ejpmr, 2019,6(3), 491-494

SJIF Impact Factor 4.897

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Research Article

ISSN 2394-3211

EJPMR

RECURRENCE OF CERVICAL CANCER, RISK FACTORS

Hilola U. Ortikova* and Mirdjalol D. Djuraev

Samarkand Branch of the Republican Specialized Scientific-Practical Medical Center of Oncology and Radiology of the Ministry of Health of the Republic of Uzbekistan.

***Corresponding Author: Hilola U. Ortikova**
Samarkand Branch of the Republican Specialized Scientific-Practical Medical Center of Oncology and Radiology of the Ministry of Health of the Republic of Uzbekistan.

Article Received on 15/12/2018 **Article Revised on 03/02/2019** **Article Accepted on 24/02/2019**

ABSTRACT

Annually more than 529.800 new patients with cervical cancer (CC) are registered in the world. The given pathology remains relevant and one of the intractable problems in view of the fact that morbidity and mortality rates throughout the world are high, which is a characteristic feature in developing countries. It should be noted that there are territorial differences and peculiarities, which require new approaches to systematization in the study of the main risk factors for development or relapse, which encourage the scientists from all countries to study the complex processes of carcinogenesis. According to statistics in the Russian Federation in the structure among all malignant neoplasms (MN), the incidence of CC is on the 5th place (5.3%), and mortality is on the 7th (5.3%)[3], at that, the disease is in the 2nd rank among oncogynecological pathology.[6] Should be noted that the majority of patients are admitted to specialized clinics with advanced forms (III, IV stage), which are determined in 37.9% of cases of patients.[1] As for statistics of the CIS countries, the number of newly diagnosed women with CC amounted to 16917 new cases in 2016. In relation to 2007 the increase in the absolute number of cases was 12.2%. In the structure of MN cases among female population, this pathology was in the 5th place in Russia (5.3%), in the 4th –in Belarus (4.4%); in the 3rd -in Armenia (6.7%), 2nd- in Kazakhstan (9.2%), in Kyrgyzstan (15.5%) and in Azerbaijan - (7.7%). Dynamics of CC percentage in the structure of cancer incidence of female population in Russia was stable.

Nowadays, morbidity and mortality from MN in Uzbekistan also continues to be one of the actual problems. According to the State Statistics Committee of the Republic of Uzbekistan, the incidence of CC was 4.6 per 100,000 of population in 2016. As well as all over the world, there is a gender difference among MN occurring in Uzbekistan, which is reflected in the high numbers of morbidity and mortality rates among female population: for example, breast cancer has been at the top of the MN structure among women for several years: morbidity is - 9.5 $^{0/}_{000}$, mortality - 4.4^{0}/000, the following ranking places belong to stomach cancer - 5.9^{0} / 000 / 5.1^{0} / 000, (second), CC- 4.6^{0} / 000 / 2.5^{0} / 000 (third).

For 2016 year throughout Uzbekistan 1465 newly identified patients with CC were registered, 10.6% of them with stage I; stage II - 51.7%; stage III - 30.6%; stage IV - 6.9%. It seems, patients with CC at stage III, IV of the disease account for 37.5%, which indicates their late detection in the advanced stages, necessitating the need to find ways to solve the problem of early diagnosis and prevention of relapses.

Traditional methods of treating CC are surgical, radial, and their combinations. The possibilities of medical and chemo-radiation therapy are being actively studied. Survival of patients with CC, the prognosis of the effectiveness of anticancer treatments depends upon the stage of the disease, the chosen method of therapy, the timing of recurrence and metastasis.[2] In the conditions of the continuing growth trend in the incidence of primary CC, high frequency and low effectiveness of treatment, leading to death even after specialized therapy, the search for factors influencing the processes of recurrence, the timing of their development, the possibility of early diagnosis and treatment is relevant.

The aim of present research is to study the frequency and timing of relapse in patients with CC with the search for the main prognostic factors.

MATERIALS AND METHODS: on the basis of a retrospective analysis of 148 clinical observations over 5-year period, the case histories of patients treated at the department of onco- gynecology of SBRSSPMCO and R were studied (over 2010-2015 yy.). According to the classification of TNM, the following stages of the disease are established: stage I - in 30 (20.2%); II - 56 (37.8%); III - 54 (36.4%); IV - 8 (5.4%);the distribution of patients by age was as follows: 20–29 years - 12 (8%); 30-39 years - 28 (18%), 40-49 years - 51 (34.4%), 50-59 years - 30 (20.4%), 60-69 years - 17 (11.4%) and over 70 years -10 (6.7%). The mean age of patients was 50.5 ±

1.3 years. All patients were examined according to standard methods of diagnosis and treatment of CC.

Analysis of case histories of 148 patients with CC has showed that 55 (37%) of them have been diagnosed with relapse of the disease, therefore they are included in the first group, the rest - 93 (62.8%) - without relapse, respectively, they are included in the second group who received combined, comprehensive treatment or standard course of combined radiation therapy. In the majority of patients, 117 (79%) - squamous cell carcinoma of varying degree of differentiation has been verified, it should be noted that squamous cell carcinoma with keratinization has been occurred most common - 68 (45.9%), rarely squamous cell carcinoma without keratinization - 49 (33.1%); adenocarcinoma - 15 (10%); glandular squamous - 9 (6%); poorly differentiated - 7 (4.7%); by tumor growth : endophytic - 40 (27.1%), exophytic - 65 (44.3%), mixed forms - 41 (27.6%).

RESULTS OF THE STUDY: Diagnosis of recurrent CC consists in comprehensive examination of patients of the III-clinical group during follow-up.

Clinically, the occurrence of recurrent CC is characterized by the presence of pain in the lower abdomen, the sacral and lower back areas (mainly night-time, dull, "gnawing" nature); at localization of recurrence in vaginal seam zone - bloody discharges (more often contact). Most often, in 18-25% of patients with relapses for a long time have an asymptomatic course, and only during the examination in the mirrors and colposcopy can be diagnosed recurrent CC. With colposcopy, can be seen edematous, ulcerated tissue or tumor with exophytic or endophytic growth pattern, atypical vascularization zone. The recurrence of cervical canal cancer following the combined radiation therapy performed in bimanual study shows the presence of increased size of the cervix and change in its shape caused by tissue infiltration. When a vaginal seam is formed after radiotherapy, the recurrence of cervical canal cancer may be accompanied by the formation of “blind bag” with mucinous and hemorrhagic contents.

At the same time, the tumor of heterogeneous consistency will be determined by palpation (preferably rectally): dense in the center of growing tissue and fluctuating in places of accumulation of mucus and decomposition products. Relapses localized in parametrium are defined as dense tumor-like formations with fuzzy contours.

The diagnosis of recurrence, according to the inspection in the mirrors, bimanual vaginal, rectal and recto-vaginal studies, is not devoid of elements of subjectivism. Therefore, in each case of estimated recurrence, it is necessary to perform a puncture or open biopsy, cytological and histological examination of the material obtained.

Using the methods of determining the recurrence of the process, the patients of the first group were diagnosed with relapse, which in 62.3% of cases occurred within the first 1.5 years after completion of the primary tumor treatment, therefore, this period can be considered as the most “dangerous” in terms of risk of recurrences. In terms from 19 to 24 months (up to 2 years), the occurrence of relapse was observed in 11 patients (20.3%); over 2 years - in 5 (9.7%).

One of the important tasks of modern oncology is the search for signs and properties of tumors, on the basis of which could be predicted the course of the disease and determine adequate therapy. The most important characteristics of MN in addition to the clinical stage are its histological version, degree of differentiation and biological aggressiveness of the tumor. In recent years, the efforts of morphologists and oncologists are aimed at identifying additional prognostic signs that allow us to determine the causes of the different behavior of tumors at the similar clinical stage and degree of differentiation.

The results of cytological and histological studies of materials puncture and open biopsy for suspected recurrent CC are decisive in making the concluding diagnosis, the choice of the method of further treatment, as well as the rehabilitation of patients.

As shown by the data from the analysis, the frequency of recurrences significantly depended on the morphological structure of primary cervical tumor and in patients with squamous cervical cancer, it was 20.6%, adenocarcinoma 33.6%, glandular squamous 28.6%, low differentiated 42.9%, i.e. depending on the tissue histostructure it increased in 2.1 times in patients with squamous histological type.

When evaluating 5-year survival of patients, it has been noted that it is also different in patients with different morphological structure, such as in patients with adenocarcinoma and squamous cell carcinoma (keratinizing and non- keratinizing), with stage II - 64.2% and 81.7%; and with stage III - 34.6% and 45.8%, respectively.

The analysis of the studies conducted on the treatment and therapy showed that in patients with adenocarcinoma and glandular squamous cervical cancer, the tumors were less sensitive not only to radiation, but also to chemotherapy. In these forms of tumors, the response to neoadjuvant chemotherapy was 67% versus 85% with squamous-cell variant, which also indicates a low sensitivity of adenocarcinoma to chemotherapy. 11 patients who underwent the treatment with cisplatin in combination with 5-fluorouracil a partial effect was observed in 63.6% of cases, and no patient was noted complete response.

Prognostically, favorable were exophytic forms of tumor growth, diagnosed in 65 (44.3%) patients, and with

exophytic growth, relapse was observed in 13.1%, endophytic growth - 39.5%, and mixed forms - 40%. Thus, already before the onset of primary treatment, patients with CC had clinical signs that define an aggressive course with a tendency to early development of relapses.

The largest proportion was represented by patients with CC stage II and stage III, and patients with advanced forms (stage III and stage IV) accounted for 40.6%, which can be considered as one of the factors with a high risk of recurrence (Table 1). The stage of the disease at the time of initial treatment was crucial for the frequency of relapses. According to the data, the majority of patients with recurrent CC initially had stage III and IV disease. Of the total number of patients with relapses, almost half were patients with stage III disease.

Table 1: Distribution of patients with CC in study groups, according to the stages of the disease

CC stage before treatment	The number of patients (n = 148),%		Number of patients with relapses (n = 55),%	
	abs. number	%	abs. number	%
stage I	30	20.2	5	16.6
stage II	56	37.8	18	30.3
stage III	54	36.4	25	46
stage IV	8	5.9	7	87.5

It was established that the age of patients with newly diagnosed CC ranged from 20 to 75 years. The prevalence of young and socially active patients of 30–39 years (20%) and 40–59 years (53.9%) was noted. Almost one third of the cases (27.8%) were women younger than 40 years old. When assessing the frequency of recurrences in each age group of CC patients, it was established that relapses occurred more often in women aged 50–59 years (25.2%) and 40–49 years (24.8%). Studies and findings suggest that the age of patients, the histological type of the tumor are the main factors in CC prognosis.

MRI in patients with suspected recurrences can detect them at an early stage, which has been confirmed by colposcopic examination methods, in comparison with cytology, in which the diagnosis of disease recurrence has not been always confirmed. In this regard, it can be concluded that the colposcopic method of investigation is more sensitive and less expensive, while the number of false-positive results does not exceed 1.2%.

One of the important facts is that almost the majority of patients with relapses (up to 98%) lived in rural areas or before the onset of treatment and diagnosis were beyond the territory of Uzbekistan, i.e. in labor migration, which allows to conclude that the place of residence of the patient and social status is one of the factors that are important in the development of relapse of CC.

When conducted combined radiotherapy, the indicators of peripheral blood composition, in particular anemia, whose frequency increases in parallel with the degree of tumor advance, are more decisive, determining the prognosis of disease recurrence.

Based on studied case histories of patients with CC, retrospective material, we concluded that the main cause of anemia in patients with CC is not only bleeding from the tumor, but also cancer intoxication. Anemia, as one of the indicators of cancer intoxication, may indirectly indicate a much greater spread of the tumor than it was established before the start of treatment.

When assessing the time of onset of recurrences after the completion of initial therapy, it was determined: in the overwhelming number of patients in analyzed group, the diagnosis of relapse was established within the first 1.5 years after treatment, while 34 out of 55 (62.3%) women in study group had further progression of the disease in terms of 7-18 months after therapy; from 19-24 months - in 11 (20.3%), over two years - 5 (9.7%).

CONCLUSION

1. Cervical cancer is currently a very topical issue that requires close attention and solutions.
2. Its significance is determined by high morbidity and mortality rates, as well as the unfavorable tendency of the increase among women of reproductive age and the occurrence of recurrences of the disease.
3. Despite numerous studies on this issue, the results of treating CC are not quite satisfactory.

All of the above allows us to conclude that the prognosis of patients with CC should be based on the totality of the clinical signs available to the practitioner, characterizing the characteristics of the organism and the tumor, taking into account their degree. The study of the factors characterizing the characteristics of the organism made possible to identify additional criteria for the prediction of the occurrence of recurrence of the disease of CC patients, which must be considered when conducting its diagnosis.

REFERENCES

1. Antipov V.A., Novikova O.V., Balakhontseva O.S. Organ-preserving treatment of initial forms of invasive adenocarcinoma of the cervix uteri // Siberian Journal of Oncology, 2010; 1(37): 5-11.
2. Bohman Ya.V. Guide oncogynecology. SPb, 2002; 544.

3. Vazhenin A.B., Zharov A.B., Shimotkina I.G. Topical issues of clinical oncogynecology. M, 2010; 6-33.
4. Davydov M.I., Axel E.M. Statistics of malignant neoplasms in Russia and in the CIS countries in 2012. // Bulletin RCRC after N.N. Blokhin RAMS, 2014; V2:# 2. (appendix1): p160.
5. Egorova I.V., Maksimov S.A. Problems of oncological diseases of the reproductive system in Krasnoyarsk Territory // Materials of the V Congress of Oncologists and Radiologists of the CIS. Tashkent, 2008; 15-16.