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Association Between Metabolic Syndrome and Risk of Endometrial Cancer

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Abstract: Back ground: Endometrial cancer is one of the most common cancers of the female reproductive system, and it is one of the rise globally. metabolic syndrome is a clustering of at least three of the five following medical conditions: central obesity, diabetes, hypertension, high serum triglyceride and low serum high density lipoprotein.

Aim: The aim of this study was to assess the association between the metabolic syndrome and the endometrial cancer.

Methods: this case control study comprised of 93 patients with abnormal uterine bleeding admitted to department of obstetrics and gynecology, Tishreen University Hospital, Lattakia Syria, during the period of February 2019 To February 2021, patients who full field the inclusion criteria for the study were divided into 2 groups, the first consisted of 31 patients had endometrial cancer with histological confirmation (cases).

The second consisted of 62 patients with normal biopsies (controls).

The determination of the metabolic syndrome is according to NCEP ATP III(2005)

Results: Baseline characteristics were matched in both study groups.

In assessment the association between the metabolic syndrome and the endometrial cancer the odd ratio (OR) was (3.31). the odd ratio (OR) for metabolic syndrome (MS) elements were (2.9 with diabetes, 3.9 with obesity, 2.05 with hypertension, 2.36 with high triglyceride and 1.2 with low high density lipoprotein).

Conclusion: the metabolic syndrome and its elements are causes of endometrial cancer.

Keywords: Endometrial Cancer (EC), Metabolic Syndrome (MS), abnormal uterine bleeding.

العلاقة بين المتلازمة الاستقلابية وخطر السرطان بأعلى الرحم

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المستخلص: يعد سرطان باطن الرحم واحداً من أبشع الخبائث في جهاز المرأة التناسلي، وتسجل نسبته ازدياداً عالمياً في الوقت الحالي.

المتلازمة الاستقلابية هي مجموعة من الأمراض تضم ثلاثة على الأقل من العناصر الخمسة التالية: بدانة مركزية، سكري، ارتفاع توتر شرياني، ارتفاع الشحوم الثلاثية وانخفاض الكوليسترول عال الكثافة.

الهدف: الهدف الأساسي من الدراسة هو تقييم العلاقة بين المتلازمة الاستقلابية وخطر سرطان باطن الرحم.

الطرق: الدراسة الحالية من نمط حالة – شاهد وقد اشتملت على 93 مريضة من المراجعات لقسم التوليد وأمراض النساء في مشفى تشرين الجامعي باللاذقية- سوريا في الفترة بين شباط 2019 حتى شباط 2021

بشكوى نزف تناسلي شاذ. وتم تقسيم المرضى المشمولين في هذه الدراسة الى مجموعتين:
المجموعة الأولى (الحالات): احتوت على 31 مريضة لديهن سرطان باطن رحم مثبت بالتشريح المرضي.
المجموعة الثانية (الشواهد): احتوت على 62 مريضة مع خزعات طبيعية.
تم تعريف المتلازمة الاستقلابية اعتماداً على تصنيف NCEP ATP III(2005)
النتائج: بدراسة العلاقة بين المتلازمة الاستقلابية وعناصرها مع سرطان باطن الرحم كانت نسب الأرجحية كالتالي:
من أجل البدانة 3.9 أجل السكري 2.9 من أجل ارتفاع التوتر الشرياني 2 من أجل ارتفاع الشحوم الثلاثية 2.3ومن أجل الملازمة الاستقلابية 3.31
الخلاصة: المتلازمة الاستقلابية وعناصرها هي مسببات لسرطان باطن الرحم.

الكلمات المفتاحية: سرطان باطن الرحم، المتلازمة الاستقلابية، نزف تناسلي شاذ.

INTRODUCTION:

Endometrial cancer (EC): is a glandular malignancy in the epithelium of the uterine endothelium caused by unopposed estrogen excitation, it is common after the menopause, the mean age is 63 years. [1]

The incidence is 26, 6 case /100000 the survival rate for 10 years is 80% with treatment by surgery, radiotherapy, chemotherapy.

the women in families who had lynch syndrome are high risk for endometrial cancer. [2]

the risk factors: age: 55- 70, unopposed estrogen high levels of estrogen with low levels of progesterone, endogenous factors (obesity, late menopause, diabetes mellitus). [2]

Clinical manifestations: abnormal uterine bleeding more than 90 %, pain, pelvic mass. [3, 4]

Diagnosi: the endometrial sampling by dilation and curettage with or without hysteroscopy is used to make the final diagnosis. [7]

Metabolic syndrome: is a multifactor disease caused by insulin resistance with dysfunction of adipose tissue. [5]

Metabolic syndrome is a risk factor of cardiac disease and many cancers. [6]

Diagnosis: Metabolic syndrome is diagnosed when there is 3 of 5 criteria according to NCEP ATP III(2005)

1- Fasting blood sugar ≥100 mg \dl.
2- Blood pressure ≥ 130\80 mmz.
3- Tri gleceride (TG) ≥150 mg\dl.
4- High rensity lipoprotine (HDL)≤ (50) mg\dl.
5- Body mass index (BMI) ≥30 KG\ M. [10]

By increasing of the metabolic disease endometrial cancer (EC) is increasing and happening with younger ages.

the exact mechanism of the role of metabolic syndrome in endometrial cancer is unknown, it has an association of high of this metabolite like glucose and triglyceride. [11, 12]

AIM:

The objective of this study was to assess the association between metabolic syndrome endometrial cancer.

IMPORTANCE OF THE STUDY: Endometrial cancer is associated with globally significant morbidity and mortality, since there are no screening programs for this disease risk, modification strategies allow controlling its incidence.

MATERIAL AND METHODS:

1- **Setting:** This case control study was carried out in department of obstetrics and gynecology, Tishreen University Hospital, Lattakia, Syria over period of February 2019 to February 2021.

2- **size of sampie:** 93 patients were participated in this study and they were divided into 2 groups; Group A(the cases) consisted of 31 patients with histological confirmation; Group B (the controls) consisted of 62 patients with normal biopsies.

3- **sampling technique:** All the patients underwent a medical questioning, clinical examinations, trans vaginal sonography, laboratory tests, pap smear and histopathological specimens.

Patients with abnormal uterine bleeding between 35 to 60 years old were taken in the study after patients demographic and routine investigation.

Patients with coagulations disorders, pregnancy, fibroid, cervical malignancy, ovarian cysts, endometrial hyperplasia, replaced hormone therapy; Were excluded from the study. The determination of the metabolic syndrome is according to NCEP ATP III(2005).

4- **Data Processing and Statistical Analysis:** A packaged computer analysis program, statistical package for the social science (IBM SPSS statisticsVersion20) will be using for statistical analysis of this data. The result is satistically significant when P- value $<$ 5% and odd ratio ≥2. the variables adjusted for age, age, at menarche, parity and menopausal status.

5- **Ethical Considerations:** Approval of the study from faculty of medicine to Tishreen Hospital manager.

RESULTS:

Table [1] gives the distribution of 31 cases of endometrial cancer and 62 controls according to sociodemographic variables, cases and controls had similar distribution according to age and menopausal status, compared with controls cases had lower age at menarche and lower parity.

	Case(31)	Contol(62)
Age		
[30- 35]	0(0%)	7(11%)
[35- 40]	1(3.2%)	3 (4%)

	Case(31)	Contol(62)
[40- 45]	3(9.7%)	9(14.5%)
[45- 50]	3(9.7%)	11 (16.1%)
[50- 55]	7(22.6%)	12(19.3%)
[55- 60]	17(54.8%)	20(32.2%)
Age at menarche		
<13	15(47.6%)	23(37.4%)
13- 14	12(40.7%)	26(41.7%)
≥15	4(11.7%)	13(20.8%)
Parity		
0	5(15%)	9(14.3%)
1- 2	7(22.3%)	11(17.5%)
3- 4	11(35.2%)	19(31.2%)
≥5	8(26.5%)	23(37.0%)
Menopausal status		
Pre\peri	18.7	18.1
post	81.3	81.9

All the following variables adjusted for age, age at menarche, parity and menopausal ststus

Table [2] The association between endometrial cancer and diabetes is presented in table 2

Diabetes Mellitus	The sample		Total
	Case	Control	
Yes	12 (38.7%)	11 (17.7%)	23
No	19 (61.3%)	51 (82.3%)	70
Total	31	62	93

As a result of studying the association between endometrial cancer and diabetes the odd ratio (OR) was OR=2.9 CI[2.1- 9.8]

diabetes is associated with a 2.9 greater risk for endometrial cancer P- value=0.001

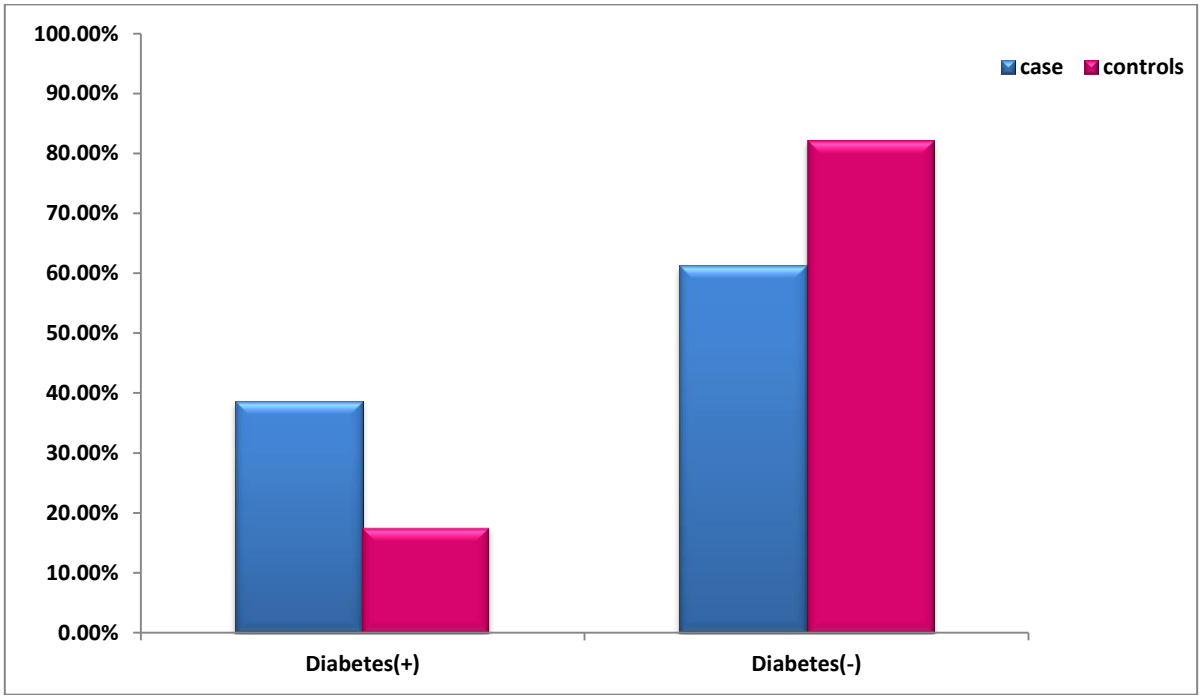

Figure (1) Distribution of the sample according to diabetes mellitus

Table [3] The association between endometrial cancer and obesity is presented in table 3

Obesity	The sample		Total
	Case	Control	
Yes	23(74.2%)	26(41.9%)	49
No	8(25.8%)	36(58.1)	44
Total	31	62	93

As a result of studying the association between endometrial cancer and obesity the odd ratio(OR) was OR=3.9 CI[2.1- 10.8]

Obesity is associated with a 3.9 greater risk for endometrial cancer P- value=0.0001

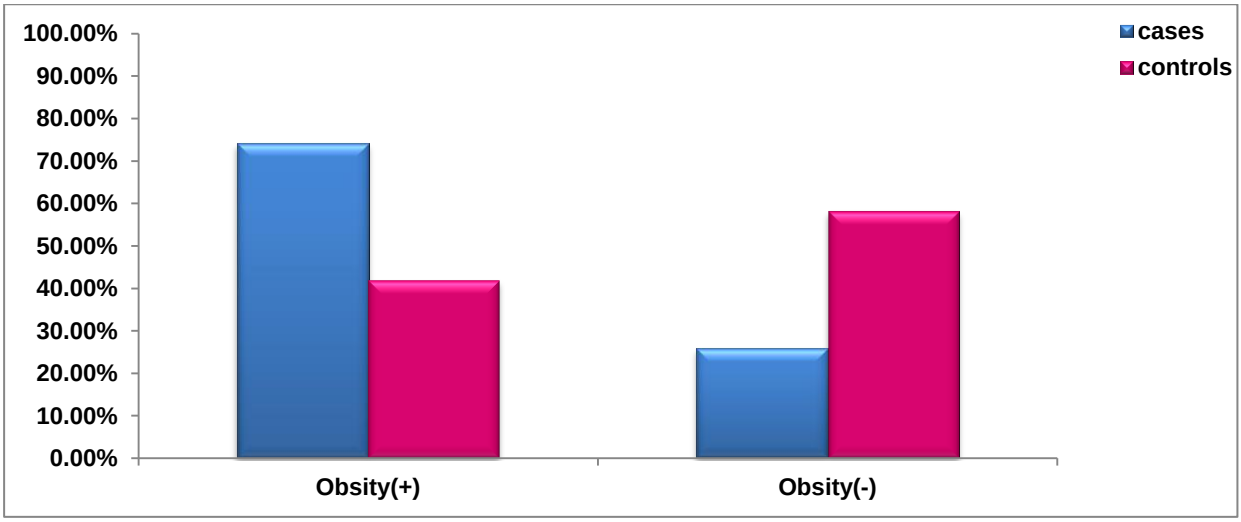

Figure (2) Distribution of the sample according to obesity

Table [4] The association between endometrial cancer and hypertension is presented in table 4

Hypertension	The sample		Total
	Case	Control	
Yes	17 (54.8%)	23 (37.1%)	40
No	14 (45.2%)	39 (62.9%)	53
Total	31	62	93

As a result of studying the association between endometrial cancer and hypertension the odd ratio (OR) was OR=2.05 CI [1.1- 6.8]

hypertension is associated with 2 greater risk for endometrial cancer P- value=0.001

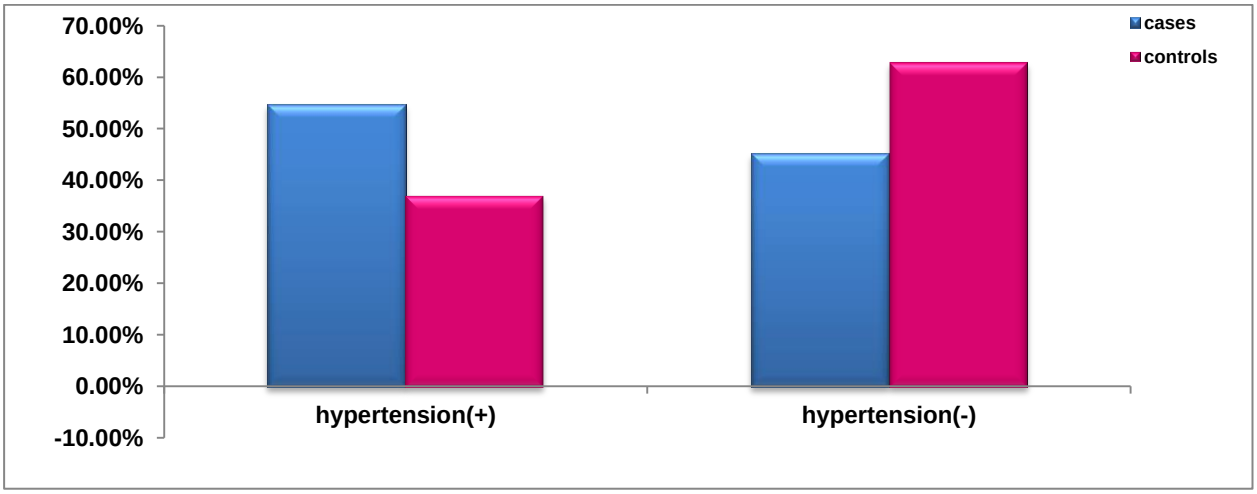

Figure (3) Distribution of the sample according to obesity Distribution of the sample according to hypertension

Table [5] The association between endometrial cancer and high triglyceride is presented in table 5

TG	The sample		Total
	Case	Control	
High	14 (45.2%)	19 (25.8%)	30
Normal	17 (54.8%)	46 (74.2%)	63
Total	31	62	93

As a result of studying the association between endometrial cancer and high triglyceride the odd ratio (OR) was OR=2.36 CI[1.6- 8.8]

high triglyceride is associated with 2.36 greater risk for endometrial cancer

P- value=0.005.

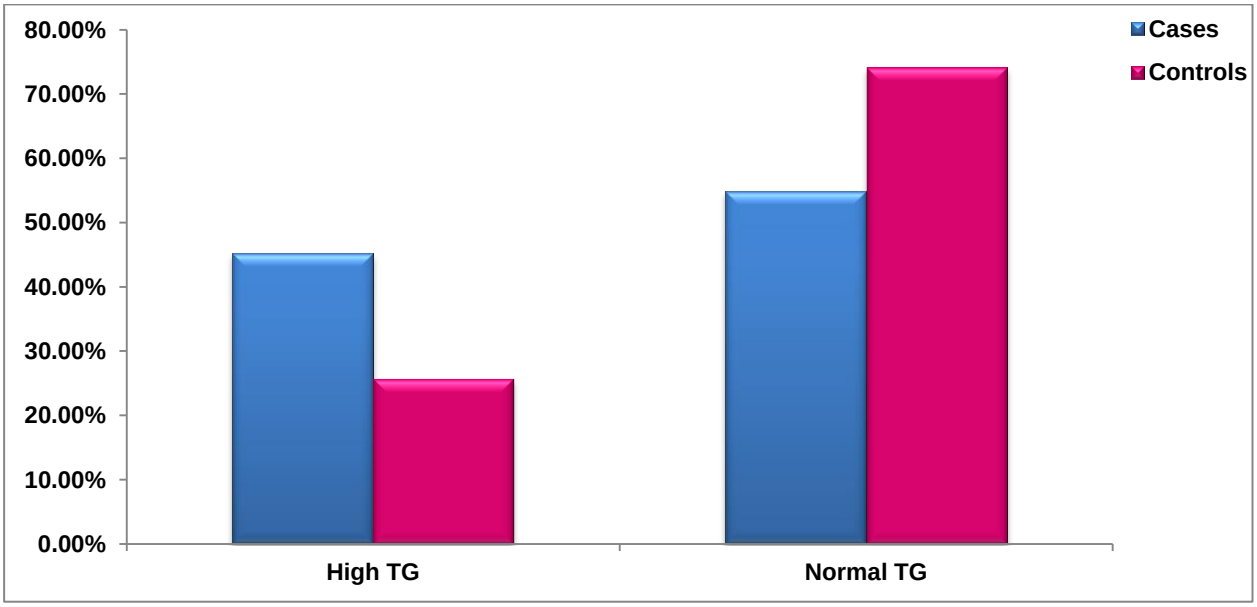

Figure (4) Distribution of the sample according to triglyceride

Table [6] The association between endometrial cancer and low of high density lipoprotein is presented in table 6

HDL	The sample		Total
	Case	Control	
Low	11 (35.5%)	19 (30.6%)	30
Normal	20 (64.5%)	43 (69.4%)	63
Total	31	62	93

As a result of studying the association between endometrial cancer and low of high density lipoprotein the odd ratio (OR) was OR=1.2 CI[0.3- 6.1] .

There is no statistically significant difference between low high density lipoprotein (HDL) and endometrial cancer, P- value=0.3:

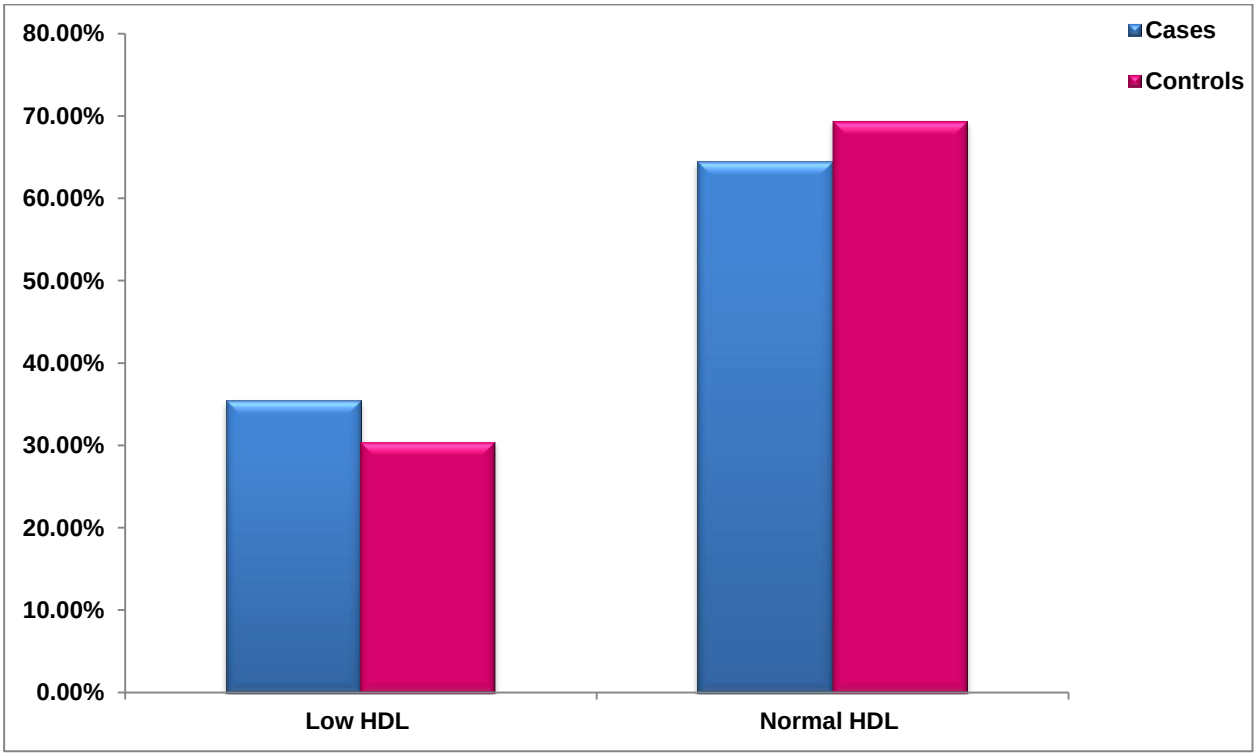

Figure (5) Distribution of the sample according to high density lipoprotein (HDL)

[7] The association between endometrial cancer and metabolic syndrome is presented in table 7.

Metabolic syndrome	The sample		Total
	Case	Control	
Yes	19 (61.3%)	22 (35.5%)	41
No	12 (38.7%)	40 (64.5%)	52
Total	31	62	93

As a result of studying the association between endometrial cancer and metabolic syndrome the odd ratio(OR) was OR=3.31 CI[1.6- 8.7]

metabolic syndrome is associated with 3.31 greater risk for endometrial cancer, P- value=0.005

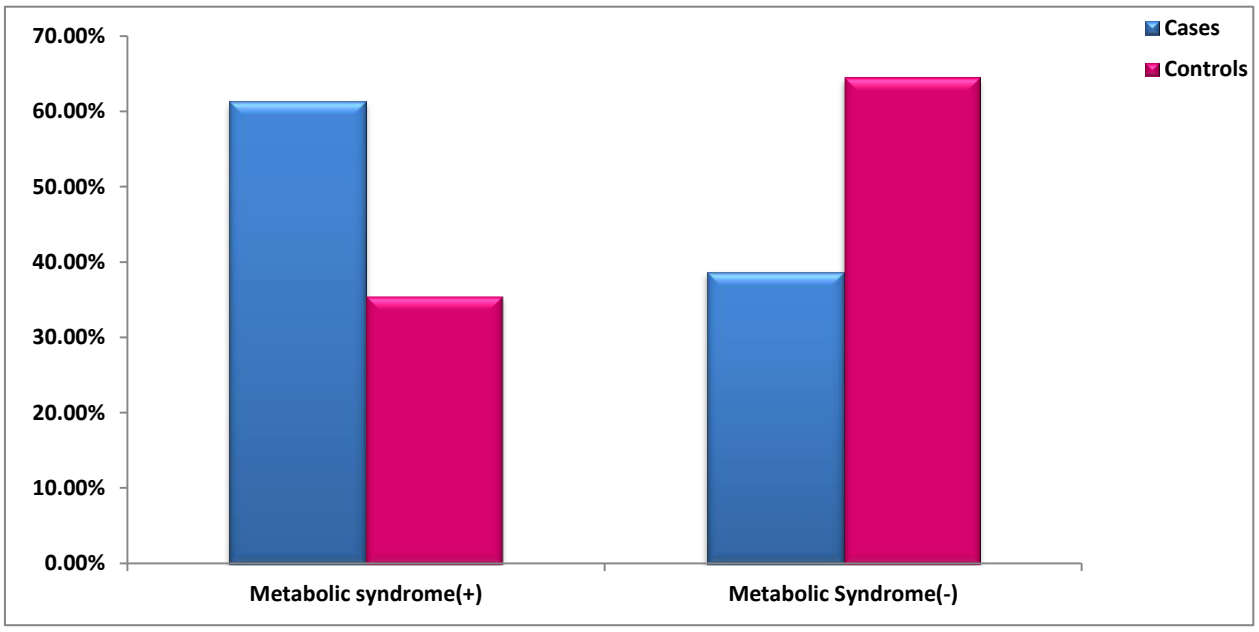

Figure (6) Distribution of the sample according to metabolic syndrome

DISCUSION:

The present study contained 93 sample the endometrial cancer patients formed 33.3 % of them, the ages ranged between 35 and 60 year the mean age was 51±6.2. cases and controls had similar distribution according to age and menopausal status, compared with controls cases had lower age at menarche and lower parity.

The obesity had the highest risk of endometrial cancer with odd ratio (OR) = 3.9 that can be explained by the high estrogen level produced by aromatase enzymes and the role of adipose tissue in secretion some elements had a role in malignant tissue development (reactive protine c, interferon). [12]

Diabetes mellitus is associated with endometrial cancer 2.9 times. that the high glucose availability provides a selective advantage for malignant cells which had high glucose need. [12]

The hypertension is associated with endometrial cancer 2 times. it is proposed that hypertension inhibits the apoptosis. [13]

High triglyceride is associated with endometrial cancer 2.36 times, hyperlipidemia may contribute to oxidative stress. [14]

Low of high density lipoprotein HDL did not have a risk of endometrial cancer. [14]

Metabolic syndrome was associated with a risk of endometrial cancer about 3 times.

Comparing with other studies:

Most of the studies reported the direct association between endometrial cancer and individual risk factor, but only a few studies considered the association between endometrial cancer and metabolic syndrome.

*In a study conducted by Rosato et al in Italy in 2011 on 545 cases and 798 controls, [14] like the present study; the metabolic syndrome and its elements were causes of endometrial cancer and the odd ratio (ORs) were 2.18 for diabetes, 1.77 with hypertension, 1.20 with high triglyceride, between 1.62and 2.23 for various definitions of central obesity, and 3.83 for women with a body mass index ≥30kg\m^2. The risk of endometrial cancer was significantly increased for subjects with metabolic syndrome, the odds ratios ranging between 1.67 and 2.77 when waist circumference was included in metabolic syndrome definition and 8.40 when body mass was considered instead. That is different from the present study which considered only body mass index to assess the obesity without measuring the waist circumference, because women tend to accumulate fat in the lower body rather than around the waist, which is more typical in men.

* In the study of Mohamad et al in Malaysia in 2020 on 119 sample, [16] the metabolic syndrome was significantly associated with increased risk of endometrial cancer, odd ratio = 3, 43 P- value <0.05%, obesity was a risk factor of endometrial cancer with odd ratio = 3.88 P- value <0.05%. And this is consistent with the present study, but unlike our study Mohamed did not find a significant difference between endometrial cancer and other metabolic components (diabetes, hypertension, triglyceride, high density lipoprotein) P- value > 0.05%. that can be explained by the high proportion of obese people in Malaysia, which made the sample size after excluding obesity very small so the variables were not statatisticaly significant.

* In the study of Wang et al in China in 2020 on 17772 cases and 150, 371 controls, [17] the metabolic syndrome was a cause of endometrial cancer with odd ratio= 1.62 and that is consistent with the present study but unlike our study he did not assess the association between endometrial cancer and metabolic syndrome elements.

Conclusion:

Most of the cases were after menopause. metabolic syndrome and its elements were risk factor for endometrial cancer Obesity was the most common risk factor for endometrial cancer.

recommendation:

screening tests for metabolic syndrome to reduce endometrial cancer.

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