Postmenopausal bleeding

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Abstract

1.Preface: Menopause is defined retrospectively as the time of the final menstrual period followed by 12 months of amenorrhea. Post menopause describes the period following the final menses. Abnormal postmenopausal bleeding should always be taken seriously and be properly investigated, no matter how minimal or no persistent.

2. The Purpose: The purpose of our study is to determine what are the causes of postmenopausal vaginal bleeding and the percentage of endometrial cancer among other causes, diagnosis and treatment of these patient in our university hospital.

3. Methods: This is a retrospective study of clinical gynecological charts of 200 patients with diagnosis of postmenopausal bleeding from 1 January 2018- 31 December 2018 in the university «Queen Geraldine».

4. Statistical Analysis: We used IBM SPSS Statistics 25 test, Anova test, Spearman 'rho and Independent Samples test for processing these data.

5.Results The causes of postmenopausal bleeding we found: 55(27.5 %) of them had Hypertrophy, 20(10%) had Atrophy;38(18.5%) had Polips;20(10%) polipoid Fragments;65(33%) had endometrial cancer;1(0.5%) had cervical cancer,1(0.5%) atipic squamous cells. Age, menopausal age, years in menopause, endometrial thickness, HTA have a significant correlation with endometrial cancer. So we can say that these factors increase the likelihood of developing of endometrial cancer. I n our study we found no significant correlation between diabetes, obesity and endometrial cancer.

6. Discussion: Endometrial cancer takes the first place in our study because the gynecologist in the cities treat all benign cases and recommend to our university hospital all difficult cases like endometrial cancer.

7.Conclussions: Endometrial cancer is the most common cause of postmenopausal bleeding with 33 %.

8. Recommendation: We recommend a large prospective study to verify the percentage of endometrial cancer in Albania and to look for other factors that can contribute in the development of endometrial cancer.

***Key words**: endometrial cancer, postmenopausal bleeding, menopause.*

Preface

Menopause, the permanent cessation of menstruation caused by ovarian failure, occurs at an average age of 52 years, with a range of 40 to 58 years. Menopause is defined retrospectively as the time of the final menstrual period followed by 12 months of amenorrhea. Post menopause describes the period following the final menses. Despite a great increase in the life expectancy of women, the age at menopause has remained remarkably constant. A woman in the developed world will live approximately 30 years, or greater than a third of her life, beyond menopause. Therefore, it is important to ensure these years are as healthy and productive as possible. The age at menopause appears to be genetically determined and is unaffected by race/ethnicity or age at menarche. Early menopause describes menopause occurring between the ages of 40 and 45 years and occurs in approximately 5% of women. Premature menopause describes permanent loss of ovarian function before the age of 40, such as following bilateral oophorectomy. Primary ovarian insufficiency (POI) describes loss of ovarian function before the age of 40 years, which may not be permanent. POI occurs in approximately 1% of women. Abnormal perimenopausal and postmenopausal bleeding should always be taken seriously and be properly investigated, no matter how minimal or no persistent. About 90% of women with endometrial carcinoma have vaginal bleeding or discharge as their only presenting symptom. Endometrial carcinoma is the most common malignancy of the female genital tract, accounting for almost one-half of all gynecologic cancers in the United States .Endometrial cancer is a disease that occurs primarily in postmenopausal women and is increasingly virulent with advancing age. The definite role of estrogen in the development of most endometrial cancers is established. Any factor that increases exposure to unopposed estrogen increases the risk for endometrial cancer.

The purpose

The purpose of our study is to determine what are the causes of postmenopausal vaginal bleeding and the percentage of endometrial cancer among other causes,

diagnosis and treatment of these patient in our university hospital. How obesity, hypertension, diabetes, age, menopausal age, years in menopause and endometrial thickness affects the endometrial cancer.

Methods

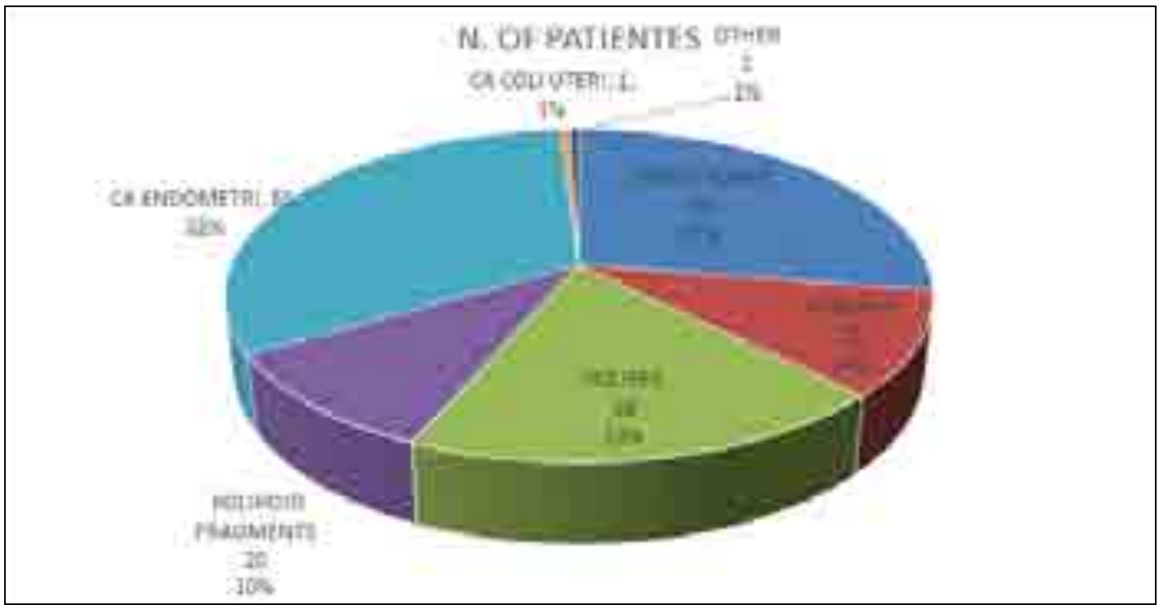
Our study is a retrospective study. Data for our study were collected from clinical gynecological charts in the university «Queen Geraldina».Object of our study were charts of 200 patients with diagnosis of postmenopausal bleeding from 1 January 2018- 31 December 2018. To provide more data we have called patients by telephone.

Statistical analysis

IBM SPSS Statistics 25 test, Anova test, Spearman's Rho and Independent Samples test were for processing these data

The results of the study

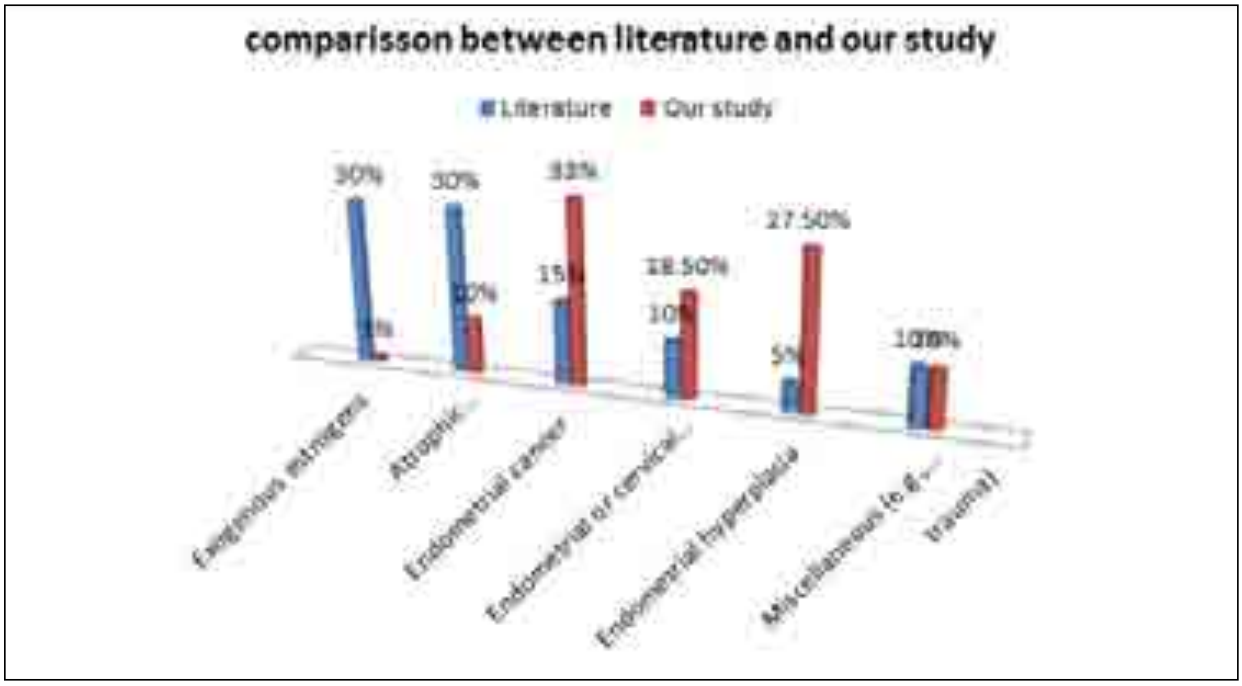
Among 200 clinical gynecological charts of the patients with the diagnosis of postmenopausal bleeding we found these results: 55(27.5 %) of them had Hypertrophy, 20(10%) had Atrophy;38(18.5%) had Polips;20(10%) polipoid Fragments;65(33%) had endometrial cancer;1(0.5%) had cervical cancer,1(0.5%) atipic squamous cells. This distribution of the cases of the postmenopausal bleeding is explained in the graph below.



As we can see from the graphic, endometrial cancer takes the first place with 33 %

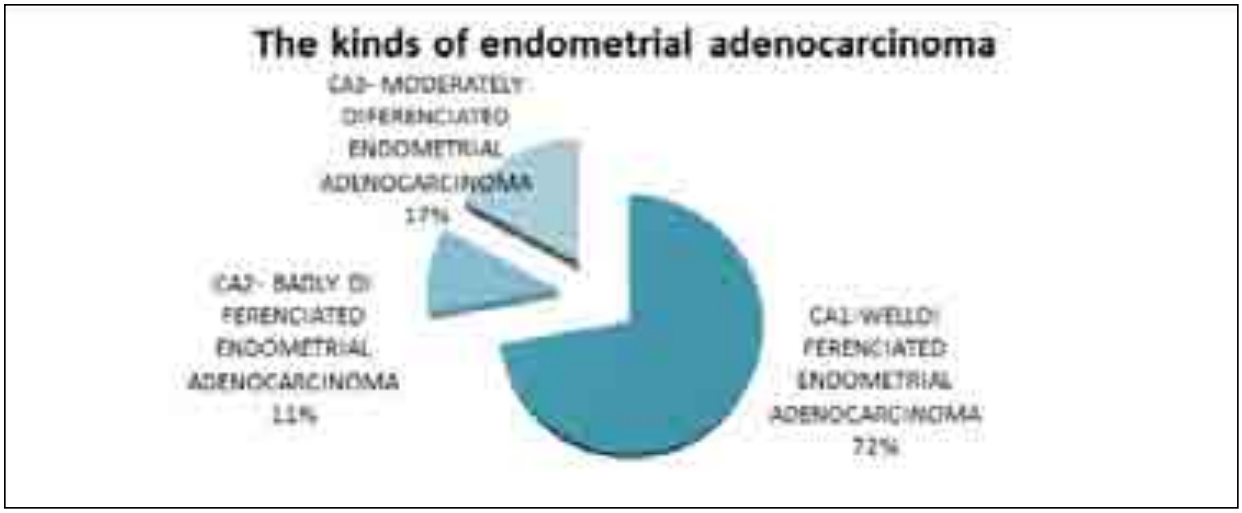
FACTOR	Literature	Our study
Exogenous estrogens	30 %	1 %
Atrophic endometritis/vaginitis	30 %	10 %
Endometrial cancer	15 %	33 %
Endometrial or cervical polyps	10 %	18.5 %
Endometrial hyperplasia	5 %	27.5 %
Miscellaneous (e.g., cervical cancer, uterine sarcoma, urethral caruncle, trauma)	10 %	10 %

Here we are comparing the results of literature studies and our studies. As we can clearly see in the graphic below endometrial cancer takes the first place in our study with 33 % but only 15 % in the studies of literature. The level of endometrial carcinoma in our study is two to three folds greater than in the literature causing a big problem. Exogenous estrogens take about 30 % in the literature but only 1% in our study making a big difference.



The kinds of endometrial adenocarcinoma

THE KINDS OF ENDOMETRIAL ADENOCARCINOMA	NUMBER (%)
CA1-WELL DIFFERENTIATED ENDOMETRIAL ADENOCARCINOMA	47 (72.2%)
CA2- BADLY DIFFERENTIATED ENDOMETRIAL ADENOCARCINOMA	7 (10.8%)
CA3- MODERATELY DIFFERENTIATED ENDOMETRIAL ADENOCARCINOMA	11 (17%)
TOTAL	65 (100%)



We see that well differentiated endometrial adenocarcinoma in our study takes about 72 % of all endometrial carcinomas. These results are nearly the same with the results of the studies in the literature that accounts for about 80 %.

Polips

Polips	Number of patients
Necrotized polip	3
Malign polip	2
Benign polipe	32
Polipoid fragments	20
Atipic polip	1
Total polips	57

As we see, the polyps are generally benign in our study. The same thing happens in the studies of the literature. We found only two malign polyps.

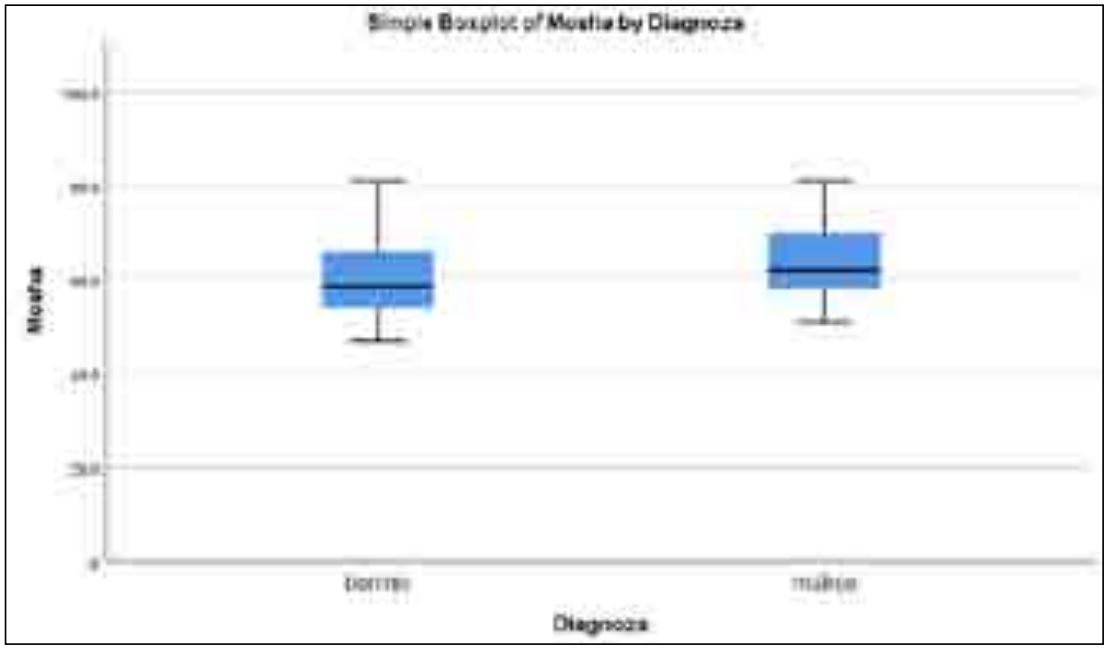
65 Of patients diagnosed with endometrial cancer distributed by age

65 OF PATIENTS DIAGNOSED WITH ENDOMETRIAL CANCER DISTRIBUTED BY AGE	
AGE	NR. OF PATIENTS
<50	1
50-55	6
55-60	17
60-65	13
65-70	14
70-75	5
75-80	7
80-85	3

We are calculating the correlation between diagnosis and age of the patients using Spearman's Rho statistical test. p= 0.032 ≤ 0.05

This p value tells us for a significant correlation between age and diagnosis. This tells us that with the increasing of the age of the patient, the likelihood of developing the endometrial cancer increases too.

Correlations				
			Diagnosis	Age
Spearman's rho	Diagnosis	Correlation Coefficient	1.000	.214*
		Sig. (2-tailed)	.	0.032
		N	200	100
	Age	Correlation Coefficient	.214*	1.000
		Sig. (2-tailed)	.032	.
		N	100	100
*. Correlation is significant at the 0.05 level (2-tailed).				



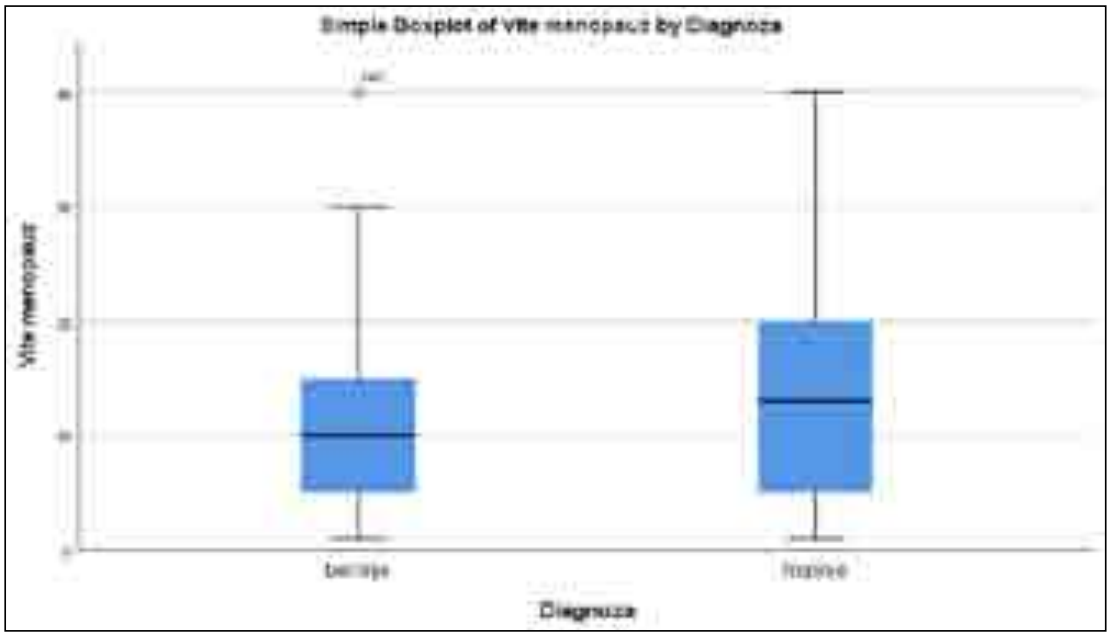
Here is the correlation between the diagnoses and years in menopause.

Years in menopause	polip	atrophy	endometrium cancer	hypertrophy
<5 vjet	3(3%)	2(2%)	5(5%)	7(7%)
5-10 vjet	3(3%)	2(2%)	10(10%)	9(9%)
10-15 vjet	2(2%)	4(4%)	4((4%)	9(9%)
≥15 vjet	8(8 %)	4(4%)	12 (12%)	10(10%)

We are calculating the correlation between diagnosis and age of the patients using Spearman's Rho statistical test. p= 0.028 ≤ 0.05.

This p value tells us for a significant correlation between years in menopause and diagnosis. This tells us that with the increasing of the years in menopause of the patient, the likelihood of developing the endometrial cancer increases too.

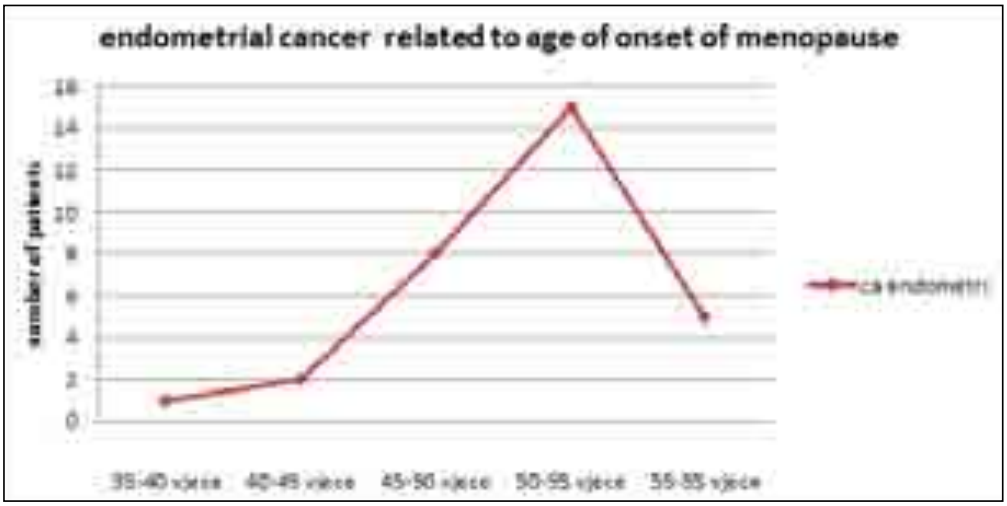
			Diagnosis	Years in menopause
Spearman's rho	Diagnosis	Correlation Coefficient	1.000	.113
		Sig. (2-tailed)	.	p=0.028
		N	200	165
	Years in menopause	Correlation Coefficient	.113	1.000
		Sig. (2-tailed)	.148	.
		N	165	165



In the table below we have presented the distribution of diagnoses depending on the age of the onset of menopause.

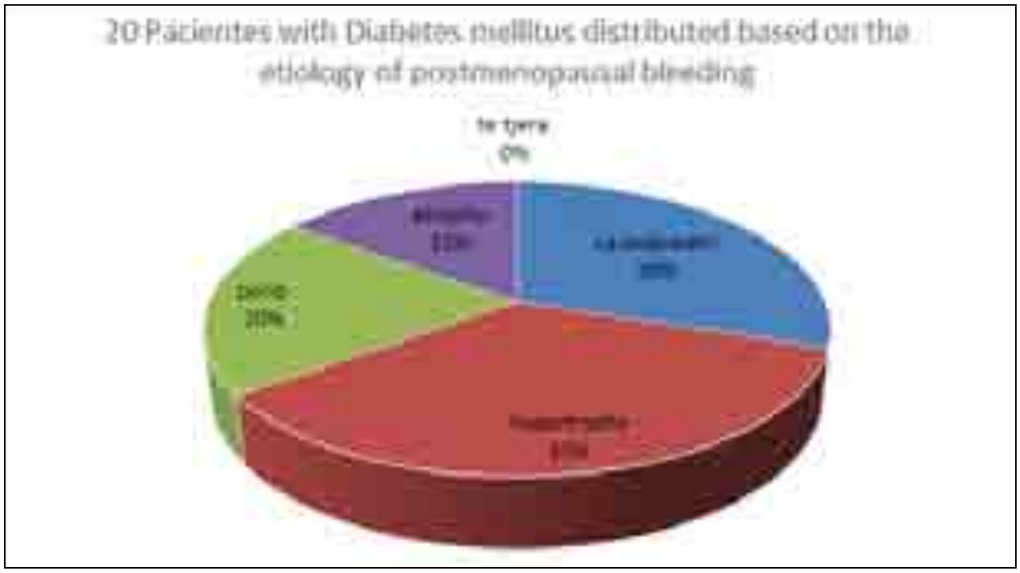
Age of onset of the menopause	polip	hypertrophy	Endometrial cancer	atrophy
35-40	0	2	1	1
40-45	2	4	2	2
45-50	4	12	8	1
50-55	7	12	15	7
55-60	3	5	5	1

We can see that endometrial cancer is more often in the age of onset of menopause 50-55 years of age.



In the table below, we have distributed the patients with diagnoses that cause postmenopausal bleeding in two group, these who have diabetes and those who have not.

paciente me,	kane diabet	nuk kane diabet	total
ca endometri	6	25	31
hipertrofi	7	18	25
polipe	4	14	18
atrofi	3	9	12
te tjera	0	14	14
total	20	80	100

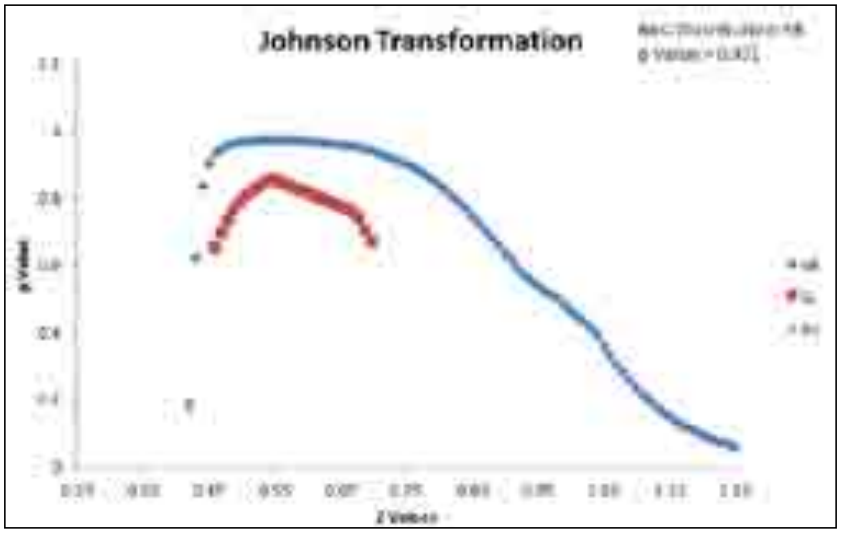


We are calculating the correlation between endometrial cancer and Diabetes mellitus of the patients using Anova statistical test. p= 0.632 ≥ 0.05

This p value tells us for a non-significant correlation between the endometrial cancer and Diabetes mellitus. This tells us that Diabetes mellitus doesn't increase the likelihood of developing the endometrial cancer increases.

Johnson Transformation Program						
	Mean	StDev	Median	Min	Max	p Value
Original data	10.00	7.688	8.000	0.000	25.00	0.632
Transformed data	-0.0111	0.964	-0.111	-1.650	1.650	0.971

We recalculated the correlation between endometrial cancer and Diabetes mellitus of the patients Johnson Transformation Program using .p= 0.971 ≥ 0.05 This p value tells us for a non-significant correlation between the endometrial cancer and Diabetes mellitus. This tells us that Diabetes mellitus doesn't increase the likelihood of developing the endometrial cancer increases .



Here is the table that shows the distribution of the patients with diagnoses that cause postmenopausal bleeding in two group, these who have HTA and those who have not.

paciente me	kane HTA	nuk kane HTA	total
atrofi	4	8	12
ca endometri	29	2	31
hipertrofi	21	14	35
polip	7	11	18
te tjera	1	3	4
total	62	38	100

To see if there are significant differences between benign /malign diagnostic groups and HTA present /not present was used Anova test. This table shows significant differences between group of patients that have HTA and endometrial carcinoma, p= 0.021<0.05.

Anova

HTA					
	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	1.256	1	1.256	5.519	p=0.021
Within Groups	22.304	98	.228		
Total	23.560	99			

We are calculating the correlation between endometrial cancer and HTA of the patients using Spearman's Rho statistical test. p= 0.021<0.05.

This p value tells us for a significant correlation between HTA and diagnosis. This tells us that with the presence of HTA of the patient, the likelihood of developing the endometrial cancer increases too.

Correlation between diagnosis and hta

			Diagnoza	HTA
Spearman's rho	Diagnoza	Correlation Coefficient	1.000	.231*
		Sig. (2-tailed)	.	p=0.021
		N	100	100
	HTA	Correlation Coefficient	.231*	1.000
		Sig. (2-tailed)	.021	.
		N	100	100

Correlation Between Endometrial Cancer and Endometrial Thickness

Endometrial thickness	polip	ca endometri	hypertrophy	other
<5mm	0 (0%)	0(0%)		2(2.7%)
5-10mm	6(8.1%)	3(4%)	5(6.7)	
10-15mm	7(9.5%)	4(5.4%)	15(20.2%)	
>15	4(5.4%)	7(9.5%)	7(9.5%)	
irregular	0(0%)	14(19%)		
TOTAL 74 PATIENTES				

We are calculating the correlation between the etiologies of the postmenopausal bleeding and endometrial thickness of the patients using Spearman's Rho statistical test. ***p***= 0.019<0.05.

This p value tells us for a significant correlation between etiologies of the postmenopausal bleeding and endometrial thickness. This tells us that with the increasing of endometrial thickness of the patient, the likelihood of developing the endometrial cancer increases too.

Correlation Between Endometrial Cancer and Endometrial Thickness

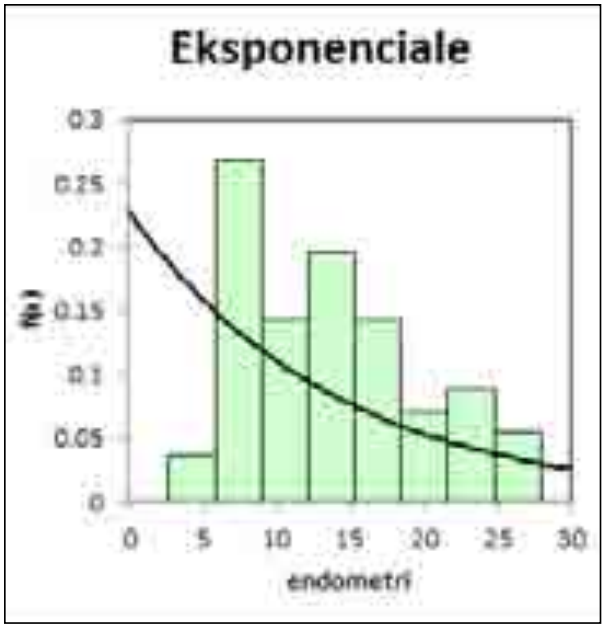
			Diagnoza	Dimensionet
Spearman's rho	Diagnoza	Correlation Coefficient	1.000	.272*
		Sig. (2-tailed)	.	0.019
		N	200	74
	Dimensionet	Correlation Coefficient	.272*	1.000
		Sig. (2-tailed)	.019	.
		N	74	74

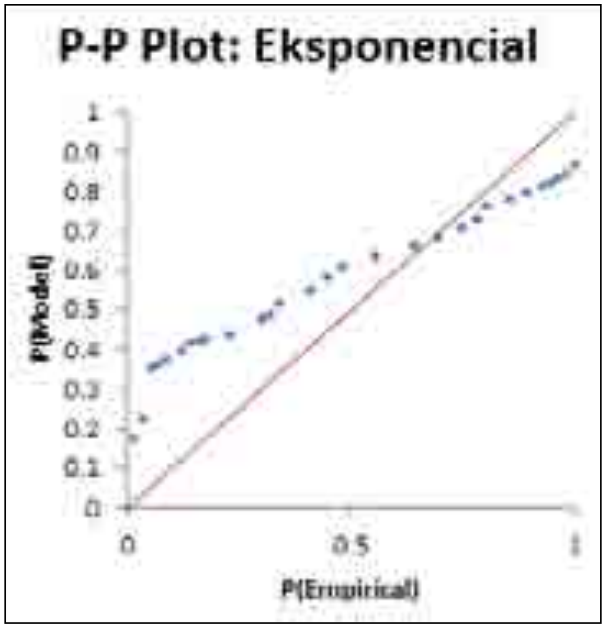
*Correlation is significant at the 0.05 level (2-tailed).

We are calculating the correlation between the endometrial cancer and endometrial thickness .***p***= 0.001<0.05.This p value tells us for a significant correlation between endometrial cancer and endometrial thickness.

Results of Eksponencial distribution

Count	Mean	StDev	Median	Min	Max	Skew
56	13.88	6.092	14.00	2.700	28.00	0.384
Location	Shape	Scale	Threshold	Log-Likelihood	AD	p Value
		13.88		-203.3	7.926	<0.001





This graphic shows us that with the increasing of endometrial thickness of the patient, the likelihood of developing the endometrial cancer increases too.

Correlation between weight and endometrial cancer

Weight	N.of Patients with Hypertrophy	N. of Patients with Endometrial Ca
Normal Weight	6(17%)	6(19%)
Overweight	29(83%)	25(81%)

We looked for a correlation between weight and endometrial cancer, was used Spearman's rho test but no important correlation was found, , p=0.855 >>> 0.05.So overweight doesn't influence development of endometrial cancer.

			Pesha	Diagnoza
Spearman's rho	weight	Correlation Coefficient	1.000	-.019
		Sig. (2-tailed)	.	.855
		N	100	99
	Diagnoses	Correlation Coefficient	-.019	1.000
		Sig. (2-tailed)	0.855	.
		N	99	99

To put the diagnosis of postmenopausal bleeding is used pelvic examination, transvaginal ultrasonography, hysteroscopy, dilatation and curettage.

Treatment was hysterectomy in endometrial carcinoma, malign polyp, cervical cancer, polipectomia in the cases of benign polyps.

Discussion

It is very important to discuss the results of endometrial cancer in our study because we found the level of endometrial cancer very high, taking the first place 33 % in comparison with other causes of posmenopausal bleeding. In comparison with the percentage of endometrial cancer of the studies of the literature , the value of our study is two to three fold greater than that of literature. These results disturbed us and we must try to find an explanation to our results.

We think that gynecologist in other cities and in private clinics treat all benign cases of postmenopausal bleeding but they refer difficult cases like endometrial cancer in our university hospital, so increasing the cases of endometrial cancer and so the percentage in our study, reducing the percentage of benign cases.

Another point is that usage of egzogene estrogens in the studies of literature is 30 % but in our study only 1 %.This can happen because our patient are frightened to use them because of negative effects. This is another factor that decreases the percentage of benign causes of posmenopausal bleeding, and allows the malign factor to take the first place.

Conclusions

In our study the causes of postmenopausal bleeding are;

1. endometrial cancer
2. hypertrophy
3. atrophy
4. polips
5. others

Endometrial cancer is in a high level, taking the first place with 33 %.

Age, menopausal age, years in menopause, endometrial thickness, HTA have a significant correlation with endometrial cancer. So we can say that these factors increase the likelihood of developing of endometrial cancer.

In our study we found no significant correlation between diabetes, obesity and endometrial cancer. So the results of our study show that diabetes and obesity don't increase the likelihood to develop endometrial cancer.

Recommendation

We recommend a large prospective study to verify the percentage of endometrial cancer in Albania and to look for other factors that can contribute in the development of endometrial cancer.

Referenca

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