

*Opšti pregledi/
General reviews*

FEMALE GENITAL TRACT CANCER

RAK ŽENSKIH POLNIH ORGANA

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Key words

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Ključne reči

Kancer, grlić uterusa, jajnik, vagina,
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Abstract

Introduction: In the morbidity and mortality women, significant role have cancer breast and genital tract cancer.

Objective was to analyze the incidence of female genital cancers from the National Cancer Registry of Republika Srpska in a five-year period.

Method: Histopathologically confirmed cancer cases of vulva, vagina, uterine cervix, uterine body, uterine non-specific localization, ovarian and of other genital parts were analyzed for a 2003 -2008 year period, with five-year survival follow up with respect to its localization and histological type.

Results: Out of total number of newly diagnosed female genital tract cancer cases, 79.4% were detected in invasive phase, which is, with statistically significant difference $p < 0.01$ ($T = 25.6$, $d f = 1875$) much more than in situ stage (20.6%). Cervical cancer was most common in fertility period (59.2%) and in this age group was more frequent than in ≥ 49 year age group, which is statistically significant ($p < 0.01$). Newly detected cases on other localizations of female genital organs in more than 2/3 occurred in ≥ 50 year age group. Squamous cell carcinoma was the most common invasive cancer of cervix (87.2%), vulva (93.8%) and vagina (85.7%). Adenocarcinoma was the most common ovarian (88.2%), uterine (83.3%) and corpus uterus (78.9%) malignancy.

Discussion: Cervical cancer occurs in highest percentage in situ stage, which is essential in prevention of this disease.

Conclusion: During the monitoring period, the largest percentage of cervical cancer occurs in women in their fertile period and squamous carcinoma in 87.2% of cases, so that with preventive programs in order to prevent this disease should begin early in the fertile period.

INTRODUCTION

Cancer is the leading cause of death worldwide and accounted for 7.9 million deaths (about 13% of all deaths) in 2007, and predicts that this number is approximated to 12 million deaths in 2030. Among the leading causes of death worldwide each year, are the cancers at following localization: lung, stomach, liver, colon and breast. About 72% of all cancer deaths in 2007 occurred in low and middle income countries. Cancer causes 20% of deaths in the European region. With more than 3 million new cases and 1.7 million deaths each year, cancer is the most important cause of death and morbidity in Europe, after cardiovascular diseases.

However, cancer can largely be avoided, and early detection greatly increases the chances for treatment. Over 40% of all cancers can be prevented. Much is already known about the causes to prevent at least one third of all cancers, and some of the most common types - including breast, colon and cervical cancers - could be healed if detected early. Among the most common types of cancer in order of mortality worldwide are lung, stomach, liver, colon, esophageal and prostate cancers in men, and breast, lung, stomach, colorectal and cervical cancers in women (1).

Cervical cancer was the third most common cancer in women, and the seventh overall, with an estimated 529 000 new cases in 2008. The mortality incidence

ratio was 52%, and cervical cancer was responsible for 274 000 deaths in 2008, about 88% of which occurred in developing countries: 53 000 in Africa, 31 400 in Latin America and the Caribbean, and 159 800 in Asia (2).

Each year 471 000 cases and 233 000 deaths occur from cervical cancer worldwide, of which 80% occur in less-developed countries that have access to less than 5% of global cancer treatment resources (3). The lifetime risk of a woman developing cervical cancer in a low-resource setting is approximately 2% to 4% (4-6).

Cancer incidence in women in Bosnia -Herzegovina (B&H) in 2008 was 138.9 (4380 cases) with mortality 65.5 (2345 deaths) and incidence of cervical cancer in B&H was 9.6 (258 cases) with mortality of 3.8 (119 deaths)(2). Five most common newly detected cases of malignant diseases that occurred in the population of Republic of Srpska- B & H in 2008 were located on lungs (15.1%), colorectum (11.6%), breast (9.2%), stomach (4.4%) and prostate (4.1%). The localizations are on the lungs, colorectum, prostate, urinary bladder and stomach in men, and on breast, colorectum, uterine cervix, lung and body of the uterus in women.

Cytology-based screening programs have markedly reduced the incidence of cervical cancer in developed countries that have the infrastructure to support these programs (7). However, screening programs have proven difficult to implement in low-resource settings.

OBJECTIVE

Our objective was of analyze the incidence of specific sites of cancer and incidence of cancer of female genitals, which are regularly reported in the National Cancer Registry in Republika Srpska (B & H) in the five-year period.

METHOD

Notifications of malignant disease were delivered by health care institutions, and the analysis included for only histologically confirmed cancer cases - vulval, vaginal, uterine cervix, corpus uterine, non-specific location of the uterus, ovarian and of other genital parts, for a 2003 -2008 year period. The survival period was followed up over the five-year interval with respect to localization and histological type of cancer. For data processing we used software program Can Reg 4 and Epi Info 2002. As statistical analysis we used frequency, mean and t-test at 0.05 level of significance.

RESULTS

Out of total number of newly diagnosed female genital tract cancer cases, 79.4% were detected in invasive phase, which was, with statistically significant difference $p < 0.01$ ($T = 25.6$, $d f = 1875$) much more than in situ stage (20.6%). Out of total carcinoma in situ, 95.1% were cervical carcinoma. Out of total invasive cancers there were 38.3% cervical, 33.0% corpus uteri, 22.2% ovarian, 1.4% vaginal and 4.3% vulval (Table 1).

Localization (ICD-10)	Invasive		In Situ	
	N	%	N	%
Vulva (C51)	64	4.3	1	0.3
Vagina (C52)	21	1.4	1	0.3
Uterine cervix (C53)	571	38.3	368	95.1
Uterine corpus (C54)	492	33.0	13	3.4
Uterus, NOS (C55)	6	0.4	0	0.0
Ovary (C56)	331	22.2	4	1.0
Other female genital (C57)	5	0.3	0	0.0
Total (C51-57)	1490	100	387	100

Table 1. Female genital tract cancers according to localization in Republika Srpska, 2008.

Cervical cancer was most common in fertility period (59.2%) and in this age group was more frequent than in ≥ 49 year age group, which is statistically significant ($p < 0.01$). Newly detected cases on other localizations of female genital organs in more than 2/3 occurred in ≥ 50 year age group. An average age of cervical cancer occurrence was 48 years, compared to total number of the disease occurring at the age between 20-90 years. Ovarian cancer occurred in the age group of 15-85 years, with 58.7 years mean value. The cancer on other genital localizations mean value was 52-68 years. (Table 2)

The highest percentage of newly detected invasive cancer cases was found in a localized clinical stage (48.5%) with statistically significant difference, compared to the number of newly detected cases that have expanded to adjacent anatomical structures ($T = 9.1$, $d f = 1047$, $p < 0.01$). The cancer in localized stages was found in corpus uteri (59.8%), vagina (57.0%), cervix (50.6%) and vulva (48.4%), while the smallest percentage was found in the ovary (27.8%). (Table 3)

Metastases outside the pelvis appeared in the peritoneum and retro peritoneum in 68 (53.5%) cases, followed by digestive organs without the rectum in 24 (18.9%), respiratory organs in 11 (8.7%) and in the bone, skin, kidney and brain in slightly smaller percentages. Squamous cell carcinoma was the most common invasive cancer in cervix (87.2%), vulva (93.8%)

Table 2. Age structure and the average age of newly detected cases according to localization

Age	Localization													
	Vulva (C 51)		Vagina (C52))		Uterine cervix* (C53)		Uterine corpus (C54)		Uterus, NOS (C55)		Ovary (C56)		Other female genital (C57)	
	N	%	N	%	N	%	N	%	N	%	N	%	N	%
<40*	2	3.1	0	0.0	278	29.6	11	2.2	0	0.0	22	6.6	1	20.0
40-49*	4	6.2	4	18.2	278	29.6	52	10.3	1	16.7	48	14.3	1	20.0
50-65	11	16.9	8	36.4	240	25.6	242	48.0	1	16.7	141	42.1	1	20.0
>=65	48	73.8	10	45.5	140	15.0	200	39.6	4	66.7	124	37.0	2	40.0
TOTAL	65	100	22	100	936°	100	505	100	6	100	335	100	5	100
M Age	67.9		61.5		48.0		61.1		64.5		58.7		52.2	
Range	36-87		47-81		20-90		24-86		41-82		15-85		14-74	

*T=5.6; df=937; p=0.00

° Excluded Patients of unknown age

M-arithmetic mean

Table 3. The number of newly detected cases, according to clinical stage of disease

Localization (ICD-10)	The clinical stage											
	Localized ^{1*}		Expanded ^{2*}		Regional ³		Distant ⁴		Unknown ⁵		Total	
	n	%	n	%	n	%	n	%	n	%	n	%
Vulva (C51)	31	48.4	10	15.6	14	21.8	2	3.1	7	10.9	64	100
Vagina (C52)	12	57.0	5	23.8	0	0	1	4.8	3	14.3	21	100
Uterine cervix (C53)	289	50.6	111	19.4	31	5.4	18	3.2	122	21.4	571	100
Uterine corpus (C54)	294	59.8	96	19.5	7	1.4	33	6.7	62	12.6	492	100
Uterus, NOS (C55)	4	66.7	0	0	0	0	1	16.7	1	16.7	6	100
Ovary (C56)	92	27.8	104	31.4	13	3.9	96	29.0	26	7.8	331	100
Other female genital (C57)	0	0	1	20.0	0	0	1	20.0	3	60.0	5	100
Total* (C51-C57)	722	48.5	327	22.0	65	4.4	153	10.2	224	15.0	1490	100

¹ Localized on source organs and tissues; ² expanded to neighboring anatomic structures; ³ affected regional lymph glands; ⁴ distant metastases; ⁵ unknown stage of disease

* T=9.1; d f= 1047; p=0.000

and vagina (85.7%). Adenocarcinoma was the most common in ovaries (88.2%), uterus (83.3%) and uterine body (78.9%). (Table 4).

In a five-year survival follow up of newly diagnosed female genital cancer cases, the highest percentage of five or more year survivals was found in corpus uteri (82.6%) and cervix (82.3%) carcinomas. As a result of these conditions, 17.4-17.7% of patients died in the first five years. In a five-year survival follow up of newly diagnosed female genital cancer cases, the

lowest percentage of five or more year survivals was found in ovary (55.2%) and vulvae (58.5%) carcinomas. As a result of these conditions, 41.5-44.8% of patients died in the first five years. (Table 5)

DISCUSSION

According to data Site-specific cancer frequencies and incidence rates are reported regularly by the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) program, cervical carcino-

Table 4. The percentage of invasive malignant carcinomas of female genital tract according to pathohistological confirmation and localization

Histology	Localization						
	Vulva (n=64)	Vagina (n=21)	Uterine cervix (n=571)	Uterine korpus (n=492)	Uterus, NOS (n=6)	Ovary (n=331)	Other female genital (n=5)
Squamous carcinomas	93.8	85.7	87.2	12.0	16.7	2.7	20.0
Basal cell carcinomas	3.1	0.0	0.0	0.0	0.0	0.0	0.0
Adenocarcinomas	0.0	9.5	10.9	78.9	83.3	88.2	60.0
Sarcomas	0.0	0.0	0.2	2.8	0.0	0.9	20.0
Adenosquamous carcinoma	0.0	0.0	0.0	1.6	0.0	0.0	0.0
Granulosa cell carcinoma	0.0	0.0	0.0	0.0	0.0	1.5	0.0
Melanom	3.1	0.0	0.0	0.0	0.0	0.0	0.0
Mullerian mixed tumor	0.0	0.0	0.4	1.8	0.0	0.3	0.0
Carcinosarcoma, NOS	0.0	0.0	0.2	0.2	0.0	0.0	0.0
Adenosarcoma	0.0	0.0	0.0	0.2	0.0	0.0	0.0
Brenner tumor, malignat	0.0	0.0	0.0	0.0	0.0	0.6	0.0
Germ cell neoplasmas	0.0	0.0	0.0	0.0	0.0	1.8	0.0
Unspecified types of cancer	0.0	4.8	1.2	0.4	0.0	3.9	0.0

Other specific carcinomas: Adenosquamous, Granulosa cell carcinoma

Other specified types of cancer: Melanom, Mullerian mixed tumor, Carcinosarcoma, NOS,

Endometrial stromal sarcoma, Adenosarcoma, Brenner tumor, malignat, Germ cell neoplasmas

ma in situ seems 91.0% of carcinoma in situ. In situ carcinoma does 78.5% of all cases of cervical cancer, vaginal cancer 35.1% and 50.4% of vulvae carcinoma (8).

The average age of the appearance of carcinoma of the cervix in Victoria was 51.7 years (2).

According to data Site-specific cancer frequencies and incidence rates are reported regularly by the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) program Squamous cell (epidermoid) carcinomas accounted for 77.1% of cervical cancers. Nearly three quarters of these were classified as squamous NOS (9988 calls), accounting for 56.5% of all cervical cancers. This was the highest percentage of cancer type in each of the three time periods. Only 6.2% were keratinizing and 6.6% nonkeratinizing. Squamous NOS along with a small number of other squamous subtypes (papillary, verrucous, spindled and adenoid) and transitional and basaloid carcinomas are designated "other specific carcinomas" under "epidermoid carcinoma". Of the squamous cancers, 9.7% were specified microinvasive (7.4% of total cervical cancers). Adenocarcinomas accounted for 13.4% of cervical cancers, including adenosquamous and other adenocarcinoma types (8).

The dissimilarity between the squamous and glandular cervical cancers is more than a histologic difference because there is also disparity in demographic characteristics.

Cervical adenocarcinoma, unlike squamous carcinoma, may be found in infants and children (9,10,11). This association of a younger age group with clear cell carcinoma was supported by one other study, in which the average age was 34 years (9) but not by a general survey, in which patients averaged 55 years (12). However, the youthfulness of patients with clear cell carcinoma is unquestioned when associated with exposure to synthetic nonsteroidal estrogens in utero (11). The average age of patients in each stage, including those with in situ carcinoma, did not vary much from the group average. One study has reported that patients with adenocarcinoma in situ were a decade younger than those with invasive cancer (13).

In Victoria squamous cervical cancer occurred in 72.2% of cases and adenocarcinoma in 18.3% (14).

Increases in adenocarcinoma compared to squamous cell carcinoma have been noted in literature, (15,16) particularly in younger women. (15,17).

Cancer registrars at 703 hospitals submitted anonymous data on 11,157 patients with cervical can-

Table 5. Female genital tract cancer according to years of survival and mortality after detection of disease

Histology		Age						Total	
		<1	1-2	2-3	3-4	4-5	>5	N	%
Vulva	Survivals	7	8	7	5	7	4	38	58.5
	Deaths	16	6	0	5	0	0	27	41.5
Vagina	Survivors	5	0	4	2	1	2	14	63.6
	Deaths	6	0	2	0	0	0	8	36.4
Uterine cervix	Survivals	170	135	103	89	137	139	773	82.3
	Deaths	83	50	19	8	6	0	166	17.7
Uterine corpus	Survivals	85	89	72	60	66	45	417	82.6
	Deaths	42	24	14	7	1	0	88	17.4
Uterus, NOS	Survivals	1	0	0	3	2	0	6	100.0
	Deaths	0	0	0	0	0	0	0	0.0
Ovary	Survivals	55	42	27	22	20	19	185	55.2
	Deaths	94	35	12	3	5	1	150	44.8
Other female genital	Survivals	1	2	1	0	0	0	4	80.0
	Deaths	1	0	0	0	0	0	1	20.0

cer diagnosed and/or treated in 1984 and 1990 for a Patient Care Evaluation Study of the American College of Surgeons. For women with Ad/SC tumors, however, the 5-year survival rate was 87.3% for those receiving combined treatment compared to those undergoing surgery alone (69.2%) or radiation alone (79.2%) (18).

According to our data Cervical cancer occurred in the largest percentage in women in fertility period, squamous cancer in 87.2% of cases, and in situ in 39.2% of all cervical cancers, while the five-year survival rate was recorded in 82.3% cases.

CONCLUSION

According to data from our registry the highest percentage of cervical cancer occurred in women during fertility period, with squamous carcinoma in 87.2% of cases. Prevention of cervical carcinoma is performed successfully with the screening program for identifying precancerous lesions that could certainly lead to a reduction in number of diseased women especially in fertility period. In order to prevent genital organs carcinoma, it is necessary to encourage young women to undergo regular controls and to provide free preventive check-ups of women for early detection of cancer.

Apstrakt

Uvod: U obolijevanju i umiranju žena značajnu ulogu imaju rak dojke i polnih organa. Cilj: Analizirati raširenost raka ženskih polnih organa prijavljenih u nacionalnom registru malignih bolesti Republike Srpske (B&H) u petogodišnjem periodu

Metod: Analiza patohistološki potvrđenih slučajeva raka vulve, vagine, cervixa uterusa, tijela uterusa, nespecifične lokacije uterusa, jajnika i raka na drugim genitalnim dijelovima, od 2003 -2008. godina, uz praćenje petogodišnjeg perioda preživljavanja u odnosu na lokalizaciju i histološki tip raka.

Rezultati: Od ukupnog broja novootkrivenih slučajeva raka ženskog genitalnog trakta 79.4% je otkriveno u invazivnoj fazi što je znatno više uz statistički značajnu razliku $p < 0.01$ ($T = 25.6$; $df = 1875$) u odnosu na in situ stadijum (20.6%). Rak cerviksa uterusa se najčešće javlja u fertilnom periodu sa 59.2% slučajeva i u ovoj dobnoj skupini se statistički signifikantno češće javlja nego u dobi ≥ 49 godina ($p < 0.01$). Novootkriveni slučajevi na ostalim lokalizacijama ženskih polnih organa u više od 2/3 slučajeva se javljaju u dobi sa i preko 50 godine starosti. Skvamozni karcinom je najčešći invazivni rak grlića materice (87.2%), vulve (93.8%) i vagine (85.7%). Adenokarcinom je bio najčešći malignitet ovarija (88.2%), uterusa (83.3%) i tijela uterusa.

Diskusija: U najvećem procentu in situ stadijumu se javlja kod karcinoma grlića maternice, što je bitno u prevenciji pojave ovog oboljenja.

Zaključak: U posmatranom periodu najvećem procentu rak grlića maternice se javlja kod žena u fertilnom periodu i to squamozni karcinoma u 87.2% slučajeva, tako da sa preventivnim programima u cilju sprečavanja ovog oboljenja treba početi u ranom fertilnom periodu.

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