

Uterine cytopathology in a public health laboratory: impact from 20 years data (1984-2003)

Citopatologia uterina em laboratório de saúde pública: impacto dos dados de 20 anos (1984-2003)

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ABSTRACT

The objective of this study was to identify the distribution of cytological diagnosis by means of Pap test on pre-neoplastic and neoplastic lesions from women at different age group in the period of 20 years. Retrospective survey of cytological cervicovaginal diagnoses was done to achieve this goal. Diagnoses results from 1,020,853 cytological samplings on Pap test, were studied according to age groups. In the period of 20 years from 1984 to 2003 the distribution of cervicovaginal cytological diagnoses according to age was analyzed four intervals of 5 year - (four quinquennia). Of analyzed cytological samples 27,314 (2.68%) were unsatisfactory, 980,985 (96.09%) were negative, and 12,554 (1.23%) resulted in squamous intraepithelial lesions and cancer. LSIL peak was observed within the four quinquennia and in the 20-24 age group, HSIL was most frequent in the 30-34 year age group, and SCC/ADENO Ca were present in women above 50 years old. In women of 15-19 years of age, a clear-increase in LSIL frequency was observed in four quinquennia, of 66 (9.19%) in the first quinquennium, 109 (9.83%) in the second, 441 (17.46%) in the third, and 467 (15.97%) in the last one. The outcome of the uterine cervix cancer prevention programs can be measured by the high frequency of LSIL type lesions in the past five years, and the data disclosed in the present study are in accordance with the data reported by the others from another continuous uterine cervix cancer prevention programs.

Key Words. screening, cervix cytology, Pap smear, age group.

RESUMO

O objetivo deste estudo foi identificar a distribuição dos diagnósticos citológicos pelo método de Papanicolaou das lesões pré neoplásicas e neoplásicas nos diferentes grupos etários no período de 20 anos. Foram utilizados dados retrospectivos dos diagnósticos citológicos cérvico-vaginais realizados no período de 1984 a 2003 no Setor de Citologia Oncótica. A distribuição dos diagnósticos de 1.020.853 amostras citológicas foi analisada por faixa etária em quatro intervalos de 5 anos (4 quinquênios). Das amostras analisadas, 27.314 (2,68%) casos foram inadequados, 980.985 (96,09%) foram negativos e 12.554 (1,23%) lesões intraepiteliais e câncer. Neste período, o pico de LSIL foi observado entre a faixa etária dos 20-24 de idade, HSIL foi mais freqüente no intervalo entre 30-34 anos de idade, e SCC/ADENO Ca foram acima dos 50 anos de idade. Nas mulheres entre 15-19 anos de idade foi observado acentuado aumento na freqüência de LSIL nos quatro quinquênios, de 66 (9,19%) no primeiro, 109 (9,83%) no segundo, 441 (17,46%) no terceiro e 467 (15,97%) no último. A qualidade dos programas de prevenção de câncer de colo uterino pode ser medido pela freqüência das lesões do tipo LSIL. Os resultados do presente estudo são concordantes com os de outros programas contínuos e importantes para evitar a mortalidade em virtude dessas lesões.

Palavras-Chave. rastreamento, citologia cervical, Método de Papanicolaou, faixa etária.

INTRODUCTION

Systematic examination of uterine cervical using the Pap test smears has been recognized as the most efficient method to detect neoplastic lesions and to identify neoplastic conditions; the Pap test, to date, seems to be the most reliable test to be applied in large populations. Continuous efforts in education to optimize the index levels of sensitivity and specificity have been made around the world, focusing strategies in diagnostic assurance quality control. Discussions on morphologic parameter evaluation have also helped to improve such quality strategies^{1,2,3}. The results show more significant protection factors in the women correlated to the number of tests performed⁴.

Many of the assurance and control strategies involve studies based on data observed in routine conditions which means that many subjects of cytological studies arose from the large data results⁵. Retrospectively, such data show frequencies of diagnosis distributed by age group that may reflect epidemiological conditions of geographic area; and also reveals a tendency of Cytology Laboratories as being more conservative or not discriminative of lesions in low or high-grade classification.

The objective of this study was to verify the distribution of cytological diagnoses of Pap tests in cancer and pre cancerous lesions in different age groups over 20 years, and to discuss the importance of such data as being strategic to cancer prevention prognosis in São Paulo, Brazil.

MATERIAL AND METHODS

The samples were examined at the Division of Pathology of Instituto Adolfo Lutz over a period of 20 years (1984 to 2003). The slides were fixed on Carbowax or absolute alcohol and stained with Papanicolaou method in samples collected with Ayres' spatula and/or cytobrush. A total of 1,020,853 cases were examined during the past 20 years. The diagnoses were compiled in intervals of 5 years, and analyzed in 4 groups: 177,975 through 1984-1988; 318,751 through 1989-1993; 294,673 through 1994-1998 and 229,454 through 1999-2003. During the period of the

study, diagnoses were made according to the WHO classification 1984⁶ and the Health Ministry in Brazil 1993⁷. Presently, the results were re-classified according to Bethesda System 2001⁸.

For the statistical analyses we used the Chi-Square test and test for likelihood ratios. Diagnoses of normal and inflammatory conditions were classified as negative. All inconclusive samplings and cases without age data were excluded from these analyses.

RESULTS

A total of 1,020,853 cases were examined over 20 years. The diagnostic classification used during this period at the Instituto Adolfo Lutz - Cytology Laboratory has not considered the analysis of the causes of inadequate samplings (2.68%); however, the selective criteria were similar to that used by the Bethesda System which recommends the internal quality control to be in accordance with at least two observers.

We reported 27,314 (2.68%) unsatisfactory samples; 980,985 (96.09%) negative (normal and inflammatory); 2,518 (0.25%) ASC/AGC; 7,277 (0.71%) LSIL; 2,429 (0.24%) HSIL and 330 (0.03%) squamous cell carcinoma (SCC) and adenocarcinoma (adenoca) (Table 1). From 1,020,853 the distribution of the diagnoses was grouped according to age, except 12,554 (1.23%) that lacked this information. From the cases classified as "unsatisfactory sample" age frequency was predominant in the 50-plus-age group. The age of the negative (normal and inflammatory) cases ranged from 20 to 35 years.

Considering the period September 98 to August 99 we have the following information, in 66,212 cases, 4.39% were inadequate samplings having as main causes: 55.43% poor fixing, 16.43% poor fixing and purulence, 20.72% purulence, 5.15% hemorrhagic, 1.5% scarce material e 0.76% thick material⁹. Still within this period, cases of ASC/AGC were undervalued because such were included in the inflammatory cytology group requiring the test to be repeated within a 6-month period or, they were reported as inconclusive atypical cells (Table 2).

Table 1. Distribution of 1,020,853 cytological diagnoses during the period 1984-2003 (4 quinquennia) realized at Instituto Adolfo Lutz.

DIAGNOSES	84-88		89-93		94-98		99-03		TOTAL	
	n	%	n	%	n	%	n	%	n	%
Unsatisfactory	3,780	2.12	8,233	2.58	4,579	1.55	10,722	4.67	27,314	2.68
Negative	172,987	97.20	308,822	96.89	286,729	97.30	212,447	92.59	980,985	96.09
ASC/AGC	-	-	4	0.001	215	0.07	2,299	1.0	2,518	0.25
LSIL	718	0.41	1,109	0.35	2,526	0.87	2,924	1.28	7,277	0.71
HSIL	431	0.24	455	0.14	572	0.19	971	0.42	2,429	0.24
SCC / AdenoCa	59	0.03	128	0.04	52	0.02	91	0.04	330	0.03
TOTAL	177,975	100	318,751	100	294,673	100	229,454	100	1,020,853	100

(p= 0,001 Chi Square Test)

The group with the largest number of LSIL was from 20 to 24 years (Table 3), corresponding to 21.85% of 7,277 cases; HSIL frequency was larger in the 30-34 year age group, which means 17.62% from 2,429 HSIL cases (Table 4). And finally the smear SCC/ADENO Ca was predominant in the 50-plus-age group or 48.79% of the 330 cases diagnosed (Table 5).

LSIL lesions showed a frequency enhanced in the teenage group (15-19 years), arising from 9.19% and 9.83 to 17.46% and 15.97% in 5-year groups respectively. Statistically we reported a significant association between age and ASC/AGC ($p=0,001$) and LSIL ($p=0,001$). We found a significant difference of HSIL ($p=0,066$) during the year, but not in SCC/ADENO Ca group ($p=0,333$).

DISCUSSION

Throughout the past 20 years many programs were undertaken against cervical cancer mortality. It's worth pointing

out that the Public Health System offers cervical cancer control procedures to women from 20 to 30 years with much more frequency, as there is spontaneous demand for family planning or even prenatal follow-up care, making this age group to be of the largest concentration. On the other hand, Nascimento et al¹⁰ observed in São Paulo City - Brazil through distribution analyses as per economic and demographic characteristics, that only 36% of the women between 15 and 24 years old acknowledged having done the Pap test.

In 2000 the Brazilian Health Ministry implemented the SISCOLO program in our laboratory. In 2004 and 2005, 2.57% and 3.00% respectively ASC and AGC cases were detected as per data from the annual report of the Division of Pathology.

The literature shows that the concentration of approximately 90% of the LSIL and HSIL cases is found in the age group of 15 to 39, thus occurring before 35 years of age and in women of 50 or older, the LSIL frequency decreases and the occurrence of cervical cancer increases with age^{11,12}. We have observed in our study that, from the total of 1,020,853 samplings

Table 2. Distribution of 2,518 cytological diagnoses of ASC/AGC by age group in the period 1989 - 2003 (3 quinquenia).

Age	89-93		94-98		99-03		TOTAL	
	n	%	n	%	n	%	n	%
<14	-	-	6	2.79	10	0.44	16	0.64
15-19	-	-	17	7.91	235	10.22	252	10.01
20-24	-	-	20	9.30	380	16.53	400	15.88
25-29	1	25	35	16.28	329	14.31	365	14.50
30-34	-	-	26	12.09	283	12.31	309	12.27
35-39	-	-	27	12.56	261	11.35	288	11.44
40-44	2	50	18	8.37	231	10.05	251	9.97
45-49	-	-	20	9.30	209	9.09	229	9.09
>50	1	25	46	21.40	361	15.70	408	16.20
TOTAL	4	100	215	100	2,299	100	2,518	100

($p=0,001$ Chi Square Test)

Table 3. Distribution of 7,277 cytological diagnoses of LSIL by age group in the period 1984 - 2003 (4 quinquenia).

Age	84-88		89-93		94-98		99-03		TOTAL	
	n	%	n	%	n	%	n	%	n	%
<14	6	0.84	8	0.72	21	0.83	29	0.99	64	0.88
15-19	66	9.19	109	9.83	441	17.46	467	15.97	1,083	14.88
20-24	128	17.83	236	21.28	584	23.12	642	21.96	1,590	21.85
25-29	152	21.17	239	21.55	430	17.02	500	17.10	1,321	18.15
30-34	135	18.80	189	17.04	337	13.34	405	13.85	1,066	14.65
35-39	79	11.0	134	12.09	240	9.50	316	10.81	769	10.57
40-44	59	8.22	68	6.13	196	7.76	216	7.39	539	7.41
45-49	34	4.73	57	5.14	125	4.95	146	4.99	362	4.97
>50	59	8.22	69	6.22	152	6.02	203	6.94	483	6.64
TOTAL	718	100	1,109	100	2,526	100	2,924	100	7,277	100

($p=0,001$ Chi Square Test)

Table 4. Distribution of 2,428 cytological diagnoses of HSIL by age group in the period 1984 - 2003 (4 quinquenia).

Age	84-88		89-93		94-98		99-03		TOTAL	
	n	%	n	%	n	%	n	%	n	%
<14	1	0.23	-	-	3	0.52	2	0.21	6	0.25
15-19	12	2.78	16	3.52	30	5.25	30	3.09	88	3.62
20-24	64	14.85	44	9.67	69	12.06	110	11.33	287	11.81
25-29	84	19.49	76	16.70	95	16.61	153	15.76	408	16.80
30-34	77	17.87	88	19.34	97	16.96	166	17.10	428	17.62
35-39	69	16.01	64	14.07	91	15.91	146	15.03	370	15.23
40-44	45	10.44	55	12.09	62	10.84	102	10.50	264	10.87
45-49	38	8.82	42	9.23	46	8.04	104	10.71	230	9.47
>50	41	9.51	70	15.38	79	13.81	158	16.27	348	14.33
TOTAL	431	100	455	100	572	100	971	100	2,429	100

(p= 0,066 Chi Square Test)

Table 5. Distribution of 330 cytological diagnoses of SCC/ADENO Ca by age group in the period 1984-2003 (4 quinquenia).

Age	84-88		89-93		94-98		99-03		TOTAL	
	n	%	n	%	n	%	n	%	n	%
<14	-	-	-	-	-	-	-	-	-	-
15-19	-	-	-	-	-	-	-	-	-	-
20-24	1	1.70	1	0.78	-	-	1	1.10	3	0.91
25-29	4	6.78	5	3.91	3	5.77	1	1.10	13	3.94
30-34	7	11.86	10	7.81	1	1.92	3	3.30	21	6.36
35-39	6	10.17	13	10.16	9	17.31	13	14.28	41	12.42
40-44	5	8.48	13	10.16	9	17.31	12	13.19	39	11.82
45-49	13	22.03	18	14.06	6	11.54	15	16.48	52	15.76
>50	23	38.98	68	53.12	24	46.15	46	50.55	161	48.79
TOTAL	59	100	128	100	52	100	91	100	330	100

(p= 0,333 Chi Square Test)

analyzed, 12,554 (1.23%) represent the distribution of pre-neoplastic and neoplastic lesions (Table 1: p=0,001), being that, in the 15-19 age group the distribution of the LSIL frequency presented a clear increase from 9.19% (1984-1988) and 9.83% (1989-1993) to 17.46% (1994-1998) and 15.97% as well as a gradual increase in the 20-24 year age group (17.83%, to 23.12 and 21.96%) (Table 3: p=0,001). In posterior age groups besides those considered of larger frequency, decrease was observed in LSIL from 25 years of age or above, as well as in HSIL from 30 or above as shown in Table 4: p=0,066; this same tendency was observed in invasive carcinoma (Table 5: p=0,333), where a clear increase was seen in the age group of 50 or higher, in agreement with the literature^{4,13}.

Rates of incidence and mortality in Brazilian women by such neoplasia are the highest concerning malignant tumors¹⁴. Taking into consideration the long detectable pre-clinical period, the temporal mortality tendency suggests that the covering of preventive tests on the feminine population has been low in the past⁹.

Our results are in accordance with other reports from cervical cancer long-term prevention programs. If detected early

through the Pap test, pre-neoplastic and neoplastic lesions of the uterine cervical are qualified for prevention and cure, and chiefly to avoid mortality by such lesions. Fender et al¹⁵ found amongst all tests completed, 1.94% pathologic test through (LSIL, HSIL and Ca) cytology. Our data relate to 0.98% (Table 1) and, 1.12% for others⁸. The identification of CIN lesions largely depends on quality of the sampling (presence or not of cells representative of squamocolumnar junction - JEC), Shirata et al.¹⁶ observed that the frequency of CIN detection on the smear with JEC representation was 10 times more frequent in those than in smears with no JEC, thus demonstrating the importance of an adequate collection.

Among adolescents, early sexual activity and multiple sexual partners, two of the major risk factors for cervical cancer are facts that involve social, cultural and educational factors. A well-conducted sexual education program for adolescent students may be an important way to prevent increase in HPV infections and SIL lesions among the young population^{17,18}. We came to the conclusion that these data reinforce the importance of implementing early cervical Pap smear screening in the sexually

active population due to the progressive and high frequency of LSIL lesions during the last ten years. Additionally, we are able to suggest screening programs with priority for the women within the age group of 25 to 40 due to the high frequency of HSIL observed; and also due to the gradually increase cases of invasive carcinomas in this group.

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