Prevalence of cervical intraepithelial neoplasia and invasive carcinoma based on cytological screening in the region of Campinas, São Paulo, Brazil

Prevalência da neoplasia intra-epitelial cervical e do carcinoma invasivo com base no rastreamento citológico na região de Campinas, São Paulo, Brasil

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Abstract

This study aimed to estimate and analyze the prevalence of cervical intraepithelial neoplasia (CIN) and invasive cervical carcinoma based on cytological diagnosis. The study included 120,635 women undergoing cytological exams in public health services in the region of Campinas, São Paulo State, Brazil, between September 1998 and March 1999. Prevalence rates per 100,000 women were: 354 for CIN I; 255 for CIN II; 141 for CIN III; and 24 for invasive carcinoma. As age increased, prevalence rates and prevalence ratios decreased for CIN grades I and II and increased for CIN III until the 50-54 age group, decreasing thereafter The prevalence rate of invasive carcinoma increased with age. The prevalence pattern of CIN II was distinct from that of CIN III, but similar to that of CIN I. This would not have been observed if the Bethesda System had been used for cytological diagnosis. Mean age at time of CIN II diagnosis was about 10 years less than for CIN III diagnosis. Therefore, a high-grade lesion diagnosed in a young woman according to the Bethesda System would probably be a CIN II, whereas in an older woman it would probably be a CIN III.

Cervical Intraepithelial Neoplasia; Uterine Neoplasms; Prevalence

Introduction

Cervical cancer, with its high incidence, is an important cause of death in developing countries, where socioeconomic conditions are precarious and screening programs do not adequately achieve their goals [1].

Cervical cancer screening in Campinas began in 1968. Since the beginning, the screening model established that Pap smear sample collection would be decentralized and that the Cytology Laboratory at the State University in Campinas (UNICAMP) would be centralized. Gradually, screening extended to other municipal districts of the region, UNICAMP being the main reference center for assisting women from community health centers who had been identified as having abnormal Pap test results [2].

Until 1998 there were no data on the prevalence rate of cervical intraepithelial neoplasia (CIN) among the population in the region of Campinas. The data available referred to the total number of exams performed in regional cytological laboratories, which only discriminated between positive and negative results. Therefore, information on age-specific prevalence was not available. In addition, until that year no population data were available on age-specific prevalence rates of cervical intraepithelial lesions in other regions of Brazil.

This study thus aimed to estimate the prevalence rate of cervical intraepithelial lesions and

invasive cervical carcinoma based on cytological diagnosis, as well as to analyze trends according to age at time of diagnosis.

Subjects and methods

This cross-sectional study was aimed at a female population of public health system clients from 64 cities situated in the region of Campinas, who were submitted to a Pap test for cervical cancer screening. Campinas, a city in the State of São Paulo with a population of approximately one million, is the hub of regional economic and university activities. The region screened for cervical cancer has approximately three and a half million inhabitants. It is estimated that almost 60% of the region's population depends on the public health system, mostly represented by the lower socioeconomic population. The samples were collected in community health units under local supervision. Current health policy suggests screening women between ages 25 and 60 every three years, after two normal tests performed at one-year intervals. Many of these municipal districts now have their own colposcopy clinics.

The study population included 131,207 women receiving Pap smears for cervical cancer screening in public health services between September 1998 and March 1999, whose slides had been processed and examined at the UNICAMP Cytology Laboratory. This Laboratory is responsible for approximately 70% of the cytological exams performed by the public health system in the Campinas region.

The study excluded pregnant women (5,278), those submitted to hysterectomy (3,472), and those of unknown or inconsistent ages (3,232). The same woman could present more than one exclusion criterion. When a woman underwent repeat tests during the study period, only the result of the first test was considered. Thus a total of 120,635 women met the inclusion criteria and were admitted to the study.

The classification proposed by Richart [3] for cervical intraepithelial neoplasia was used in this study because the goal was to study CIN grades II and III separately. Samples were collected with an Ayre spatula and cytobrush.

Data were collected from the Pap test form adopted by the Cytology Laboratory and available in all public health services, designed for reading on optical mark readers. This form was introduced in August 1998 after a development period and performance test in two community outpatient clinics. The first month that this form was used was dedicated to identifying system errors and difficulties met by the community health centers. During this period a computer-based system was developed to detect data incompatibility or inconsistencies during the form's optical reading. Forms presenting incompatibilities and inconsistencies were rejected. The system could accept only one cytological diagnosis for each cell type, either squamous or glandular, in addition to the diagnosis of "cytopathic effect suggestive of HPV".

Prevalence rates for each cytological diagnosis and the prevalence ratio (PR) with 95% confidence interval (CI) were calculated according to age at diagnosis. The reference group for CIN PR was women aged 19 or younger and for invasive carcinoma PR was women aged 20 to 24, since no diagnosis of this lesion was observed in the group aged 19 or younger. Linear PR variations with increasing age group were tested using the Cochran-Armitage Trend Test [4].

Results

Some 20% of the women were under 25 years of age and two-thirds were 39 or younger, while only 5.4% were over 59. Approximately 50% of the women undergoing a Pap smear for the first time were under 25 (Figure 1). Almost one-sixth (19,635) of the women were receiving their first Pap smear, and 40%, 19.9%, 8.7%, and 6.2% were repeating the test, after one-, two-, three-, and more than five-year intervals, respectively (data not shown).

Mean ages at cytological diagnoses were 28.0, 29.3, 38.1, and 51.7 years for CIN grades I, II, III, and invasive carcinoma, respectively. For all diagnoses, the 50th age percentile varied from one to three years below the mean age (Table 1).

The overall prevalence rate of intraepithelial and invasive lesions was 774 per 100,000 women. Prevalence rates were 354 per 100,000 women for CIN I, 255 for CIN II, 141 for CIN III, and 24 for invasive carcinoma (Table 2).

According to the Cochran-Armitage Trend Test, prevalence ratios for CIN grades I and II decreased significantly as age increased. Conversely, prevalence ratios for CIN III and invasive carcinoma presented an upward trend as age increased, despite a slight decrease in CIN III above 50-54 years. Prevalence ratios for CIN I were less than 0.10 for the 50-54 age group or older. The highest CIN III prevalence ratio was in the 50-54-year group (Table 3).

Figure 1

Distribution (%) of total screened women (n = 120,635 women) and the women doing first
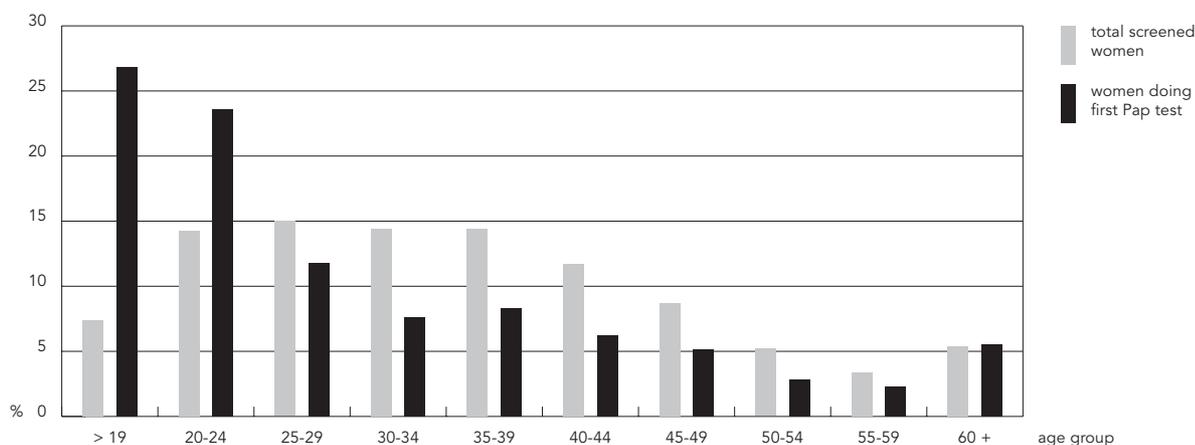Pap test (n = 19,304) by age group.

Table 1

Mean and percentile of age (years) according to cytological diagnosis.

	25th percentile	50th percentile	75th percentile	Mean (SD)	Total women
CIN I	20	25	34	28.0 (9.7)	427
CIN II	22	27	35	29.3 (9.5)	308
CIN III	28	37	46	38.1 (12.1)	170
Invasive carcinoma	43	49	59	51.7 (14.7)	29
Total women	26	34	43	35.7 (12.8)	120,635

CIN = cervical intraepithelial neoplasia.

Discussion

Data from 1988 for the State of São Paulo, Brazil, on prevalence rates of cervical lesions showed 860 CIN I per 100,000 cytological tests, 270 CIN II per 100,000, 160 CIN III per 100,000, and 70 invasive carcinomas per 100,000 tests. This database registered 170,754 tests in 120,604 women. Some women thus had repeat tests. Furthermore, there was no information as to whether tests from the cervical pathology outpatient clinic had been excluded. These tests could bias estimates of the prevalence rates due to the higher number of abnormal cytological tests in this group of women. There is also no information on the variability of CIN prevalence rates according to age [5].

Brazilian data from the cervical cancer screening information system of the Health Ministry (SISCOLO) for the year 2000 showed 2,262, 383, and 54 per 100,000 Pap tests with cytological diagnoses of low-grade squamous intraepithelial lesion (LSIL), high-grade squamous intraepithelial lesion (HSIL), and invasive cervical cancer, respectively [6]. The LSIL diagnosis of the Bethesda System includes the Richart CIN I diagnosis [3] plus the HPV cytological diagnosis, and therefore there is no equivalent diagnosis in our study. The HSIL cytological diagnosis of the Bethesda System is equivalent to the combined diagnoses of CIN grades II and III [7]. Thus, the HSIL prevalence rate in the Brazilian data could be con-

Table 2

Prevalence (per 100,000 women) of CIN and invasive carcinoma by age-group.

Age group	CIN I		CIN II		CIN III		Invasive carcinoma		Total women
	n	Prevalence	n	Prevalence	n	Prevalence	n	Prevalence	
19	86	958	46	512	3	33	0	0	8,977
20-24	113	653	67	387	18	104	1	7	17,295
25-29	63	347	65	358	26	143	1	6	18,147
30-34	61	352	50	289	25	144	2	12	17,326
35-39	50	288	34	196	29	167	0	0	17,377
40-44	22	156	17	121	18	128	6	43	14,100
45-49	22	210	17	163	21	201	5	48	10,459
50-54	4	63	9	143	16	254	4	63	6,309
55-59	4	97	3	72	6	145	3	72	4,145
60	2	31	0	0	8	123	7	108	6,500
Total women	427	354	308	255	170	141	29	24	120,635

CIN = cervical intraepithelial neoplasia.

Table 3

Prevalence ratio of CIN and invasive carcinoma by age group.

Age group	CIN I		CIN II		CIN III		Invasive carcinoma	
	PR	95% CI	PR	95% CI	PR	95% CI	PR	95% CI
< 19	1.00	–	1.00	–	1.00	–	–	–
20-24	0.68	0.52-0.90	0.75	0.52-1.10	3.11	0.92-10.57	1.00	–
25-29	0.36	0.26-0.50	0.69	0.48-1.02	4.28	1.30-14.16	0.95	0.02-36.40
30-34	0.36	0.26-0.51	0.56	0.38-0.84	4.31	1.30-14.30	1.99	0.09-46.80
35-39	0.30	0.21-0.43	0.38	0.25-0.59	4.99	1.52-16.39	–	–
40-44	0.16	0.10-0.26	0.23	0.13-0.41	3.82	1.13-12.96	7.35	0.46-118.87
45-49	0.21	0.14-0.35	0.31	0.18-0.55	6.00	1.79-20.14	8.26	0.49-138.92
50-54	0.06	0.02-0.18	0.27	0.14-0.57	7.58	2.21-26.03	10.96	0.62-195.26
55-59	0.10	0.04-0.27	0.14	0.04-0.45	4.3	1.08-17.31	12.51	0.64-244.96
> 60	0.03	0.01-0.13	–	–	3.68	0.98-13.88	18.62	1.19-292.35
CATT	-12.52		-8.81		2.61		5.88	
	p < 0.001		p < 0.001		p < 0.01		p < 0.001	

PR = prevalence ratio; CIN = cervical intraepithelial neoplasia; CI = confidence interval; CATT = Cochran-Armitage Trend Test [4].
There were no invasive carcinoma cases among women in the "19 years and under" and "35-39 year" age groups.

sidered similar to the CIN II plus CIN III prevalence rates observed in this study, i.e., 396 per 100,000.

SISCOLO data from the State of Paraná, Brazil, from January to October 2002 showed prevalence rates for CIN grades I, II, and III of 262, 249, and 124 per 100,000 women, respectively [8], and the data are similar to those obtained in the current study. The SISCOLO reports consulted had no information available on age-specific prevalence rates.

Other studies have shown prevalence rates for overall abnormal cytological diagnoses from screening programs in different countries. In two studies in Holland, rates of abnormal Pap tests, including all abnormal diagnoses, were 540 per 100,000 [9] and 800 per 100,000 [10]. In Thailand, 1,250 abnormal cytological diagnoses per 100,000 women [11] and in Chile 1,430 abnormal cytological diagnoses per 100,000 women were observed [12]. More recently, a study in a rural Costa Rican population showed a

prevalence rate of abnormal Pap tests of 2.2% LSIL and 1.5% HSIL [13]. An American study included 628,085 women, almost half of whom from ethnic minority groups. Prevalence rates of abnormal results were 3.2%, 3.0%, and 2.7%, respectively, among blacks, whites, and Hispanics, according to the Bethesda System [14].

Research using the Bethesda System has shown a higher prevalence rate than the current study and others. In fact, the Bethesda System includes atypical squamous cells of undetermined significance, atypical glandular cells of undetermined significance, and HPV cytological diagnoses, which increase the overall prevalence of abnormal results [7]. These diagnostic classes do not exist in the Richart system [3].

At any rate, prevalence rates of cervical intraepithelial lesions, regardless of classification, present widely varied values. This may be attributed to cervical cancer screening, diverse collection techniques, quality of samples, and especially differences in diagnostic criteria. In addition, all prevalence rates mentioned are crude rates that do not consider the difference in age distribution for each population.

The decreasing range of prevalence rates for CIN grades I and II according to age observed in this study was wider than the increasing range in prevalence rates for CIN III or invasive carcinoma. Therefore, the decrease in the prevalence rates of CIN grades I and II could be due mainly to cytological screening or spontaneous regression of these lesions, rather than progression to more severe diagnoses [15]. The decreasing trend of prevalence rates for CIN grades I and II is consistent with a higher HPV infection rate among younger women and spontaneous cure with follow-up time [13,16,17].

On the other hand, CIN III is associated with persistent oncogenic HPV infection [18,19]. Compared to CIN grades I and II, CIN III has a lower percentage of spontaneous regression and a higher percentage of progression to invasive carcinoma [15]. Furthermore, the mean estimated duration of CIN III is approximately 10 years, meaning that there is a cumulative annual incidence which influences the prevalence rates [20].

CIN III prevalence peaked in the 55 to 59 age group and decreased in the older age groups, and this trend could be due to spontaneous regression or progression to invasive carcinoma in this age group [15]. Treatment of CIN III could also lead to a decrease in its prevalence rate due to cervical cancer screening. Data from Sweden, Canada, United States, and Great Britain presented a peak prevalence for in situ carcinoma between ages 35 and 40, thus earlier than the peak found in Campinas [21]. However, these countries had established their cervical cancer screening programs earlier and for several decades in a more systematic way. As a consequence, the prevalence rate peaked in younger women and its decline was earlier and more abrupt, possibly due to earlier detection and efficient treatment of these lesions.

As previously mentioned, the Bethesda System considers the combined diagnoses of CIN grades II e III as HSIL. But the prevalence rate of CIN II according to age is similar to that of CIN I and different from that of CIN III, which would not have been observed if the Bethesda classification had been used. Also, mean age at the time CIN grades I and II were diagnosed was similar and about 10 years younger than the mean age in which CIN III was diagnosed.

Therefore, an HSIL diagnosed in a young woman would probably be a CIN II. If it were diagnosed in a woman over 50, it would probably be a CIN III. Results observed by Herrero et al. [13] in his population-based study in a rural Costa Rican population emphasize this possibility, since the prevalence rate of HSIL presented two peaks, the first around age 30, possibly due to CIN II, and the second around age 65, possibly due to CIN III.

Although this is not a population-based study, the results represent a significant sample of the user population of the Brazilian public health system. Therefore, these estimates should be close to the actual values of a lower-income population and could provide a reference for planning, assessment, and follow-up of cervical cancer screening activities.

Resumo

O objetivo deste estudo foi estimar e analisar a prevalência das neoplasias intra-epiteliais cervicais (NIC) e do carcinoma invasivo do colo uterino, com base no diagnóstico citológico. Foram incluídas 120.635 mulheres que realizaram o exame citológico, entre setembro de 1998 a março de 1999, nos serviços públicos de saúde da região de Campinas, Brasil. As prevalências por 100 mil mulheres foram: 354 para NIC I; 255 para NIC II; 141 para NIC III e 24 de carcinoma invasivo. À medida que a idade aumentou, as prevalências e razões de prevalência diminuíram para NIC I e NIC II, e aumentaram para NIC III até 50-54 anos, decrescendo após. A prevalência do carcinoma invasivo aumentou com a idade. O padrão da prevalência da NIC II é distinto do padrão da NIC III e semelhante ao da NIC I, o que não teria sido observado se fosse utilizado o Sistema de Bethesda. Ainda, a média da idade ao diagnóstico da NIC II foi cerca de dez anos menor que para NIC III. Portanto, um diagnóstico de lesão de alto grau, de acordo com o Sistema de Bethesda, em uma mulher jovem provavelmente seria NIC II e em uma mulher mais velha seria NIC III.

Neoplasia Intra-epitelial Cervical; Neoplasias Uterinas; Prevalência

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