

Cervical Pap smear is gold diagnostic tool for cervical cancer

Dr. Manal Abd Ali BSC&S, M.S.C

Dr. Aseel Al Qzweni B.C, F.I.C.P

*Microbiology Department/ College of Medicine/University of Kufa

**Pathology Department /College of Medicine/University of Kufa

الخلاصة: تم دراسة ١٠٠ مريضة من اللاتي راجعن مستشفى الزهراء التعليمي لأمراض وعوارض نسائية مختلفة أو لمتابعة عمليات وعلاجات سابقة وحديثه مشكوك بإصابتهن بحالات سوء نمو ظهاريه حشفيه لغرض إجراء مسحة لعنق الرحم. وقد تم تقسيم نتائج فحص المسح الخلوي لعنق أرحامهن إلى ثلاثة مجاميع :- حالات التهاب عنق الرحم مع سوء نمو ظهاريه حشفيه وحالات التهاب عنق الرحم بدون سوء نمو وحالات عنق رحم صحيحة بدون تغيرات. حيث تم اخذ تاريخ المرض والفحص السريري لجميع هذه الحالات الثلاث. أظهرت الدراسة النتائج التالية:

١- كانت نسبة حالات التهاب عنق الرحم مع سوء نمو ظهاريه حشفيه ٢٢% والتي تضمنت الأنواع التالية (٥٠%) حالات سوء نمو ظهاريه حشفيه عالية الدرجة و ٦٣% حالات سوء نمو ظهاريه حشفيه واطنة الدرجة و ٣٢% خلايا حشفيه سيئة النمو غير محددة الدرجة) أما نسبة حالات التهاب عنق الرحم بدون سوء نمو ظهاريه حشفيه كانت ٦٨% بينما نسبة الأصحاء كانت ١٠%.

٢- إن متوسط أعمار المريضات المصابات بحالات سوء نمو ظهاريه (٤٤,٢٣ ± ١٠,٢) سنة و كانت أعلى نسبة إصابة في الفئة العمرية (٣٦-٥٠) سنة.

٣- الأعراض السريرية للمريضات المصابات بحالات سوء نمو ظهاريه مميزة عن بقية المجاميع الخلوية الأخرى التي تم ذكرها في البحث. فقد وجد بأنه من بين العديد من المعلومات المستخلصة من التاريخ المرضي والفحوص السريرية بان الزواج المبكر وتعدد الولادات والتدخين والنزف المهلي الغير طبيعي لها علاقة مهمة بحالات سوء نمو ظهاريه حشفيه.

Abstract:

One hundred (100) female patients referring to AL-Zahraa Teaching Hospital in AL-Najaf Province who were suspected to harbor Cervical squamous intraepithelial lesions were included in this study. Cytological examination were performed for their Pap-smear and stained cervical cellular scrapes and according to their main cytological finding they were divided into three cytological groups: Cervicitis with Squamous intraepithelial lesions, Cervicitis without Squamous intraepithelial lesions and healthy group.

A full history taking and clinical gynecological examination of all these (3) groups was performed.

The following summarized results were found:

1-Cervicitis with SILs was 22% (HSILs 5%, LSILs 63% and Asc-us 32%),Cervicitis without SILs was 58% and 10% healthy patients.

2-The mean age of patients presented with cervical intraepithelial lesions was (44.23± 10.2)years. The highest percentage was diagnosed in the age stratum (36-50) years. 3-the clinical presentation of the patients with cervical neoplasia were indistinguishable from other cytological group, However, among many other finding related to the history and clinical examinations, early of marriage, multiparity, smoker behavior, abnormal vaginal bleeding were found significantly higher in cervical premalignant lesions than other cytological group.

Introduction:

Cervical cancer is the second most common cancer in women worldwide, and it is the second cancer of women in most developing countries, where 80 percent of cases occur(4). The rationale for cervical cancer screening programs is that considerable morbidity and mortality could be avoided by early cytological detection and treatment of these lesion (6)

These facts should stress the need for early detection these cervical lesions by cytological screening and hopefully prevent the development of cervical cancer (1).This cytomorphological examination is the most widely applied and accepted screening methods for diagnosis of SIL. In addition, the implementation of such cervical screening programs has led to decrease in number of deaths due to cervical cancer by more than 40% during the last 20 years (19).Unfortunately in countries of the third world , such screening is often not routinely performed since it is expensive,complex to organize and often difficult (7).

An overview of Iraqi Cancer Registry of cervical cancer revealed that the incidence of this cancer in Iraq constitutes 1.4% among the total number of cancer with mean annual number of 113 new cases during the period (1995-1997) (5).The last report of Iraqi cancer registry in Iraqi Ministry of health announced an incidence of 1.04% for cervical cancer occurrence in 2004, the annual number of new cases of cancers of cervix uteri increased to 151 in these years(5). Current estimates indicate that every year 311 women are diagnosed with cervical cancer and 212 die from the disease (20) This could be related to that the plans of Ministry of Health for establishing centers for early diagnosis and screening programmed of cervical cancers are only very recently applied and still a milestones in these respects that not yet reaching the minimal wanted wishes.

Patients & Methods:

Cervical pap smears screening applied on one hindered (100) female patients referring to AL-Zahra teaching hospital in AL-Najaf province who suspected to harbor Cervical Intraepithelial Lesions, a sample for cervical pap smear stained with Papanicolaou stain and Hematoxylin& Eosin stain for examination and diagnosis by pathologist in Al-sader medical city laboratories (Cytology unit) according to Bethesda system.

All sample were taken under supervision of special Gynecologist, the sample of cells was collected from the ectocervix and endocervix by scraping it with an wooden Ayre"s spatula. The cells are smeared on a glass slide and immediately fixed by 95% ethyl alcohol. Pap smear were processed according to the cytology laboratory routine practice for Papanicolaou staining and Hematoxylin & Eosin staining methods.

Results:

The results of Pap smear screening that applied on one hindered female (100) patients according to Bethesda system were : the total number of patients with cervicitis was 90, among them, the number of patient with Cervical Squamous Intraepithelial Lesions (SILs) was 22{High grade squamous intraepithelial lesion (HILS) was 5%(1 out of total 22) (figure 2), Low grade squamous intraepithelial lesion (LILS) was 63%(14 out of total 22) (figure 3), and Atypical squamous cells of undetermined significance constituted(Asc-us) 32%(7 out of total 22) (figure 4)}, the residue of patients without SILs but with different types of Cervicitis was(68%), and the number of cases who were appeared cytopathologically healthy was (10 %). As in figure (1)

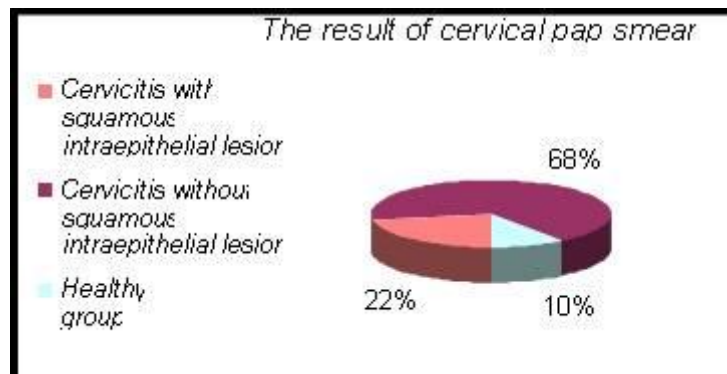
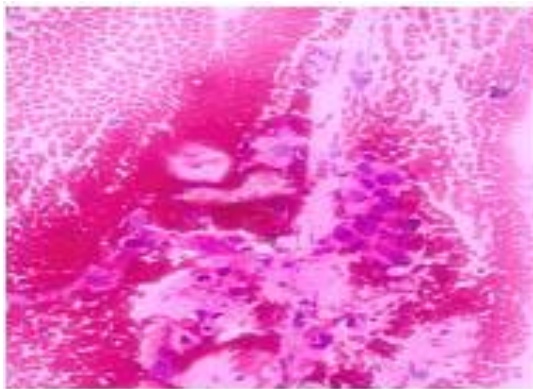
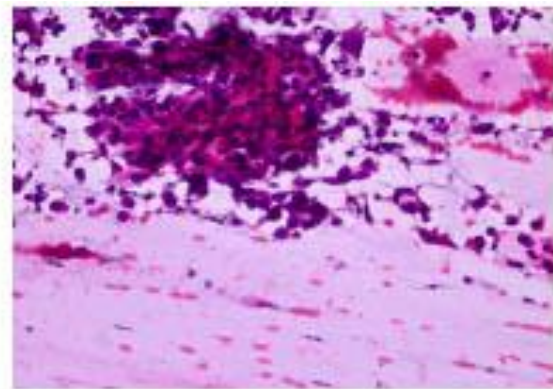


Figure (1): Distribution the results of cervical pap smear screening according to Bethesda system.

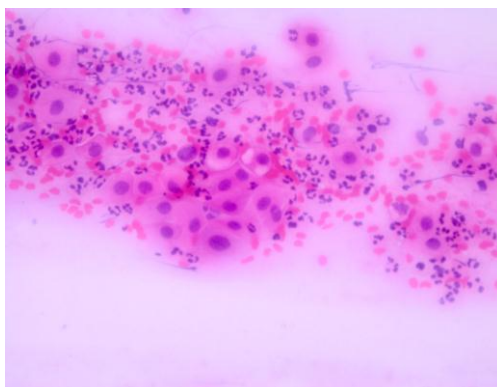


Hematoxylin and eosin stain

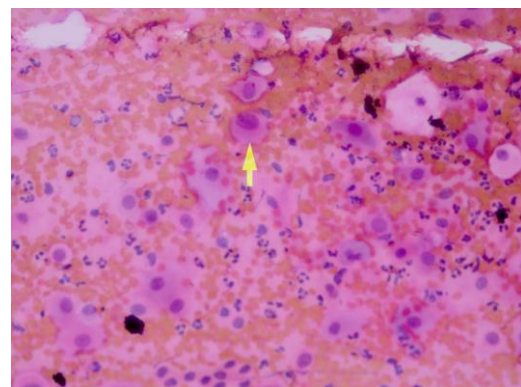


Papanicolaou stain

Figure (2): Cervical Pap smear staining with H&E stain and Papanicolaou stain, High grad squamous intraepithelial lesion, power40x.

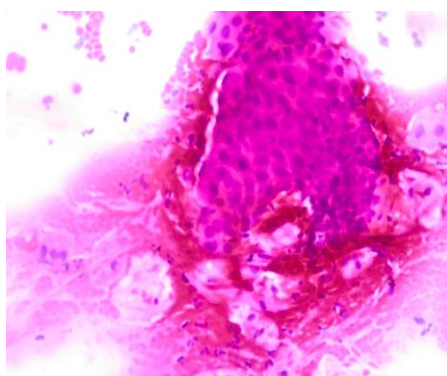


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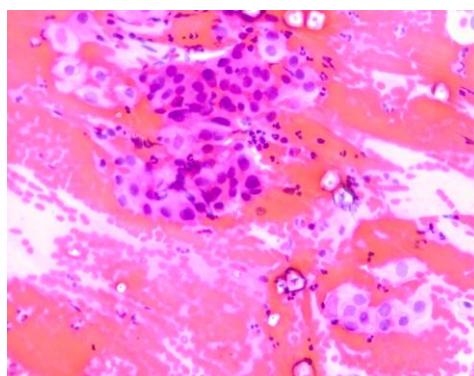


Papanicolaou stain

Figure (3): Cervical Pap smear staining with H &E stain and Papanicolaou stain, Low grad squamous intraepithelial lesion power400x.



Hematoxylin and eosin stain



Papanicolaou stain

Figure (4): Cervical Pap smear staining with H & E stain and Papanicolaou stain, Atypical squamous cell of undetermined significance power 40x.

Clinical types of Cervicitis: The prevalence of different types of cervicitis detected in our patients are shown in table(1)

Table (1): Distribution of different types of cervicitis according to their SILs

Studied groups	Types of Cervicitis						healthy		Statistical analysis
	Acute non-specific cervicitis		Acute specific cervicitis		Chronic cervicitis				
Cervicitis with SILs		%		%		%		%	$\chi^2 = 3.229$ $P = 0.199$
	17	17%	5	5%	0	0%			
Cervicitis without SILs & healthy	52	52%	9	9%	7	7%	10	10%	
Total	69	69%	14	14%	7	7%	10	10%	

It appears from these results that 17%, and 5%, of patients with cervical SIL were presented with acute non-specific cervicitis and acute specific cervicitis respectively, also, the patients of cervicitis without SIL had 52%, 9%, and 7% of acute non-specific cervicitis, acute specific cervicitis and chronic cervicitis respectively,

Among acute specific cervicitis there were 9.09% (2 out of total 22)of cervical SIL group and 3.5%(2 out of total 52)of cervicitis without SIL group complained acute *chlamydial* infection, (figure 6)

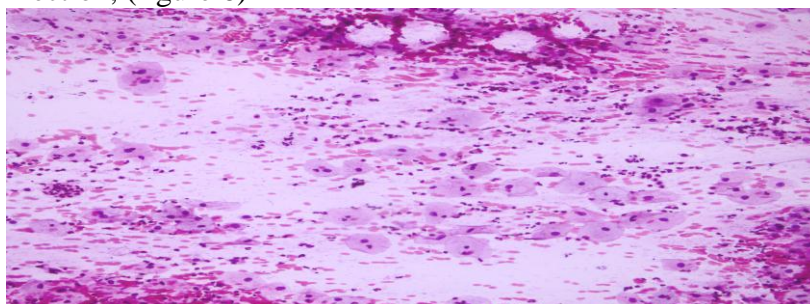


Figure (5): Cervical Pap smear stained with hematoxylin and eosin stain, Acute none specific cervicitis, power 20x.

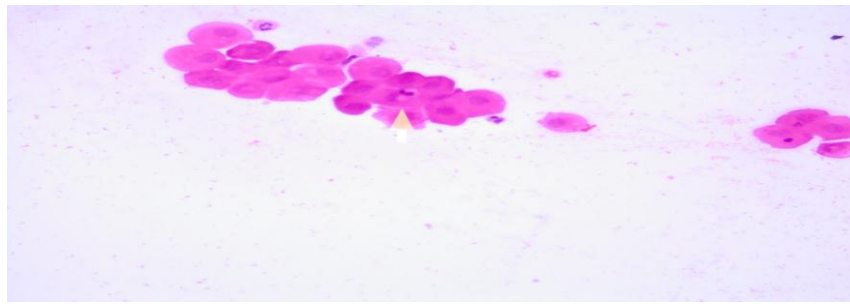


Figure (6): Cervical Pap smear stained with hematoxylin and eosin stain, Acute specific Cervicitis –*Chlamydial infection*(Cytoplasmic vacuoles)
Power 40x.

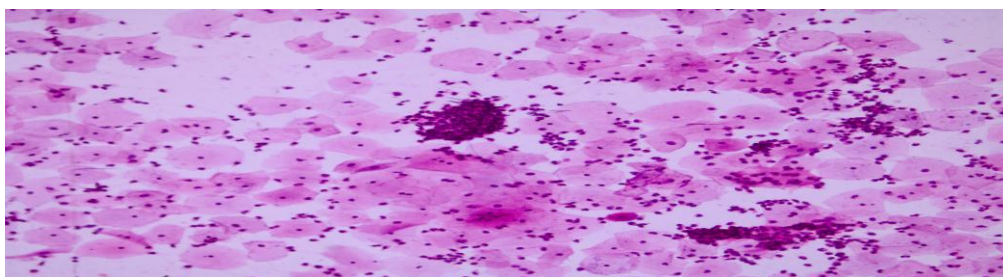


Figure (7):Cervical Pap smear stained with hematoxylin and eosin stain, power 20x Acute specific cervicitis –*Trichomonus vaginalis* infection(leukocytes agglomeration).

Also, with cervical SIL group there were 13.63%(3 out of total 22) and 15.78% of cervicitis without SIL group that were presented as acute *Trichomonus vaginalis* infection (figure 7)

Table (2): Distribution of mean age (years) among the studied groups (Cervicitis with SIL, Cervicitis without SIL and healthy group) according to age strata

Studied groups	N	Mean Age	SD	SE	Mini.	Maxi.	Comparison of significant
Cervicitis with SIL	22	44.23	10.197	2.170	22	64	Highly significant P value=0.0001
Cervicitis without SIL	68	38.68	10.131	1.229	22	64	
Healthy	10	25.50	6.570	2.078	20	40	
Total	100	38.58	10.934	1.094	20	64	

The highest percentages among age strata were 63.6% for cervical intraepithelial lesion and cervicitis patients were noticed in the age group (36-50 years) as shown in figure (8).This age group was followed by the percentages of age strata 30.0% for healthy group ,respectively.

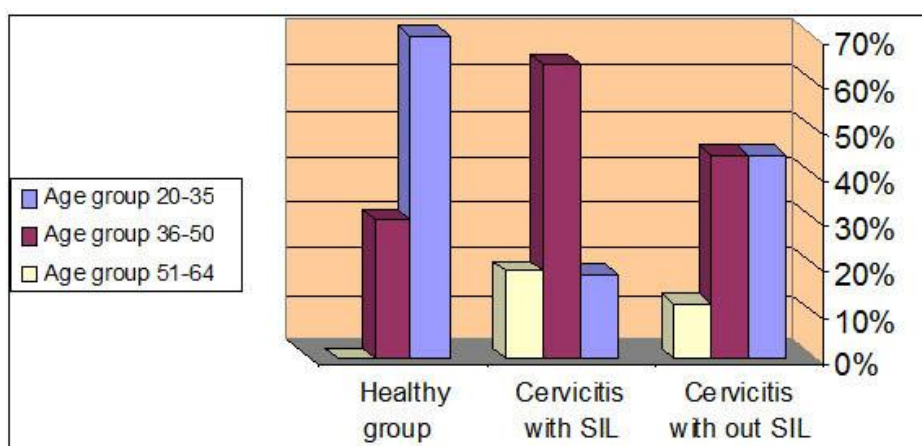


Figure (8): Age groups distribution in the patients of Cervicitis with SIL, Cervicitis without SIL and healthy group.

Discussion

Cervical cancer prevention and control can be divided into several components. One includes cytological screening and management of Pap smear abnormalities. Another is the histological diagnosis and removal of precancerous lesion(16).

The cytomorphological examination of cervical smear is the most widely applied and accepted screening methods for dysplasia, cancer, and HPV infection (17).The reason that cytological screening is so effective in preventing cervical cancer is that the majority of cancers are preceded by a long-standing precancerous lesion. This lesion may exist in the noninvasive stage for years and shed abnormal cells that can be detected on cytologic examination (16). The pap test aims to detect potentially pre-cancerous changes (called cervical squamous intraepithelial lesion (SIL) or cervical dysplasia) and cervical cancer, The test may also detect many infections in the endocervix and endometrium.(14) It was estimated that the progression rate of LSIL to HSIL is about 20% (17). Another study found that about one third of high-grade lesions (HSIL) have progressed to cancer within ten years. (12).

Abnormal cells could also be missed either by the cytologist or due to sampling error giving rise to false negative result, the presence of false-negative smears varies from 15% to 20% (3). Moreover, over diagnosis on the basis of cytological criteria is also a growing problem due to the number of false-positive smears is about 10% (13). This constituted a major problem to colposcopy units in dealing with numerous unjustifiable referrals of border line cytologies and mildly dyskaryotic smears, which vary considerably in their underlying pathology (16).This mean that the sensitivity of cytology for cancer and SIL screening is low (50%-85%) and it is specificity high about 90% (13).

There were highly significant differences ($P<0.01$) noticed between both groups when the mean age of the patients who suffered from Cervicitis with SIL (44.23 years) when compared with the mean age of patients with cervicitis without SIL and healthy group(38.68 years) and (25.50 years) respectively, Regarding the age of these patients with cervical neoplasia as a relatively rough indicator for their average age at first intercourse and sexual activity, an obvious differences were noticed in this study between the mean age of different groups (Table 2) .

The present results were consistent with the notion that malignant transformation requires a long latency period that extend between, cervical intraepithelial lesions that

frequently occur in the younger women (often in 40 years of age) and cervical cancer that tends to affect women ,usually in the fifth or sixth decade at a mean age of 54 years(11).

statistical analysis shows significant differences in the age groups distribution of Cervicitis with Squamous intraepithelial lesions and Cervicitis without Squamous intraepithelial lesions and Healthy.

There are many potential risk factors have been implicated as an important risk factors that influencing the rate of cervical cancer including marital and sexual history, smoking ,gynecologic and obstetric events, infectious agents(on top of the list is HPV), oral contraceptive, occupational factors, immunosuppression, and dietary habits. Recent studies indicate the number of sexual partners of women, age at first intercourse, number of pregnancies, and number of sexual partners of the husbands are independent risk factors(14)

As shown in table (1) the prevalence of acute non specific cervicitis with all grade of SILs and the highest incidence of acute none-specific cervicitis was observed in low grade squamous intraepithelial lesions subgroup, then followed by atypical squamous cells of undetermined significance.

However, the acute cervicitis could be related to many physiological and gynecological factors, disease and disorder. The result indicated that many infectious (protozoa and bacteria) associate with preinvasive cervical neoplasia. These are true when reviewing our results and finding many trichomoniasis and bacteria (*Chlamydial infection*) associated many low grads of SILs and to a lesser extent atypical squamous cell of undetermined significance. The present results of different types of cervicitis in cervical premalignant lesions are in line with previous reported finding by (13) .

References

1. Clifford GM., Smith 3S., Aguado T., Franceschi S. (2003) Comparison of HPV type distribution in high-grade cervical. lesions and cervical cancer: a meta-analysis. BrJ. Cancer, 89:10.
2. Edmund S., and Barbara S. (2009) Cytology-Diagnostic Principles and Clinical Corrlates Third Edition, 1:1-68.
3. Goldie S.J., Grima D., Kohli M., Wright T.C., Weinstein M. and Franco E.A. (2003) Comprehensive natural history model of HPV infection and cervical cancer to estimate the clinical impact of a prophylactic HPV-16/18 vaccine. Int. J. Cancer.; 106: 896-904.
4. Hesselink A.T.(2007) High-risk human papillomavirus testing in cervical screening .Netherlands Organization for Health Research and Development; grant 2200.0147.
5. Iraqi Cancer Board (1999) Results of Iraqi Cancer Registry 1995-1997. Ministry of Health (editor).Baghdad. Iraqi. P.11-13,34,and 32-39.
6. Health Promotion Council (2010) Facts about smoking and cervical cancer. Beabridge, philadeliphia,PA 19102.
7. Iraqi Cancer Registry Center (2004) Results of Iraqi Cancer Registry.Ministry of Health (editor). Baghdad. Iraqi 2008:.P15.
8. Jenkins D., Johnson CSW. and Gallivan S. (1996) Can papillomavirus testing be used to improve cervical cancer screening .Int J Cancer.65:768-773.
9. Koyama T.,Tamai K. ,Togashi K. (2007) Staging of carcinoma of the uterine cervix and endometrium.Eur Radiol ,17:2009-2019.

10. Louise A., Catherine S., William H. , Paul S., Herman F. Lehman D., Robert L., David A. (1986): Cigarette Smoking and Invasive Cervical Cancer JAMA. 255(23):3265-3269.
11. Malloy C., Sherris J. and Herdman C. (2000): HPV DNA testing: technical and programmatic issues for cervical cancer prevention in low-resource setting. P.A.T.H. (Program for Appropriate Technology in Health) 1-27.
12. Monsonego J., Bosch FX., Coursaget P., Cox JT., Franco E., Frazer I., Sankaranarayanan R., Schiller J., Singer A., Wright T. , Kinney W. , Meijer C. and Linder J. (2004): Cervical cancer control , priorities and new direction. Int. J. Cancer. 108: 329-333.
13. Mohammed Ali S. H. (2001): Molecular Biological Studies of Human Papillomavirus Infections in Patients with Cervical Neoplasia. A thesis submitted to the Collage of Medicine AL- Nahrain University in partial fulfillment of the PhD degree in Medical Microbiology.
14. Olsen A.O., Gioen K., Sauer T., Orstavik I., Ness O., Kierulf, Sponland G. and Magnus P. (1995): Human papillomavirus and cervical intraepithelial neoplasia grade II-III: A population-based case-control study. Int J.Cancer. 61:312-315.
15. Pirog E.C., Kleter B., Olgac S., Bobkiewicz P., Lindmeman J., Qunt W.G.V., Richart R.M. and Isacson C. (2000): Prevalence of human papillomavirus DNA in different histological subtypes of cervical adenocarcinoma. Am J pathol. 157(4):1055-1062.
16. Robbins and Cotran :Pathologic basis of disease 8th edition, 2010.
17. Rozendaal L., Walboomers J. M. M., Van Der Linden J. C. , Voorhorst, F. J. , Kenemans P. , Helmerhorst T. J. M. , Van Ballegooljen M. and Meijer C. J. L. M. (1996): PCR-based high-risk HPV test in cervical cancer screening gives objective risk assessment of women with cytomorphologically normal cervical smears. In J. Cancer. 68:766-769.
18. Sasieni P., Castanon A., Cuzick J., Snow J. (2009): Effectiveness of Cervical Screening with Age: Population based Case-Control Study of Prospectively Recorded Data". BMJ. 339: 2968-2974.
19. Walker P. (2005) The English National Health Service Cervical Screening Programme-approach to new technologies and quality assurance .J Low Genit Tract Dis. 9:118-123.
20. WHO/ ICO (2011) Information center on HPV (http://www.who.int/hpv_center).
21. Young T K., McNicol P. and Beauvais J. (1997): Factors associated with human papillomavirus infection detected by polymerase chain reaction among urban Canadian aboriginal and non-aboriginal women. Sex Transm Dis. 24 (5):293-298.
22. Zehbe, Strand L., Chua Z-L and Wilander P. (1996): Cytological evaluation and molecular human papillomavirus test of cervical scrapings from women treated for condyloma. Gynecol Invest. 42:128-132.