

ORIGINAL ARTICLE

New software for collecting data from the organized cervical cancer screening program in Serbia. Are we on the threshold of a new screening registry? – A multicentric study

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Summary

Purpose: The purpose of this study was to present the Screening Registry and the results of organized cervical cancer screening program (OCCSP) in the Republic of Serbia using a database made as an output model, linked with the Screening Registry.

Methods: Data were respectively collected over a one-month period from 3 state primary health care centers (and related hospitals/clinical center) in central Serbia in which OCCSP was conducted. The sample consisted of women of the target population (25 to 64 years old) who responded the call for Pap test.

Results: The most frequent abnormal cytological diagnosis was in the 38-50 years age group, and consisted of atypical squamous cells of undetermined significance - ASCUS (7.5%) and low grade squamous intraepithelial lesions - L-SIL (7.3%). The most frequent abnormal colposcopic finding in the youngest age group of women (25-37 years)

was iodine negative epithelium (35.7%) and in the group of women aged 38-50 and 51-64 years acid-white epithelium. The most common histopathological diagnosis was L-SIL. Positive predictive value of colposcopy in relation to the Pap test was 0.64 (95% CI=0.56-0.70). Interrater agreement (between cytotechnicians and supervisors) measured by the Cohen's coefficient was 0.94 (95% CI=0.91 to 0.97), but between cytology (supervisors) and pathology findings it was 0.83 (95% CI = 0.67 to 0.99).

Conclusion: The existence of a screening registry contributes to a better epidemiological surveillance of a screening program, and to a possibility for development of various epidemiological researches.

Key words: abnormal colposcopic findings, abnormal cytological diagnosis, organized cervical cancer screening program, Screening Registry

Introduction

Screening Registry plays an important role in screening programs for countries that have it

- better organization of screening programs, collecting data of the results of Pap test, linking re-

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sults of cytology with histopathological findings, better monitoring of women, especially those with a positive Pap test, as well as better overall monitoring of the results [1-13].

In Australia, full monitoring of the results of the national cervical cancer screening program is enabled with screening Registries. Cervical screening Registries operate in each state and territory [14].

In European countries (Finland, Belgium and the Czech Republic) the existence of screening registry also means increasing the quality of implementation of screening programs, as well as improving the quality, volume and speed in obtaining results. In these countries, screening registry also serves for pooling and collecting individual data of each woman who participated in the screening program [4,5,12].

The Swedish National Cervical Screening Registry was established to monitor the cervical screening program, as well as to provide information about the performed Pap tests within OCCSP, including the cytological and histological diagnoses and the laboratory where the samples were analyzed [15].

One of the phases of the pilot program for cervical cancer screening, which was conducted in a Serbian district with the highest incidence of this disease (Branicevo) in 2004-2005, was the development of information technology (IT) support and software for screening. This software was used only in the framework of this pilot project [16].

For the present research, a pilot version of the Screening Registry was made in the form of web application for the first time in Serbia. It is designed to follow the methodology of the National OCCSP from the moment of receiving the participants till the final diagnosis [17]. In designing OCCSP methodology Serbia followed the European recommendations [18]. At the request of researchers, and according to the expert guidance of medical school teachers, a software system was made by the master students of the informatics from Faculty of Mathematics, University of Belgrade. The team was supplemented with two more programmers.

Screening Registry constructed for this study consists of seven orders - for each step of the OCCSP (and for each health care professional who is engaged in the program) till the pathological diagnosis. The first order is for an administrative officer who invites women (by the year of birth) and schedules the testing. The second order is for

administrative officer - serves for the collection of data on women who have responded to the invitation and did a screening test (age, place of residence, unified screening number under which the woman is followed until establishment of the final diagnosis). The third order is for cytotechnician - for data collection on the Pap test findings: whether the examination is negative or positive, and, if positive, collection of the cytological diagnosis according to Bethesda classification. The fourth is the Supervisor's order - for collection of findings of Pap test according to Bethesda classification for all positive and 10% of randomly selected negative findings of Pap test according to the methodology set out in the Regulation of the National Programme for Early Detection of Cervical Cancer ("Regulation" from now on) [17]. The fifth order is made for collection of colposcopy findings for women with positive Pap tests - according to the methodology set out in the Regulation [17] and the sixth order for pathologist - to collect pathological diagnoses of women who underwent biopsy.

The purpose of this study was to present for the first time the results of OCCSP in Serbia, using a database - model linked with the Screening Registry.

Methods

This was an epidemiological cross-sectional preliminary study. Data were collected retrospectively from 3 state primary health care centers (PHCC) and related hospitals/clinical centers in central Serbia in which OCCSP was conducted. The sample consisted of women of the target population (25 to 64 years old) who responded the call for Pap test, and had no symptoms. Women who have had a total hysterectomy, women with other malignancies or previously treated for precancerous lesions in the cervix were excluded from the OCCSP. Data were collected over a one-month period of OCCSP implementation. For this research, data were used from the database made as an output model which corresponded to the 5 of the existing 7 orders (all except the first and third) from the Screening Registry.

Statistics

Categorical variables were expressed in absolute numbers and percentages. Continuous numerical variables were expressed as mean \pm standard deviation. Cytological findings were classified as mildly abnormal cytology (slight degree of change) and more severe change in cervical cells. Colposcopic findings were classified as normal or abnormal according to the colposcopic terminology of the International Federation for Cervical Pathology and Colposcopy [19]. Chi-square

was used to determine the significance of differences between the groups of women who have had a slight degree of change and more severe change in cervical cells, compared to the age groups. Statistical analysis also included the determination and assessment of Cohen's Kappa-K coefficient as a measure of agreement between cytotechnicians and supervisors reports, as well as a measure of agreement of cytological and pathological reports. Positive predictive value (PPV) of colposcopy in relation to Pap smears and in relation to the pathological findings was also determined.

SPSS software v.20.0 (IBM, Chicago, Ill, USA) was used for data analysis, while for assessing the Kappa coefficient and the PPV with corresponding 95% confidence intervals (95% CI), Med Calc v.16.2 software was used. P value less than 0.05 for type-1 statistical error (alpha) was considered as statistically significant for bi-directional testing hypotheses.

Results

The total number of the participants was 1092 and their average age was 43.1±11 years.

The frequency of diagnosis of ASCUS was 7.5%, almost equal as the diagnosis of L-SIL (7.3%) (Table 1).

Around 5% of the specimens were unsatisfactory for evaluation in the records from PHCCs.

The most frequent abnormal Pap test findings were in women aged from 38 to 50 years (Table 2).

There was no statistically significant difference between the mild and severe grade of cervical cells changes by age groups ($\chi^2=2.84$, $p=0.242$).

One colposcopic examination was carried out in of every 5.6 Pap tests performed in OCCSP. The most frequent abnormal colposcopic finding was acid-white (AW) epithelium (19%), followed by iodine negative epithelium (erosion Lugol's non stained) (17.4%) and mosaic (11.8%) (Table 3).

The largest number of women with abnormal colposcopy findings belonged to the age group from 38 to 50 years (45.6%) (Table 3).

The most common diagnosis in the youngest age group of women (25-37 years) was iodine

Table 1. Findings of Pap smear according to Bethesda classification

Pap smear findings	N	%
NILM	897	82.1*
ASCUS	82	7.5
ASCH	13	1.2
AGC NOS	17	1.6
L-SIL	80	7.3
H-SIL	3	0.3
Total	1092	100

*cytotechnicians' findings (for negative results of Pap smear)+supervisors' findings (for 10% randomly selected negative cytotechnicians' Pap smear results).

For abbreviations see text.

Table 2. Positive findings of Pap test according to age groups of women of target population

Age categories (years)	Mildly abnormal cytology (ASCUS; ASCH; AGC-NOS)	Higher grade of cervical cell lesions (LSIL, HSIL)
	N (%)	N (%)
25-37	44 (39.3)	23 (27.7)
38-50	46 (41.1)	41 (49.4)
51-64	22 (19.6)	19 (22.9)
Total	112 (100)	83 (100)

For abbreviations see text

negative epithelium (erosion Lugol's non stained) (35.7%) and in the group of women aged 38-50 and 51-64 years AW epithelium (Table 3). There was no statistically significant difference between these groups of women ($\chi^2=9.33$, $p>0.05$). Every colposcopic lesion characterized as severe, was send for pathological examination.

The most common pathological diagnosis was L-SIL (Table 4). Malignant tumors have not been reported for a month.

The PPV of Pap test in relation to colposcopy was 0.64 (95% CI=0.56-0.70).

Interrater agreement (between cytotechnicians and supervisors) measured by the Cohen's Kappa K coefficient was 0.94 (95% CI=0.91-0.97).

Table 3. Abnormal colposcopic findings according to age categories

Age categories (years)	AW epithel	Punctation	Mosaic	Leukoplakia	Lugol negative staining	Total
	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)
25-37	10 (23.8)	4 (9.5)	10 (23.8)	3 (7.1)	15 (35.7)	42 (100.0)
38-50	17 (29.8)	11 (19.3)	11 (19.3)	7 (12.3)	11 (19.3)	57 (100.0)
51-64	10 (38.5)	5 (19.2)	2 (7.7)	1 (3.8)	8 (30.8)	26 (100.0)
Total, N (%)	37 (29.6)	20 (16.0)	23 (18.4)	11 (8.8)	34 (27.2)	125 (100.0)

Table 4. Pathological findings

<i>Pathological findings</i>	<i>N</i>	<i>%*</i>
Cervicitis chr.	3	0.3
Metaplasia	6	0.5
Polypus cervicis	8	0.7
L-SIL	28	2.6
H-SIL	2	0.2
Hyperkeratosis/Parakeratosis	6	0.5
Leiomyoma	1	0.1
Total	54	4.9

*of the total number of women

Discussion

In an effort to adequately adjust the pilot project (Screening Register) to the screening program objectives it was decided to follow all the steps of methodological guidance covered by the Regulation [17], from admission of a woman to the establishment of definitive pathological diagnosis.

Many epidemiological studies carried out based on the existing Screening Registers showed and analyzed data in a similar way as our study [9,10,20-23].

Screening Registers in Finland, Sweden and the Czech Republic serve to collect all the results from OCCSP, including cytological findings, colposcopy findings and consequent pathological confirmation of the diagnosis of cervical cells changes [8,15,22,24].

In Finland, the Screening Registry is established and implemented since the end of the 1960s [4]. Finnish Mass Screening Registry serves for coordination, evaluation and further development of the screening programs. Complete data at the individual level in an organized screening program are available in the Screening Registry in electronic form [4,8].

Data analysis from a database extracted from our pilot Screening Registry enabled us to see that the majority of the tested women had secondary education, permanent partner, were non-smokers, and had two children.

In Norway, Cancer Registry is used for the purpose of screening as Screening Registry. Accordingly, data collected in this country are obtained by the questionnaires and they are associated with those included in the Cancer Registry. The results indicated that the Pap smear was less frequently carried out in women of younger age groups [11].

In our study, the results of cytology showed

that the most common changes of the cervical cells were ASCUS (7.5%) and L-SIL (7.3%) and that H-SIL was found in 0.3% of women only.

In a study conducted in Sweden, the most common abnormal findings of cervical cytology was ASCUS (2%) [25].

Data and results from the Czech National Registry for cervical cancer screening, presented in a recently published study, showed that 96% of women had negative findings of Pap smear in 2012, and ASCUS (46.6%) was the most common among women with abnormal findings (women with epithelial cell abnormalities, squamous or glandular), followed by L-SIL (34.7%) and H-SIL (4.5%) [24].

The results obtained from the Finnish Mass Screening Registry over the one-year of implementation of organized screening program were as follows: Pap test results were normal or negative in 93.1% (PAP I) of the examined women, suspicious (PAP II) in 6.4%, and positive (PAP III,IV,V) in 0.55% [4]. Around 6-7% of the smears were inadequate for full interpretation [4], which is similar to the result from our study.

According to the annual report from Australian-New South Wales, diagnosis of low-grade squamous epithelial and high-grade abnormalities were found in 1.6% and 0.63% of the tested women, respectively. Most women with histologically confirmed high-grade lesions were aged from 20 to 24 years [10].

The results obtained from the ZORA program in Slovenia showed that in 2014, a total of 91.1% of women had normal results. Abnormal changes of cervical cells were evidenced in 4.5% of women and included low-level of ASCUS-ASCH (2.7%), L-SIL (1.1%), H-SIL (0.7%) while no case showed squamous cell carcinoma. High-grade pathological changes in cervical cells was most common in women aged 30-39 years. Unlike our pilot project, ZORA Registry did not collect information of the performed colposcopies [26].

Our results showed that one colposcopic examination was carried out in every 5.6 Pap tests. In Belgium, the corresponding figure was 3.2 Pap tests [27].

The most frequent histological finding in our study was L-SIL. The highest percentage of histological findings in our study accounted for L-SIL changes (2.6%) and polyps (0.7%). In the study of Bodal et al. the rate of malignant lesions was 10% [28].

Getting information from the Screening Registry enabled us to compare our results with the

results from other studies coming from countries having well-organized data collection and reporting.

The existence of a Screening Registry contributes to a better epidemiological surveillance of a screening program through the recommended indicators [18], or new indicators (e.g. number of women of a certain age with precancerous lesions). At the same time Screening Registry allows obtaining more detailed information about women from the target population who presented to the screening examination within OCCSP, quality control (interrater accuracy, diagnostic accu-

racy) as well as support for the development of various epidemiological researches.

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Conflict of interests

The authors declare no conflict of interests.

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