

## DIRECTIONS IN THE EVOLUTION OF CERVICAL L-SIL LESIONS

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Molecular activities in the basic cytopathological substratum of the lesions on uterus cervix, in case of HPV infection in form of squamous intraepithelial lesions of the low (L – SIL) and high (H – SIL) level, are defined by Bethesda terminological system. More frequent, L – SIL changes include CIN I, coil atypia and condilomata lata and can be recognized by cellular abnormalities in the basal and parabasal layer with minor cellular structural changes, nuclei hyperchromasia with chromatin condensation, acantosis, parakeratosis with well differentiated cells and faster exfoliation. Women more prone to develop L-SIL are those older than 41, with III degree of vaginal secretion, with the colposcopic finding of aceto-white epithelium and Papa-Nicholaus test of III group. The control cervical, colposcopically controlled biopsy was resumed after four control medical check-ups done every three months after the L-SIL diagnosis. The results showed that lesions remained at the same stage (41,67%), whereas regression appeared in every third examinee (33,33%), slight progression in every eight examinee (12,50%), and significant progression in every twelfth examinee (8,33%). Our conclusion was that L-SIL lesions do not require the ablative therapy a priori, and what is needed is a regular colposcycytological check-up every three months and cervical biopsy, if necessary. Diagnosis of HPV infection certainly changes one's attitude and requires loop diameter because of the additional diagnostic indications and final therapy. *Acta Medica Medianae* 2005; 44 (1):11–14.

**Key words:** cervix, L-sil lesions, evolution

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### Introduction

The cytohistological recognition of the squamous intraepithelial changes on the uterus cervix, which was defined by Bethesda system in 1988, resolved doubts regarding all known nomenclatures. This nomenclature system is based on the completion of molecular changes in case of presence or absence of HPV infection with the basic cytopathological substratum presented in the form of coilocytosis (1,2,3).

Therefore, lesions of the low (L-SIL) and high (H-SIL) level can be differentiated. Lesions of the high level include CIN I, coil atypia and flat condilomas. They are characterised by cellular atypia that spreads over parabasal and basal cells of the mature squamous or metaplastic epithelium as well as spare cells of endocervix. The origin of these changes is polyclonal if in association with oncogene types of the HPV virus, and it is monoclonal if it appears together with the oncogenic HPV virus infection.

Dominant histological abnormalities of L-SIL are in the form of minimal cellular changes localised in deep cervical intraepithelial layers. The basal and parabasal layers proliferate intensively accompanied by acantosis, parakeratosis and papillomatos and seriously disrupt natural epithelial architecture. With proper differentiation, nuclei enlarge five times being hyperchromatically coloured, with the chromatin condensation that loses polarity. Certain cells obtain irregular cisterns due to the cytotoxic effect of HPV virus on the cytoskeleton protein of the cell matrix. It is exactly these changes in deep layers that lessen the reliability of the cytological method whose level of so-called negative results remains in about 50%. The degree of reliability of the colposcopic method is maintained in 90% approximately.

The most frequent colposcopic finding is acetous-white with epithelium of pale colour and unclear contours. It is often accompanied by changes in the vascular net in the form of the delicate mosaic or clear punctations.

The evolutive process of L-SIL into H-SIL is slow, so that the leading evolutive courses are in the form of regression and stagnation. The most frequently cited is the evolution towards regression in about 40%, towards persistence in 38% and towards progression, in about 42%. All this occurs within 4-5 days (4,5,6,7).

Such a long period of relative stagnation, with the help of cervical colposcopy and cytology, makes it

possible to recognize the critical moments of evolutive transition into the following phase, H-SIL, in which a small ablative intervention represents a reliable method of the additional diagnosis and complete healing.

### Aim of the research

The aim of the research is to determine the evolutive developmental courses of the cervical intraepithelial lesions of the low level (L-SIL), analysed in two time intervals with one-year pause in-between (1) and, at the same time, to estimate the reliability of the colposcopic and cytologic diagnosis, as well as the possibility to predict a negative development of L-SIL with these methods (2).

### Results and discussion

The research was carried out at the Gynecology and Obstetrics Clinic "KBC Kragujevac" in Kragujevac including women who, either because of a regular gynaecological check-up or being advised by their gynaecologist, visited The Department for early diagnosis of malignant diseases in the period from November 2002 to April 2003.

The level of vaginal secretion cleanliness was analysed by Peter-Jirovec method (1), then colposcopic status was estimated (2), the cytological smear was coloured by Papa-Nicholaus method (3) and colposcopic cervical biopsy was taken (4) from all examinees. The study included only 24 examinees in whom L-SIL was diagnosed by cervical biopsy. The medical check-ups of women with cervical L-SIL were done every three months (1,2,3), whereas the complete initial examination (1,2,3,4) was done after approximately one year in the period from November 2003 to June 2004.

The results are shown in Table 1.

Table 1. Distribution of patients according to age

| Age     | Absolute number | Relative number |
|---------|-----------------|-----------------|
| < 20    | 2               | 8,33            |
| 21 – 30 | 5               | 20,83           |
| 31 – 40 | 8               | 33,34           |
| 41 >    | 9               | 37,50           |
| Total   | 24              | 100,00          |

The most frequent age of women with L-SIL is above 41 (37,50%), though it is also frequent in women of 31 to 40 years of age (33,34%). L-SIL is almost never diagnosed under 20 years of age.

The squamous intraepithelial low level lesions are most often found in cases of pathological vaginal secretion cleanliness, primarily in group III which appears due to various causes. L-SIL often persists synergically with fungal germs, and rarely in protozoal infestations. We should add that the existence of L-SIL was diagnosed in physiological levels of the vaginal secretion cleanliness (Table 3).

The main colposcopic finding in L-SIL is acetous- white epithelium of delicate mosaic, of the leucoplakia basis and leucoplakia.

The cytologic study of the cervical plaque-layered cells' exfoliation in cases with L-SIL appears to be more frequent in Papa-Nicholaus group III. L-SIL is often found in Papa-Nicholaus group II which lessens the sensitivity of this method (Table 4).

A year later, when colposcopic cervical biopsy was done again, it was concluded that the same status of L-SIL lesions was mainly maintained (41,67%), that regression appeared in 33,33%, whereas slight progression was noted in 12,5% and great progression in 8,33%.

Table 2. Distribution of patients according to the level of vaginal secretion cleanliness

| Age   | II<br>Physiological VS | III<br>Various | IV<br>N. gonorrhoe | V<br>T. vaginalis | VI<br>C. albicans |
|-------|------------------------|----------------|--------------------|-------------------|-------------------|
| < 20  |                        | 1 (4,17)       |                    | 1 (4,17)          |                   |
| 21–30 | 1 (4,17)               | 3 (12,5)       |                    |                   | 3 (12,5)          |
| 31–40 | 2 (8,33)               | 6 (25,0)       |                    | 2 (8,33)          | 3 (12,5)          |
| 41 >  |                        | 1 (4,17)       |                    |                   |                   |
| Total | 3 (12,5)               | 12<br>(50,00)  | 0 (0,00)           | 3 (12,5)          | 6 (25,0)          |

Table 3. Distribution of patients according to the colposcopic status

| Age     | Ectopia  | TZ       | Acetous White | Mosaic   | Punct.   | Baza Leukopl. | Leukopl. |
|---------|----------|----------|---------------|----------|----------|---------------|----------|
| < 20    | 1 (4,17) |          |               |          |          |               |          |
| 21 – 30 | 1 (4,17) | 2 (8,33) | 2 (8,33)      |          | 1 (4,17) |               |          |
| 31 – 40 |          |          | 5 (20,8)      | 3 (12,5) |          |               |          |
| 41 >    |          |          | 1 (4,17)      | 3 (12,5) |          | 3 (12,5)      | 2 (8,33) |
| Total   | 2 (8,33) | 2 (8,33) | 8 (33,33)     | 6 (25,0) | 1 (4,17) | 3 (12,5)      | 2 (8,33) |

Table 4. Distribution of patients according to the cytological status

| Age     | Papanicolaou II | Papanicolaou III | Papanicolaou IV | Papanicolaou V |
|---------|-----------------|------------------|-----------------|----------------|
| < 20    |                 | 1 (4,17)         |                 |                |
| 21 – 30 | 6 (25,0)        |                  |                 |                |
| 31 – 40 | 1 (4,17)        | 6 (25,0)         | 2 (8,33)        |                |
| 41 >    | 1 (4,17)        | 7 (29,17)        |                 |                |
| Total   | 8 (33,33)       | 14 (58,33)       | 2 (8,33)        |                |

### Conclusion

1. The squamous cervical intraepithelial low level (L-SIL) lesions mostly remained at the same stage one year after (41,67%). Regression was noted in every third examinee (33,33%), slight progression in every eighth (12,5%) and great progression in every twelfth examinee (8,33%). Due to the low level of L-SIL progression, especially when not associated with HPV infection, the applied therapy need not be aggressive. Colpocytologic supervision with regular check-ups every three months during the first year of changes is enough.

2. The colposcopic method in detection of the state and progression of L-SIL is quite sensitive so that, being non-aggressive and cheap, it should be regarded as

Table 5. Distribution of the bioptical cervical HP findings one year after the beginning of the L-SIL evolution supervision

| Age     | Positive finding | CIN I      | CIN II   | CIN III  |
|---------|------------------|------------|----------|----------|
| < 20    | 1 (4,17)         |            |          |          |
| 21 – 30 | 4 (16,7)         | 1 (4,17)   | 1 (4,17) |          |
| 31 – 40 | 3 (12,5)         | 7 (29,17)  | 1 (4,17) | 2 (8,33) |
| 41 >    |                  | 2 (8,33)   | 1 (4,17) |          |
| Total   | 8 (33,33)        | 10 (41,67) | 3 (12,5) | 2 (8,33) |

the main method of the cervical status supervision, unlike the cytological method which results with false results in high percentage.

3. The most reliable methods can be obtained by the combination of colposcopic and cytological methods with assessing of the vaginal secretion cleanliness in regular medical examinations every three months and by the colposcopic cervical biopsy which should be done one year after the L-SIL lesions have been diagnosed. In case of lesions with turbulent epithelium and HPV infection, the supervision ought to be widened with minor ablativ interventions which, along with diagnostic and therapeutic procedures, provides complete curing in most of the cases.

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## PRAVCI U EVOLUCIJI CERVIKALNIH L-SIL LEZIJA

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Bethesda terminološkim sistemom definisana su molekularna zbivanja u osnovnom citopatološkom supstratu lezija na cerviksu uterusa u okolnostima postojanja HPV infekcije kao skvamozne intraepitelne lezije niskog (L-SIL) i visokog stepena (H-SIL). Učestalije po prisustvu, L-SIL promene obuhvataju CIN I, koilocitnu atipiju i condilomata lata i prepoznaju se prema celularnim abnormalnostima u bazalnom i parabazalnom sloju, sa manjim celularnim izmenama strukture, hiperhromazijom jedara sa kondenzacijom hromatina, akantozom, parakeratozom uz dobro diferentovane ćelije i bržu eksfolijaciju. Incidentnija grupa žena za pojavu L-SIL u ispitivanom uzorku je ona u starosti iza 41. godine, uz III stepen čistoće vaginalnog sekreta, sa kolposkopskim nalazom aceto-withe epitela i Papanicolaou testom III grupe. Nakon četiri kontrolna pregleda od dijagnostikovanja L-SIL lezija od kojih je svaki bio na tri meseca od prethodnog, obnovljena je kontrolna cervikalna, kolposkopski kontrolisana biopsija. Dobijeni rezultati su pokazali održavanje lezija u istom stadijumu u 41,67%, regresiju smo konstatovali kod svake treće ispitanice (33,33%), laku progresiju kod svake osme (12,50%) i tešku progresiju kod svake dvanaeste (8,33%). Iz ovih podataka zaključili smo da L-SIL lezije ne zahvataju a priori agresivnu ablativnu terapiju, već je dovoljan redovni, tromesečni kolpocitološki nadzor i po potrebi obnavljanje cervikalne biopsije. Svakako, utvrđivanje postojanja HPV infekcije, menja u značajnoj meri stav i nalaže loop dijometriju, kako zbog dodatnih dijagnostičkih indikacija tako i u smislu konačne terapije. *Acta Medica Medianae* 2005; 44(1):11–14.

***Ključne reči:*** cervix, L-sil lezije, evolucija