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Cervical Intraepithelial Neoplasia in the "Dr. Salvator Vuia" Clinical Obstetrics and Gynecology Hospital - Arad During the 2000-2009 Period

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ABSTRACT

Objectives: *This study intends to analyze some statistical data concerning Cervical Intraepithelial Neoplasia diagnosed in our hospital.*

Material and Methods: *Our study concerning the incidence of Cervical Intraepithelial Neoplasia (CIN) covers the 2000-2009 time-span, the data being collected from the Histopathology Exams (HPE) registers.*

Results: *During this period, CIN lesions were discovered in 1256 cases and Cervical Intraglandular Dysplasia (CIGD) in 53 cases. CIN I, CIN II and CIN III lesions represented 65.92% (828 cases), 19.67% (247 cases), and 14.41% (181 cases) of the total CIN cases, respectively. There were 26 cases combined with cervical carcinoma (2.07% of all CIN cases, 3.56% of the 731 cervical cancer cases). The mean patients' age was 44.65± 9.83 years for all cervical dysplasia cases, 44.58± 9.75 years for all CIN cases, 43.81±9.22, 46.50±10.17, and 45.46±11.05 years for CIN I, CIN II, and CIN III, respectively, and 46.45 ± 11.63 years for CIGD. The t-test revealed the following significant differences: all cases versus CIN I ($p<0.05$) and CIN II ($p<0.01$), CIGD versus CIN I ($p<0.05$), all cases versus CIN II ($p<0.01$), CIN I versus CIN II ($p<0.0001$) and versus CIN III ($p<0.05$). The mean age of the 731 cervical cancer cases diagnosed in our hospital during that same period was 52.94±12.96 years,and it was statistically significantly different from the mean ages of patients with CIN I, II and III ($p <0.00000001$) and with CIGD ($p<0.0005$).*

Conclusions: *Early detection of CIN is of utmost importance for preventing cervical cancer, a serious and frequent health problem in Romania.*

Keywords: cervical intraepithelial neoplasia, cervical intraglandular dysplasia, cervical biopsy, cervical cancer

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INTRODUCTION

All squamous cell carcinomas of the ectocervix are preceded by cervical intraepithelial neoplasia (CIN), and in most instances are related to infection with human papilloma viruses (1,2).

Experience with the CIN terminology led to further reclassification of the terminology for reporting cytologic abnormalities consistent with preinvasive disease (3,4). The CIN grading is very subjective, (3-6), while separating CIN 2 from CIN 3 is again often not reproducible (7). A continuous range of morphologic abnormalities exists among these lesions, which provide a rough indication of the likelihood with which they will evolve into invasive carcinoma if left untreated (8).

The rubric CIN 3 includes not only severe dysplasia but also carcinoma in situ of the cervix; these 2 lesions cannot be separated objectively. Intraepithelial lesions also may be graded in a binary system as low-grade squamous intraepithelial lesions (LSIL) or high-grade squamous intraepithelial lesions (HSIL) (9). The 3-tiered system of grading is currently the most widely used. It includes the following categories:

- CIN 1, mild squamous dysplasia.
- CIN 2, moderate squamous dysplasia.
- CIN 3, severe squamous dysplasia/carcinoma *in situ* (10,11). CIN 3 is reliably distinguished from recently acquired HPV infection and is a genuine surrogate marker of subsequent cancer risk (12, 13).

CIN 1 is increasingly viewed as an insensitive histological marker of HPV infection. (14). Standardized for positivity for a given high-risk HPV type, a diagnosis of CIN 1 does not predict a meaningfully higher risk of CIN 3 than does a negative biopsy (12).

Histologically confirmed CIN 1 lesions confer a lower risk of developing cervical cancer than does a Pap smear report of low-grade squamous intraepithelial lesion (12,13). CIN 2 can be produced by noncarcinogenic HPV types and is equivocal in cancer potential (13).

The stepwise progression of increasingly severe cervical intraepithelial neoplasia to invasive cancer, implicit in the CIN continuum, remains an important histopathological concept to assist clinical management (14).

HPV infection is a broad transition state between normal and precancer stages (16). CIN 3, particularly full thickness carcinoma in situ, shares the same HPV-type spectrum and cofactor profile as invasive cancer; at this time there is no reliable predictor of CIN 3 lesions likely to progress to cancer and as such all are managed as definite precancer (16).

CIN 2 demonstrates greater heterogeneity in biology and definition (14). It can be caused by low-risk HPV types rarely found in cancer and have a greater regression potential. A diagnosis of CIN 2 is not a reliable surrogate for cancer risk. Although of equivocal malignant potential, in the absence of reliable predictors of risk of progression, CIN 2 lesions tend to be managed as precancer to provide a further safety margin against development of cancer (14).

A histological diagnosis of low-grade cervical intraepithelial lesions (HPV infection/CIN 1) is increasingly viewed as not representing precancer. Persistence of oncogenic HPV types is strongly linked to precancer (18-20). Only a fraction of precancers arise from HPV infection in the absence of mild or equivocal microscopic abnormalities (18-20).

High-grade lesions are commonly found within a broader field of low-grade disease, suggesting that CIN 3 may develop in high-risk HPV-infected epithelium independent of and within a CIN 1 lesion, rather than as a classical stepwise progression (1).

Positive margins and glandular involvement by CIN II or CIN III are independent predictors of residual or recurrent disease (21-23), but that may not be the case for low-grade CIN (CIN I) (24). ❑

OBJECTIVES

The purpose of this study is to analyze the type and age distribution of cervical dysplasia cases in our hospital over a ten year period and to statistically compare the mean ages of each dysplasia type with all other types and with the mean age of the patients with cervical cancer. ❑

MATERIALS AND METHODS

Our study concerning the incidence of Cervical Intraepithelial Neoplasia (CIN) covers the 2000-2009 time-span, the data being collected from the Histopathology Exams (HPE)

Age (years)	≤20	21-30	31-40	41-50	51-60	61-70	71-80	81-90
CIN I	0.36	6.76	26.09	47.22	15.22	3.50	0.72	0.12
CIN II	0.00	6.48	16.19	49.80	18.62	7.29	1.21	0.40
CIN III	0.00	7.73	27.07	34.25	21.55	6.63	2.76	0.00
All CIN	0.24	6.85	24.28	45.86	16.80	4.70	1.11	0.16
CIGD	0.00	7.55	18.87	47.17	15.09	9.43	0.00	1.89
All CIN	0.23	6.88	24.06	45.91	16.73	4.89	1.07	0.23

TABLE 1. Distribution of cervical dysplasia age groups

registers. During this period, 83.006 Obstetrics -Gynecology patients and newborns were admitted in our hospital and 16.063 HPEs were performed (19.35% of all patients). ❑

RESULTS

During the 2000-2009 period, 1309 cases of cervical dysplasia cases were discovered: 1256 CIN cases (95.95%) and 53 CIGD cases (4.05%).

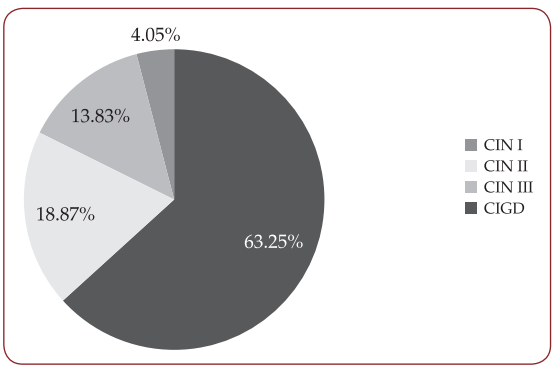

FIGURE 1. Distribution of cervical dysplasia types

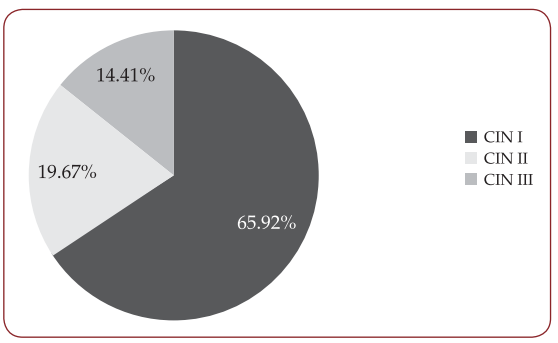

FIGURE 2. Distribution of CIN types

	Mean (years)	SD (years)
All	44.65	9.83
CIN	44.58	9.75
CIN I	43.81	9.22
CIN II	46.50	10.17
CIN III	45.46	11.05
CIGD	46.45	11.63

TABLE 2. Mean ages of cervical dysplasia types

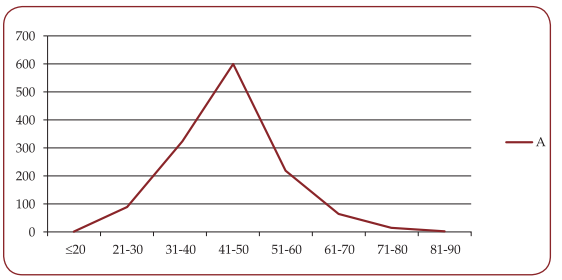

FIGURE 3. Distribution of cervical dysplasia age groups

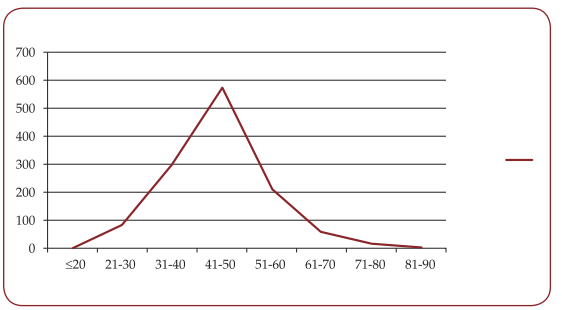

FIGURE 4. Distribution of CIN age groups

A number of 844 cases (64.48%) were diagnosed from tissue fragments obtained from exo- and/or endocervical biopsies, while 465 (35.52%) were found after analyzing surgical specimens.

There were 828 cases of CIN I (65.92% of all CIN cases, 63.25% of all dysplasia cases), 247 cases of CIN II (19.67% of all CIN cases, 18.87% of all dysplasia cases), and 181 cases of CIN III (14.41% of all CIN cases, 13.83% of all dysplasia cases) (Figure 1, Figure 2).

Table 1 and Figures 3-6 show the age distribution for the cervical dysplasia cases, while Table 2 and Figure 7 show the mean age and standard deviation for each group.

There were 26 cases of CIN lesions combined with carcinoma: 18 cases of CIN III with microinvasive carcinoma (1.43% of the CIN cases, 2.46% of the 731 cervical cancer cases diagnosed during the same ten year period) and eight cases of CIN lesions combined with invasive carcinoma (0.64% of the CIN cases,

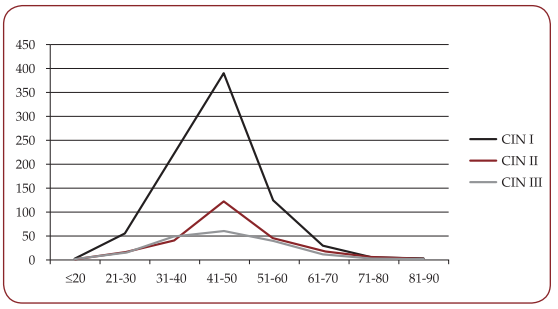

FIGURE 5. Distribution of CIN types age groups

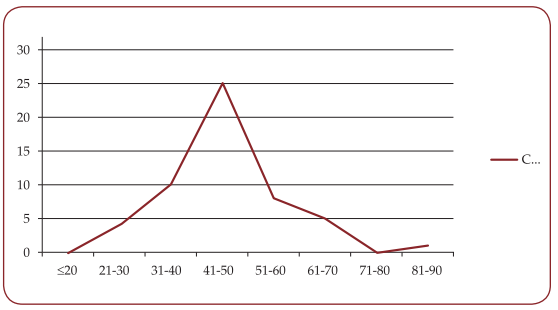

FIGURE 6. Distribution of CIGD age groups

1.09% of the 731 cervical cancer cases), comprising six CIN I cases (four with non-squamous macrocellular epidermoid carcinoma, one with squamous macrocellular epidermoid carcinoma, and one with neuroendocrine cell carcinoma), one CIN II case with non-squamous macrocellular epidermoid carcinoma, and one CIN III case with squamous macrocellular epidermoid carcinoma.

Table 3 shows the comparisons and the statistical significance between the mean ages of different groups by using Student's t-test, while Table 4 compares the mean ages of the four different types of dysplasia with the mean age of the 731 patients diagnosed with cervical cancer in our hospital during the 2000-2009 period (mean age 52.90 ±12.97 years) by using Student's t-test. ❑

DISCUSSIONS, CONCLUSIONS

Early detection of CIN lesions through adequate clinical and paraclinical exams is of utmost importance for preventing cervical cancer, which remains a serious and frequent health problem in Romania, as there are, besides the clinical exam, several paraclinical methods which can achieve this goal.

If the mean ages of each type of cervical dysplasia are statistically more or less different among them, all of them are highly different from the mean age of the patients with cervical cancer, thus proving that the evolution from CIN lesions to invasive cervical cancer takes several years, leaving enough time for detection and adequate treatment.

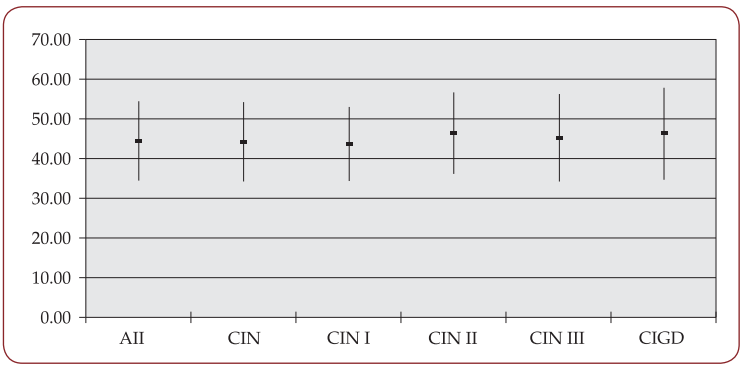

FIGURE 7. Mean ages ± SD

Comparison	p
All vs CIGD	0.19
All vs CIN	0.86
All vs CIN I	**<0.05**
All vs CIN II	**<0.01**
All vs CIN III	0.31
CIGD vs CIN	0.18
CIGD vs CIN I	**<0.05**
CIGD vs CIN II	0.97
CIGD vs CIN III	0.57
CIN vs CIN I	0.07
CIN vs CIN II	**<0.01**
CIN vs CIN III	0.26
CIN I vs CIN II	**<0.0001**
CIN I vs CIN III	**<0.05**
CIN II vs CIN III	0.31

TABLE 3. Comparisons and the statistical significance between the mean ages of different groups using Student's t-test

Comparison	p
Cervical cancer vs CIN I	<0.00000001
Cervical cancer vs CIN II	<0.00000001
Cervical cancer vs CIN III	**<0.00000001**
Cervical cancer vs CIGD	**<0.0005**

TABLE 4. Comparisons between the mean ages of the four different types of dysplasia with the mean age of the 731 patients

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