ISSN (Online): 2455-3662
EPRA International Journal of Multidisciplinary Research (IJMR) - Peer Reviewed Journal
Volume: 6 | Issue: 1 | January 2020 || Journal DOI: 10.36713/epra2013 || SJIF Impact Factor: 5.614||ISI Value: 1.188

STUDY OF THE EPIDEMIOLOGICAL CHARACTERISTICS OF DEVELOPMENT OF CERVICAL CANCER AND RELATED CANCER DISEASES

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ABSTRACT

The aim of this research was to study the epidemiological characteristics of cervical cancer in Uzbekistan, to compare the data obtained with studies conducted in the world. Define a strategy for preventive measures aimed at preventing cervical cancer by introducing a cervical cancer screening system, as well as introducing vaccination against human papillomavirus infection.

KEYWORDS: ***cervical cancer, epidemiology, prevalence, prevention.***

1. INTRODUCTION

Cervical cancer is the third most common cancer among women worldwide, with an estimated global cancer tracking program (GLOBOCAN) of 569,847 new cases of cancer and 311,365 deaths due to cervical cancer were reported in 2018 [1]. The incidence of cervical cancer throughout the world varies greatly. The highest rates were found in the African region: for example, in Esvatini (Swaziland), the incidence of cervical cancer among women is 75.3 per 100,000 women, while in Malawi this indicator was 72.9 per 100,000 women. The lowest rates of 1.9 per 100,000 women were found in Yemen and Iraq [2, 3]. If we consider the whole region, the highest average for the African region was 27.6, for the Pan-American region - 11.2, for the Asian region - 11.9, for the European region - 11.2 per 100,000 women [1] .

2. MATERIALS AND METHODS

For a retrospective analysis to study the long-term dynamics of the incidence of cervical cancer, we used data from the cancer registry of the Tashkent city branch of the RSNPMTSOR 2180 patients for 2007-2019.

All databases of cancer registries were entered into the electronic database of Excel. After cleaning and encoding the data, all the data was processed in the statistical analysis program IBM SPSS Statistics V22.0 (www.ibm.com). This program intended for statistical analysis of complex survey data and used for prognostic calculations of weighted prevalence and standard error (SE) with a 95% confidence interval using descriptive statistics methods.

3.RESULTS

In order to assess the epidemiological characteristics of the incidence of cervical cancer in Uzbekistan, a retrospective analysis of the incidence data in cervical cancer in Uzbekistan carried out. To study the long-term dynamics of the incidence of cervical cancer, the data of the cancer registry of the Tashkent city branch of RSNPMTSOiR used. The database contains information about each patient, the date of diagnosis, diagnosis, and prescribed treatment measures, as well as information about nationality and age. The frequency of visits used as a temporary gradation. Individual characteristics of patients can lead to different durations between visits. The multiplicity of calls is due to either the prescribed therapy or clinical manifestation. This approach will reduce the impact of personality characteristics on the time aspect.

In order to determine the epidemiological characteristics of the manifestation of cervical cancer in the female population of the Republic of Uzbekistan, it is necessary to have data on each case of cervical cancer in the Republic of Uzbekistan, indicating clinical and epidemiological indicators. The most relevant source of such data is the registry of cancer patients of the Tashkent branch of the

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Republican Specialized Scientific and Practical Medical Center for Oncology and Radiology.

In total, from 2006 to the first half of 2019, with the diagnosis of Malignant neoplasm of the cervix (Code C53 according to ICD 10), 2180 primary patients were registered. For this period, an uneven distribution of cases is noted. Therefore, there is a period of a decrease in the number of cases from 168 in 2006 to 80 cases in 2011, and a rise from 96 cases in 2012 to 217 cases in 2015. Then a "plateau" is noted when the level approximately fluctuates between 213 - 221 cases. These fluctuations are due to the heterogeneity of the application for medical care to this institution. Thus, when analyzing the appeal for medical care to this medical institution, it was found that almost 30% of all applicants are residents of the regions of the Republic, and 70% are residents of the city of Tashkent.

When analyzing the applicants at the place of residence, dividing all patients into residents of Tashkent (the main contingent to be served in this institution) and residents of the regions (Uzbekistan), a picture emerges on the face (Fig. 1.), circulation from Tashkent residents fluctuates in the range of 74 - 149 cases per year. The circulation from residents of other regions has a wave-like picture, which as a result forms general fluctuations in the numbers of circulation over the years.

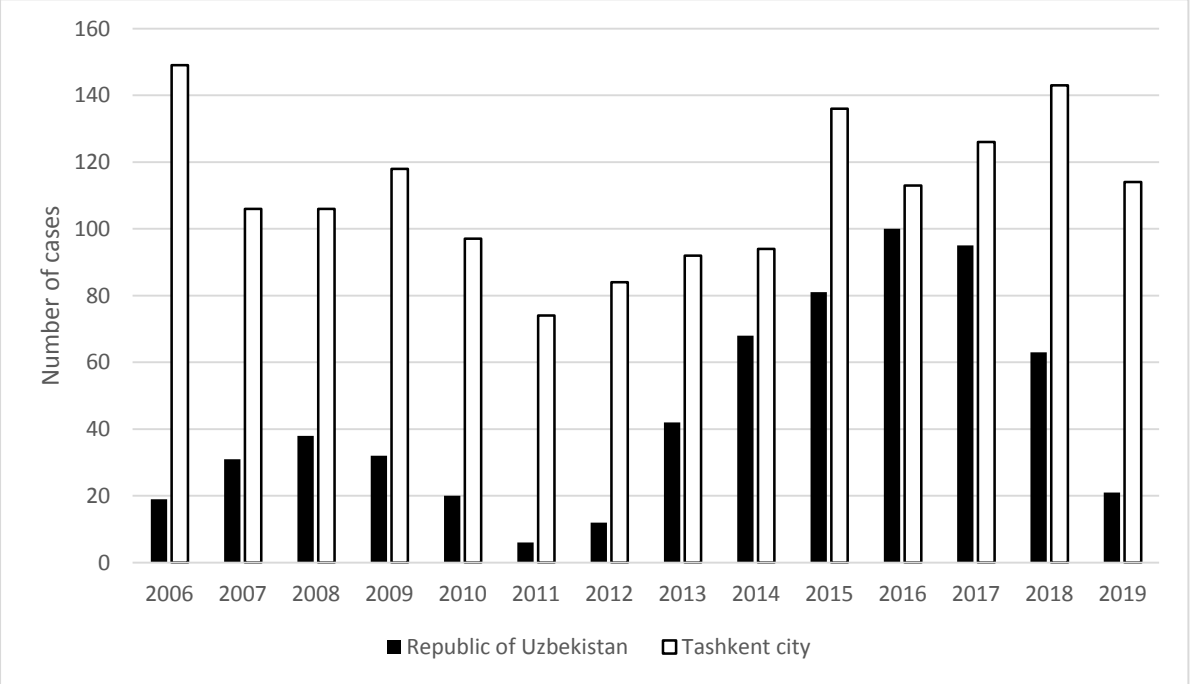

Fig. 1. The frequency of primary referral of patients with cervical cancer included in the analysis of the register of cancer patients of the Tashkent branch of the Republican Specialized Scientific and Practical Medical Center of Oncology and Radiology from 2006 to 2019 depending on the place of residence

These fluctuations in the circulation of residents of the regions of the Republic of Uzbekistan are explained by ongoing reforms in the healthcare system and increasing the availability of medical services for the population of the Republic of Uzbekistan. The relative uniformity of circulation on the part of residents of the city of Tashkent indicates the epidemiological constancy of the cervical ecosystem within the city of Tashkent, which suggests that the data obtained representatively describe the epidemiological process for a closed ecosystem and allow extrapolating data to the entire population of the Republic of Uzbekistan.

An analysis of the intra-annual (monthly) dynamics of primary circulation shows a complete absence of seasonal fluctuations, with the exception of the month of December, which can be explained by the New Year mood and holidays. On average, the number of initial complaints about cervical cancer observed at a level of 8 to 25 cases per month.

The average age of all primary patients was 52.1 ± 0.23 years, with a 95% confidence interval for the average being only 51.6 - 52.5 years (Table 1). This is a narrow range and indicates representativeness of the sample. The minimum-recorded age was 21.7 years; the oldest patient was 85.2 years old. In this case, the median of age is almost equal to the average indicator, which indicates the normal distribution of the indicator of age, which in turn determines the possibility of using parametric methods of statistical processing. The normal distribution of cervical cancer cases confirmed by the age distribution chart among patients.

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Table 1. Characteristic of the age indicator of patients included in the study

Age, years		Statistics	Standard Error
Mean		52,1	0,23
95% Confidence interval for medium	Bottom line	51,6	
	Upper bound	52,5	
Median		51,9	
Minimum		21,7	
Maximum		85,2	
Range		63,5	
Age groups		Frequency	Interest
20-29 years old		15	0,7
30-39 years old		241	11,1
40-49 years old		552	25,3
50-59 years old		657	30,1
60-69 years old		354	16,2
70-79 years old		118	5,4
80 years and older		4	,2
Total		1941	89,0
Missing age data		688	11,1

Using demographic data on the number of women in Tashkent provided by the State Committee of the Republic of Uzbekistan on Statistics (www.stat.uz) and the data on the distribution of patients aged 20 to 80 years, it is possible to determine the incidence of cervical cancer among the population of Tashkent for the period from 2006 to 2019 (Table 2).

Table 2. Standardized indicator of the incidence of cervical cancer by age and population

Year	Total	Tashkent resident		Female population between the ages of 20 and 80 *	Per 100,000 population
		no	yes		
2006	168	19	149	1205797	12,4
2007	137	31	106	1235902	8,6
2008	144	38	106	1266007	8,4
2009	150	32	118	1278027	9,2
2010	117	20	97	1307411	7,4
2011	80	6	74	1371261	5,4
2012	96	12	84	1398679	6
2013	134	42	92	1435542	6,4
2014	162	68	94	1456927	6,5
2015	217	81	136	1478670	9,2
2016	213	100	113	1503501	7,5
2017	221	95	126	1530296	8,2
2018	206	63	143	1562099	9,2
2019	135	21	114	1590615	7,2
	2180	628	1552	1401481	8,0 (7,6)**

*Note: * - Data of the State Committee of the Republic of Uzbekistan on Statistics (www.stat.uz). ** - The indicator is calculated without taking into account the year 2006 due to the possible error of including indicators of previous years in the data of this.*

In total, from 2006 to 2019, the studied medical institution received 1,552 residents of Tashkent city aged 20 to 80 years old, while the average number of women in this age group in the city of Tashkent is 1,401,481 women. Substituting these data, we found that the average incidence of cervical cancer in Tashkent is 8.0 per 100,000 women, and if we take into account the fact that in any program the first reporting year is subject to various kinds of errors and it is necessary to exclude the impact of this year. As a result, we got an indicator equal to 7.6 per 100,000 women. The lowest rate was recorded in 2011 - 5.4 per 100,000, and the highest rate was recorded in 2009 and 2018.

Given the fact that many studies indicate the relationship of genetic predisposition and the development of cancer pathology, as well as the possible influence of ethnicity, we studied the ethnic composition of primary patients. In total, among 2180 patients, we found 11 diverse nationalities that belong to 3 ethnic groups. The peoples of the Central Asian region make up the bulk and account for 67.5%,

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followed by 30.5% of the Caucasian, and the smaller group are Asians (2.0%), represented only by Koreans.

Among the nationalities, the most numerous, of course, were Uzbeks - 61.5%, followed by Russians 23.7%, Tatars and Kazakhs make up about 4.5-4.8%. Other nationalities do not exceed 1% of the total number of applicants for medical care. We analyzed the age distribution of cases depending on the ethnic group, in order to determine whether the ethnic group affects the epidemiology of cervical cancer in the Republic of Uzbekistan. So, the average age in the group of caucasoids was 53.9 ± 0.4 years, in the group of Central Asia 51.2 ± 0.2 years, and among Asians this figure was 53.2 ± 1.8 years. At the same time, the average age indicator between the Caucasoids and Central Asia (CA) differ statistically significantly (p <0.001), Asians occupy an intermediate position that do not have a statistically significant difference with the other two groups. However, when studying the differences between the ages based on the median distribution, it was found that the median for the age among the Caucasoids was 53.6 years, for CA 51.0 years, which is very close to the average, for Asians this indicator was 55.5 years. this, as well as the quartile shift down in fig. 6, which suggests that among this ethnic group there is a large number of fairly young cases of cervical cancer, which shifts the average to the left. The average hospital stay for all cases in this medical institution was 7.3 ± 0.08 days (Table 3). The maximum duration was 18 days, the minimum is less than 1 day. Most often, patients were in hospital for 4 days. Moreover, the duration of the visit did not depend on age or ethnic group. The confidence index for these groups was p> 0.05.

Table 3.Statistical characteristics of the indicator average duration of hospitalization

Duration of hospitalization, days		Statistics
Mean		7,3±0,08
95% confidence interval for the average	Bottom line	7,1
	Upper bound	7,5
Median		7,0
Minimum		0,5
Maximum		18
Range		17,5
Interquartile range		6,00

Once, 1196 patients, representing 54.8%, sought medical help from 2180 primary patients. 95% of all patients went to the hospital no more than 9 times, more than 18 times only 3 patients came to the hospital. On average, each patient went to the hospital 3.3 ± 0.03 times.

We also analyzed the likely dependence of the hospitalization rate on age and ethnicity. Thus, the distribution of the frequency of hospital visits by age is shown in Fig. 3.27, and represents a normal distribution with a slight shift to the right, which indicates the existence of a relationship between age and frequency of treatment. Moreover, the correlation coefficient has statistical significance p = 0.002. The dependence of the frequency of treatment and age is described by the following equation: $y = 2.66 + 0.01 * x$

Where, y is the multiplicity of treatment

x is the age in years.

We also analyzed the dependence of the multiplicity of treatment on belonging to an ethnic group. So, for the Caucasoids, an average of 3.7 ± 0.07 times was admitted to the hospital, CA turned 3.1 ± 0.04, Asians turned 3.3 ± 0.2 times. Moreover, the indicator between the Caucasoids and Central Asia (CA) differ statistically significantly (p <0.001), Asians occupy an intermediate position that do not have a statistically significant difference with the other two groups. Moreover, the presence of extremely multiple hospital stays was characteristic of the Caucasoids. Patients from this group turned to the hospital more than 25 times. For the Central Asian ethnic group, the maximum number of calls was 23, for the Asian 10 times.

We also analyzed the relationship between the length of hospitalization and the frequency of visits to health facilities. A strong inverse correlation was revealed (p = 0.027) between the frequency of the visit and its duration. Therefore, with an increase in the frequency of the visit, the length of stay in the hospital was shortened.

The length of hospital stay is described by the following equation:

$$y = 7.32 - 0.21 * x$$

Where, y is the length of hospital stay

x - the frequency of visits.

We also analyzed the dependence of the length of hospitalization on the month of the year, taking into account the fact that there is an opinion that in the summer and winter months due to climatic changes, patients are less in hospital. On the graph of the linear regression distribution of the dependence of the duration of hospitalization and the frequency of seeking medical help, we see a uniform distribution, which, surprisingly, has a statistically pronounced tendency to decrease (p = 0.001).

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The length of hospital stay, depending on the season of the year, is described by the following equation:

$$y = 6.87 - 0.04 * x$$

Where, y is the length of hospital stay

x is the month of the year.

Although, given the fact that the decrease is noted only by 0.04 days, this trend can be neglected in further analysis.

Among concomitant oncological pathologies during initial treatment, in addition to Malignant neoplasm of the cervix uteri (C53 according to ICD10), 30 out of 2180 (1.38 ± 0.25%) malignant neoplasms of the uterine body (C54) were noted, in 21 cases (0.96 ± 0.21%) Malignant neoplasm of the mammary gland (C50), in 17 cases (0.78 ± 0.19%), malignant neoplasm of the ovary (C56) was noted. Concomitant pathologies such as In situ neoplasms (D00-09), Digestive malignant neoplasms (C15-26), Respiratory malignant neoplasms (C30-39), and Skin malignant neoplasms (C43-44) were found in less than 0.5% of cases. In isolated cases, Nephollular lymphoma (C83), malignant neoplasm of other and unspecified female genital organs (C57), and Malignant neoplasm of the urinary tract (C64-C68) were found (Table 3.14).

Table 3.

Incidence of concomitant oncological diseases during initial treatment for malignant neoplasms of the cervix uteri (C53 according to ICD10)

Concomitant diseases (n = 2180)	Number	Mean
C54 Malignant neoplasm of the uterus	30	1,38±0,25
C50 Malignant neoplasm of the mammary gland	21	0,96±0,21
C56 Ovarian Cancer	17	0,78±0,19
D00-09 In situ neoplasms	8	0,37±0,13
C15-26 Digestive malignant neoplasm	3	0,14±0,08
C30-39 Malignant neoplasm of the respiratory system	2	0,09±0,06
C43-44 Malignant neoplasm of the skin	2	0,09±0,06
C83 Nephollular lymphoma	1	0,05±0,05
C57 Malignant neoplasm of other and unspecified female genital organs	1	0,05±0,05
C64-C68 Urinary malignancy	1	0,05±0,05

Thus, even taking into account the fact that there are concomitant pathologies, their share is so insignificant that it can argued that the initial treatment for cervical cancer occurs at the immunopathology phase, which in turn indicates a possible high role in the control of this disease preventive screening.

We have analyzed the incidence of distant metastases in patients with each new call for medical care. When conducting a linear regression analysis, it was found that there is a strong statistical relationship (p = 0.009) between the frequency of treatment and the appearance of distant tumor metastases. So with each new treatment, the likelihood of developing distant metastases increased according to the following equation:

$$y = 0{,}03 + 6{,}25e^{-3x}$$

Where, **y** - the presence of distant metastases (0,1)

x - frequency of seeking medical care

We have studied the likelihood of developing concomitant forms of oncological pathology over time. So, on the basis of the analysis of repeated requests for medical help, it was found that starting from the second visit, the incidence of breast cancer increases. Its prevalence increases from 0.5% to 3.5% by the 9th visit. The risk of nephollular lymphoma increases from 0% to 1.2% at the 8th visit. The risk of malignant ovarian formation (up to 1.75%) and respiratory organs (0.6%) is also significantly increased. But, neoplasms of the uterine body, on the contrary, decrease from 1.4% to 0.8%.

Of all 6208 visits, only 13 (0.2 ± 0.05%) were diagnostic; in other cases, any therapy was prescribed (Table 3.18). Of all the procedures prescribed for patients with cervical cancer, surgery was prescribed in 493 (7.9 ± 0.3%) cases, radiation therapy in 977 (15.7 ± 0.4%), chemotherapy in 3834 (61.8 ± 0.6) %) of cases and symptomatic treatment in 819 (13.2 ± 0.4%) of all 6208 visits during the study period.

4. DISCUSSION

Thus, even taking into account the fact that there are concomitant pathologies, their share is so insignificant that it can argued that the initial treatment for cervical cancer occurs at the mono-pathology phase, which in turn indicates a possible high role in the control of this disease screening. On the other hand, the incidence of concomitant oncopathology after primary cervical cancer is also not high. Of the most common, it is breast cancer. However, it is necessary to take into account the high mortality of both the primary disease and secondary complications.

Given the data obtained in the USA on the role of ethnicity on the frequency of cancer (white / black) [4, 5]. Studies have shown a higher risk of cancer in African Americans compared to

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Caucasoids. In our study, we studied the effect of ethnicity on the frequency and characteristics of cervical cancer in Uzbekistan. There were no differences between ethnic groups, with the exception of one fact that among Asians, a younger age for the development of cervical cancer, which has no statistical significance, is noted.

The average duration of the patient's stay in the hospital was 7.3 ± 0.08 days, and the frequency of visits can reach 18 times.

Among the concomitant oncological pathologies during the initial treatment, in addition to the Malignant neoplasm of the cervix (C53 according to ICD10), only 86 of 2180 cases had concomitant oncopathology. Given the fact that there are concomitant pathologies, their share is not so significant, it can argued that the initial treatment for cervical cancer occurs at the immunopathology phase, which in turn indicates a possible high role in the control of this disease of preventive screening. A similar situation was noted in the USA in the 70-80s, before the cervical cancer-screening program was introduced [6, 7]. After the introduction of the screening program, the incidence of cervical cancer of grade 3 and 4 decreased by 70%, i.e. milder cases of cervical cancer began to clear out, which indicated a high efficiency of screening programs [8].

5. CONCLUSION

Thus, the problem of cervical cancer in Uzbekistan is relevant. Since the introduction of the Papanicolaou (Papanicolaou) test, the incidence of cervical cancer in the United States has declined by more than 60% [9]. Theoretically, cervical cancer can prevented with a timely qualitative examination; all women aged 21 to 65 years should examined. Currently, there are three options for screening for cervical cancer: only the Pap test, the pap-HPV contest and the high-risk HPV test [10, 11, 12]. In our country, it is necessary to take measures to introduce high-quality screening aimed at early detection of inflammatory processes in the cervix. It is also necessary to introduce vaccination against HPV [12, 13], which will make it possible to prevent the spread of HPV, the main reason for the development of cervical cancer.

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