Obesity and Endometrial Cancer: Increase in Frequency over a Period of 44 Years

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Abstract: 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. Retrospective study of patients with EC treated in the Oncology Service (OS) General Hospital of Mexico (GHM), 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. 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. 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, Endometrial, Cancer, Increase, Frequency

1. Background

Endometrial cancer (CE) is the first gynecological neoplasm diagnosed in developed countries [1, 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 [5, 6]. The metabolic and endocrinological effects of menopause 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 [6]. However, many unresolved questions arise from the interaction between obesity, estrogens, and insulin as mediators of endometrial carcinogenesis [6, 7].

The National Institute of Public Health in Mexico published in 2018 that 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 [8]. In adults aged 20 years and 78 over, the prevalence of overweight and obesity in 2016 was 72.5%

and, according to the National Survey of Health and Nutrition (NSHN) this percentage increased to 74.9% in 2018 [9].

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. We attribute it to its association with overweight and the obesity.

2. Material and Methods

Retrospective and observational study in patients with a histopathological diagnosis of EC treated at the MGH 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, 10, 11].

We compared the frequency of EC in three time periods, the first from 1983-1984 [12], the second from 2010-2011 [13] and finally from 2016-2017. The results obtained in terms of risk factors and CE from the period 2000 to 2017 were compared with the data recorded for the period 1966-1993 [14]. A body mass index (BMI) of 25-29.9 was considered overweight and a BMI of 30.0 - 50 obesity [6, 9]. For statistical analysis we use the Epi-info v 7 system and the Chi square test. Confidence values of less than 95% were specific without statistical significance (N. S.).

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.

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.

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.

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 from period 2000 to 2009 were 48 years old or younger compared to 28.0% of those in the period 2020 to 2017 (p=0.011) Table 4.

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, 10].

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.

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 and stages Ib: myometrial infiltration equal to or more than 50%) [1, 10, 11].

Table 1. Endometrial cancer. Registered patients in 44 years.

Period	No. of years	No. Of patients	Significance
(a).1966-1993	27	260	P<0.05
(b).2000-2017	17	785	
Total:	44	1045	

(a) vs (b): (9 cases vs 46 cases by year).

Table 2. Gynecological cancer. Relative frequency at different times.

Neoplasm	(I) 1983-1984		(II) 2010-2011		(III) 2016-2017		Significance
	No.	%	No.	%	No.	%	
1. Cancer of cervix	727	88.9	632	60.6	427	47.0	I vs. II p<.05
Corpus uterine cancer	38	4.6	197	18.9	274	30.2	I vs. II p<.05
Epithelial ovarian cancer	52	6.3	213	20.4	206	22.7	I vs. II p<.05
Total:	817	99.8	1,042	99.9	907	99.9	

1.(II) vs.(III) p<.05 2.(II) vs. (III) p. 0001 3.(II) vs. (III) p=0.2245.

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		785	

*Average age: 57 years. **Average age: 55 years.
Significance: 1 (a) vs. (b) p<0.05, 2 (a) vs. (b) p=0.412 3 (a) vs. (b) p=0.048.

***Table 4.** Frequency in premenopausal patients.*

Age groups	Period	Nº	%	Significance
<40 years	1966-1993	16/260	6.1	P=0.095
	2000-2017	69/723	9.5	
48 years and<	2000-2009	40/210	19.0	P=0.011
	2010-2017	144/513	28.0	

3. Discussion

The increase in the number of overweight and obesity documented in several countries after 1975 [15] was associated with a higher incidence of EC as in the USA [5]. 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, 15]. 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 [14], 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).

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 [9]. In 2012, the figures for overweight and obesity for women were 73% and 76.8%

for 2018 [9]. Figure 1 shows the correlation between overweight and obesity, with the increase in EC reported in our Unit for the intervals 1966-1993 and 2000-2017.

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 EC 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, 4].

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 and that 42.0% of the overall series, had advanced malignancies [1, 10, 11].
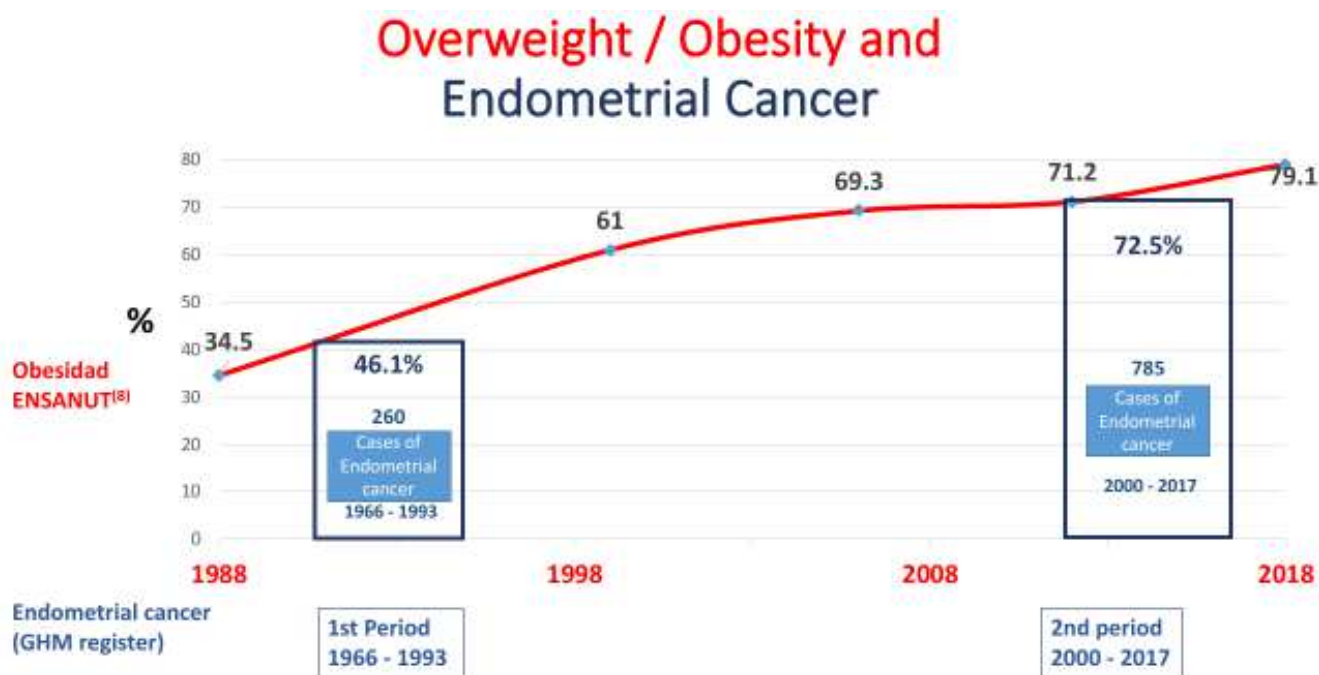
***Figure 1.** Correlation of overweight and obesity in Mexico from 1988 to 2018. Endometrial cancer in Mexico General Hospital in the periods 1966-1993 and 2000-2017.*

4. 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 observed 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

All the authors do not have any possible conflict of interest.

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Biography

Alfonso Torres Lobaton: Founder of Oncology Gynecology Residence in Mexico and Professor of the Oncological Gynecology Specialty, Graduate Division of the National Autonomous University of Mexico School of Medicine. Emeritus Member of the Mexican Academy of Surgery, Full Member of the Mexican Society of Oncology, Former Head of Gynecology Oncology, Former Head and Technical Consultant of the Oncology Service Hospital General de México. Former president of the Mexican Council of Oncology. Author of 110 articles on cancer and 2 books on Gynecological Cancer: 1st. Ed Think ISBN 968-882-061-x, 2000 and 2nd. Ed. Mc Graw Hill ISBN 970-10-4376-6.2004.

Rosalva Barra Martinez: Surgeon Oncologist, Master of Science, Full Member of the Mexican Society of Oncology. Associate Professor of the Specialties of Oncological Surgery and Oncological Gynecology. Graduate Division of the Faculty of Medicine of the National Autonomous University of Mexico, Tutor of 10 theses of the specialty and Author of 5 chapters of Oncology books and publication of 20 articles on cancer.

Elisa Paola Jimenez Arroyo: Gynaecological Oncologist who started her medical training in the Autonomous University of The State of Mexico. Afterwards, she made the Gynecology and Obstetrics specialty and Oncoloical Gynaecology subspecialty at General Hospital of Mexico, with both degrees endorsed by National Autonomous University of Mexico. She has training in colposcopy, as well as minimal invasive surgery. She has participated in papers such as vulvar cancer surgery and its evolution in time, and the changes in epidemiology of gynaecological cancer in Mexico.

Juan Carlos Oliva Posada: General Surgeon and Oncologist Surgeon. Head of the Gynecological Tumors Unit in the Oncology Unit of the General Hospital of Mexico. Counselor of the Mexican Council of Oncology. Professor at Anahuac University in cancer biology course. Member of the National Unit of the Angeles group. He has participated in international papers of Vulvar, Endometrial and Cervical Cancer.

Carla America Suarez Juarez: Gynecological Oncologist who began her medical training at the La Salle Mexico School of Medicine, she completed the specialty of Gynecology and Obstetrics and the subspecialty of Oncological Gynecology at the General Hospital of Mexico. She is trained in colposcopy as well as minimally invasive surgery. He has participated in international papers of Vulvar, Endometrial and Cervical Cancer. She currently works at the Angeles Metropolitano Hospital, and his member of the Mexican Society of Oncology.

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