Obesity and Endometrial Cancer: The impact of a public health problem

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Abstract

Objective: To draw attention to the increase in the frequency of endometrial cancer (CE) in recent decades and its association with overweight and obesity in a highly specialized institution.

Material and Methods: Retrospective study of patients with EC treated in the Oncology Service of Mexico General Hospital, in the years 2000 to 2017, obtaining information related to some risk factors and their classification. The data were compared with a previous study from the years 1966-1993.

Results: Of the record of 1,045 EC treated during the studied time of 44 years, 785 corresponded to the period 2000-2017 and 260 to the previous report, which meant an increase of 200% for this disease. Of gynecological cancers, the EC figures increased from 17.9% in 2010-2011 to 29.4% in 2016-2017 (p = 0.0001). Overweight and obesity were in 572/785 (72.8%) of the current series vs. 120/260 (46.1%) of the previous series (p <0.05). An increase of 19% to 28% was found in women younger than 48 years when comparing the periods 2000 - 2009 vs. 2010-2017 (p = 0.011); 119/389 classified as stage I, (30.5%) had risk factors for tumor recurrence and 378/898 (42.0%) had advanced malignancies.

Conclusions: An increase in CE reported in this series and its association with overweight and obesity, may highlight the public health problem that this association represents in our country.

keywords: obesity and endometrial cancer a public health problem

Background: Endometrial cancer (CE) is the first gynecological neoplasm diagnosed in developed countries [1]. In the United States of America (USA) the American Cancer Society (ACS) published a total of 63,230 cases for 2018, representing 57.7% of the gynecological cancers registered that year[2].
The World Health Organization (WHO) registered in 2018 in Mexico a frequency of CE of 7,266 cases, so it is the second gynecological malignancy just below cervical cancer [3]. This was the first time in our country that EC replaced the epithelial ovarian cancer (EOC) that had occupied this place until then, according to the Epidemiology Directorate of the Ministry of Health [4].
It has been established that overweight and obesity are closely linked to the development of EC, proof of it is that USA is having a dramatic impact on the incidence of CE because de epidemy of obesity[5,6.]
The metabolic and endocrinological effects of menopause and obesity may explain them association with EC, such as high levels of estrogens resulting from the conversion of androstenedione to estrone, the aromatization of androgens to estrogens in peripheral adipose tissue and high insulin levels. However, many unresolved questions arise from the interaction between obesity, estrogens, and insulin as mediators of endometrial carcinogenesis [6].
The National Institute of Public Health (NIPH) published in 2018 that in Mexico the prevalence of overweight and obesity has increased in the last 3 decades, making it one of the two countries with the highest prevalence of obesity in the world. In adults aged 20 years and over, the prevalence of overweight and obesity in 2016 was 72.5% [7] and, according to the National Survey of Health and Nutrition (NSHN) this percentage increased to 74.9% in 2018.[8].
This article shows the frequency and increase in recent decades of EC in the General Hospital of Mexico (MGH) and its relationship with the rest of gynecological cancers over time, [9,10] we attribute it to its association

with overweight and the obesity.

Material and methods: Retrospective and observational study in patients with a histopathological diagnosis of EC treated at the MGH Oncology Unit during the years 2000 to 2017, obtaining risk factors for EC such as age, overweight and obesity, hypertension and diabetes. The cases were classified according to the Clinical Stage (CS) of the International Federation of Gynecology and Obstetrics (FIGO) in its 2009 version. [1,11].

We compared the frequency of EC in three time periods, the first from 1983-1984, the second from 2010-2011 and finally from 2016-2017 10. The results obtained in terms of risk factors and CS from the period 2000 to 2017 were compared with the data recorded for the period 1966-199312. A body mass index (BMI) of 25-29.9 was considered overweight and a BMI of 30.0 - 50 obesity [6.8.] For statistical analysis we use the Epi-info v7 system and the Chi square test. Confidence values of less than 95% were specific without statistical significance (NS).

Results: In this study we registered a total of 1,045 patients with CE in a 44-year period, of these, 785 cases corresponded to the time period between 2000 and 2017. In a first period of 27 years, we treated 260 patients, while in the last 17 years a total of 785 patients, which meant a 200% increase in the frequency of this disease. Table 1

Table 1
Endometrial Cancer
Patients registered in 44 years

Period	Nº. of years	Nº. of patients
1966-1993	27	260
2000-2009	10	243
2010-2014	5	268
2016-2017	2	274
Total	44	1,045

The analysis of the relative frequency of gynecological cancers in 3 different variables, selected when comparing the periods 2010-2011 vs. 2016-2017; an increase in EC figures from 17.9% to 29.4%. (p = 0001), data that place it in second place among gynecological cancers of the Oncology Unit Table 2.

Table 2
Gynecological cancer. Relative frequency at different times.

Neoplasm	(I)1983-1984		(II) 2010-2011		(III)2016-2017		Significance
	Nº	%	Nº	%	Nº	%	
1. Cervical cancer	727	86.8	632	57.8	427	45.8	I vs.II p<.05
2. Uterine corpus cancer	38	4.5	197	17.9	274	29.4	I vs. II p<.05
3. Epithelial ovarian cancer	52	6.2	213	19.7	206	22.1	I vs. II p<.05
4. Vulvar cancer	16	1.9	22	2.0	22	2.3	I vs.II p=.845
5. Vaginal cancer	4	0.4	16	1.4	2	0.2	I vs.II p=.032
Total:	837	99.8	1,080	99.8	931	99.8	

1.(II) vs.(III) p<.05   2.(II) vs. (III) p.0001   3.(II) vs. (III) p=.185   4.(II vs.III) p=.618   5.(II) vs. (III) p=.003

When comparing the risk factors analyzed for EC, for the 1966-1993 vs 2000-2017 intervals, an increase from 46.1% to 72.5% (p = <05) was found in terms of overweight and obesity; of hypertension from 30 to 33% (p = 0.412) and diabetes from 25.0% to 31.4% (p = 0.048) Table 3

Table 3
Risk Factors

| Variable | Period analyzed | | | |
| | 1966-1993* | | 2000-20017** | |
	N° of patients	%	N° of patients	%
Obesity	120	46.1	(b) 572	72.5
Hypertension	78	30.0	(b) 260	33.0
Diabetes	65	25.0	(b) 248	31.4
Total:	260		788	

*Average age: 57 years. **Average age: 55 years.
Significance: (1) (a) vs. (b) p<0.05 . (2) (a) vs. (b) p= 0.412
(a) vs. (b) p= 0.048

The average age for the 1966-1993 period was 57 years and for the 2000-2017 period it was 55 years. In the first, only 6.1% of the patients were 40 years old or younger compared to 9.5% of the patients in the second period (p = 0.095). Likewise, 19.0% of the patients in the first period were 48 years old or younger compared to 28.0% of those in the second period (p = 0.011). Table 4.

Table 4
Frequency in premenopausal patients

Age groups	Period	N°	%	Significance
≤ 40 years	1966-1993	16/260	6.1	P=0.095
	2000-2017	69/723	9.5	
> 40 and ≤ 48 years	2000-2009	40/210	19.0	P=0.011

Only in 874 cases did we obtain the histopathological varieties, 745 (85.2%) corresponded to endometroid carcinomas (Type 1) and 129 (14.7%) to non-endometroid carcinomas (Type 2) [1,11] Table 5.

Table 5
Histopathological classification

Histopathological classification	N° of patients	%
Endometroid (Type 1)	745	85.2
Non endometroid (Type 2)	129	14.7
Total:	874	99.9

CS was obtained in 898 patients. A ratio of 116 (48.7%) patients in the first group was classified in stage I compared to 404 (61.2%) of those in the second (p = 0.001). We consider advanced neoplasm as CS II, III and IV, of these we added 378/898 (42.0%) patients in the global series Table 6.

Table 6
Relation of clinical stages in two different periods

| Clinical stage | Period analyzed | | | | Significance |
| | 1966-1993 | | 2000-2017 | | |
	Nº of patients	%	Nº of patients	%	
I	116	48.7	404	61.2	P=0.001
II	35	14.7	77	11.6	P=0.224
III	54	22.6	118	17.8	P=0.128
IV	33	13.8	61	9.2	P=0.045
Total:	238	99.8	660	99.8	

Of the patients classified in CS I from the period 2000 to 2009, 113/147 (84.0%) were diagnosed as overweight and obese. And of the stage I patients diagnosed between 2000 and 2017, 119/389 (30.5%) had risk factors for tumor recurrence (Stages Ia: vascular infiltration and / or high degree of malignancy 3 and stages Ib: myometrial infiltration equal to or more than 50%) [1,11]

Discussion: Although cervical cancer remains the predominant gynecological cancer in the MGH Oncology Unit 10, its frequency has shown a decrease, which coincides with the WHO publication in 2018 for Mexico. This may contribute to the increase in the incidence of EC, which is now the second gynecological neoplasm in our country[3].
The increase in the number of overweight and obesity documented in several countries after 1975 [5,13] was associated with a higher incidence of EC as in the USA. This obesity epidemic has had a dramatic impact on public health. The average age of presentation of this disease is 60 years or more, but in overweight and obese patients it is less than 60 years. [5,6,13].
In the authors series from the years 1966-1993, the average age was 57 years and 46.1% of the patients reported overweight and obesity [12], while for the age from 2000 to 2017, the average age was 55 years and 72.5% were overweight and obese (p = <05). Up to 28% of the patients in this last series were premenopausal (48 years of age and younger).

It is surprising the 274 cases of EC diagnosed in the last period of 2016-2017, which exceeded those that we remember in the previous period of 27 years of duration [5,10,12]. The NSHN published in 2018 data on overweight and obesity registered in our country in the last 30 years with figures of 34.5% for 1988, 61% for 1999, 69.3% for 2006, 71.2% for 2012 and 74.9% for 2018 8. In 2012, the figures for overweight and obesity for women were 73% and 76.8% for 2018 8. Figure 1 shows the correlation between overweight and obesity, with the increase in EC reported in our Oncology Unit for the intervals 1966-1993[12] and 2000-2017.

In a series of 274 cases of EC published in 2013 by the Mexico National Cancerology Institute (MNCI), reference was made to an age of 54 years for these patients, and an overweight and obesity of 72.6% [14]. BMI is the main factor for predicting the risk of other chronic diseases such as diabetes and hypertension, conditions that influence the incidence and prognosis of EC [1,5,6]. These factors are currently present in 31.4% and 33% of the present study for the years 2000-2017 with statistically specific differences for the increase in diabetes in the period 2000-2017 (p = 048).

Although more than 80% of endometroid-type ECs are linked to overweight and obesity, current reports are also related to these risk factors with type 2 non-endometroid cancers whose prognosis is less favorable [1,5].

The increase from 19% to 28% of CE cases in women younger than 48 years diagnosed in 2000-2009 vs 2010-2017 (p = 0.011) stands out, which 84% of those classified in Stage I of the 2000-2009 period, they were overweight and obese; that 30.5% of this last group had risk factors for tumor recurrence [1,11] and that 42.0% of the overall series, had advanced malignancies[1,11].

Abnormal genital bleeding in overweight and obese premenopausal women with EC was present in only 28% of patients in the current series, which may delay timely diagnosis. [1,5,6,11].

On the other hand, the treatment of choice for CE is surgical; in stage I injuries with recurrence factors and advanced injuries, surgery should include systematic lymphadenectomy or at least lymph node biopsy, [1,11]. These complex procedures, in addition to promoting morbidity in overweight and obese patients [1,5,6], must be accompanied by adjuvant therapies including radiotherapy or chemoradiotherapy. [1,11] The patients who had a less favorable prognosis are those with obesity, additional comorbidities, EC type 2 and advanced lesions (stages II, III and IV) [1,5,6,14]

Conclusions: In this series we find an increase in EC of 200% in relation to what was published in the previous study of our institution. For overweight and obesity, the figures rose from 46% to 72.5% (p = 0.05). Likewise, an increase from 19% to 28% of EC was reduced in women younger than 48 years (p = 0.01).

It was found that 30.5% of the patients with early stages of EC had risk factors for tumor recurrence and 42% of the overall series had advanced malignancies, which has affected their prognosis.

The increase in overweight and obesity and in the EC figures reported in this series, may highlight the public health problem that this association is representing in our country.

Conflict of interests
The authors declare that they have no conflict of interest.

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