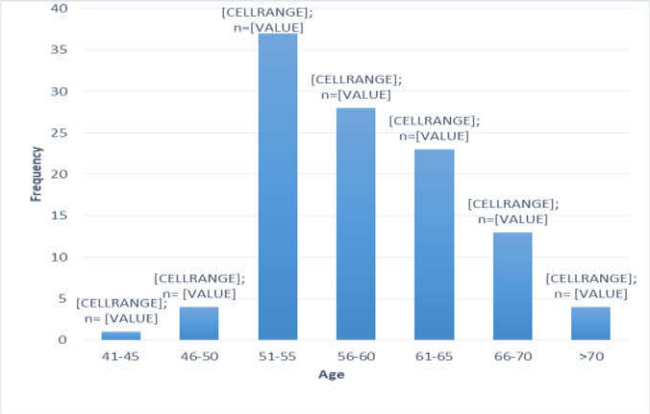

Figure 1: Age distribution of the sampled women.

The frequency of associated medical illness in sampled women

Hypertension and diabetes

In this study, 110 cases (Table 1) were collected for the designated objectives; 29(26.36%) of patients were found have history of hypertension, while only 19 (17.2%) cases had diabetes mellitus. The history of both diabetes and hypertension was detected in 18(16.3%) cases. As such, the remaining 44 (40%) cases show negative history for hypertension and diabetes.

Table 1: Frequency of associated medical illness.

Associated medical illness	Frequency	Percentage
Diabetes and hypertension		
Diabetes	19	17.27%
Hypertension	29	26.36%
Both	18	16.36%
Negative	44	40%
Total		110

Parity distribution

The parity distribution of women with PMB was depicted as shown in Figure 2. It is evident from the figure that the parity distribution ranged from (0 – 14). Where only 5 (4.5%) cases recognized as nulliparous, and 105 (95.4%) were multiparous.

The frequency of Ultrasonographic findings of the cases with PMB

Endometrial thickness and Uterine size

Figure 3 illustrates the ultrasonographics findings of the collected data .In this study the endometrial thickness obtained from ultrasonography ranged from (3-25) mm and distributed as following: 22 (20%) cases were equal to or less than 4 mm, and (80%) were more than 4mm. Most cases in this study had a normal size uterus 67 (60.9%) cases.

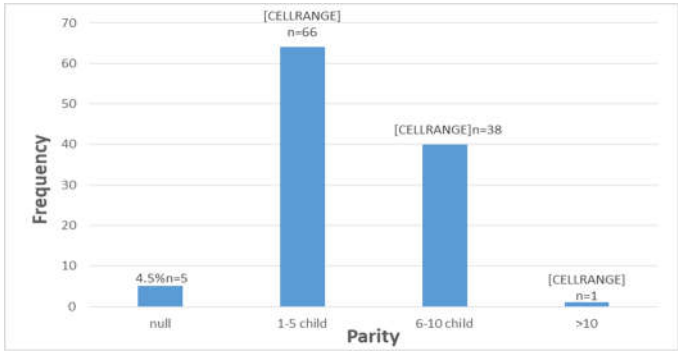

Figure 2: Parity distribution of women with postmenopausal bleeding.

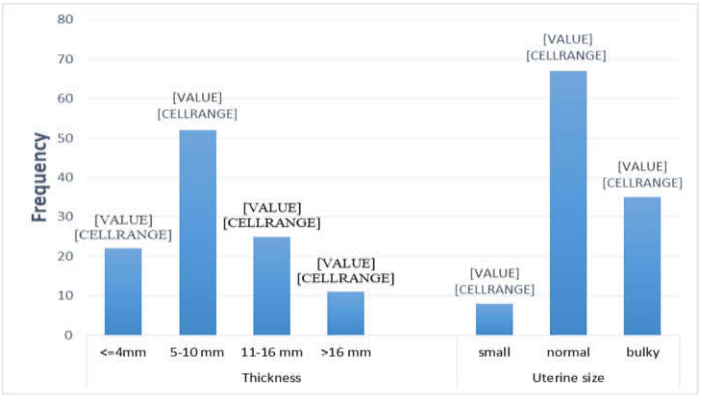

Figure 3: Frequency of ultrasonographic finding in women with postmenopausal bleeding.

The frequency of Histopathological findings of the cases with PMB

Table 2 lists the frequency distribution and the percentages of the histopathological findings of the PMB women. The most common diagnosis was endometrial hyperplasia with frequency of 34 (28.5%) of cases. It was found that endometrial hyperplasia with atypia (figure4) and without atypia constitute (35.29%) and (64.71%) respectively out of the total number of patient with hyperplasia (34 cases). The endometrial atrophy was diagnosed in 21 (17.6%) and 20 (16.8%) cases were diagnosed as polyp .It was found that 13 (10.9%) cases were diagnosed as carcinoma, type of malignant cases obtain from this study was as follow (type I (endometeriod adenocarcinoma) was the commonest type and represent 10 (76.92%) from the entire cases, While 2(15.38%) and 1(7.69%) cases represented cervical squamous cell carcinoma and endometrial serous carcinoma type II (figure 5) respectively) .Nine (7.56%) cases were inadequate tissue. The leiomyoma was diagnosed in 8 (6.7%). Weak Proliferative endometrium was found in almost 8 (6.7%) of cases, and 5 (4.2%) cases show more than one pathology, as having 2 or 3 lesions as (polyp, leiomyoma and adenomyosis), the less common finding was chronic endometritis only one (0.8%) case.

The Relationship of endometrial hyperplasia and malignancy with medical parameters

Table 3 below shows the association of endometrial hyperplasia and malignancy with medical parameters (age, parity, medical illness, and endometrial thickness). It can be seen that 19 (55.8%) cases of endometrial hyperplasia out of 34 were in age group between (51-60) years old and 13 (38.2%) cases were above 60 years old .Malignancy was identified in 11(84.6%) cases out of 13 in age above 55 years old and 2 (15.4%) cases were in age group (51-55). In other side It can be raised that 17(50%) cases of endometrial hyperplasia and 10 cases of malignant condition have 1-5 child and only 2(5.9%) of cases of endometrial hyperplasia and 2 (15%) cases of malignancy were nulliparous, It is also observable that there are 24 cases of hyperplasia had positive medical illness of which 11(32.4%) cases had HTN, 7 (20.6%) cases had DM, 6 (17.6%) cases had both. The analysis shown also that there are seven cases of malignancy had positive history for chronic illness, among these seven cases there were only 3(23.1%) cases had HTN, 2(15.4%) cases had DM, 2 (15.4%) cases had both. Regarding the endometrial thickness it was found that 2(5.9%) cases of endometrial hyperplasia have endometrial thickness less than or equal to 4 mm , 19(55%)of cases were have thickness rang 5-10mm, and 10 (29%) cases have thickness rang 10-16mm. while most malignant cases 8 (61%) have thickness rang 10-16 mm. The association of endometrial hyperplasia and malignancy with age, parity ,medical illness and thickness was significant in p values (0.02,0.023,0.033,0,04) respectively.

Table 2: Frequency of histopathological finding of the cases with PMB.

Histopathological finding	Frequency	Percentage
Endometrial hyperplasia	34	28.57%
Endometrial atrophy	21	17.65%
polyp	20	16.81%
Malignancy	13	10.92%
Inadequate	9	7.56%
leiomyoma	8	6.72%
Weak Proliferative endometrium	8	6.72%
multiple pathology	5	4.20%
Chronic endometritis	1	0.84%
Total	119	100.00%

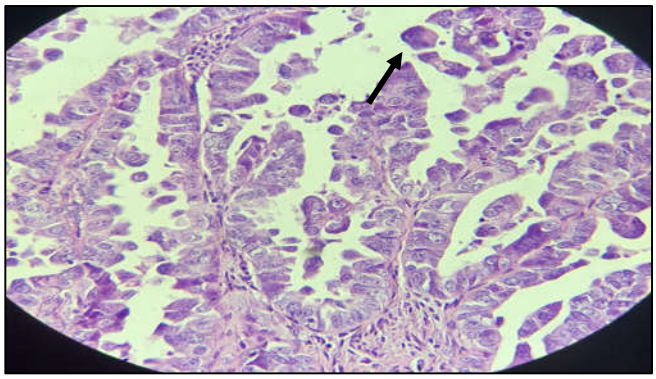

Figure 4: Section from endometrium show increase gland to stroma ratio and abnormal architectural pattern of the glands with cytological atypia (enlarged, round irregular, pleomorphic nuclei and prominent nucleoli (arrow)).(H&E) (40X).

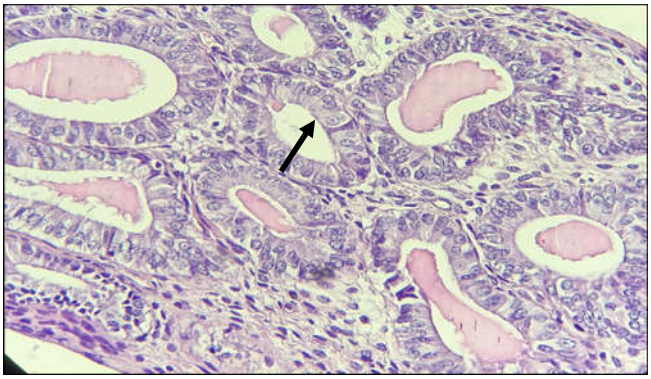

Figure 5: Endometrial serous carcinoma showing papillary architectural growth pattern and high grade nuclear atypia (striking pleomorphism, enlargement, and marked prominent nucleoli) and bizarre nuclear feature (arrow). (H&E) (40x).

Table 3:Relationship between medical parameters with endometrial hyperplasia and malignancy.

			Endometrial hyperplasia	Malignancy	
		Frequency	%	Frequency	%
Age (years)	41-45 (n=1)	0	0	0	0
	46-50 (n=4)	2	5.9%	0	0
	51-55 (n=37)	13	38.2%	2	15.4%
	56-60 (n=28)	6	17.6%	3	23.1%
	61-65 (n=23)	9	26.5%	4	30.8%
	66-70 (n=13)	3	8.8%	2	15.4%
	>70 (n=4)	1	2.9%	2	15.4%
	Total	34	100%	13	100%
p value 0.02					
Parity	Null (n=5)	2	5.9%	2	15.4%
	1-5 child (n=66)	17	50%	10	76.9%
	6-10 child (n=38)	14	41.2%	1	7.7%
	> 10 child (n=1)	1	29%	0	0
	Total	34	100%	13	100%
	P value 0.023				
medical illness	HT (n=29)	11	32.4%	3	23.1%
	DM (n=19	7	20.6%	2	15.4%
	Both (n=18)	6	17.6%	2	15.4%
	Negative (n=44)	10	29.4%	6	46.2%
	Total	34	100%	13	100%
	P value 0.033				
Thickness	=<4 mm (n=22)	2	5.9%	0	0
	5-10 mm (n=52)	19	55.9%	1	7.7%
	11-16 mm (n=25)	10	29.4%	8	61.5%
	>16 mm (n=11)	3	8.8%	4	30.8%
	total	34	100%	13	100%
	p value 0.04				

DISCUSSION:

Patients in this study ranged in age from (45-90 years) with a mean age of 58 years. The maximum number of cases were in the age group 51-55 years (33.6%) followed by the age group 56-60 years (25.4%). This is in concordance with another Iraqi study conducted in Kufa by Al-Turiahi et al (2016) who obtained exactly the same mean age of patients (58 years) with the maximum number of patients in the age group (50-59 years) [9]. It is well established that although the incidence of PMB declines with succeeding years after menopause,[10] the incidence of endometrial carcinoma increases as the age of the patient with PMB increases.[11]

This is in concordance with the present study in which although most (63.5%) of the studied sample were below 60 years of age, the majority {8 (72.7%) patients} of endometrial malignancy cases were ≥60 years old.

Hypertension was the most common associated illness as it was present in 47 (42.7%) patients either as a single chronic disease in 29 (26.36%) or associated with diabetes in 18 (16.36%).

This is comparable to the results by Al-Turiahi et al. in Kufa in which hypertension was found in (52.9%) and higher than Singh V et al.(2017), and Kothapally K et al(2013). in India in which hypertension was found in 32%, and 36.6% respectively.[9, 12, 13]

DM was present in 37 (33.6%) patients either as a single morbidity in 19 (17.27%) or associated with hypertension in 18 (16.36%). This is comparable to the results by Al-Tuhiari et al. in Kufa in which DM was found in (29.2%) of the studied sample but much higher than Singh V et al (2017). and Kothapally K et al (2013). in India in which DM was found in (5%) and (13.3%) respectively.[9,12, 13]

Nullparity was only recognized in 5 (4.5%) cases in our study since it is uncommon in our society. Similar small percentages of nulliparity were also found in other Iraqi studies in Babylon (Shatha Zakar 2005), and Mosul (Al-Neaimy et al 2010.). [14,15]. In the present study, most histopathological findings were identified in the category of women with (1-5 children). This contradicts the research by Shatha Zakar, which revealed that more than 50% of endometrial changes were found in women who had 6-10 children including endometrial hyperplasia and adenocarcinoma.[14] However, it is in concordance with Jillani et al (2010). Who found a strong correlation of endometrial carcinoma with nulliparity and low parity.[16]

In the present study, an endometrial pathology was correlated with endometrial thickness in 88 (80%) cases. Among 11 patients with endometrial carcinoma, 10 (90.9%) had endometrial thickness of more than 10mm. Moreover, only 2 (5.7%) cases of endometrial hyperplasia had normal endometrial thickness; as the majority had thickened endometrium as follows: 19 (55.9%) had a thickness of (5-10 mm), 10 (29.4%) had a thickness of (11-16 mm) and 3 (8.8%) had an endometrial thickness of >16mm. The result of this study is in concordance with the studies by Kothapally K et al (2013), and Jillani et al (2010). Who observed that women with an endometrial thickness >4 mm are at risk of endometrial carcinoma.[13,16]

Endometrial hyperplasia was the most common histopathological finding (28.57%) followed by endometrial atrophy (17.65%). Similar studies in Iraq by Al-Turiahi et al (2016). And Shatha Zakar(2005). Also found endometrial hyperplasia to be the most common. Out of 13 (10.92%) cases of malignancy in our study, endometrial adenocarcinoma was detected in 10 cases and endometrial serous carcinoma type II was detected in only one case. Cervical squamous cell carcinoma was detected in only 2 (1.6%) cases. This is in agreement with studies from other conservative societies such as Bani-Irshaid et al (2011) in Jordan (0.6%);[17] however, these data must be evaluated in the context of our country's lack of a cervical screening program, as good screening programs reduce the risk of cervical cancer. Polyps were found in 20 (16.81%) cases. Endometrial polyp cancer prevalence has been reported to range from 0.5–3%.[18,19] Risk factors for malignancy within uterine polyps include abnormal uterine bleeding, increasing age, postmenopausal status, obesity, diabetes an increased polyp size and tamoxifen[20]. A systematic review found that 4.2% of women with symptomatic bleeding had endometrial hyperplasia or cancer within polyps, compared to 2.2% of women without bleeding[21].

CONCLUSION:

The most common etiology for postmenopausal bleeding in this study was endometrial hyperplasia ,and the lowest one was chronic endometritis, malignant cases in women presented with PMB was constitute 10.9%, the commonest type of cancer was endometrioid adenocarcinoma. There is an increasing risk of endometrial hyperplasia and malignancy in associated with medical illness i.e. DM and HTN and the suspicion of hyperplasia and malignancy increase if endometrial thickness more than 4 mm. The incidence of endometrial carcinoma increases as the age of the patient with PMB increases so any women with post-menopausal bleeding need thorough evaluation to exclude premalignant and malignant conditions

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