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CERVICAL INTRAEPITHELIAL NEOPLASIA IN THE "DR. SALVATOR VUIA" CLINICAL OBSTETRICS AND GYNECOLOGY HOSPITAL ARAD DURING THE 2004-2008 PERIOD

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ABSTRACT. Cervical Intraepithelial Neoplasia (CIN) lesions are of high importance because of their relatively high frequency, potential evolution towards cervical cancer and relatively easy diagnosis. Our study concerning the incidence of Cervical Intraepithelial Neoplasia (CIN) covers the 2004-2008 time span, the data being collected from the Histopathology Exams (HPE) registers. During the 2004-2008 period, 631 cases of cervical dysplasia cases were discovered: 606 CIN cases (96.04%) and 25 CIGD (cervical intraglandular dysplasia) cases (3.96%). There were 377 cases of CIN I (62.21% of all CIN cases, 59.75% of all dysplasia cases), 121 cases of CIN II (19.97% of all CIN cases, 19.18% of all dysplasia cases), and 108 cases of CIN III (17.82% of all CIN cases, 17.12% of all dysplasia cases).The mean patients' age was 44.52± 9.92 years for all cervical dysplasia cases, 44.41± 9.84 years for all CIN cases, 44.70± 9.34 years, 47.15± 10.40, and 45.94±10.66years for CIN I, CIN II, and CIN III, respectively. The mean patients' age for the CIG case was 48.12 ± 10.66 years. There were 12 cases (3.27% of the 367cervical cancer cases diagnosed during the same period, 1.98% of the 606 CIN cases) of microinvasive carcinomas combined with CIN lesions (all of them with CIN III) and one case of cervical carcinoma combined with CIN I (0.27% of the 367 cervical cancer cases diagnosed during the same period, 0.17% of the 606 CIN cases). 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.

KEYWORDS: cervical intraepithelial neoplasia, cervical intraglandular neoplasia, CIN, LSIL, HSIL, human papilloma virus, cervical cancer, mean age, Student's t-test, statistical significance

INTRODUCTION

Squamous cell carcinomas of the ectocervix are preceded by cervical intraepithelial neoplasia (CIN), and are usually related to infection with human papilloma viruses (HPV) (Cannistra et al, 1996; Giannoudis et al, 2001).

Experience with the CIN terminology led to further reclassification of the terminology for reporting cytologic abnormalities consistent with preinvasive disease (Solomon et al, 2002; Stoler et al, 2002), the CIN grading being very subjective, (Solomon et al, 2002; Stoler et al, 2002; Wright et al, 2007; Stoler et al, 2001); separating CIN 2 from CIN 3 is often not reproducible (Wright et al, 2006). A continuous range of morphologic abnormalities exists among these lesions (Ostor, 1993).

The rubric CIN 3 includes not only severe dysplasia, but also carcinoma in situ of the cervix (they 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) (Sindos et al, 2003). The 3-tiered system of grading is currently the most widely used: CIN 1 (mild squamous dysplasia), CIN 2 (moderate squamous dysplasia), and CIN 3 (severe squamous dysplasia/carcinoma in situ) (Melnikow et al, 1998; Robertson et al, 1989). CIN 3 is a genuine surrogate marker of subsequent cancer risk (Cox et al, 2003; ASCUS-LSIL Triage Study (ALTS) Group, 2003).CIN 1 is viewed as an insensitive histologic marker of HPV infection. (Greenberg et al, 1999). 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 (Cox et al, 2003).

Histologically confirmed CIN 1 lesions confer a lower risk of developing cervical cancer than does a Pap smear report of LSIL (Cox et al, 2003; ASCUS-

LSIL Triage Study (ALTS) Group, 2003). CIN 2 can be produced by noncarcinogenic HPV types and is equivocal in cancer potential (ASCUS-LSIL Triage Study (ALTS) Group, 2003). The stepwise progression of increasingly severe CIN to invasive cancer, implicit in the CIN continuum, remains an important histopathological concept to assist clinical management (Greenberg et al, 1999).

HPV infection is a broad transition state between normal and precancer stages (Schiffman et al, 2007). 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 (Schiffman M et al, 2007). CIN 2 demonstrates greater heterogeneity in biology and definition (Greenberg et al, 1999), being often caused by low-risk HPV types rarely found in cancer and with a greater regression potential. 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 (Greenberg et al, 1999).

A histological diagnosis of LSIL (HPV infection/CIN 1) is increasingly viewed as not representing precancer, while persistence of oncogenic HPV types is strongly linked to precancer. Only a fraction of precancers arise from HPV infection in the absence of mild or equivocal microscopic abnormalities (Schiffman et al, 2005; Kjaer S et al, 2006; Khan et al, 2005).

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 (Demopoulos et al, 1991;, Livasy et al, 1999; Paterson-Brown et al, 1992), but that may not be the case for low-grade CIN (CIN I) (Cardoza-Favarato et al, 2007).

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 2004-2008 time-span, the data being collected from the Histopathology Exams (HPE) registers.

RESULTS

During the 2004-2008 period, 631 cases of cervical dysplasia cases were discovered: 606 CIN cases (96.04%) and 25 CIGD (cervical intraglandular dysplasia) cases (3.96%).

There were 377 cases of CIN I (62.21% of all CIN cases, 59.75% of all dysplasia cases), 121 cases of CIN II (19.97% of all CIN cases, 19.18% of all dysplasia cases), and 108 cases of CIN III (17.82% of all CIN cases, 17.12% of all dysplasia cases).

The mean patients' age was 44.52± 9.92 years for all cervical dysplasia cases, 44.41± 9.84 years for all CIN cases, 44.70± 9.34 years, 47.15± 10.40, and 45.94±10.66years for CIN I, CIN II, and CIN III, respectively. The mean patients' age for the CIG case was 48.12 ± 10.66 years.

Table 1 shows the mean ages and SD for each dysplasia type, while table 2 shows the age groups thereof. Figures 1-3 show the didtribution of the dysplasia types; the age groups thereof are represented in figures 4-7.

	Mean	SD
All	44.52	9.92
CIGD	48.12	11.68
CIN	44.41	9.84
CIN I	44.7	9.34
CIN II	47.15	10.4
CIN III	45.94	10.66

Table 1 Mean ages and SD

	21-30	31-40	41-50	51-60	61-70	71-80	81-90
All	6.02	23.93	44.37	18.23	5.86	1.43	0.16
CIN	6.11	24.42	43.73	18.48	5.78	1.49	0.00
CIN I	6.37	25.46	45.89	16.18	5.31	0.80	0
CIN II	4.96	19.83	46.28	19.01	7.44	2.48	0
CIN III	6.48	25.93	33.33	25.93	5.56	2.78	0
CIGD	4	12	60	12	8	0	4

Table 2 Cervical dysplasia age groups

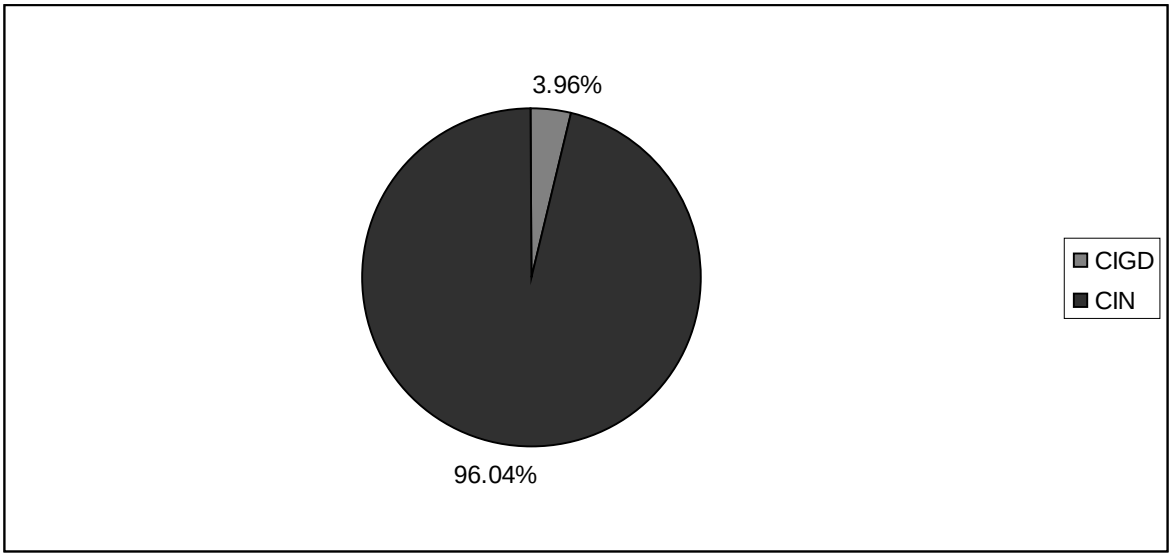

Fig. 1 Dysplasia types

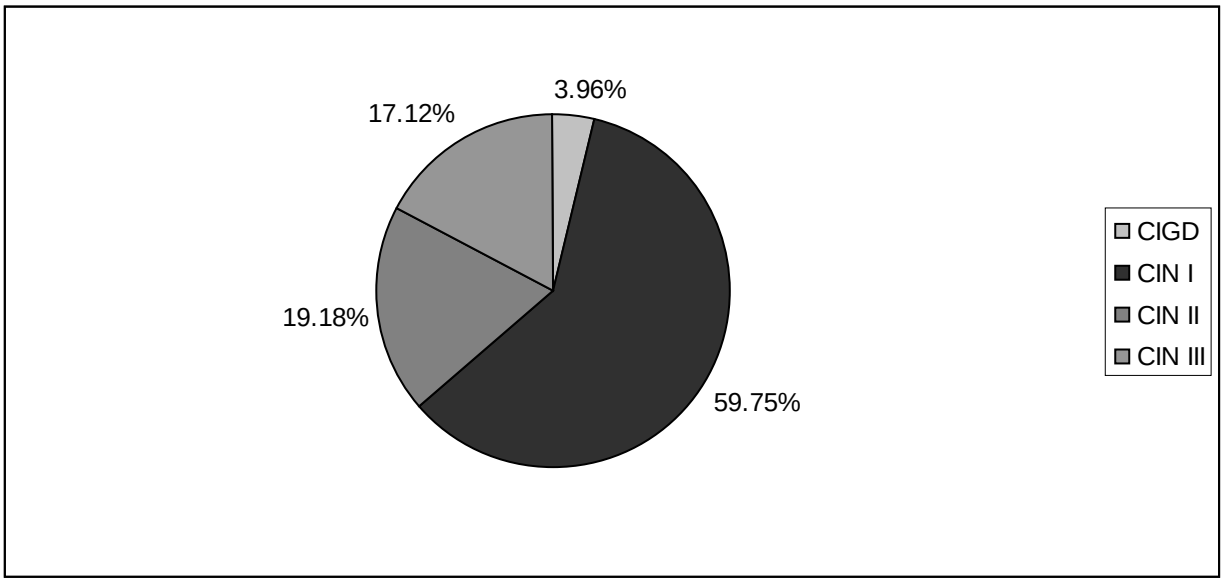

Fig. 2 Percentage of dysplasia types

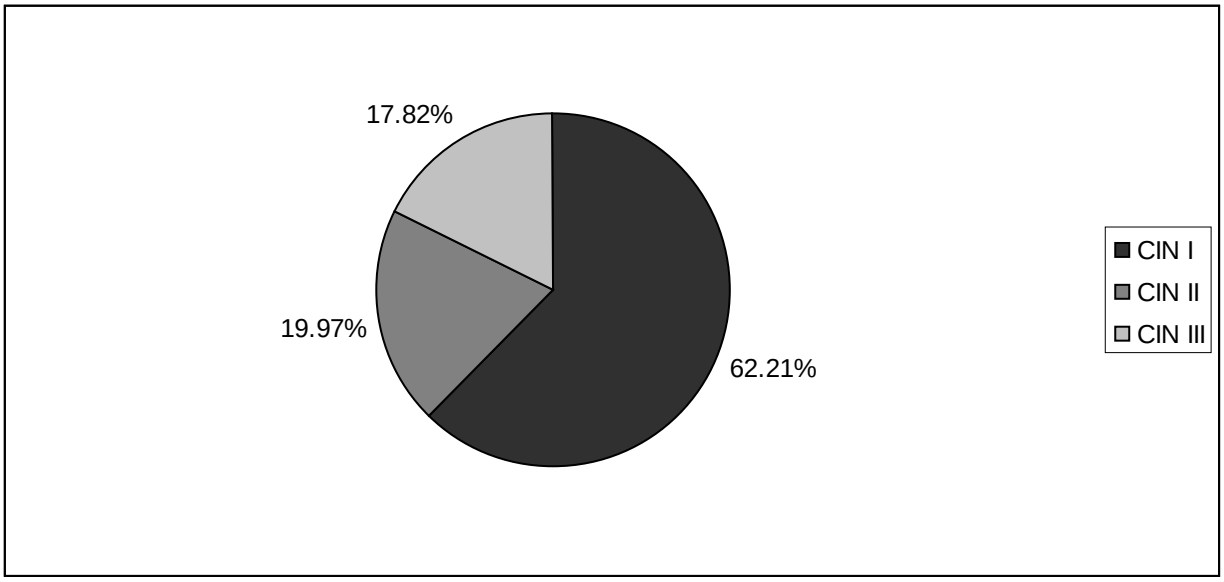

Fig. 3 Percentage of CIN types of the total CIN cases

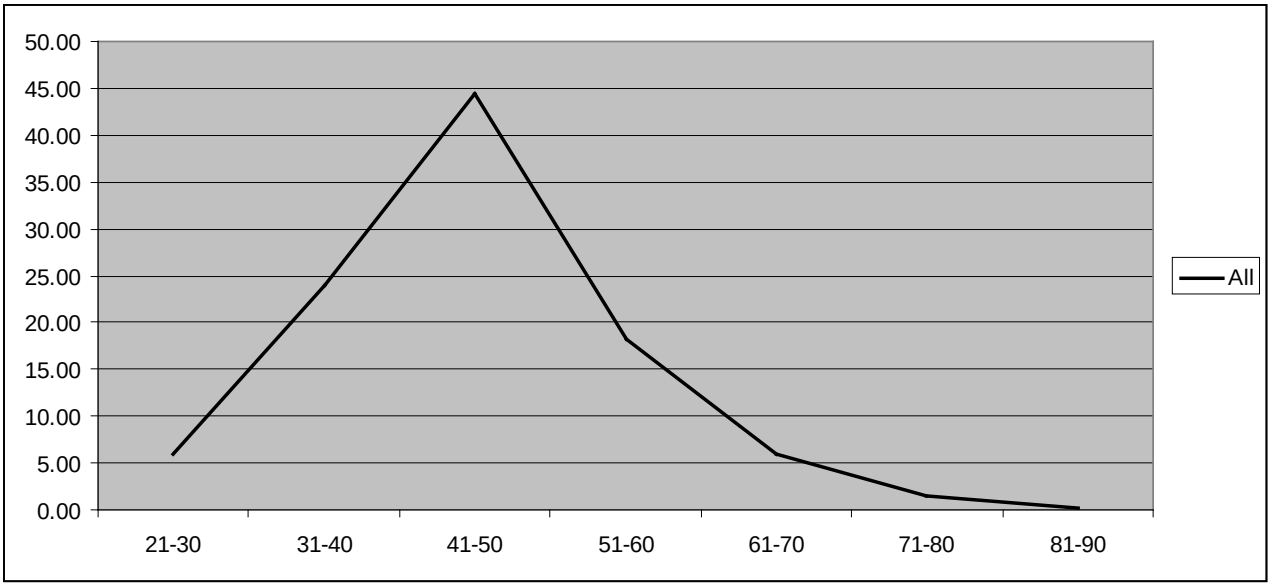

Fig. 4 All age groups

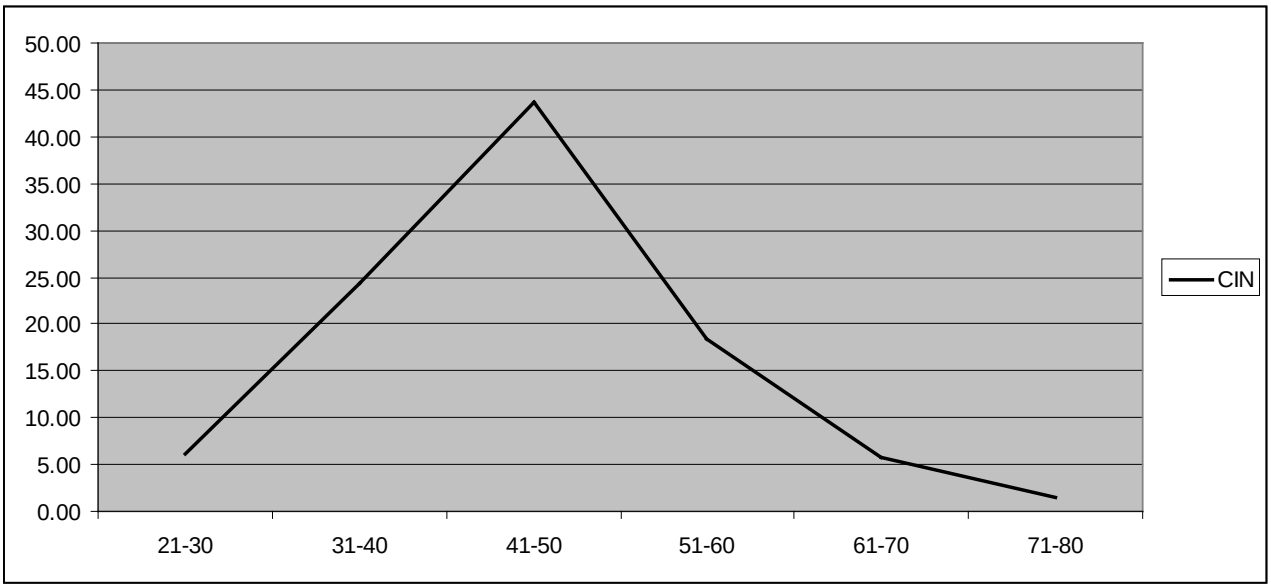

Fig. 5 CIN age groups

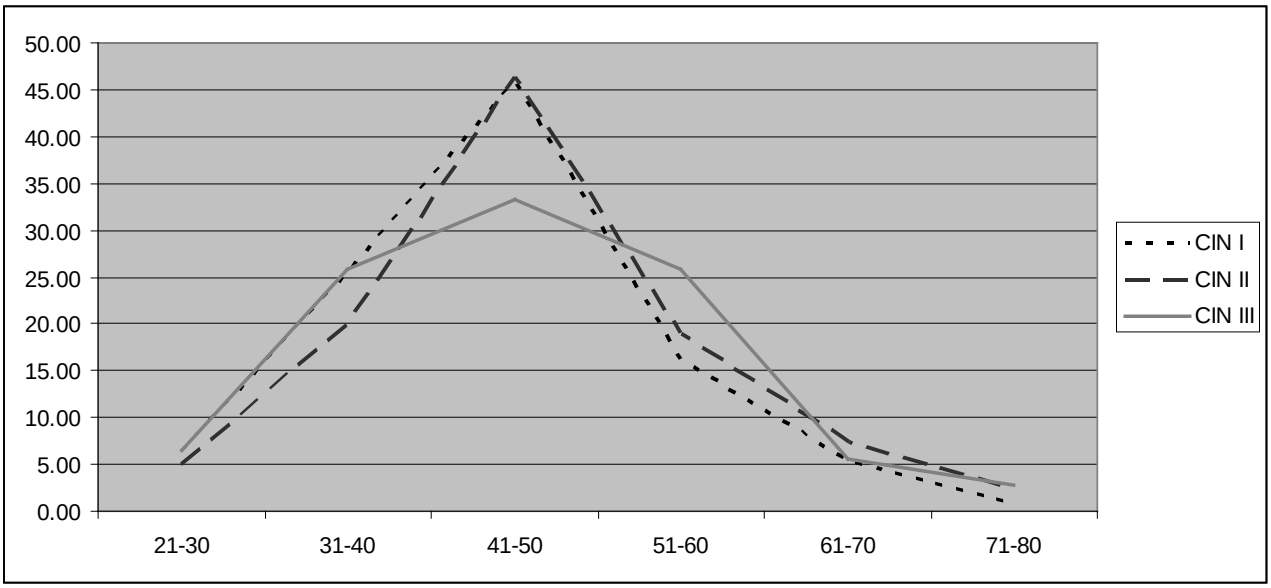

Fig. 6 CIN I-III age groups

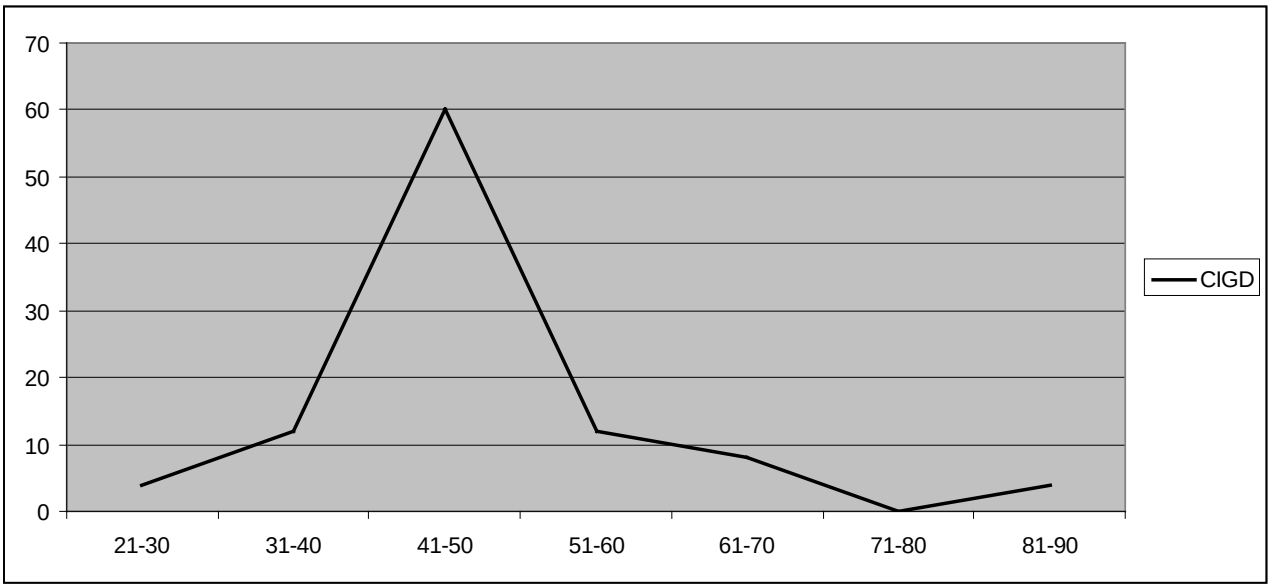

Fig. 7 CIGD age groups

There were 12 cases (3.27% of the 367cervical cancer cases diagnosed during the same period, 1.98% of the 606 CIN cases) of microinvasive carcinomas combined with CIN lesions (all of them with CIN III) and one case of cervical carcinoma combined with CIN I (0.27% of the 367 cervical cancer cases diagnosed during the same period, 0.17% of the 606 CIN cases).

Table 3 shows the statistically significant differences between the mean ages of different groups and between dysplasia cases and the 367 cervical cancer cases (mean age 53.66 ±13.29years) by using Student's t-test.

Comparison	p
All vs CIGD	0.390
All vs CIN	0.889
All vs CIN I	0.358
All vs CIN II	0.631
All vs CIN III	0.478
CIGD vs CIN	0.363
CIGD vs CIN I	0.235
CIGD vs CIN II	0.583
CIGD vs CIN III	0.675
CIN vs CIN I	0.430
CIN vs CIN II	0.569
CIN vs CIN III	0.430
CIN I vs CIN II	0.290
CIN I vs CIN III	0.212
CIN II vs CIN III	0.849
Cervical cancer vs all	**<0.00001**
Cervical cancer vs CIN	**<0.00001**
Cervical cancer vs CIN I	**<0.00001**
Cervical cancer vs CIN II	**<0.05**
Cervical cancer vs CIN III	0.059
Cervical cancer vs CIGD	0.556

Table 3 Age comparisons

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 not statistically different among them in the present study, all dysplasia cases, all CIN, the CIN I and CIN II cases 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; CIN III and CIGD cases are not statistically different from the cervical cancer cases, due probably to the small number of cases.

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