



Hospitalization burden associated with malignant neoplasia and in situ carcinoma in vulva and vagina during a 5-year period (2009–2013) in Spain: An epidemiological study



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ABSTRACT

Background: Vulvar and vaginal cancers are considered rare cancers in women. Human Papillomavirus is responsible for 30–76% of them. The aim of this study was to describe the burden of hospital admissions by malignant neoplasia (MN) and in situ carcinoma (ISC) of vulva and vagina from 2009 to 2013, in Spain. **Methods:** This observational, descriptive study used discharge information obtained from the national surveillance system for hospital data, Conjunto Mínimo Básico de Datos, CMBD, provided by the Ministry of Health. **Results:** From 2009–2013, we found 9,896 hospitalizations coded as MN or ISC of vulva and vagina. Mean age of hospitalization was 69.94 ± 15.16 years; average length of hospital stay (ALOS) was 10.02 ± 12.40 days, and mean hospitalization costs were $5,140.31 \pm 3,220.61$ euros. Mean hospitalization rate was 9.874 per 100,000 women aged > 14 years old (95% CI: 9.689–10.058); mean mortality rate was 0.932 per 100,000 women aged > 14 years old (95% CI: 0.872–0.991) and mean case fatality rate was 9.438% (95% CI: 8.862–10.014). **Conclusion:** MN and ISC of vulva and vagina are responsible for a considerable hospitalization burden. Information about these hospitalizations could be useful for cost effectiveness analysis and monitoring of HPV vaccination effectiveness.

1. Introduction

According to IARC (International Agency Research of Cancer) estimations, around 14.1 million new cancer cases and 8.2 million cancer deaths occurred during 2012 worldwide [1]. Previous data indicated that gynecological cancers accounted for 19% of total female cancers [2]. Vulvar and vaginal cancers are considered as rare cancers in women [3]. It is estimated that 34,000 new cases of vulvar cancer and 15,000 new cases of vaginal cancer occurred in 2012 worldwide [4]. Around 68% of the vaginal cancer cases occur in less developed countries. In contrast, 60% of vulvar cancer cases occur in more developed countries [3]. While cervical cancer is estimated to be higher in women between 30 and 39 years old, vulvar and vaginal cancers occur more frequently in older women, aged 70+ [5].

In Europe, the estimated annual number of cases of vulvar and vaginal cancer is 9,544 and 2,171, respectively [6].

Data about incidence of vulvar and vaginal intraepithelial neoplasia

(VIN and VaIN, respectively) is estimated based on registries from Scandinavian countries. The age-standardized incidence rate of high grade VIN ranged between 2.5 and 8.8 per 100,000 women and, for high grade VaIN, between $0.5/10^5$ and $1.3/10^5$, worldwide [5]. The age of appearance of these lesions is also higher than for cervical neoplasia; as vulvar and vaginal pre-invasive neoplasia peaked in women aged 40–49 and 60–69, respectively [5]. In Europe, between 13,886–27,592 high-grade VIN (VIN2/3) cases and 2,549–4,719 high-grade VaIN (VaIN 2/3) cases are estimated to occur each year [6].

According to the most recent studies, human papillomavirus DNA was detected in 86.7% and 28.6% of VIN and invasive vulvar carcinoma (IVC), respectively and in 74% of invasive vaginal cancers and 96% of VaIN2/3. Most of the HPV positive invasive vulvar and vaginal carcinomas were squamous cell carcinoma basaloid or warty basaloid, and the prevalence of HPV was higher among women up to 55 years old [7,8].

Apart from the age of appearance and the type of carcinoma, there

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are other factors that can differentiate HPV positive from HPV negative vulvar and vaginal cancer. HPV positive vulvar cancers are usually preceded by precancerous high grade lesions and risk factors are similar to cervical cancer ones; such as number of sexual partners, age of sexual debut and other cofactors involved in human papillomavirus carcinogenesis such as tobacco smoking. In contrast, HPV negative vulvar cancers are usually associated with p53 mutations and it usually appears after long-term chronic lesions such as lichen sclerosus and no cervical cancer risk factors are usually found [9].

Regarding HPV type specific contribution, based on HPV DNA, type 16 is the most commonly detected one. It is estimated that HPV16/18 and HPV31/33/45/52/58 are present in 72.6% and 13% of HPV vulvar cancers; and 79.8% and 13% HPV VIN2/3, respectively. For HPV vaginal disease, HPV16/18 and HPV31/33/45/52/58 are present in 63.7% and 20.3% in cancer, and in 63.8% and 13.5% in high-grade lesions, respectively. The percentage of multiple infections in vulvar invasive cancer was 6.1%, in vaginal cancer 4.0%, in VaIN 2/3 11.0% and in high grade vulvar precancerous lesions 9.0% [10].

In Spain, information about vulvar and vaginal cancer incidence comes from the Spanish Regional System of Cancer Registry, REDECAN, which includes 14 regional registries from different areas of Spain. No national cancer registry exists currently. According to this registry, the age-standardized incidence of vulvar and vaginal cancer ranges between 0.8–1.5 and 1.5 and 0.0–0.5 cases per 100,000 women per year, respectively [3]. In line with global figures, Spanish incidence rates are highest in women aged 70+ [3].

Last published data about burden of hospitalizations of malignant neoplasia and in situ carcinoma of vulva and vagina in Spain in 2011 showed that the time trend in hospitalization incidence rate had remained quite stable from 1997 to 2008 [11]. This paper showed, for the first time in Spain, the national burden of hospital admissions due to these diseases. During this period, almost 18,000 hospitalizations related to malignant neoplasia of vulva and vagina, and over 2,000 hospitalizations related to in situ carcinomas in these sites occurred in our country. The fact that no significant changes in the hospitalization rate were observed during 1997–2008 in that study can be explained by the absence of standardized screening programs for these types of cancers [12]. However, a decrease in the incidence of HPV related vulvar and vaginal cancers and precancerous lesions could be expected during the next decades as result of the HPV vaccination program. In Spain, this program started in 2007 and targeted 11–14 year-old girls with a 3-vaccine dose schedule [13,14]. Nowadays, the immunization program against papillomavirus has decreased the vaccination age to 12 years with a 2-dose schedule reaching a vaccine coverage rate of around 77% [15]. No formal catch up for women older than 15 years-old was implemented at the beginning of the HPV vaccination program, thus, vaccine coverage rate in females out of the national vaccination program is very low, under 1% [16].

This study, like the previous study, used a hospital discharge database, Conjunto Mínimo Básico de Datos (CMBD), that has proven to be useful for the evaluation of HPV related hospitalizations and other hospitalization associated diseases [11,17,18].

Our aim is to describe the burden of hospital admissions by malignant neoplasia (MN) and in situ carcinoma (ISC) of vulva and vagina in Spain from 2009 to 2013.

2. Methods

This was an epidemiological, descriptive study that used discharge information obtained from the national surveillance system for hospital data, CMBD, provided by the Ministry of Health. This database contains data about admission and discharge date, age, sex, geographical region, diagnosis and discharge status for all hospitalizations in our country. It uses clinical codes from the Spanish version of the 9th Internal Classification of Diseases (CIE-9-MC) [19]. It is estimated to cover around 98% of public hospital admissions, and 99.5% of the population

in Spain [20]. We assumed that for population and hospitalizations not covered by CMBD, epidemiological characteristics are very similar.

We selected all hospital discharges related to MN and ISC of vulva and vagina in any diagnostic position during a 5 year period (2009–2013) (ICD-9-CM: 184, malignant neoplasia of other female genital organs and unspecified; 184.0 vagina; 184.1 labia majora, 184.2 labia minora, 184.3 clitoris, 184.4 vulva, unspecified, 184.8 other specified female genital organs; malignant neoplasia affecting sites next to female genital organs whose origin cannot be specified; 184.9, female genital organ, unspecified; 233.3 in situ carcinoma of other female genital organs and unspecified female genital organs; 233.30 unspecified female genital organ, 233.31 vagina, 233.32 vulva, 233.39 other female genital organ) [19]. For each case, we collected data about age, geographic region, funding scheme, type of discharge, average length of hospital stay (ALOS), diagnosis and therapeutic procedures associated to each hospitalization and outcome (recovery or death). Costs related to hospitalization were estimated by the Ministry of Health using the diagnostic cost group (DCG) system, which classifies hospitalizations into groups that are expected to generate similar use of hospital resources. Classification is based on diagnoses, procedures, age, presence of complications and co-morbidities.

For statistical analysis, we calculated the average number of hospitalizations, ALOS and the average hospitalization cost (euros), per year and by age. Incidence rates of hospitalization (per 100,000 women aged more than 14 years old), mortality rates (per 100,000 women aged more than 14 years old), and case fatality rates (%) were calculated per year, age and region. As denominator we used the data of the female population aged more than 14 years old from the municipal registers adjusted by the population targeted by hospitals covered by the CMBD.

We used Chi square test to assess significant differences in proportions, and ANOVA for multiple comparisons. Poisson models were used to assess differences in the hospitalization and mortality rates (per 100,000 women aged > 14 years old) between the years of the studied period (2009–2013) and the age group. Hospitalization rate and mortality rate were used as dependent variables, and the year and the age were used as independent variables.

All of the results were reported with their corresponding 95% confidence intervals (95% CI). For all tests, we considered a p value less than 0,05 to be significant.

3. Results

From 2009–2013, we found 9,896 hospitalizations coded MN or ISC of vulva and vagina in 6,600 females, which corresponded to a number of 1.5 hospitalizations per patient. During the studied period, mean age of hospitalization was 69.94 ± 15.16 years, and no significant changes in age of hospitalization was observed ($p = 0.2811$). 1,741 hospitalizations were registered in women up to 55 years old, and 8,155 in women above 55 years old. Average length of hospital stay (ALOS) was 10.02 ± 12.40 days, and mean hospitalization costs were $5,140.31 \pm 3,219.61$ euros. During the study period, we found a significant decrease in ALOS, from 11.00 ± 13.51 days in 2009, to 9.59 ± 11.88 days in 2013, $p < 0.001$. By contrast, hospitalization costs significantly increased during the same period; from $4,565.99 \pm 2,892.41$ euros in 2009; to $5,131.69 \pm 3,186.18$ euros in 2013, $p < 0.001$. Both variables showed significant increase with the age ($p < 0.001$ for ALOS and $p < 0.001$ for hospitalization costs). In women up to 55 years old, ALOS was 7.47 ± 8.08 days and mean hospitalization cost was $5,189 \pm 4,513$ euros; while in women above 55 years old, ALOS was 10.56 ± 10.25 days and mean hospitalization cost was $5,122 \pm 4,002$ euros. Women between 25 and 29 years old registered the maximum hospitalization cost.

Mean hospitalization rate was 9.874 per 100,000 women aged more than 14 years old (95% CI: 9.689–10.058); mean mortality rate was 0.932 per 100,000 women aged more than 14 years old (95% CI: 0.872–0.991) and mean case fatality rate was 9.438% (95% CI:

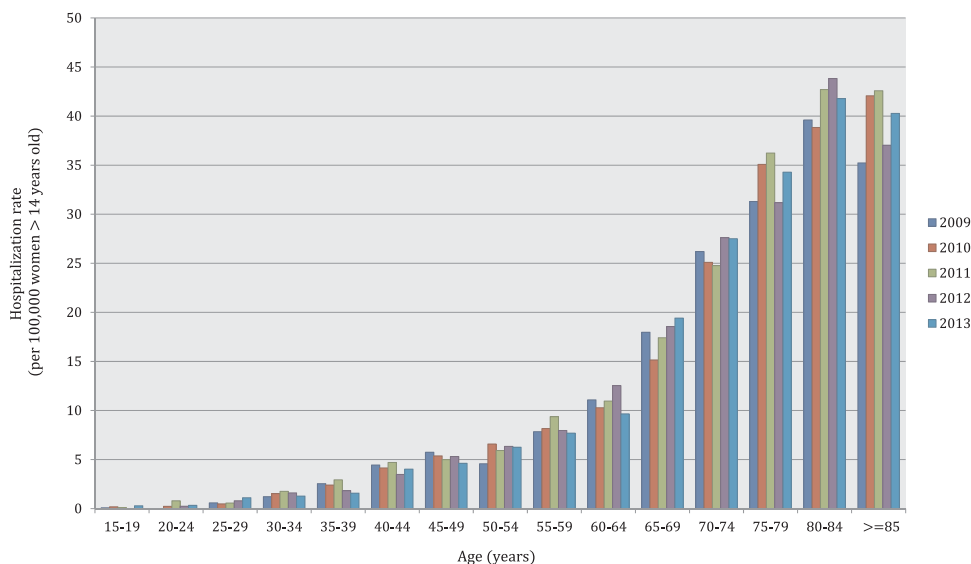


Fig. 1. Hospitalization rate (per 100,000) due to MN and ISC in vulva and vagina per age group and per year.

8.862–10.014). We did not observe significant differences across the study period for any of the assessed rates (hospitalization, mortality and case fatality rate). By contrast, we found a significant increase by age for all of them ($p < 0.001$) (Fig. 1), especially above 55 years of age. Mean hospitalization rate in females up to 55 years old was 2.697 per 100,000 women aged more than 14 years old (95% CI: 2.570–2.824); by contrast in females above 55 years old, mean hospitalization rate was 22.861 per 100,000 women aged more than 14 years old (95% CI: 22.365–23.357).

Different disease patterns were observed when we analyzed MN and ISC separately.

3.1. Malignant neoplasia of vulva and vagina

8,469 hospitalizations were coded for MN from 2009 to 2013; most of them (5,951) were related to the vulva. Of the 8,469 hospitalizations, 5,593 listed MN of vulva and vagina as first position.

Mean age of hospitalizations was 72.18 ± 13.54 years old and remained quite stable during the studied period ($p = 0.1326$); being women aged above 70 the ones with higher number of hospitalizations registered. Mean ALOS was 10.92 ± 12.97 days and we found significant differences by year ($p = 0.0015$) and by age groups ($p < 0.001$). Mean hospitalization cost was $5,276.98 \pm 3,281.45$ euros, and also differed significantly during the period ($p < 0.0001$) registering the highest mean cost in 2011 (5,580.37 \pm 3,274.53 euros) (Table 1). According to the age group, significant differences were also observed ($p < 0.0001$) and highest mean cost corresponded to women aged between 25 and 29 years old (Fig. 2).

Mean hospitalization rate was 8.450 per 100,000 females aged > 14 years old (95% CI: 8.278–8.622) and it remained quite stable during the studied period ($p = 0.397$), but it differed significantly by the age group ($p < 0.001$) (Table 2). By location (Fig. 3), hospitalization rate due to MN in the vulva is higher than for the rest of anatomic sites, and there was also an increasing trend with the age. According to the geographical distribution, Aragón, Galicia, Cantabria and Castilla León showed the highest values while Canarias, Baleares, Melilla and Andalucía showed the lowest value.

During this period, 922 deaths due to MN of vulva and vagina were registered within the hospital setting. Most of the deaths happened in women aged 70+. Mean mortality rate during the studied period, based on hospital registries, was 0.920 deaths per 100,000 women aged > 14 years old (95% CI: 0.861–0.979). As happened with hospitalization rate, only significant differences by age group were found

Table 1

Mean cost (euros) and mean average length stay (days) related to MN (malignant neoplasia) and ISC (in situ carcinoma) in vulva and vagina, in women per year of the studied period.

Year	Malignant neoplasia vulva and vagina			In situ carcinoma vulva and vagina		
	N	Mean cost in euros (SD)	Mean Average Length Stay in days (SD)	N	Mean cost in euros (SD)	Mean Average Length Stay in days (SD)
2009	1602.00	4701.23 (2965.14)	11.94 (14.13)	248.00	3753.98 (2231.41)	5.15 (6.26)
2010	1645.00	5527.30 (3718.96)	11.27 (13.96)	299.00	4303.73 (2614.11)	4.95 (6.58)
2011	1768.00	5580.37 (3274.53)	10.70 (12.48)	327.00	4696.07 (2971.23)	4.94 (6.30)
2012	1728.00	5293.40 (3080.72)	10.34 (11.79)	304.00	4613.18 (2935.14)	5.17 (7.18)
2013	1726.00	5245.60 (3251.08)	10.43 (12.44)	342.00	4509.80 (2742.18)	5.52 (7.11)
Total	8469.00	5276.98 (3281.45)	10.92 (12.97)	1520.00	4406.69 (2748.10)	5.15 (6.71)

($p < 0.001$) (Table 2). Within Spanish regions, Castilla León, Galicia, Melilla, Asturias and Aragón showed the highest mortality rates, and Baleares, Cataluña, Comunidad Valencia and Murcia recorded the lowest values for this rate.

Mean case fatality rate was 10.853% (95% CI: 10.189–11.517). Only significant differences by age were found, being highest for women aged more than 85 years old; 15.702% (95%CI: 17.620–13.784) (Table 2).

3.2. In situ carcinoma (ISC) of vulva and vagina

1,520 hospitalizations due to ISC of vulva and vagina were registered over the 5-year period, and 1,120 were listed as primary position. Most of them, 858, were record as ISC of vulva and the average number of hospitalizations per patient was 1.20.

Mean age of hospitalizations was 57.30 ± 17.45 years old and it was not stable during the period of the study ($p = 0.03$) (Table 1), being highest in 2013, 59.54 ± 18.06 years old. Mean ALOS was 5.15 ± 6.71 days, and this value remained quite stable over the 5 years. However, we observed a significant trend to increase according

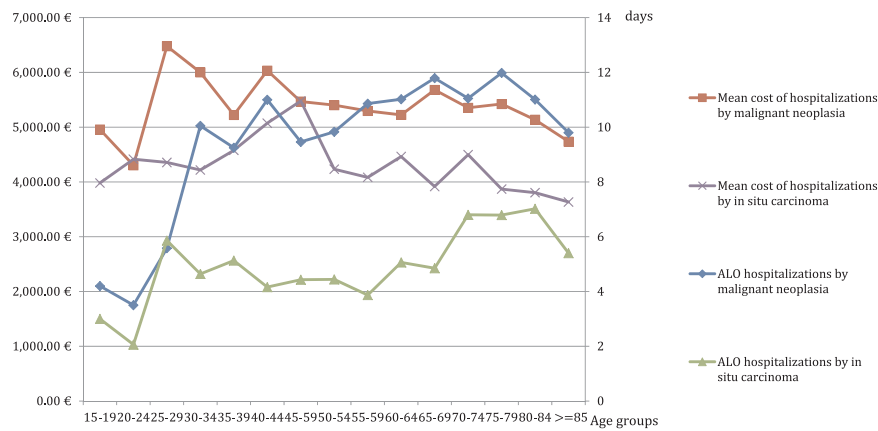


Fig. 2. Mean hospitalization cost, in euros, (left axis) and mean ALOS, in days, (right axis) associated to MN and ISC of vulva and vagina during the studied period (2009–2013) per age group.

to the age ($p < 0.001$). Mean hospitalization cost was $4,406.69 \pm 2,748.10$ euros (Table 1, Fig. 2).

Mean hospitalization rate was 1.516 per 100,000 women aged > 14 years old (95% CI: 1.441–1.592), and differed significantly during the period ($p = 0.029$) and by age group ($p < 0.001$) (Table 2, Fig. 4).

During the studied period, 13 deaths due to ISC of vulva and vagina were registered within the hospital environment. Mean mortality rate was 0.013 per 100,000 women aged > 14 years old (95%CI:

0.006–0.020) and the mean fatality rate was 0.860% (95% CI: 0.395–1.326%).

4. Discussion

A total of 9,896 hospitalizations related to MN and ISC of vulva and vagina occurred in Spain during 2009–2013. This corresponds to a hospitalization rate of 9.874 per 100,000 women aged > 14 years old.

Table 2

Hospitalization rate, mortality rate (per 100,000 aged > 14 years old) and case fatality rate (%) associated to MN and ISC of vulva and vagina during the studied period (2009–2013) per age group.

Age group	Malignant neoplasia vulva and vagina					In situ carcinoma vulva and vagina				
	Hospitalizations		Deaths			Hospitalizations		Deaths		
	N	Hospitalization rate (per 100,000 habitants > 14 years old) 95% CI	N	Mortality rate (per 100,000 habitants > 14 years old) 95% CI	Case fatality rate (%) 95% CI	N	Hospitalization rate (per 100,000 habitants > 14 years old) 95% CI	N	Mortality rate (per 100,000 habitants > 14 years old) 95% CI	Case fatality rate (%) 95% CI
15–19	5	0.093 (0.011–0.174)				2	0.037 (–0.014 to 0.089)			
20–24	4	0.063 (0.001–0.125)				16	0.253 (0.129–0.378)			
25–29	26	0.329 (0.203–0.456)				29	0.367 (0.234–0.501)	1	0.013 (0.000–0.037)	3.448% (0.000%–11.813%)
30–34	59	0.618 (0.460–0.776)	2	0.021 (0.000–0.050)	3.390% (0.000–8.007%)	85	0.891 (0.701–1.080)			
35–39	105	1.085 (0.877–1.292)	4	0.041 (0.002–0.082)	3.810% (0.148–7.471%)	118	1.219 (0.999–1.439)			
40–44	209	2.262 (1.956–2.569)	5	0.054 (0.007–0.102)	2.392% (0.321–4.464%)	181	1.959 (1.674–2.245)			
45–59	285	3.276 (2.896–3.656)	19	0.218 (0.120–0.317)	6.667% (3.771–9.563%)	171	1.966 (1.671–2.260)			
50–54	320	4.103 (3.654–4.553)	19	0.244 (0.134–0.353)	5.938% (3.348–8.527%)	149	1.911 (1.604–2.217)	1	0.013 (0.000–0.038)	0.671% (0.000%–1.982%)
55–59	453	6.766 (6.143–7.389)	38	0.568 (0.387–0.748)	8.389% (5.836–10.941%)	100	1.494 (1.201–1.786)			
60–64	581	9.256 (8.504–10.009)	43	0.685 (0.480–0.890)	7.401% (5.272–9.530%)	112	1.784 (1.454–2.115)			
65–69	879	15.955 (14.900–17.009)	87	1.579 (1.247–1.911)	9.898% (7.923–11.872%)	106	1.924 (1.558–2.290)	1	0.018 (0.000–0.054)	0.943% (0.000%–2.784%)
70–74	1146	24.170 (22.771–25.569)	127	2.679 (2.213–3.144)	11.082% (9.265–12.899%)	106	2.236 (1.810–2.661)	2	0.042 (0.000–0.101)	1.887% (0.000%–4.477%)
75–79	1519	31.000 (29.441–32.559)	168	3.429 (2.910–3.947)	11.060% (9.483–12.637)	143	2.918 (2.440–3.397)	1	0.020 (0.000–0.060)	0.699% (0.000%–2.065%)
80–84	1496	38.543 (36.590–40.496)	193	4.972 (4.271–5.674)	12.901% (11.202–14.600%)	124	3.195 (2.632–3.757)	3	0.077 (0.000–0.165)	2.419% (0.000%–5.124%)
> =85	1382	37.680 (35.694–39.666)	217	5.916 (5.129–6.704)	15.702% (13.784–17.620%)	78	2.127 (1.655–2.599)	4	0.109 (0.002–0.216)	5.128% (0.233%–10.023%)
Total	8469	8.450 (8.278–8.622)	922	0.920 (0.861–0.979)	10.853% (10.189–11.517%)	1520	1.516 (1.441–1.592)	13	0.013 (0.006–0.020)	0.860% (0.395%–1.326%)

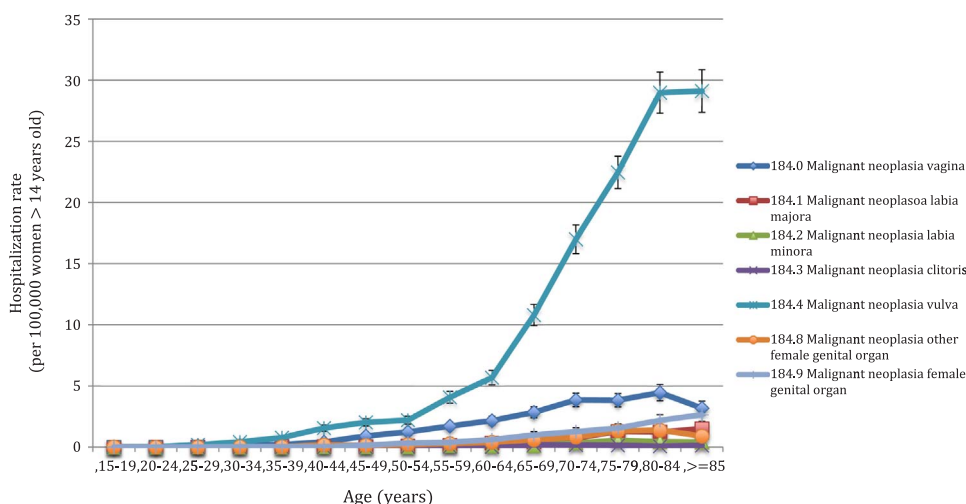


Fig. 3. Hospitalization rate (per 100,000 women > 14 years old) due to malignant neoplasia, by location, during the study period (2009–2013).

As the number of hospitalization per patient was 1.50, the estimated annual rate of patients hospitalized is 6.583 per 100,000 women aged > 14 years old.

We have observed that in general, there is an increase in all assessed rates by age. The same happened for ALOS, which means that in females above 55 years old, the hospital burden of these diseases is higher. In fact, more than 82% of hospitalizations are registered in women above 55 years old. This could be due to the fact that these diseases are more frequent in older women; hospitalization rate in women above 55 years old is 8.4-fold higher than in younger women. Additionally, when we assessed hospital burden, we are mainly considering the most severe cases of the disease. Other lesions, such as precancerous lesions in vagina and vulva, that affect younger females, are usually managed outpatient.

It is also important to note that HPV related vulvar disease is diagnosed more frequently in women up to 55 years old, which means that the majority of hospital burden would be non-HPV related.

Although ALOS and mean hospitalization costs were usually higher in older women, we found that the highest hospitalization costs for MN are registered in females between 25 and 29 years old. In those younger women, preserving genital anatomy and functionality is a factor that needs to be considered for disease management, thus, more conservative approaches could be recommended in these cases [21].

Over the studied period, we found almost no differences in

hospitalization, mortality and case fatality rates. ALOS has decreased, probably due to the advances in the management of these diseases during the last years. We also found important differences related to MN and ISC patterns: number of hospitalizations for MN was 5.6 fold higher than the ones for ISC, leading to a higher hospitalization rate for MN versus ISC. In addition, for MN, mean age of hospitalization was 72.18 years old, but in contrast, for ISC, mean age of hospitalization was 57.30 years old. Mean ALOS and costs were usually higher for MN than for ISC and case fatality rate for malignant neoplasia was 10.853% while for ISC, it was 0.860%.

Most of the burden of hospitalizations due to vulva and vagina MN and ISC corresponded to vulva related diseases. This is in concordance with the overall incidence rates of these diseases in Spain and Europe [3,6].

Comparing these results with the ones from the previous period, 1997–2008 [11], we observed a potential increasing trend in almost all assessed parameters. Hospitalization incidence rate due to MN and ISC increased from 7.054 and 0.862 cases per 100,000 women in 1997–2008 to 8.450 and 1.516 cases per 100,000 women > 14 years old during 2009–2013, respectively. Mortality rates for MN and ISC during 1997–2008 were 0.7 and 0.004 cases per 100,000 women, and 0.920 and 0.013 cases per 100,000 women aged > 14 years old during 2009–2013. Fatality rate has also increased; from 9.34% and 0.46% for MN and ISC during the previous period, to 10.853% and 0.860% for

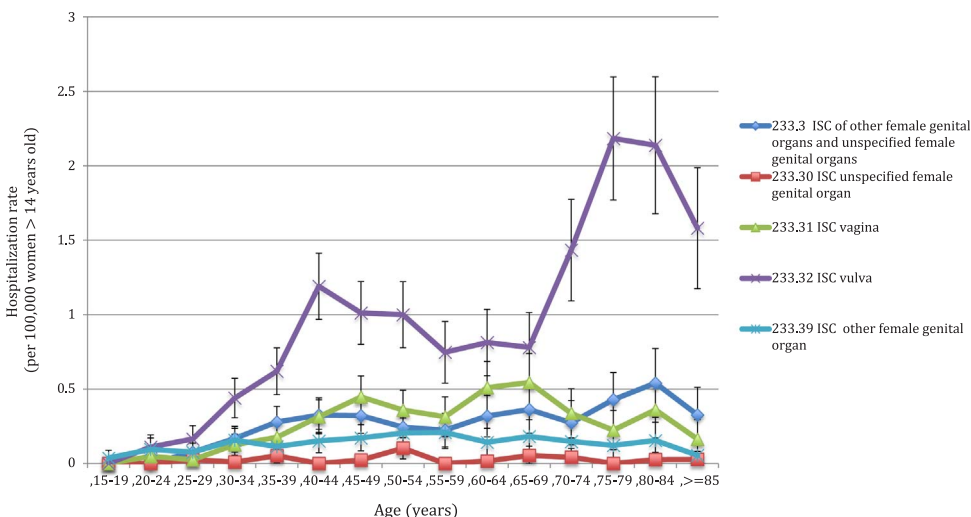


Fig. 4. Hospitalization rate (per 100,000 women > 14 years old) due to in situ carcinoma, by location, during the study period (2009–2013).

respectively, during 2009–2013. However, both studies are not identical, and comparison needs to be done cautiously.

We have also observed some differences among the different Spanish regions in the hospitalization rate, mortality rate and fatality rate. A north-south distribution for hospitalization rate associated to vulvar and vaginal MN was shown. This distribution was previously described during the period 1997–2008 [11]. These differences could be attributable to variability in informatics and codification systems, patient related factors or other factors related to clinical procedures or bed availability. However, the fact that this pattern remains stable during 16 years could be an interesting topic for future research. Data from CLEOPATRE study, which aimed to estimate the prevalence of cervical HPV infection in Spanish women attending cervical cancer screening, showed no statistically significant differences in HPV prevalence or in distribution of the HPV genotype between the geographical areas. Based on this, it is less likely that geographical differences could be due to differences in HPV prevalence [22].

In contrast, during 1997–2008, a north southwest pattern of hospitalization rate of vulva and vagina ISC was also described, however this distribution is not so evident in this follow up.

Our data also shows an important economic burden related to hospitalizations due to MN and ISC of vulva and vagina, that could represent around half of the annual cost related to hospitalizations due to cervical cancer in Spain, which has been previously estimated in 19 million of euros per year [18]. Apart from hospitalization costs, there are other outpatient costs that must be taken into consideration for economic evaluations. A recent study in Canada showed that hospitalizations for cervical cancer accounts just for 35% of total annual costs related to this cancer [23], which means that total economic burden of these cancers is markedly higher if we consider outpatient costs. A European review of economic burden of non-cervical cancers attributable to HPV showed that annual total costs for HPV related vulvar and vaginal cancers were 8.19 million euros in France during 2006. The same publication collected data from UK, that estimated lifetime treatment cost of 13,650£ per case of these types of HPV cancers [24]. In our case, we were not able to differentiate HPV related vulva and vagina MN and CIS from non-HPV related.

However, vulvar and vaginal cancers represent a small percentage of all HPV related diseases. In Spain, crude incidence rates of vulvar and vagina cancer are 1.9–3.6 cases and 0.0–1.1 cases per 100,000 women, respectively [3]. The attributable fraction to HPV is 74.3% for vaginal invasive cancers and 28.6% for vulvar invasive cancers; these percentages are higher for precancerous lesions in these locations. An organized screening program is not justified due to the low incidences of these diseases. Few years ago, the only prevention method was early diagnosis and adequate treatment of precancerous lesions [25]. Nowadays, HPV vaccines have shown to be effective in the prevention of HPV-related vulvar and vaginal lesions [26–31]. Although this study presents data from post vaccine era, it is expected that incidence rates associated to HPV diseases, included vulva and vagina cancers, will decrease in the following decades, when vaccinated girls approach ages of maximum incidence of these diseases. However, no reduction in non-HPV related vulvar and vaginal disease is expected as result of HPV vaccination program.

This study presents some limitations due to the use of the database, CMBD. The reliability of this database is influenced by the quality of gathering clinical histories and hospital discharge codifications [32]. There is a possibility of overcounting patients with multiple hospital admissions. Moreover, mortality rate estimations should be interpreted with caution as deaths could occur out of the hospital environment. Additionally, HPV infection is not always documented. However, hospital discharges database have shown to be adequate tools for cancer surveillance [33]. Other countries, like France, have also published data about number of cases of vulvar and vaginal cancers and dysplasia, using hospital medical information systems [34]. Finally, mortality rate could be affected by deaths happened out of the hospital environment.

Despite these limitations, our study could add important information about hospital burden of the assessed diseases.

5. Conclusion

Our analysis suggests that vulvar and vaginal malignant neoplasia and in situ carcinoma are responsible for a considerable hospitalization burden in our country that mainly affects women above 55 years old. These hospitalizations have changed substantially during the study period, probably due to clinical progresses: ALOS has decreased, in contrast with hospitalization costs that have increased during the last years... Information about these hospitalizations could be useful for Public Health decision-making and surveillance and also for cost effectiveness analysis and HPV vaccination monitoring.

Acknowledgement

Not applicable.

Conflict of interest

NL works for MSD Spain- Medical Department, AGM and RGP have received travel and research grants from SPMSD and GSK. JMRyC has received travel, medical education and research grants from SPMSD, MSD, GSK and Qiagen.

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Appendix A. Supplementary material

Supplementary data associated with this article can be found in the online version at <http://dx.doi.org/10.1016/j.pvr.2018.02.001>.

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