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ORIGINAL ARTICLE

Urban and rural differences in characteristics of ovarian cancer patients

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Abstract

Introduction and objective. The aim of the study was evaluation of the urban and rural differences in ovarian cancer patients' characteristics at the moment of diagnosis.

Materials and methods. The study comprised women with ovarian cancer diagnosed and treated in the Division of Gynecological Surgery of Poznan University of Medical Sciences between 2004–2011. The patients were divided into 3 groups based on their place of residence: 1) patients residing in large cities (over 50,000 people), 2) inhabitants of small towns (below 50,000 people), 3) women from rural areas.

Results. Among the studied groups of patients no differences were found in the FIGO stage at diagnosis (p=0.453), histological grade of the tumour (p=0.916), histopathological types of ovarian neoplasms (p=0.431), median tumour volume (p=0.855), presence of fluid in the pouch of Douglas (p=0.872). Women with ovarian cancer residing in large cities had lower median parity (p=0.0005), higher education level status (p=0.0001), and experienced menarche at an earlier age (p=0.039). There were no differences in the use of oral contraception (p=0.93) and body mass index (p=0.23) between the women included in the study.

Conclusions. There were no differences in advancement of ovarian cancer at the moment of diagnosis or in tumour type and size between women residing large cities, small towns and rural areas. Several ovarian cancer risk factors were more common among ovarian cancer patients living in urbanized areas.

Key words

ovarian cancer, place of residence, urban rural differences

INTRODUCTION

Ovarian cancer remains one of the most challenging problems in contemporary gynecological oncology worldwide. It concerns women from different countries, regions, socio-economic, age and ethnic groups. It is also a very important cause of mortality among malignant diseases in every population [1]. This is why research into epidemiology and ovarian cancer patients' characteristics is of particular interest and importance for the improvement of early diagnosis and effective treatment of this disease. Unfortunately, to date, there are no effective screening programmes for women with ovarian cancer. Screening may significantly improve the results of treatment and reduce mortality in this patient group. Early diagnosis may be helpful for pre-operative malignancy prediction, and if the pre-operative risk of malignancy is high, patients should be transferred to tertiary gynecological oncology centres in big cities for surgical treatment where there is a better prognosis [2].

There is evidence that there are some differences in ovarian cancer incidence and mortality in different populations according to place of residence, socio-economic and educational status [3]. It may be related to differing lifestyle and exposure to risk factors, as well as different access to healthcare and its diagnostic tools and treatment. It is hypothesised that low social status, low income and low educational level are connected with delayed diagnosis and a poorer prognosis in ovarian cancer patients. It is also possible that patients from rural regions have fears and bad habits associated with gynecological examinations and screening programmes. The situation quite often arises in which the only contact with a gynecologist takes place during pregnancy and childbirth, and later on, in the situation where a gynecological malignancy is at an advanced, usually inoperable stage of the disease. The differences between urban and rural accessibility to healthcare centres are also connected with longer travel distances and times, as well as higher costs in reaching medical care units. The level of education and awareness of the threat of cancer may also affect the regularity and frequency of preventive medical examinations. Previous research concerning the relationship between the place of residence and stage of disease at diagnosis of malignancy demonstrated that the rural population is affected by delayed discovery of cancer [4, 5].

OBJECTIVES

The aim of the presented study was evaluation of the urban and rural differences in ovarian cancer patients' characteristics at the moment of diagnosis. The research concerned analysis of tumour characteristics at diagnosis, according to the place of residence and educational level of the women analyzed.

MATERIALS AND METHOD

An exploration of the archives of the Division of Gynecological Surgery of Poznan University of Medical Sciences was

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undertaken between 2004–2011. A group of 363 women, diagnosed and treated in the Division for malignant ovarian tumor were included in the study. The patients were divided into 3 groups, based on their place of residence. The first group consisted patients residing in a large city (over 50,000 inhabitants), the second group consisted of patients living in a smaller town that had city rights and with a population below 50,000 inhabitants, and the third group consisted of patients living in rural areas.

The diagnosis of ovarian tumour was based on histopathological examination of the tumour, obtained during surgery. The tumours were subdivided according to the WHO criteria, and the histological grade of the tumour was defined in a 3-step grading scale. The clinical stage of the disease was specified using the criteria of the International Federation of Gynecology and Obstetrics [6]. Borderline ovarian tumours and metastatic adnexal tumours were classified as malignant adnexal masses. For each patient, their age, menopausal status, age at menarche and menopause, duration of reproductive period and body mass index (BMI) were determined. Postmenopausal status was defined as more than 12 months of amenorrhea or age above 50 years in women who had undergone hysterectomy. All other women were considered premenopausal. From each patient an anamnesis considering parity and the use of oral contraceptives (OC) was taken. The use of OC pills for longer than 5 years was considered relevant for the study. Data about educational status was available for 152 women.

Ovarian tumour volume was estimated by means of transvaginal and abdominal ultrasonography performed within 5 days of operation. The volume of the majority of tumours was measured by means of transvaginal ultrasonography. In the case of large tumours, transabdominal ultrasonography was performed. Tumour volume was assessed according to the formula: volume [cm^3]= A [cm] x B [cm] x C [cm] x 0.532, where A, B and C were the largest perpendicular dimensions of the tumour expressed in centimeters. The presence of fluid in the pouch of Douglas was determined according to the International Ovarian Tumor Analysis (IOTA) Group recommendations [7]. Fluid in the pouch of Douglas (ascites) was considered as present when the largest anterior-posterior diameter was greater than 10 mm [7].

Statistical analysis was calculated by means of Cytel Studio StatXact 9 and GraphPad Instat 3. Finally, a systematic review of the literature concerning the subject of the study was performed.

RESULTS

The median age of patients in the study was 52, ranging from 12–85. In the group of studied women, 176 were premenopausal and 187 postmenopausal. It was found that 176 patients (48%) resided in large cities, 65 (18%) and 122 (34%) patients lived in smaller towns and rural areas, respectively. There were no differences between patients' ages, menopausal status and BMI in the 3 studied groups. Demographic characteristics, as well as the results of statistical calculations, are presented in Table 1.

No difference was found in the FIGO stages at diagnosis of malignant ovarian tumours between the 3 studied groups (p=0.453). The difference in the FIGO stage at diagnosis was not statistically significant, even when the group of women residing in large cities and small towns were combined and compared to women from rural areas (p=0.235). Similarly, there were no differences regarding the grading of the tumour between the 3 studied groups (p=0.916) (Tab. 2).

Table 1. Demographic characteristics of studied patients.

	Large cities	Small towns	Rural areas	p-value
Median age of patients (minimum – maximum)	54 (21 – 80)	53 (29–78)	50 (12–85)	p=0.182
Number (%) of premenopausal and postmenopausal	82 (47%) and 94 (53%)	32 (49%) and 33 (51%)	62 (51%) and 60 (49%)	p=0.760
Median Body Mass Index (minimum – maximum)	24 (17–39)	25 (18–50)	24 (15–38)	p=0.239

Table 2. FIGO stages and histological grade of ovarian neoplasms among studied groups.

	Large cities (No. of patients)	Small towns (No. of patients)	Rural areas (No. of patients)	p-value
FIGO stage				
FIGO I	64	22	31	p=0.453
FIGO II	14	8	11	
FIGO III	82	27	66	
FIGO IV	16	8	14	
Histological grade				
G1	56	18	34	p=0.916
G2	53	21	35	
G3	64	22	48	

There were no differences in the frequency of diagnosis of main histopathological types of ovarian neoplasms between the analyzed groups of patients (p=0.431). Additionally, no differences were found in the presence of specific types of epithelial ovarian cancer (p=0.765) (Tab. 3).

Table 3. Histopathological tumor characteristics.

	Large cities (No. of patients)	Small towns (No. of patients)	Rural areas (No. of patients)	p-value
Main types of ovarian neoplasms				
Epithelial ovarian cancer	140	50	103	p= 0.431
Granulosa cell tumor	10	2	5	
Malignant germ cell tumors*	4	1	5	
Borderline ovarian tumors	19	9	6	
Metastatic ovarian tumors	2	2	3	
Epithelial ovarian cancers				
Serous	60	23	57	p= 0.765
Mucinous	16	6	11	
Endometrioid	20	8	13	
Clear-cell	11	3	4	
Undifferentiated carcinoma	33	10	18	

* The group of malignant germ cell tumors included: 5 cases of dysgerminoma, 4 diagnosed in patients living in rural areas and 1 found in a large city; 3 immature teratomas diagnosed in one patient from each group; one case of embryonal carcinoma and one case of mixed germ cell tumor containing elements of embryonal carcinoma, dysgerminoma and yolk sac tumor were found in patients residing in large cities.

Median tumuor volume among patients residing in large cities was 382.0 cm^3, ranging from 14.1–9369.1 cm^3, compared to 430.0 cm^3 (14.7–5753.0 cm^3) and 418.0 cm^3 (16.5–6297.6 cm^3) in the groups of patients living in small towns and rural areas, respectively. The difference was not statistically significant (p=0.855). 104 (59.1%) women living in large cities showed ascites at the time of diagnosis. There were 39 (60%) and 69 (56.6%) patients diagnosed with fluid in the pouch of Douglas who resided in small towns and rural areas, respectively. This difference was not statistically significant (p=0.872).

Median parity for women residing in large cities was 1 (range 0–4). The corresponding values for women living in small towns and rural areas were 2 (range 0–5) and 2 (range 0–7). The difference was statistically significant (p=0.0005). However, when a *post-hoc* test was performed, the only statistically significant difference was between the parity of women living in rural areas and large cities (p<0.001). There was no difference either in the parity between women residing in small towns and rural areas, or between patients living in large cities and small towns (p>0.05).

A statistically significant difference was found in educational status between the studied groups (p=0.0001). There were 36% (22/62), 45% (28/62) and 19% (12/65) of women with higher, secondary and primary education, respectively, among women living in large cities. The corresponding values for women residing in small towns and rural areas were, respectively, 45% (21/47), 34% (16/47), 21% (10/47), and 12% (5/43), 30% (13/43), 58% (25/43). No differences were found between educational status and the FIGO stage of the diseases at the moment of diagnosis (p=0.112) (Tab. 4).

Table 4. Distribution of FIGO stages of ovarian cancer at the moment of diagnosis within different educational levels of the studied women.

	Higher education (No. of patients)	Secondary education (No. of patients)	Primary education (No. of patients)	p-value
FIGO I	10	11	13	p= 0.112
FIGO II	7	9	7	
FIGO III	22	30	12	
FIGO IV	10	8	16	

9% (16/175) of women living in large cities declared the use of oral contraception for more than 5 years. A similar percentage was found among women from small towns (8%, 5/65) and rural areas (9%, 11/122), (p=0.93).

A statistically significant difference in age at menarche was found across the 3 studied groups (p=0.039). The *post-hoc* test showed that women with ovarian cancer residing in large cities experience menarche at an earlier age compared to women from rural areas (mean rank difference – 22.351; p<0.05). The Kruskal-Wallis Test (Nonparametric ANOVA) revealed a significant difference between age at menopause across the 3 studied groups (p=0.047). The *post-hoc* test, however, did not find significant differences. Data concerning the reproductive cycle characteristic of the patients studied are summarized in Table 5.

Table 5. Menstruation characteristics of studied patients.

	Large city	Small town	Rural areas	p-value
Median age at menarche (Range)	14 (11–18)*	14 (12–18)	14 (11–18)*	p= 0.039
Median Duration of reproduction period (Range)	36 (24–43)	33 (29–40)	34 (20–40)	p= 0.417
Median age at menopause (Range)	50 (38–55)	49 (42–49)	50 (36–57)	p= 0.047[$]

* Dunn's multiple comparisons post-hoc test revealed a statistically significant difference (p<0.05) in age at menarche between women residing in large cities and rural areas. There were no differences when other groups were compared.
[$] Performed pos-hoc test revealed no difference between the groups studied.

DISCUSSION

The incidence of ovarian cancer and mortality remains high among all cancers in women, in Europe and worldwide. Age Standardized Rate per 100,000 for incidence and mortality in the European Union in 2008 were 13.5 and 7.6, respectively. In these statistics, Poland is situated very high among European countries. Incidence and mortality rates for Poland in 2008 were 17.0 (7th place) and 10.1 (5th place), respectively [8]. The level of 5-year survival is inextricably linked with the stage of the disease at diagnosis. The lack of effective screening programmes for ovarian cancer means that most diagnoses occur at an advanced stage of the disease [9]. However, recent studies involving novel methods of screening (multimodal screening and transvaginal ultrasound screening) have achieved encouraging results [10]. Nevertheless, it should be noted that effective screening requires high-quality gynecological ultrasound with subjective ultrasound assessment performed by an experienced clinician, which is not globally available [11, 12]. The search for effective first-line diagnostic methods and access to centers experienced in ultrasound and surgery seems to be the primary goal to improve the results of treatment of women with ovarian cancer, because the prognosis is best when the treatment takes place at a tertiary centre for gynecological oncology [2].

It has been shown that there are differences in tumour characteristics at diagnosis according to the place of residence, educational level and socio-economic status of women affected by cancer [13]. One reason for delayed diagnosis might be caused by poor access to health care and thus the higher stage of the disease according the FIGO at diagnosis. It is important to assess whether patients from rural areas have a more advanced stage of the disease at diagnosis, and whether the prognosis in such a situation is worse. This could then be taken into account when planning organization of medical care. Campbell et al. analyzed this situation in patients with lung or colorectal cancer and their findings suggest that patients who live far from cities and associated cancer centres have less chances of survival because of the more advanced stage of the disease at diagnosis [14]. Krzyzak et al. also reported that the proportion of early breast cancer diagnosis is low and prognoses are poorer in the rural population [4, 5]. They suggest the explanation of this situation is the more difficult access to early diagnosis and treatment methods [4, 5]. In the presented study, this situation was not confirmed in ovarian cancer patients in the Poznan region, because no differences were found in the stages of the diagnosis between women residing in different areas. Furthermore, there were no differences in tumour size and presence of ascites, based on place of residence in the analyzed group of women. This may be explained in several ways. For instance, there is lack of organized ovarian cancer screening in Poland. Although, women residing in large cities and have a higher educational status tend to

visit the gynecologist more often compared to women from rural areas.

The most encouraging results of ovarian cancer screening were achieved with the use of the organized multimodal screening method (assessment of ovarian cancer biomarker CA125 level and ultrasound evaluation by referral to a gynecologist in selected cases) which, however, is not routinely performed in Poland [10, 15, 16]. Furthermore, ovarian cancer was once regarded as a 'silent killer', but nowadays opinions have changed because as many as 95% of patients reported non-specific symptoms at the time of ovarian cancer diagnosis [17, 18]. As reported by Goff et al. [18], only 11% of patients with stage I/II ovarian cancer reported no symptoms before diagnosis. Although women residing in urban areas mostly have better access to a general practitioner (GP) [19], the delayed time from the first report of symptoms to appropriate referral may contribute to the lack of difference in the stage of ovarian cancer diagnosis between women residing urban and rural areas [20]. It was shown that both women and GPs fail to recognize the symptoms of ovarian cancer, due to this, 50% of women are not referred directly to a gynecological oncologist [18, 21]. Lastly, the lack of difference in stage at diagnosis may be related to tumour biology. As proposed by Brown and Palmer [22], the median diameter of ovarian cancer before progression to stage III or IV is 3 cm, and recognition of 50% of stages I-II ovarian cancer would be possible if tumours of 1.3 cm could be detected at annual screening. Currently, such a sensitive screening programme is not available.

Numerous studies have revealed increased cancer incidence with increased population density and urbanization [23]. The difference is explained by increased exposure to cancer risk factors related with personal behaviours (cigarette smoking, alcohol consumption, sexual promiscuity, exposure to ultraviolet light, type of diet and family size), atmospheric pollution and occupational hazards [24]. However, in the case of ovarian cancer, the interrelation between incidence and urbanization is not clear. S. Dey et al. [3] observed a twice higher incidence of ovarian cancer among women living in urban versus rural areas. This difference in the incidence between the studied populations was similar to that for leukemia, which is a neoplasm of mainly genetic etiology. Nevertheless, the highest urban-rural incidence rate ratio was found for uterine cancer, where, the incidence was 6 times higher in urban areas.

Another interesting observation by Dey et al. was the fact that the comparison of age-specific incidence of ovarian cancer at an early age showed a higher urban incidence than rural incidence, and the urban incidence kept increasing with age to its maximum in the age group over 70 years old. Rural incidence, however, was maximal in the 60–69 age group, after which it declined [3]. In the study by Minelli et al. [25] the difference in incidence of ovarian cancer between urban and rural regions of central Italy was not statistically significant. Contrary to Dey et al. [3, 25], Minelli et al. found no difference in the incidence of uterine neoplasms among the studied populations. However, the authors showed a higher incidence of breast cancer among women residing in urban areas [24].

The difference in incidence of female cancers was shown to be particularly related to estrogen-dependent cancers (such as breast and endometrial cancer), where lifestyle, socio-economic status, dietary habits and exposure to external factors is especially important. In estrogen-dependent malignancies the urban population is exposed to a higher concentration of xenoestrogens. In ovarian cancer patients, these factors are not so important and this tendency is not so strongly reflected [3]. Although several risk factors were shown to influence the development of ovarian cancer, the most important are associated with reproductive history, where nulliparous women are at increased risk, while increasing parity reduces the risk of ovarian cancer [26, 27].

A higher level of education was also shown to be associated with an elevated risk of ovarian cancer [28, 29]. In the presented study, significant differences were found in the educational status among women suffering from ovarian cancer, depending on place of residence. In this case, women from rural areas tended to have lower educational status. However, no relationship was found between educational status and the FIGO stage of ovarian cancer at the moment of diagnosis.

The use of oral contraceptives is also associated with lowered risk of development of ovarian cancer. The presented study shows that the use of oral contraception is generally infrequent, and there were no differences depending on place of residence. There is multiple data on the correlation between duration of the reproductive period and the risk of ovarian cancer. Generally, it is considered that the increased number of ovulations associated with a prolonged reproductive period is a risk factor of ovarian cancer [27]. The presented study shows that women living in large cities experience menarche at an earlier age, compared to women from rural areas. This is in accordance with the secular trend present in Poland [30]. However, a recent large study conducted by Tsilidis et al. [31] showed that age at menarche is not a predictive factor for ovarian cancer, contrary to age at menopause. No difference was found in the presented study in the length of reproductive period and age at menopause.

Data on the association of the BMI with risk of ovarian cancer is inconsistent. Meta-analysis performed by Olsen et al. [32] revealed a positive correlation between the BMI and increased risk of ovarian cancer. On the other hand, there is data showing that the BMI may be protective [33]. In the presented study, no differences were found in the BMI between women suffering from ovarian cancer residing in different areas. However, in the analysis of some cancer risk factors in Poland, Romundstad et al. showed that obesity increased with age, especially in females, and was less frequent among people with high education and people residing in urban areas [34].

CONCLUSIONS

To sum up, no differences were found in the advancement of ovarian cancer disease at the moment of diagnosis, or in the tumour type and size among women residing in large cities, small towns and rural areas. Several ovarian cancer risk factors were more common among ovarian cancer patients living in urban areas.

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