Trend of incidence in the last five years of breast, cervical, ovarian and uterine cancer in the main hospital in Romania

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ABSTRACT

In the time of modern medicine, gynecologic cancers kill millions of people annually. Worldwide, breast cancer is the first among cancer types in terms of incidence rate. Cervical cancer continues to be a public health issue, despite all methods of prevention and early detection. Ovarian cancer is considered a "silent killer" and associates high incidence and mortality in women. The incidence of uterine cancer has increased by one percent per year in the last ten years. We analyzed the histopathological results of gynecologic neoplasms during 2016-2021, using the database of the pathological anatomy department within the Bucharest University Emergency Hospital. Breast cancer was the most common type, with an incidence of 34.86%, followed by cervix cancer - 29.44%, uterine cancer - 24.93%, and ovarian cancer - 10.76%. The proportion of each form of cancer respected the reports declared for the worldwide female population. In our opinion, all forces should orient themselves towards campaigns of correct information, promotion of prevention methods, and awareness of unfavorable prognosis.

Keywords: gynecologic cancer, incidence trend, distribution by age

INTRODUCTION

In the era of continuous progress of medicine, cancer remains the condition that kills millions of people. Cancer-related deaths for 2030 are estimated to be 11 million (1).

Data from World Health Organization (WHO) show that in 2020 breast cancer remains first in terms of incidence rate worldwide, with an estimated age-standardized rate of 47.8 per 100,000 people (1). About 70% of breast cancer-related deaths occur in developing countries, with an associated five-year survival rate of about 40% (2). The four main categories of gynecologic cancers that target breast, cervix uteri, corpus uteri, and ovaries are the first ten types of cancers in terms of age-standardized incidence in 2020.

Multidisciplinary approaches, new therapeutic strategies appropriations, and participating in national screening programs help reduce breast cancer-related mortality (3). In contrast to other countries that report a breast cancer screening rate of over 80%, like Finland and Denmark, Romania has reported data from 2015 with a rate of 0.2% in women aged 50-69 years (4). 90% of newly diagnosed breast cancer cases in Romania are in an advanced stage, leading to an economic burden as the average oncological cost for a stage IV breast cancer treatment is three times higher than the average cost of the oncological management of a stage I breast cancer (5). In 2017, estimations showed that 70% of the fares related to breast cancer were societal and indirect economic, and only 30% were medical expenditure (5).

These data are worrying and require an attitude with the participation of all parties involved. In 2017, the European Commission conducted a thorough analysis of the health system in Romania, highlighting the deficits responsible for the situation described above. As a result, the European committee depicted that the health system in Romania is underfunded and centralized, where local health care providers do not have the opportunity to adjust their demand for medical materials and technology according to their needs (6).

Worldwide, cervical cancer is the fourth in terms of incidence (7). Early detection of cervical cancer is possible through screening, yet it is preventable with vaccination. These approaches are the way for eliminating cervical cancer from the list of public health matters.

In Romania, cervical cancer is the second most common female cancer of women aged 15 to 44 years, with about 3.380 new diagnosed cases and about 1,805 cervical cancer deaths in 2020 (8). Even though awareness strategies and screening programs were implemented starting with the year 2012, for the last few decades, Romania has the highest incidence (28.6/100,000) and mortality (10.8/100,000) of cervical cancer in Europe (9,10).

Ovarian cancer is a "silent killer" disease, as screening and prevention methods are still limited. Worldwide, ovarian cancer ranks seventh in terms of incidence and associated mortality in women, with a five-year survival rate of approximately 35% (11). In Romania, ovarian cancer has an estimated incidence of 4% among all female types of cancer and places in the first 25 countries with the highest incidence of ovarian cancer cases, with 10.4% of thousands of inhabitants (12).

The incidence of ovarian cancer is directly proportional to age and is rare in women younger than forty (13). Identifying the risk factors can guide the frequency of gynecological consults. Recognizing signs and symptoms suggestive of ovarian cancer is the key to an early diagnosis and proper management. Associated factors with an increased risk of developing ovarian cancer are advanced age, obesity, nulliparity or late pregnancy, hormone replacement therapy, family history of ovarian, breast, or colorectal cancer, and history of family cancer syndromes. Inherited BRCA1 and BRCA2 genes mutation, or hereditary nonpolyposis colon cancer associated with MLH1, MSH2, MSH6, PMS2, and EPCAM genes, treatment for infertility in medical history, antecedents of breast cancer, and smoking are factors that increase the risk for the mucinous type of ovarian cancer (14).

As regards uterine cancer, more than 90% occur in the endometrium. Obesity is one risk factor to be considered. After increasing obesity incidence, uterine cancer has extended by one percent per year in the last ten years (15). In Romania, corpus uteri cancer represents 5.2% of all female types of cancer, with 2 355 new diagnosed cases in 2020 and 516 associated death cases. In Romania, endometrial cancer ranks the 4th among gynecological cancers, accounting for 7.8% of these, and the 4th among the causes of genital cancer mortality (5.7% -5.9%). The diagnosis advantage for this type of cancer is the early manifestation through vaginal bleeding, present in more than 90% of cases.

Uterine sarcomas are less frequent, representing 2-6% of uterine cancers, but are characterized by a poor prognosis when compared to endometrial cancer (16). For this type of cancer, early diagnosis and aggressive management are crucial for prognosis.

Beginning from observational data that suggested a continuous ascendant incidence of gynecological cancer with cases diagnosed at younger ages and in more advanced stages, we aimed to analyze the data from the anatomic-pathological department regarding incidence trends in the University Emergency Hospital of Bucharest, the main hospital of Romania.

MATERIAL AND METHOD

The present study is a retrospective analysis of histopathological results from patients with diagnosed gynecological cancers. Our team collected data from the last five years (October 2016-October 2021), using the database of the pathological anatomy department within the University Emergency Hospital of Bucharest.

Cervical, ovarian, uterine, and breast specimens with neoplastic characteristics, were included. We conducted a study of the most common histopathological forms and their trend. The analysis also regarded the age of the patients at the time of diagnosis. We present the results in graphical forms.

1,440 histopathological results matched our selection criteria. We carried out a descriptive analysis of data, calculating indicators as mean, median, standard deviations, maximum and minimum values, percentages of variables. Kruskal-Wallis one-way analysis of variance was used in the statistical analysis. If significant, it indicates that at least one sample stochastically dominates one other sample.

The Ethical Committee of the University Emergency Hospital of Bucharest approved our study. Statistical analysis was performed using the software SPSS 23.0 (SPSS Statistical Software, IBM Corp, Armonk) and Excel software.

RESULTS

1,440 cases with histopathological diagnoses of breast, cervix, ovarian, and uterine cancer were

registered. Breast cancer was the most common type, with an incidence of 34.86%, followed by cervix cancer - 29.44%, uterine cancer - 24.93%, and ovarian cancer - 10.76%.

Distribution by the age of each type of analyzed cancer showed that uterine cancer has the highest median age, opposed to cervical cancer that associates the lowest median age (Figure 1, Table 1).

Referring to the proportion of the histopathological forms, we found that ductal and lobular carcinomas accounted for more than 90% of the breast cancer cases diagnosed in this period. The most common histopathological form of ovarian cancer diagnosed in our unit was serous ovarian cancer, accounting for more than 58%. Squamous cell carcinoma of the cervix had a proportion of about 89% in our database, and as expected, endometrial cancer accounted for more than 93% of the uterine cancer cases. Relationship between the histopathological type of cancer and age showed statistical significance (Chi-squared =111,7, df- 21, Sig = .000).

The mean age for breast cancer was 62 years, with the youngest patient of 25 years old and the oldest, 91 years old. The mean age for ovarian cancer was 57 years, with the youngest diagnosed patient of 19 years. The mean age for the cervix uteri cancer was similar to ovarian cancer, 56 years old, with the youngest patient of 19 years old. Regarding uterine cancer, the average age was 63 years with a minimum recorded age of 37 years (Table 1).

Table 1. Statistical descriptive analysis of the type of cancers included in the study, according to age.

Breast cancer	Mean		62.0643
	95% Confidence interval for mean	Lower bound	60.9656
		Upper bound	63.1629
	5% Trimmed mean		62.2941
	Median		63.0000
	Variance		155.726
	Std. deviation		12.47903
	Minimum		25.00
	Maximum		91.00
Ovarian cancer	Mean		57.2418
	95% Confidence interval for mean	Lower bound	55.0109
		Upper bound	59.4727
	5% Trimmed mean		57.5007
	Median		60.0000
	Variance		195.079
	Std. deviation		13.96708
	Minimum		19.00
	Maximum		87.00

Cervix uteri cancer	Mean		56.3017
	95% Confidence interval for mean	Lower bound	55.0595
		Upper bound	57.5438
	5% Trimmed mean		56.2557
	Median		57.0000
	Variance		168.130
	Std. deviation		12.96650
	Minimum		19.00
	Maximum		91.00
Uterine cancer	Mean		63.7311
	95% Confidence interval for mean	Lower bound	62.7819
		Upper bound	64.6803
	5% Trimmed mean		63.7403
	Median		64.0000
	Variance		83.158
	Std. deviation		9.11909
	Minimum		37.00
	Maximum		91.00

The distribution by age for breast cancer showed an increased prevalence. In our study group, 4.6% of women diagnosed with breast cancer aged under 40 years. About 14% of the women diagnosed with ovarian cancer were young women aged between 19 and 40 years. About 11% of these cases were under the age of 40. 60% of women were under 60 years old. The median age for uterine cancer was 64 years. We reported only one patient with endometrial cancer under the age of 40, respectively, the age of 37 years. There were no cases of uterine sarcomas below this age limit.

Further, we analyzed the incidence trend for the last five years. We noticed that the incidence of uterine and cervical cancer had a slight decrease (Figure 2). Breast cancer had a peak incidence in 2019, and ovarian cancer did not have significant changes in the incidence during the studied years.

There was no significant difference in the number of cases per mean age during the studied period. The diagnosis of each type of cancer has maintained its age range (Figure 3).

DISCUSSIONS

Our results show that most cancers were diagnosed in advanced stages.

The proportion of each type of cancer included in the analysis follows the estimated age-standardized incidence rate for the worldwide female population. Specifically, breast cancer has the highest incidence among gynecological cancers, followed
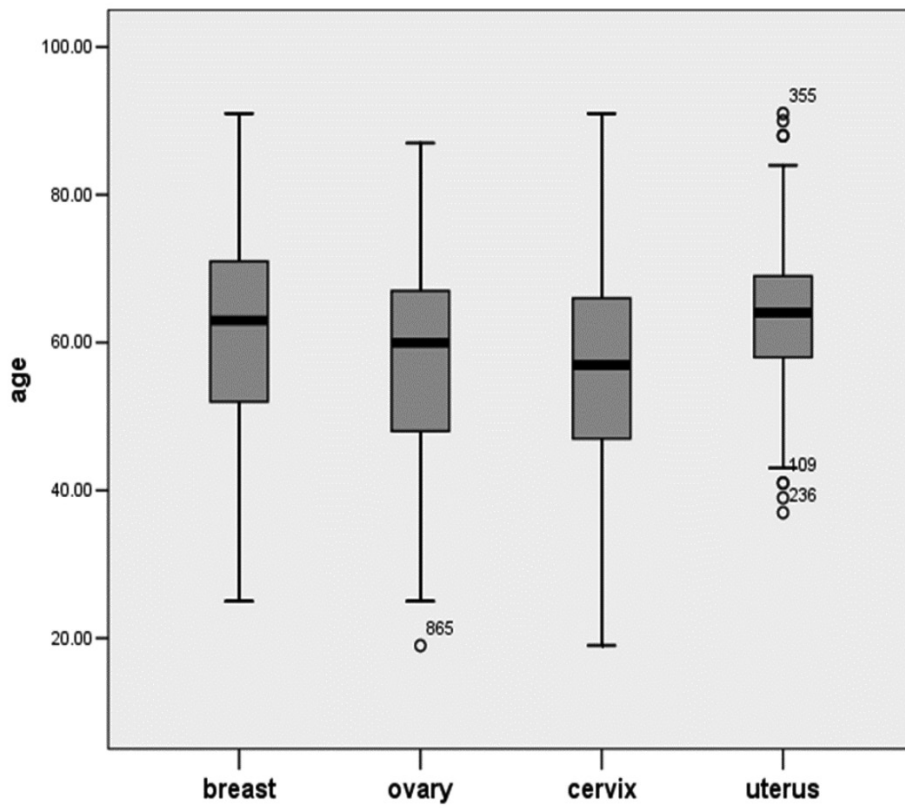
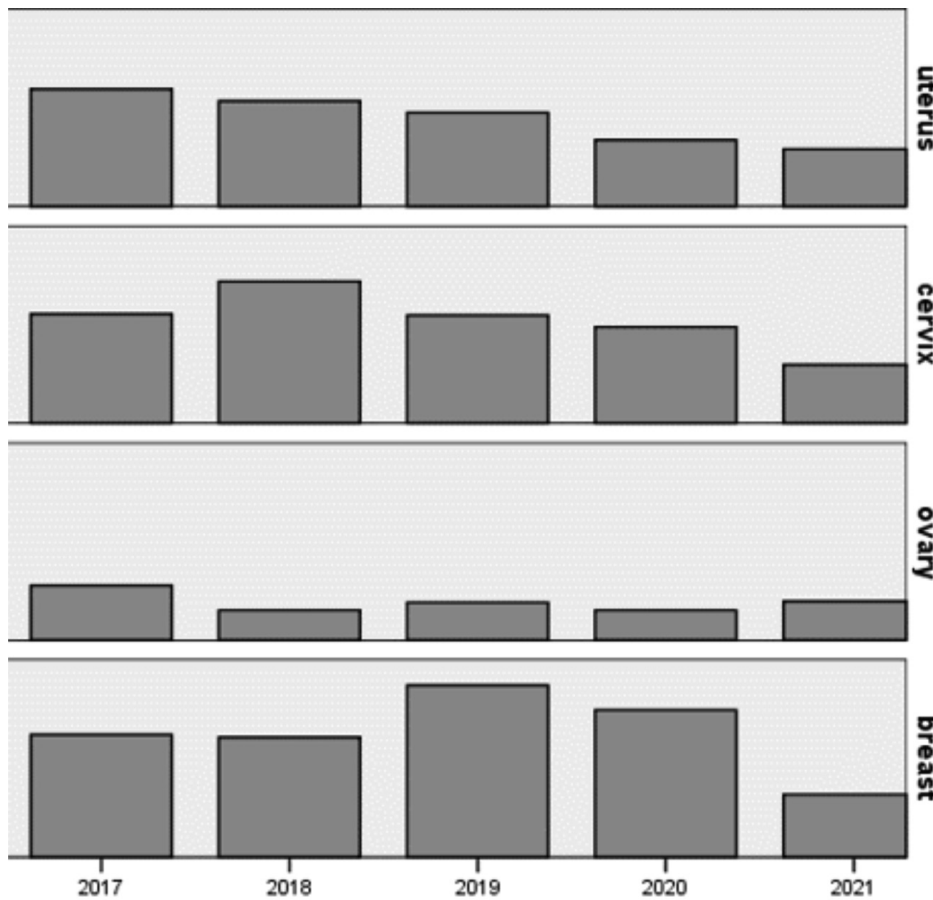**FIGURE 1.** Distribution of the analyzed types of cancer, by age

FIGURE 2. Incidence trend for the analyzed types of cancer in the University Emergency Hospital of Bucharest (2016-2021)
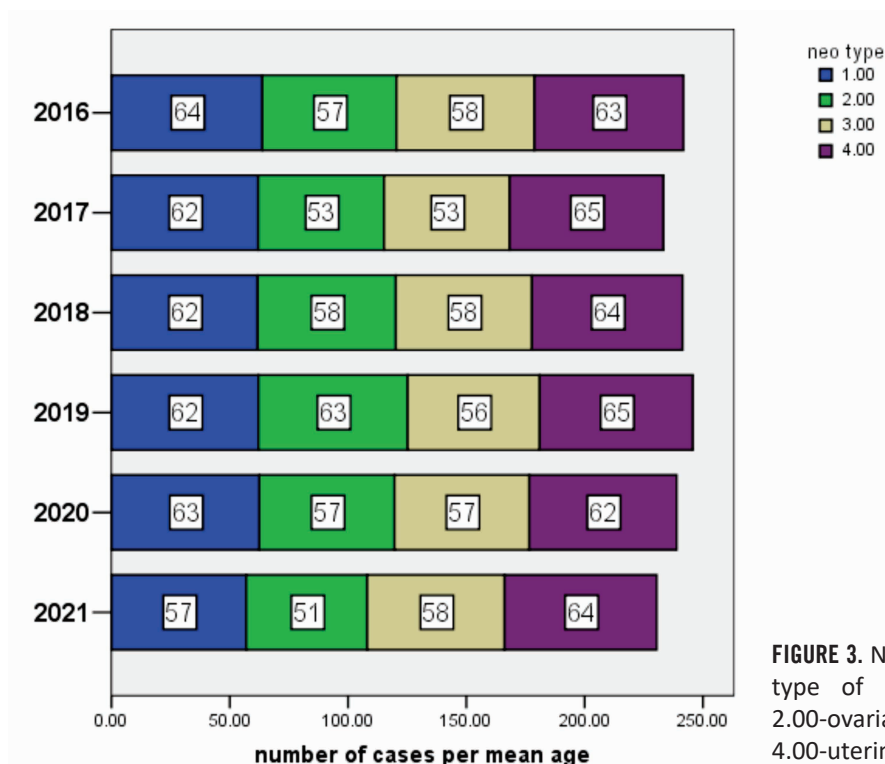
FIGURE 3. Number of cases per mean age for each type of cancer studied (1.00-breast cancer, 2.00-ovarian cancer, 3.00 cervix uteri cancer, 4.00-uterine cancer)

by cervix uteri cancer, corpus uteri cancer, and finally, ovarian cancer (17).

In Romania, breast cancer has an estimated age-standardized incidence of 65.8 with an estimated mortality rate of 17.4 per 100.000 people. These values are significantly higher than those declared for the worldwide population. According to the last official report for breast cancer incidence in Europe in 2016, the lowest number of newly diagnosed cases were in Romania. The low proportion of mammographic screenings of 6%, is therefore explained (18).

It is to notice that the youngest patient diagnosed with breast cancer was 25 years old. According to Cathcart-Rake et al. (18), one in 196 women aged under 40 is diagnosed with breast cancer, and this form of cancer accounts for 30% of cancers among women from this category of age. The median age of 63 years corresponds to data from the medical literature (19,20).

Our data regarding the median age for ovarian cancer is in line with reported data in the literature of 65 years, with a slight difference (21). Ovarian cancer is the one gynecological cancer that has the worst prognosis and the highest mortality rate. It is three-time more lethal compared to breast cancer (7). The particularity in our study is the younger ages for ovarian cancer.

Clarification of the etiopathogenetic diagnosis of cervical cancer and subsequent approval of HPV vaccines as primary prevention and the existence of a screening tool, namely the Pap test, was the

gateway to eradicating cervical cancer among public health problems. However, the number of cervical cancer cases has increased worldwide in the last decades. The estimation was 471,000 cases in 2000, 529,000 in 2008, and 570,000 in 2018 (7,22).

Romania's screening program for cervical cancer, started in 2012, failed. The consequences of a frail medical system, with limited funding, expose an unfavorable reflection over the mentioned results. In 2017, the Romanian Ministry of Health asked for help from the World Health Organization (WHO) and the International Agency for Research on Cancer (IARC) to revise and offer a solution on improving the efficiency of the cervical cancer screening program. The expert analysis summarized the following elements:

1. The coverage of the screening program was low, with no more than 10% of the targeted population participating in the screening program.
2. The follow-up of the patients screened positive was not included in the program.
3. The quality of the screening process, diagnosis, and treatment was questionable.
4. There was not a proper data recording for monitoring and evaluation of the screening program.

The following recommendations of the expertise included the reintroduction of HPV vaccination in the routine immunization program and the appropriate follow-up of patients screened positive (10).

In 2021, in Romania, another cervical cancer screening program has been implemented, a program that is mainly focused on vulnerable groups with difficult access to health services and includes the HPV vaccination in the immunization program for female teenagers aged 11-18 years.

Endometrial cancer, globally, accounts for 5% of all cancer cases and 2% of cancer-related death cases in women (23). This type of cancer occurs in reproductive and menopausal patients with a characteristic age range of 50-59 years. About 5% of the cases are under 40 years old (24).

In our study population, we obtained a median age for uterine cancer of 64 years, the value that exceeds the interval mentioned above.

Apparently, in our unit, the incidence of endometrial cancer has constantly decreased in the last five years. In the last four years, the incidence of cervical cancer also presented a downward trend. We need to mention that pandemic years came with restrictions regarding the hospitalization and surgical management of non-urgent cases. Overall, the addressability of a chronic patient was lower in 2020 and 2021.

As the values for 2019 remain as a reference, we can say that the incidence of breast cancer remains high.

As an observation for ovarian cancer, most cases were diagnosed at least in stage II, without this circumstance changing in the years studied.

CONCLUSIONS

Women with gynecological cancer are young women, for whom the stage at the time of diagnosis is the factor that dictates the subsequent prognosis. In our opinion, all forces should be oriented towards campaigns of correct information, promotion of prevention methods, and awareness of unfavorable prognosis. As cancers can run silently into advanced stages, we believe that access to specialized medical services with a presentation for routine gynecological check-ups is the solution for good management.

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