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Secondary cervical cancer prevention in routine prenatal care — coverage, results and lessons for the future

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ABSTRACT

Objectives: Cervical cancer is the fourth most common type of cancer among women worldwide and one of the most common malignancies diagnosed in gravidas. Therefore, routine antenatal Pap smear is such an important examination. The aim of the study was to assess the prevalence of Pap smear performance during prenatal care and to determine possible factors affecting it.

Material and methods: A self-composed questionnaire was distributed among 638 women managed in a tertiary obstetric referral center. 33 questions regarded cervical cancer prevention and risk factors.

Results: 96.9% of respondents had undergone Pap smear and 80.6% had it performed during pregnancy. For 11.5% women Pap smear in pregnancy was the first one in their life. The most common reasons for lack of Pap smear performance were: no subjective need to perform it (40.9%), no doctor's recommendation (28.6%) and lack of gynecological care (16.3%). Among professionally active women the percentage of those who had not undergone Pap smear during pregnancy was statistically higher (28.5%) than among those who were on sick leave (13.5%) ($p = 0.0003$). Also, younger women were at risk of less frequent participation in cervical cancer screening

Conclusions: Although performance of Pap smear among surveyed patients was relatively high, there was a significant group of women who had undergone their first test during pregnancy, which makes secondary cervical cancer prevention in prenatal care a useful prophylactic strategy. Special attention should be given to younger and professionally active women.

Key words: cervical cancer; pap smear; prenatal care; pregnancy; secondary prevention

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INTRODUCTION

According to GLOBOCAN cervical cancer is the fourth most common type of cancer among women worldwide, with the incidence of 569,847 cases and the cause of 311,365 deaths a year [1]. In Poland, in 2018 the number of new cases was 3,220 with an incidence age- standardized rate of 9.4 per 100,000 and the number of deaths was 1,947 with a mortality age-standardized rate of 4.9 per 100,000 [1]. Nevertheless, according to GLOBOCAN, the age-adjusted cervical cancer incidence in 2018 was lower in Poland than in Europe as a whole (9.4 vs 11.2) and the number of new cases decreased by almost 2.3 times during the end of the first decade of the 21st century, which was possibly due to the introduction of a population based cervical cancer screening program initiated in 2006 by the Polish National Health Fund [1, 2]. The program is dedicated to women covered by health insurance between 25 and 59 years of age and offers performance of Pap smear once in three years — in case of negative results. Whereas patients classified as high-risk groups — HIV or HPV positive or on immunosuppressive therapy - can participate in examinations every 12 months [2]. Over the years participation in the cytology screening program in Poland increased from 12.7% in 2006 to 42.11% in 2015 [3]. This suggests that the universal, free access to cytology examinations may result in increased population coverage.

Another factor, which contributes to incidence reduction, is the vaccination against human papillomavirus (HPV)

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which is recommended in Poland, but is not among the publicly funded healthcare benefits [4]. Only two EU member states, including Poland, are not financing HPV vaccinations in selected age groups (10–15) [5]. However, various local governments and autonomies as well as charity organizations and schools conduct free, preventive HPV vaccination actions. The Polish National Vaccination Program recommends HPV vaccination prior to sexual initiation, however it does not indicate the specific age when such vaccination should be performed [4].

Additionally, in order to improve cervical cancer screening effectiveness, according to the Ordinance of the Polish Minister of Health, Pap smear should be performed in every pregnant woman till the end of the 10th gestational week as a part of standard prenatal care, unless she had undergone it within the last six months [6]. For most women, pregnancy is a period of increased medical supervision, which makes it a good opportunity for secondary cervical cancer prevention.

Objectives

The aim of the study was to assess the performance of Pap smear in pregnant women and to determine possible factors affecting it.

MATERIAL AND METHODS

A cross-sectional study was performed by means of a self-composed questionnaire (*see* Annex no. 1) distributed among 638 patients from different regions of Poland who were managed in the 3rd trimester or within the first month after birth in a tertiary referral obstetric center. The entire group of patients who agreed to take part in the study was surveyed between December 2017 and February 2018. The survey was composed of 33 questions regarding obstetric history, performance, frequency and results of Pap smear examinations, reasons for not performing it (if applicable), gynecological care, vaccination against HPV, use of hormonal contraception, family history of cervical cancer, and performance of further diagnostic procedures: colposcopy or histopathological examination. Informed consent was obtained from all individual participants included in the study. Statistical analysis was performed with the use of Statistica 13.3. Since the differences between groups were based on the categorical variables, they were tested with the use of chi-squared test. P-values < 0.05 were considered statistically significant.

RESULTS

The average age of surveyed women was 25.8 ± 4.89 years (17–45 years). The study group was diverse in terms of place of residence, level of education, professional activity and marital status, which is presented in Table 1.

More than half of respondents were primigravid (54.4%; n = 347), 29.9% (n = 191) were in their second pregnancy and for 15.7% (n = 100) of women it was the third or subsequent pregnancy.

All surveyed women were under gynecological supervision during pregnancy but as many as 10.2% (n = 65) of them had never visited a gynecologist before pregnancy. Out of those who were attending appointments regularly before pregnancy, 34.1% (n = 206) did it once in 6 months or more often, 41.9% (n = 253) once a year, 12.7% (n = 77) once in 2 or 3 years and 6% (n = 36) less often.

The analysis of Pap smear performance among surveyed women revealed that the vast majority of them (96.9%; n = 618) had undergone Pap smear examination, yet fewer (80.6%; n = 497) did it during pregnancy. This includes a small group of women (4.9%; n = 23) who performed the test as a preparation for planned pregnancy. Among women who underwent Pap smear during pregnancy those who had it in the first trimester (72.2%; n = 324) dominated, whereas 23.6% (n = 106) had it in the second and 4.2% (n = 19) in the third trimester. Among multiparas the per-

Table 1. Group characteristics: number of women (%)

Level of highest achieved education				
Primary	**Vocational**	**Secondary**	**Higher**	
19 (3%)	36 (6%)	238 (37%)	345 (54%)	
Place of residence				
Village	**City < 10,000 inhabitants**	**City 10,000–100,000 inhabitants**	**City > 100,000 inhabitants**	
128 (20%)	55 (9%)	149 (23%)	306 (48%)	
Professional activity				
Unemployed	**Professionally active**	**Sick leave during pregnancy**	**Maternity leave**	**Other**
99 (16%)	137 (21%)	283 (44%)	75 (12%)	44 (7%)
Marital status				
Married		**Unmarried**		
457 (72%)		181 (28%)		

centage of Pap smear performance in previous pregnancies was 79.9% (n = 226).

The analysis of Pap smear results performed during pregnancy revealed that in 67.8% (n = 328) of cases they were normal, in 23.6% (n = 114) the test detected inflammation and 2.3% (n = 11) of women had an abnormal test result such as: atypical squamous cells of undetermined significance (ASC-US), low grade squamous intraepithelial lesion (LSIL) or high grade squamous intraepithelial lesion (HSIL) (Fig. 1).

The analysis of questions regarding frequency of Pap smear performance showed that almost half of the women (47.4%; n = 293) performed the test regularly every year, 22.7% (n = 140) every 2 years, 7.8% (n = 47) every 3 years and 7.9% (n = 49) less often. For 11.5% (n = 71) of women Pap smear in pregnancy was the first in their lifetime and 1% (n = 6) underwent the test mainly in pregnancies. The average age during the first Pap smear was 20.6 ± 3.4 years (12–35 years).

Similarly, among women who were over 25 years old and were qualified for the population-based cervical cancer screening program, almost half (48.1%; n = 232) performed the test once a year, 24.5% (n = 118) every 2 years, 9.3% (n = 45) every 3 years and 8.5% (n = 41) less often. For 7.5% (n = 36) of women Pap smear in pregnancy was the first in their lifetime.

The most common reasons for not performing Pap smear were: no subjective need to perform it (40.9%; n = 83), no doctor's recommendation (28.6%; n = 58) and lack of gynecological care (16.3%; n = 33). No doctor's recommendation was reported by 26% (n = 39) women who were over 25 years old and were covered by a population-based screening program. Other listed reasons were: feeling of shame (5.4%; n = 11), cost of the test (3%; n = 6), fear of pain (2.5%; n = 5) and concern about the test result (2%; n = 4).

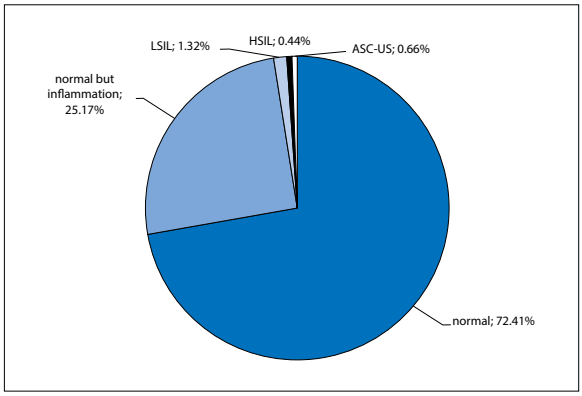

Figure 1. Results of performed Pap smears in current pregnancy

As for the reasons which affected the Pap smear performance, it was observed that among professionally active women the percentage of those who did not perform Pap smear during pregnancy was statistically higher (n = 41; 28.5%) than among those who were on sick leave (n = 37; 13.5%) (p = 0.0003). Another statistically significant factor was women's age (Tab. 2). Analysis of the following age groups: under 25 years (< 25), between 25 and 35 years (≤ 25 and < 35) and over 35 years (> 35) revealed that the youngest women much more often had never performed Pap smear (9.1% vs. 1.2% in other age groups; p = 0.0001) and that the test during pregnancy was more often the first one in their life (25.7% vs. 7.2% in other age groups; p = 0.0001). The most important fact is that they much more frequently did not perform Pap smear in their current pregnancy (27.1% vs. 16.7% in other age groups; p = 0.02). No significant association between place of residence, level of education or marital status and Pap smear performance was observed.

8.8% of women (n = 56) admitted to having a positive family history of cervical cancer. Yet the majority of them (67.9%; n = 38) did not indicate any impact of this fact on the frequency of Pap smear performance. 50.9% (n = 324) of women declared their use of hormonal contraception (HC) in the past, 85.4% (n = 274) of them reported no association between HC use and regular Pap smear control.

The study also showed that vaccination against HPV was not widespread among respondents (6.1%; n = 39). Those who had been vaccinated were asked whether they had undergone it before or after sexual initiation, but no marked predominance of either option was observed (38.5% vs. 46.2%, respectively).

A history of further diagnostic procedures due to suspicion of cervical abnormalities was reported by 10.1% (n = 64) of surveyed women, revealing one case of LSIL and four cases of HSIL in histology examinations.

DISCUSSION

Despite the development of a National Population-Based Cervical Cancer Screening Program in 2006 by the Polish Ministry of Health, the National Health Fund and

Table 2. Pap smear performance in different age groups: number of patients (%)

	< 25 years n = 150	25–34 years n = 404	≥ 35 years n = 70	P
Had never performed Pap smear	14 (9.1%)	4 (1.2%)	1 (1.4%)	0.0001
Pap smear in pregnancy was the first in a lifetime	39 (25.7%)	31 (7.6%)	4 (5.6%)	0.0001
Did not perform Pap smear in current pregnancy	41 (27.1%)	69 (17%)	12 (17.1%)	0.02

the Polish Gynecological Society, following World Health Organization and International Agency for Research on Cancer (WHO/IARC) guidelines, percentage of women performing the test was still unsatisfactorily low according to the Supreme Audit Office of Poland performed in the Lubelskie Province [7]. In order to increase cervical cancer screening coverage, since 2012 every pregnant woman should undergo Pap smear during her initial prenatal visit as ordinated by the Polish Ministry of Health [8]. However, it is stated that cervical samples collected during pregnancy are more difficult to interpret because of hormonal changes in the epithelial cells [9]. Similarly, WHO provides the information that cervical specimens taken during pregnancy can give misleading results [10]. Nevertheless, results of Pap smear performed in pregnant women are not less accurate than in non-pregnant patients and it is recommended to perform the test if the woman is likely to give up gynecological care after delivery and when she is in the target age group [11, 12]. This includes women over 20 years old or sexually active for more than 3 years [13]. On the contrary, several publications reported that pregnancy did not modify or affect HPV infection, nor cervical cytomorphology [14, 15]. It is also proved that the intraepithelial lesions in gravidas are cytometrically identical to those in nonpregnat women [13]. Therefore, a specimen collected during pregnancy is adequate for evaluation but only if the pathologist is notified of patient's pregnancy status [9, 16]. It may be even more difficult to interpret the colposcopic appearance of the cervix, even in the first trimester. Nevertheless, it should be always performed in women with an abnormal Pap test result [13].

Cervical cancer is one of the most common malignancies diagnosed in gravidas, complicating 1 in 2200 pregnancies [13, 17]. Therefore, routine antenatal Pap smear is such an important examination. Abnormal cervical cytology is observed in about 5% of gravidas [17–19]. In our study the percentage was slightly lower than the average — 2.3%. Pregnancy is a special period and sometimes the only one when women pay more attention to their health condition so especially during this time physicians should motivate their patients to conduct screening examinations. In the Norwegian study Nygård et al. [20] indicated that screening during pregnancy increases the coverage of the cervical cancer prevention program. They reported that 69% of pregnant women had the Pap smear performed during one year of follow-up since the beginning of pregnancy and that the majority of tests were performed before the delivery [21]. Our study showed that the percentage of Pap smear performance during pregnancy in Poland was even higher (80.6%). However, more important is the fact that for 11.5% of women cervical cytology performed during pregnancy was the first in their life and it does not apply only to women who were under the age of 25, not routinely covered by screening. As many as 16.7% of women over 25 years of age had never had the test performed before pregnancy, while according to the screening guidelines — should have had [22]. Similarly, a French study conducted by Brun-Micaleff et al. suggested that Pap smear combined with HPV infection testing may be an effective method of covering young women with poor adherence to cervical cancer screening. It is estimated that in France 40% of women do not perform regular cytology examinations. By enrolling in the study women with poor adherence the researchers detected high risk HPV-infections in 20.2% gravidas and cervical intraepithelial neoplasia grade 1 or 2 in 2% of the tested population [23].

It may be the subject of controversy whether it is wrong that women under the age of 25 much more often do not perform Pap tests. It is believed that the majority of dysplastic cervical lesions, which are common in this age group have a tendency to regress spontaneously [21]. Therefore, covering this age group with screening may lead to overdiagnosis and subsequently — overtreatment of precancerous lesions [24]. However, Nygård et al. [20] showed that women who perform Pap smear frequently have a tendency to follow this pattern, whereas those who do it seldomly or never, have no tendency to participate in screening in the near future. This is why teaching young women a regular Pap smear scheme may lead to increased screening coverage when they are older. This approach is also in line with the study conducted by Brun-Micaleff et al. Although they detected that 20% of the young pregnant women were positive for HPV infection, they were aware that most of them developed transient infections. Nevertheless, they stated that a positive result may prompt women to repeat Pap smears in the following years at regular intervals [23].

In a Polish study regarding awareness of cervical cancer prevention performed by Ulman-Włodarz et al. [25] the most common reasons for avoiding Pap smear performance were: fear of pain (40.9%), no symptoms of the disease (18%) and carelessness (15%). These causes are quite different in our results, where no subjective need to perform the test was the most frequently reported reason (40.9%) and fear of pain was quoted only by 2.5% of respondents. Nevertheless, the alarming fact is that in both studies a significant number of patients — 28.6% in our study and 11.0% in Ulman-Włodarz et al. [25] study — reported no doctor's recommendation to perform the test. Monteiro et al. [26] showed that the problem does not only concern the Polish society. In their study from Brazil the majority of gravidas who did not undergo cytological examination did not receive an offer from healthcare professional to do so. They emphasized that it was crucial to perform the Pap smear during antenatal consultations as women less frequently schedule an appointment exclusively in order to undergo Pap smear but they usually participate in prenatal consultations, which

makes pregnancy a good opportunity for screening. Similar recommendations are given by the authors of the Thai research [18]. In their study 31% of gravidas had no previous Pap smear screening. Therefore, the proposition of the examination is clinically relevant because these women may not attend regular gynecological appointments in future. In addition, in a Swedish study by Eaker et al. [27] respondents stated that receiving an invitation or offer from a gynecologist motivated them to perform the test. Thus, it is crucial to put emphasis on the greater frequency of these proposals. In addition, the most commonly reported reason for avoiding Pap smear performance, which was 'no subjective need to perform the test', can be interpreted as no disease symptoms. This misunderstanding that Pap smear should be performed only in the presence of gynecological symptoms is quite common among patients all over the world. Augusto et al. [28] in their Brazilian study proved that the absence of symptomatic episodes of sexually transmitted disease was one of the most common reasons for no participation in the screening program. Also, research by Khaengkhor et al. [18] revealed that for 53% of women Pap smear performance seemed necessary only in case of symptoms, such as vaginal bleeding or leucorrhea.

Authors of different studies tried to identify factors affecting the Pap smear performance in order to define under-screened groups requiring special attention. Spaczyński et al. [29] reported that the place of residence and level of education have an impact on cervical cancer screening. According to their study, living in the village and low level of education contribute to less frequent secondary prevention. On the contrary, our study did not show any influence of the place of residence, level of education or marital status on cervical cancer screening — both during pregnancy and in general. The only association we observed was the fact that women who were professionally active during pregnancy less often underwent Pap smear in comparison to women who were on sick leave (28.5% vs. 13.5%; $p = 0.0003$). This problem does not only affect our population — in the Brazilian study Augusto et al. [28] revealed that for 30.4% of women no participation in the screening program was caused by time-consuming job responsibilities and childcare. It may indicate that numerous duties affect prenatal testing and that this group of women requires more attention.

Ulman-Włodarz et al. [25] mentioned that almost 31% of patients who had an incidence of cervical cancer in their family were more motivated to perform Pap smear. It is consistent with the results obtained in our study (32.1%). Other forms of cervical cancer prophylaxis such as vaccination against HPV for primary prevention is not widespread in Poland — Ulman-Włodarz et al. [25] reported that only 4% of respondents were vaccinated, whereas in our study it was declared by 6.1% of surveyed women.

CONCLUSIONS

In conclusion, although the prevalence of Pap smear performance in analyzed population was relatively high, there was a substantial group of women who performed their first Pap smear as a part of prenatal care. Therefore, secondary cervical cancer prevention should remain an important element of prenatal consultations, combined with educating women about the necessity of regular control in future and more frequent doctors' proposals to perform it. Special attention should be given to younger and professionally active women as they are at risk of less frequent participation in cervical cancer screening in comparison to older women and those who resign from work during pregnancy.

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Annex 1. PAP SMEAR IN PREGNANCY — QUESTIONNAIRE

1.	How old are you? .....
2.	Place of residence:
	Countryside
	City < 10,000 inhabitants
	City of 10,000–100,000 inhabitants
	City > 100,000 inhabitants
3.	Education:
	Basic
	Professional
	Medium
	Higher incomplete
	Higher
4.	Professional activity:
	Professionally active
	Sick leave during pregnancy
	Social benefits
	Unemployed
	Maternity leave
5.	Marital status:
	Single
	Married
	Separated
	After divorce
	Widow
6.	How many times have you been pregnant (including your current pregnancy)?

0	1	2	3	4	5	6	7	8	9+

7.	How many times have you given birth?

0	1	2	3	4	5	6	7	8	9+

Pap smear is a screening test that gives an opportunity to diagnose and monitor cervical cancer. It relates to the diagnosis of cancer, based on microscopic evaluation of cells taken from the cervical smear. Thanks to cytology, most abnormalities can be detected at an early stage.

8.	Have you ever had undergone Pap smear examination?
	Yes
	No
9.	If you answered "Yes" to question number 8: How many times have you had undergone Pap smear examination? .....
10.	If you answered "Yes" to question number 8: How often do you undergo Pap smear?
	Every 1 year
	Every 2 years
	Every 3 years
	Less often
	Other: .....
11.	If you answered "Yes" to question number 8: How old were you at the time of your first cytology? .....
12.	If you answered "Yes" to question number 8: Did you perform cytology during your current pregnancy?
	Yes
	No
	I performed it before pregnancy
12 a.	In which week of pregnancy did you perform cytology? .....
12 b.	What was the result of the examination? .....

12 c.	The evaluation of the last cytology was made with the use of scale:
	Papanicolau Scale: result as group I, II, III, IV or V.
	Bethesda scale: normal result, ASCUS, LSIL, HSIL, AGUS, ASC-H, cancer cells
	I do not know
13.	If you answered "Yes" to question number 8 and were pregnant before: Did you perform cytology during your previous pregnancy(ies)?
	Yes
	No
14.	If you answered "Yes" to question number 8: When was the last time you have had undergone Pap smear (before pregnancy)?
	< 1 year
	1–2 years ago
	2–3 years ago
	3 years
	I do not remember
	Never
15.	If you answered "Yes" to question number 8: What were the results of these cytology examinations?
	Always correct
	Mostly correct
	Usually incorrect — exactly how? .....
	Always incorrect — exactly how? .....
	I do not remember
16.	If you answered "Yes" to question number 8: Did the abnormal cytology result affected the frequency of your Pap smear performance?
	Yes
	No
17.	If you have not undergone Pap smear before, why was that?
	No subjective need to perform it
	Concern about the test result
	No doctor's recommendation
	Lack of gynecological care
	Fear of pain
	Feeling of shame
	Cost of the test
	Other — what? .....
18.	Have you ever been to a gynecologist before your pregnancy?
	Yes
	No
19.	If you answered "Yes" to question number 18: How often did you go to the gynecologist for a check-up before pregnancy?
	Once every 6 months or more often
	Once a year
	Once every 2–3 years
	Less often than every three years
	Never

20.	Have you been vaccinated against HPV (human papilloma virus causing cervical cancer)?
	Yes
	No
20 a.	If you answered "Yes" to question number 20, has it been before your sexual initiation?
	Yes
	No.
21.	Has anyone in your family had cervical cancer?
	Yes — who? .....
	No
	I do not know
21 a.	If you answered "Yes" to question number 21, has it affected the frequency of your Pap smear performance?
	Yes
	No
22.	Did you use hormonal contraception before getting pregnant?
	Yes
	No
22 a.	If you answered "Yes" to question number 22, what kind of contraception did you use?
	Oral contraception
	Intrauterine device
	Vaginal ring
	Subcutaneous implant
	Injections
	Contraceptive patch
	Other - what? .....
22 b.	Have you performed Pap smear more often while using hormonal contraception?
	Yes
	No
23.	Have you ever had a colposcopy (endoscopic examination of the cervix, assessing the cervix by a doctor using an optical device - colposcope)?
	Yes
	No
	I do not know
23 a.	If you answered "Yes" to question number 23, do you remember the result of the colposcopy?
	Correct result
	Incorrect result: .....
24.	Have you had a histopathological examination of the cervical tissue?
	Yes
	No
	I do not know
24 a.	If you answered "Yes" to question number 23, do you remember the result of the histopathological examination?
	Correct result
	Incorrect result: .....