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Trend of uterine cancer at Hiwa Cancer Hospital of the Sulaymaniyah Province of Iraqi Kurdistan over a five-year period

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Abstract---Background: Uterine cancer is the sixth most frequent cancer in women worldwide, with broad international variations in incidence rates due to lifestyle changes and exposure types. In changing economies, uterine cancer is the most frequent gynecological malignancy, but it is still less common than cervix carcinoma. Methods: From 2014 to 2018, data from 135 individuals with corpus uterine cancer were extracted from the Hiwa cancer center, the governorate's only tertiary care facility with a population of around two million people. Age, parietal and menopausal status, number of children, BMI, previous medical history, date of diagnosis, tumor morphology, tumor stage and grade, and kind of surgery were among the information collected. Also, we estimated the Age-Standardized Specific Rate (ASR) / for 100,000 women. The researchers looked at 135 cases of corpus uterine carcinoma. 3.84 was the age-standardized specific rate (ASR). The median age at diagnosis was 58 years, with more than half of the patients (67%) being postmenopausal and living in cities. In half of the instances, 53.3 percent had other medical comorbidities, and 54 percent had a BMI of less than 30, with 17% having a BMI of more than 40. Adenocarcinoma was found in the majority of patients detected early (73.7 percent stage I and 8.9 percent stage II). Conclusion: The study found a greater risk of uterine cancer diagnosis in middle-aged women, with a rising incidence rate over time, which could be due to epidemiological causes and socio-economic transitions.

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Keywords---corpus uterine cancer, Hiwa cancer center, Sulaymanyia, Iraq.

Introduction

Uterine cancer is the sixth most frequent cancer in women worldwide and the fourth most common in the United States. According to the American Cancer Society, there were 61,380 new instances of uterine corpus cancer and 10,920 fatalities in 2017, but it is less common in developing nations than in cervix carcinoma. (1,2,3). The bulk of uterine cancers come from the endometrial epithelium (endometrial carcinomas), which account for 90% of all uterine cancers, followed by uterine sarcomas, which account for 3-7 percent of all uterine cancers, and less common kinds of cancer (2 percent).

Endometrial carcinoma can be classified into several histological subgroups, including endometroid, serous, papillary serous, clear cell, mucinous, papillary, undifferentiated, squamous, carcinosarcoma (malignant mixed Müllerian tumor), and adenocarcinoma with squamous differentiation (2,4). The remainder of uterine malignancies is stromal or mesenchymal tumors, such as uterine leimyosarcoma (ULMS), which is the most common, followed by low grade endometrial stromal sarcoma (LGESS), high-grade endometrial sarcoma (HGESS), adenosarcomas, undifferentiated uterine sarcoma (UUS), previously known as high-grade undifferent (PEComa). 4,5 In individuals with adenocarcinoma of the endometrium, a number of risk factors have been found, including advanced age [>55], obesity, and diabetes mellitus. 6,7 Lynch syndrome, tamoxifen use, nulliparity, late menopause [age >52y], and unopposed estrogen all play a role in the pathogenesis of this cancer when used as a hormone replacement therapy for some patients and endogenously produced by conditions like polycystic ovarian syndrome and feminizing ovarian tumors. Uterine sarcomas have also been linked to unopposed estrogen stimulation and tamoxifen use. 8,9. The most prevalent symptom of corpus uterine cancer in postmenopausal and premenopausal women is abnormal vaginal bleeding, which includes any unexpected bleeding after menopause, bleeding between periods, or bleeding after sex.

3 Pelvic pain, bowel irregularities, and frequent urination are common late symptoms in women with endometrial cancer. 4,5 It is a disease that affects postmenopausal women, with a median age of 62 years at diagnosis, whereas uterine sarcomas strike women in their early 50s. The majority of uterine malignancies are detected early in their development (80 percent in stage I). 5,6
The goal of this study is to present for the first time the demographic, clinical, and pathological characteristics of corpus uterine malignancies treated at Hiwa cancer center in Iraqi Kurdistan's Sulaymaniah region from 2014 to 2018, as well as to shed light on modifiable risk factors.

Methodology

Study population and data management: From January 2014 to December 2018, a retrospective and prospective study were done to examine all corpus uterine cancer patients at Hiwa Hospital, based on documented data, telephone

interviews, and direct interviews with the patients. The patients gave their informed permission. Various documents were acquired from the archives of the Shorish hospital's Hiwa, Zhyanawa, and pathology departments, where the findings of clinical data at presentation, past medical history, and histological reports were available. Name, age, date of diagnosis, BMI, menopausal, marital, and parietal status, the pattern of presentation, previous medical history and associated comorbidities, type of surgery, and histopathology report were among the information collected.

Sulaymaniyah is a lovely city in Iraqi Kurdistan, situated 700 feet above sea level and home to a population of roughly 2 million people. The number of women at risk was calculated using the World Standard Population (WHO 2001). The age-standardized incidence rate (ASR) for Hiwa center patients was determined using Sulaymaniyah's population. The data was entered into SPSS version 20 (Statistical Software for Social Science). At a statistical level of 0.05, the rates of each variable were determined, and the chi-square test and person correlation were utilized.

During the study, ethical considerations governed by the Ministry of Health and the Ministry of Higher Education in Kurdistan were observed.
Criteria for Inclusion and Exclusion:
The original tumor site and the period of diagnosis were used as inclusion criteria. Patients with secondary uterine cancer of ovarian or cervical origin, as well as those with the recurring disease, were eliminated, as were those who lived outside of Sulaymaniyah and had lost contact.

Results

Between January 2014 and December 2018, the Hiwa cancer center analyzed 135 instances of primary uterine cancer, with 119 cases from Sulaymaniyah province and 16 cases from other cities. The participants' ages ranged from 28 to 88 years old, with the average age being 57 years old and the median age at diagnosis being 58. (Figure:1)

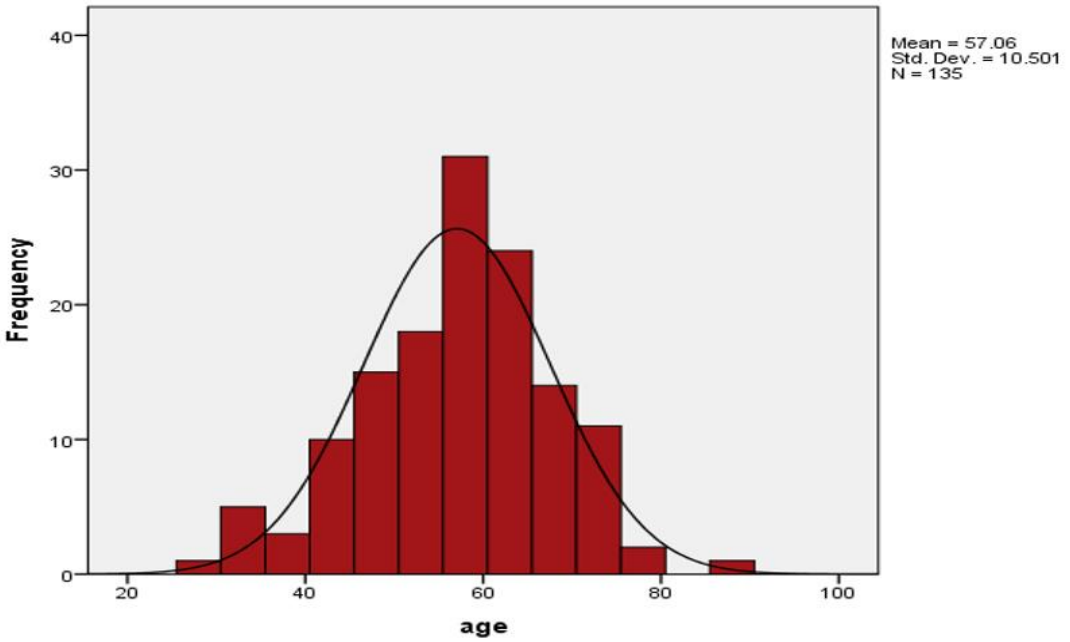

Figure 1: Uterine Cancer Cases by Age Distribution Concerning the residency: 51.1 percent came from Sulymania's city core, while 36.3 percent came from the countryside; nonetheless, 12.6 percent came from other governorates, with urban 5.9% and rural 6.6% respectively. During the study period, the age-standardized rate of uterine cancer was 4.31 per 100 000 women, with 135 cases.

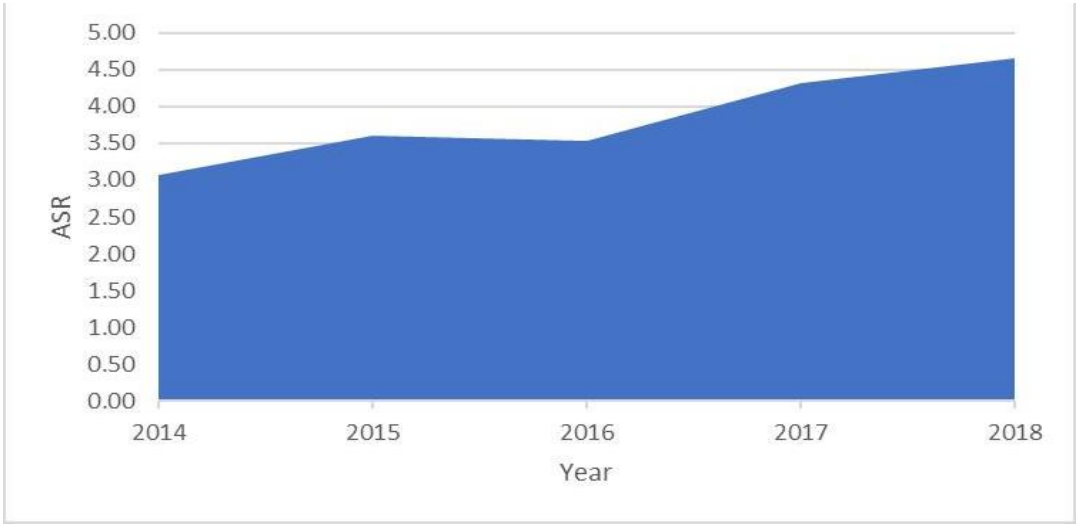

Figure 3.1: the Age-Specific Incidence Rate of 119 Uterine Cancer Sulaymaniyah cases per 100 000 from Jan. 2014-Dec. 2018

Table 1 summarizes the clinical and demographic features of the patients included in the study. At the time of diagnosis, 67 percent of the patients were postmenopausal.

In general, the individuals' BMI was high, with 57 percent being obese (BMI >30), 14.8 percent having morbid obesity, and 23.4 percent being overweight. Only 7.9% of people were at a healthy weight when they were diagnosed.

Table 3.1: Demographic and clinicopathological characteristics of 135 uterine cancer patients in Hiwa cancer center between 2014 and 2018

Variables		Frequency	Percent
Age Group	20-29	1	.7
	30-39	7	5.6
	40-49	24	18.5
	50-59	44	32.1
	60-69	44	32.1
	=>70	15	11.8
Menopausal status	Premenopause	44	32.8
	Postmenopause	91	67.2
Residency	Urban	84	57.6
	Rural	51	42.4
BMI(n=127)	20_24.9	10	7.9
	25_25.9	26	23.4
	30_34.9	35	31.4
	35_39.9	19	18.0
	>=40	19	17.1
Parity Status(n=88)	Nulliparous	22	15.4
	Low parity	33	24.1
	High parity	33	24.1
Past Medical History(n=122)	Hypertension	26	19.7
	DM	13	9.5
	DM & Hypertension	23	16.8
	Others	10	7.3
	Uterine fibroid	9	6.6
	No medical history	42	30.7
Tumor stage(n=130)	Localized	112	73.7
	Regional	9	16.1
	Distant	9	6.6
	I	52	38,7

Tumor grade(n=129)	II	42	30.7
	III	35	26.3
Tumor Histology(n=135)	Adenocarcinoma	105	76.7
	Other carcinoma	11	8
	carcinosarcoma	7	5.1
	Sarcoma	12	8.8

The most prevalent symptom was postmenopausal vaginal bleeding (54%), followed by perimenopausal vaginal bleeding (43%), menorraghea, menstrual cycle irregularity, lower stomach pain, vaginal discharge, and a few of them (3%) were discovered by accident during routine pelvic ultrasound.

The majority of our patients (86) had a total abdominal hysterectomy with BSO, while (24) had a hysterectomy with BSO with or without pelvic LN sampling, omental sampling, and peritoneal wash. Only (7) individuals had a total abdominal hysterectomy without BSO, and (3) cases had unilateral SO. As a result, most patients' staging was based on T stage (FIGO staging) with uncertain nodal status. 73.7 percent were in stage I, 8.8 percent in stage II, 7.3 percent in stage III, and 6.6 percent in stage IV.

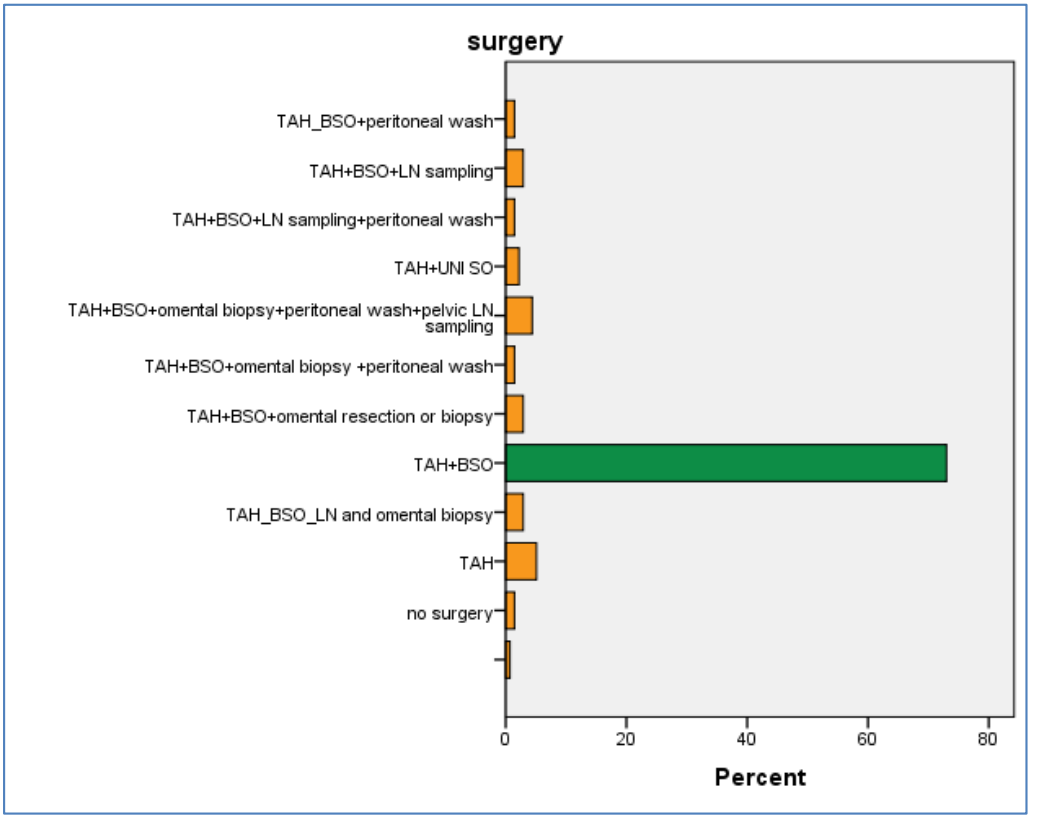

Figure 3.3: Type of Surgical Management of Participants

Table 3.2: Histological Types of Uterine Cancer

Histological type	Frequency	Percent %
EIN	2	1.5
Endometroid type	93	67.9
Endometroid type with squamous diff.	10	7.3
Clear cell type	2	1.5
Mucinous type	1	0.7
Papillary serous type	7	5.1
MMMT	7	5.1
Leimyosarcoma	6	4.4
ESS	6	4.4
Small cell type	1	0.7
Total	135	100

Some of the cases had additional tumor at the time of diagnosis, including endometroid adenocarcinoma, ovarian cyst serous adenoma, and ovarian mucinous cyst in 5% of the cases (6 instances). In addition, one instance was diagnosed with cervical metaplasia and uterine cancer.

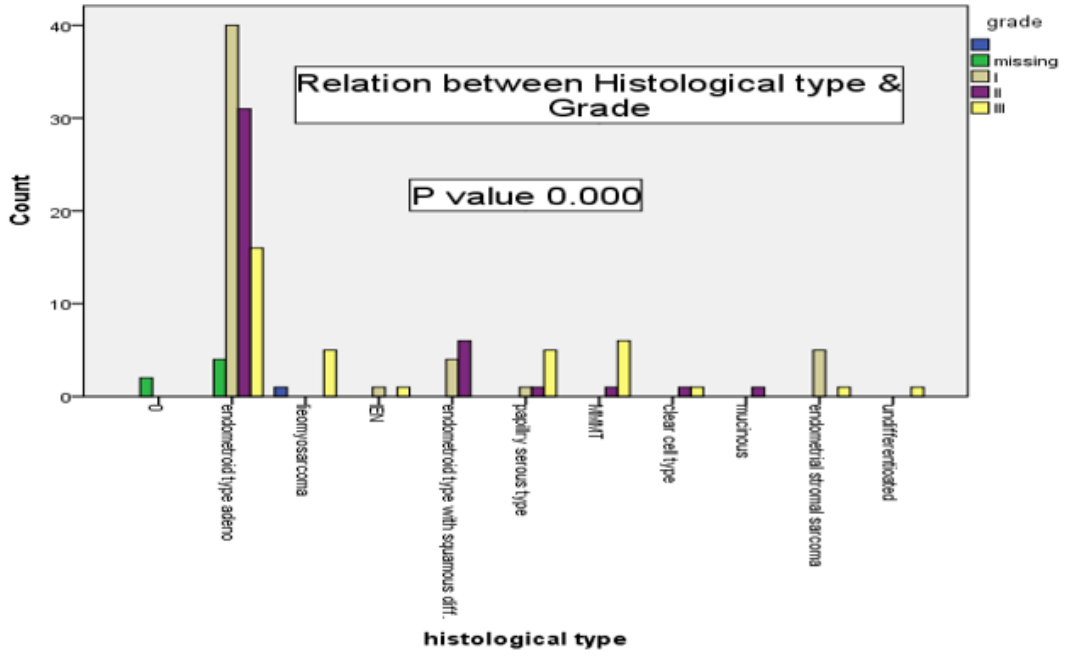

Figure 3.4: Relation between Histological type &Grade

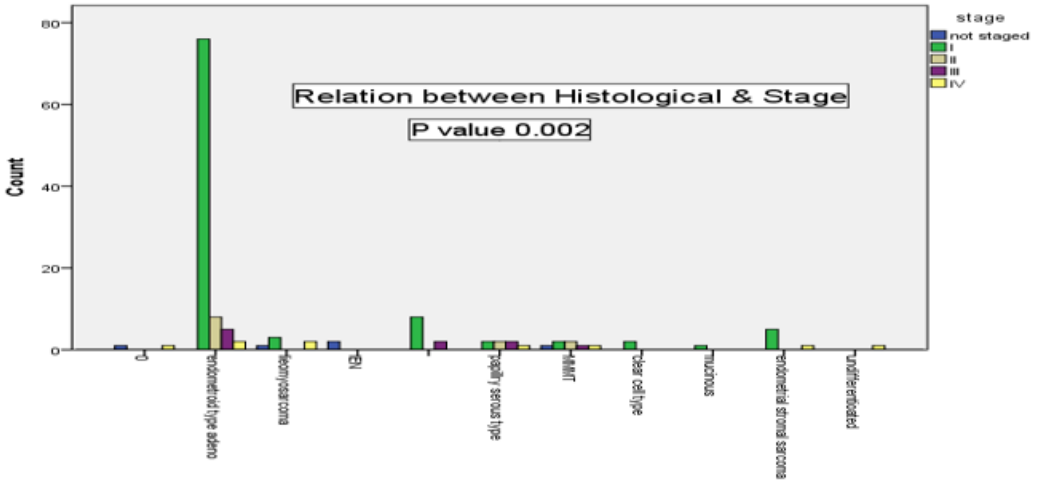

Figure 3.5: Relation between Histological type and Stage

During the research, the correlation between menopausal state and different factors was assessed; it is significant for histological type and stage (p value=0.04). This can be seen in the following table:

Table 6: the association of the menopausal state with cancer characteristics

Factors	Premenopausal	Postmenopausal	P-value
Histology	68.3% Endometroid type 14.7 Sarcoma 4.9% MMMT 7.2% Other Carcinomas 4.9% EIN	80% Endometroid type 6.4% Sarcoma 6.3% MMMT 7.6% Other Carcinomas	0.04
Stage	65.9% stage I	77.5% Stage I	0.04
Grade	39% grade I	40% grade I	0.9

Discussion

In Iraq, particularly in Kurdistan, there is a dearth of study on corpus uterine cancer patterns. This is the first report on the epidemiology of corpus uterine cancer in the Kurdistan Region of Iraq. It reflects cancer's incidence, demographics, and clinicopathological pattern in Iraq's Sulaymaniyah province and Kurdistan region.

This research yielded some intriguing results. First, the ASR for corpus uterine cancer in the Hiwa cancer center, which represents Sulaymaniyah, was reasonably high (3.84 per 100 000 women) for the entire study period from 2014 to 2018, compared to the time prior to 2014, which was notably low. According to a study published by Khoshnaw N et al. 20 on cancer patterns in Sulaymaniyah province from 2006 to 2014, it was around 1.34. Furthermore, according to (GLOBOCAN 2018)10, the ASR of corpus uterine cancer for high/high HDI

regions is 11.1 and for low/medium HDI regions is 3.3, which is similar to our ASR of 4.66 in 2018.

The highest rates of endometrial cancer were found in North America, Eastern, and Northern Europe, and the lowest rates were found in middle-income nations, according to a comprehensive international study on the pattern and trend of endometrial cancer in 46 different populations from 1978 to 2013. Rates grew in 26 of the 43 populations studied, with the biggest increases occurring in South Africa and numerous Asian countries. 11 Increased risk factors, improved screening and diagnostic procedures, and a higher-quality cancer registry are all contributing to the rising incidence of uterine cancer in our community.

Second, the peak age groups in our study were 50-59 and 60-69 years, with a median age of 58, which is lower than the peak age of 65-69 years in a study on female genital tract cancer in Basrah city/northern Iraq between 2005 and 200919, and also in an Egyptian study on 660 patients (1999-2010) by Alshahrani S, et al. 2, where the peak age was 60-69 years. While a study in Tunisia by Nabiha M et al. 18 estimated the median age at diagnosis to be 60 years old. Another study conducted in Yazd, Iran, on 84 patients with endometrial cancer with clinicopathological characteristics between 2005 and 2012 found that the median age was 58. 63
Furthermore, between 2013 and 201516, the peak age in the UK was 75-79 years, and >40 percent of women with endometrial cancer in the US are elderly. 12

In our area, there is a younger age group for corpus uterine cancer, which could be due to lifestyle changes and early exposure to risk factors or underlying hereditary causes. In addition, our population is youthful and rising. Although there is no more data to compare, our study found that 67 percent of participants were in menopause at the time of diagnosis, but in Egypt, 83 percent were postmenopause 2. Although there is no more data to compare, this also shows that uterine cancer develops at a younger age in our area. More than two-thirds of patients had a localized stage at the time of diagnosis, which matches various studies from different countries. 4-1 table

Table 4.1: Uterine cancer stages in various populations

Stage	Hiwa Center (%)	US (%)[3]	Gharbiah/Egypt (%)[2]
Localized	73.7	66.7	59.6
Regional	16.1	20.7	3.4
Distant	6.7	8.6	12.7
Unknown	3.6	3.7	24.1
Total	100	100	100

Endometroid type adenocarcinoma comprised for 75% of all instances, which is equivalent to the US study's 68 percent three and Egypt's 68 percent 2. Between 2005 and 2012, endometroid adenocarcinoma accounted for 85.7 percent of endometrial cancer in Yazd, Iran. 60 Furthermore, uterine sarcoma comprised for 8.8% of the total, which is a little lower than Egypt's 11.0 percent two but much higher than the United States' 3%. 3

Obesity is one of the factors leading to the rise in uterine cancer incidence; women who are overweight (BMI= 25.0-29.9 kg/m2) or obese (BMI 30 kg/m2) are two to four times more likely than women of normal weight to develop endometrial cancer13,14. This aspect was highlighted in this study by the fact that the majority of our cases were overweight to morbidly obese at the time of diagnosis, with just 7.9% having a healthy body weight. As a result, obesity appears to be the most important risk factor in our research. There may be other risk factors, as 46% of the patients had hypertension, type II diabetes, or both at the time of presentation. Diabetes is linked to obesity and has been linked to tumor genesis and progression through insulin resistance and hyperinsulinemia, increased steroid hormone bioavailability, and localized inflammation61. Type II diabetes causes an increase in insulin levels for long periods of time, both before and after disease onset, and is linked to an increased risk of typical hyperplasia and endometrial cancer independent of obesity because insulin has a direct proliferative effect. 62 In patients with endometrial cancer, both fasting insulin levels and non-fasting C peptide were considerably higher, according to a meta-analysis. 63

Even though the women had similar BMIs, Modesitt et al. 64 observed that obese women with and without endometrial cancer had inferior physical fitness and higher glucose levels as compared to those without endometrial cancer. In a prior study in Yazd, Iran, 33.3 percent of patients had hypertension, and 32.1 percent had diabetes when they were diagnosed.60 According to a meta-analysis of published observational studies on hypertension and the risk of endometrial cancer, women with hypertension have a 61% higher relative risk of having endometrial cancer. 65

Conclusions

This study verified that middle-aged women have the greatest rates of uterine cancer, with an increasing incidence over time; it also demonstrated the impact of environmental factors, particularly obesity, on the incidence of uterine cancer.

Recommendations

Effective primary care programs to assist women in achieving and maintaining a healthy weight; additionally, public awareness of the need of adequate physical exercise in reducing the incidence of endometrial cancer and other risk factors such as diabetes and high blood pressure. Future research should concentrate on the effect of environmental factors on the occurrence of uterine cancer. Abnormal vaginal bleeding should be evaluated as soon as possible to maximize the chances of early discovery and correct therapy of uterine cancer.

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