

# Cytopathological pattern of cervical Pap smear according to the Bethesda system in Southwestern Saudi Arabia

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## ABSTRACT

**Objective:** Cervical carcinoma is an important women's health problem worldwide. The aim of this study is to evaluate the abnormal cytological entities detected by cervical Pap smear in Al-Baha region of KSA, to reclassify the cytological findings according to the recently recommended Bethesda system and to discuss the significance of Pap smear's screening programs.

**Methods:** A retrospective study was designed to review the Pap smears from the archives of the Department of Pathology, King Fahad Hospital, Al-Baha over the last 10 years starting from 1994 to 2003 with correlation to the Bethesda system. Cytopathological aspects of Pap smears were reviewed with age distribution.

**Results:** Of the 2100 cases reviewed there were 166 cases (7.9%) with epithelial abnormalities that included: atypical squamous cells of undeterminate significance (ASCUS) were seen in 58 cases (2.76%) with age peak incidence (API) between 30-39 years; atypical squamous epithelium, cannot exclude high squamous intraepithelial

lesion (HSIL) was seen in 4 cases (0.19%); low grade squamous intraepithelial lesion (LSIL) including human papillomavirus was seen in 27 cases (1.3%) with API between 50-59 years and HSIL was seen in 14 cases (0.66%) with API between 40-49 years. Squamous cell carcinoma was seen in 7 cases (0.33%) with API between 50-59 years. There were 54 cases (2.57%) of atypical endocervical cells and 2 cases (0.09%) of atypical endometrial cells.

**Conclusion:** Atypical squamous cells of undeterminate significance, LSIL, HSIL, invasive cervical carcinoma and sexually related infectious diseases are less frequently encountered in Saudi women and occur at older age compared to the Western countries. Fewer women are screened for this disease in this region and health education is very important to encourage more Saudi female to have this important screening test particularly in this region of KSA.

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Today, the vast majority of cervical cancer cases are diagnosed at the in-situ stage.<sup>1,2</sup> Worldwide, cervical cancer is the second or third most common cancer in incidence and mortality among women and continues to be a significant health problem on a worldwide scale.<sup>1,3</sup> In some developing countries, it is the most common cancer despite advances in the detection and management of cervical

carcinoma.<sup>1,3</sup> Screening for cervical carcinoma by cervicovaginal cytology has led to a marked reduction in the incidence of and mortality from this tumor over the last 50 years, essentially in all countries with a functioning screening program.<sup>4,5</sup> The greatest barrier of effective cervical screening is patient's ignorance.<sup>6</sup> In the Kingdom of Saudi Arabia (KSA), carcinoma of the cervix ranks as the

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eighth in the National Registry of KSA in its frequency with the prevalence of 3.8%.<sup>7</sup> The literature overwhelmed with evidence supporting the importance of early detection of precancerous lesions in cervix by cytological examination using Pap smear. It is the most successful cancer prevention program of all times. Approximately 80% of the current incidence and mortality from this disease occurs in geographic areas of underserved and under screened women and the most important reason for the remaining mortality from cervical cancer in developed countries is lack of complete screening coverage.<sup>4</sup> The objective of this study is to evaluate the abnormal cytological entities detected by cervical Pap smear in Southwestern region of KSA and to discuss the importance of Pap smear screening programs.

**Methods.** A retrospective study is designed to review the Pap smears from the archives of the Department of Pathology, King Fahad Hospital Al-Baha, KSA over the last 10 years starting from 1994 to 2003, with correlation to the Bethesda system. Cytopathological aspects of Pap smears were reviewed with the age distribution and the percentage distribution. A total number of 2100 cases were reviewed for the study. King Fahad Hospital is the major referral hospital in the region that receives most of the Pap smear cases. No specific classification scheme was followed in reporting smears, so we reclassified them according to the Bethesda system, which is the newly recommended system of reporting Pap smear.

**Results.** Of the 2100 cases reviewed, there were 166 (7.9%) Pap smears with epithelial abnormalities, 1934 (92.1%) were negative for intraepithelial lesions, 420 (20%) showed benign reactive changes, 1100 (52%) showed chronic cervicitis not otherwise specified (NOS), 356 (16.9%) were within normal limits and 58 (2.8%) were unsatisfactory (Table 1). Out of the 166 Pap smear cases with epithelial abnormalities, atypical squamous cells of undeterminate significance (ASCUS) were seen in 58 cases (2.8%) with an age peak incidence (API) between 30 and 39 years; atypical squamous epithelium cannot exclude high squamous intraepithelial lesion (HSIL) was seen in 4 cases (0.19%) with API between 40-49 years; low grade squamous intraepithelial lesion including human papillomavirus (HPV)/mild dysplasia/cervical intraepithelial neoplasia (CIN I) was seen in 27 cases (1.3%) with API between 50-59 years; high grade intraepithelial lesion encompassing moderate to severe dysplasia, CIS/CIN II was seen in 14 cases (0.7%) with API between 40-49 years; squamous cell carcinoma was seen in 7 cases (0.3%) with API between 50-59

years. There were 54 cases (2.6%) of atypical endocervical cells NOS and 2 cases (0.09%) of atypical endometrial cells, NOS. Pap smears that are negative for intraepithelial lesion were seen in 1934 cases (92.1%), out of them 420 cases (20%) showed benign reactive changes. Among the benign reactive changes 127 cases (6%) showed cellular changes associated with inflammation including typical repair; 66 cases (3.1%) showed shift in the flora suggestive of bacterial vaginosis; 26 cases (1.2%) and 23 cases (1.3%) showed fungal organism consistent with *Candida* species and *Trichomonas vaginalis*; 5 cases (0.23%) showed cellular changes consistent with Herpes simplex virus; one case of Actinomycosis and 2 cases showed radiation changes; 50 cases (2.38%) showed reactive changes due to intrauterine device and 10 cases (0.85) showed endometrial cells in women of  $\geq 40$ .

**Discussion.** In 1988, the National Cancer Institute Workshop proposed the Bethesda system of Nomenclature for reporting cervical/vaginal cytological diagnosis.<sup>8-11</sup> The goal of the Bethesda system is to provide a uniform system of cytopathological reporting. Effective communication between the pathologist and the clinician is essential for patient care. The Bethesda system is a complete diagnostic system that recognizes the cytopathology report as a medical consultation. The Bethesda system addresses 4 points: 1) the need for a standard system of nomenclature so that results are comparable among various laboratories; 2) a clear statement of specimen adequacy (satisfactory or limited or unsatisfactory); 3) a general categorization for triage; 4) the appropriateness of making recommendation for further evaluation if clinically indicated.<sup>8-11</sup> There is a little doubt that cytological screening programs play a major role in reducing both the incidence and mortality of invasive cervical cancer.<sup>12-14</sup> Declining trends in cervical cancer in USA appear to be related to the widespread use of cervical cytological screening programs, which have counteracted increases anticipated from changes in risk factor prevalence.<sup>15</sup> The first attractive point is the total number of the pap smear which is relatively less than an expectation if we compare this with other institution in the western region taking into consideration, the total number of hospital beds and total number of surgical specimens received.<sup>15</sup> In our study (Table 2), we found that there were 166 (7.9%) abnormal Pap smears out of a total of 2100 smears. The rate of abnormal Pap smear in Saudi Arabia ranged between 0.2% and 18.1%.<sup>15-17</sup> The percentage of patient with benign and reactive cellular changes is 5.4% (0.9% of total pap smears). Atypical squamous cells of undeterminate significance was seen in 58 cases (2.8%) with API

Table 1 - Cytological diagnosis of Pap smears with their age distribution and percent distribution. Negative for intraepithelial lesion or malignancy.

Cytological diagnosis	Age groups							Total number	Abnormal (%)	Pap smear (%)
	20-29	30-39	40-49	50-59	60-69	70-79	80-89			
Trichomonas vaginalis	5	9	7	1	0	0	1	23	(5.5)	(1.1)
Fungal organism morphologically consistent with <i>Candida species</i>	7	16	3	0	0	0	0	26	(6.2)	(1.2)
Shift in the flora suggestive of bacterial vaginosis	10	33	18	4	0	1	0	66	(15.7)	(3.1)
Bacteria morphologically consistent with Actinomycosis	1	0	0	0	0	0	0	1	(0.2)	(0.1)
Cellular changes consistent with Herpes simplex virus	5	0	0	0	0	0	0	5	(1.2)	(0.2)
Cellular changes associated with inflammation (includes typical repair)	7	46	28	32	7	4	3	127	(30.2)	(6.1)
Radiation	0	2	0	0	0	0	0	2	(0.5)	(0.1)
Intrauterine contraceptive device	3	32	15	0	0	0	0	50	(11.9)	(2.4)
Atrophy	0	0	14	36	20	7	5	82	(19.5)	(3.9)
Glandular cell status post hysterectomy	0	0	12	8	0	0	0	20	(4.8)	(0.1)
Endometrial cells in women of $\geq 40$ years	0	0	12	4	1	1	0	18	(4.3)	(0.9)
<b>Total</b>	<b>38</b>	<b>138</b>	<b>109</b>	<b>85</b>	<b>28</b>	<b>13</b>	<b>9</b>	<b>420</b>		<b>(20)</b>

Table 2 - Cytological diagnosis of Pap smears with their age distribution and percent distribution. Epithelial abnormalities.

Cytological diagnosis	Age groups								Total number	Abnormal (%)	Pap smear (%)
	20-29	30-39	40-49	50-59	60-69	70-79	80-89	90-99			
ASCUS	0	23	13	10	08	2	2	0	58	(34.9)	(2.8)
Cannot exclude HSIL	0	0	4	0	0	0	0	0	4	(2.4)	(0.2)
Low-grade squamous intraepithelial lesion encompassing HPV/mild dysplasia/CIN 1	0	5	9	10	03	0	0	0	27	(16.3)	(1.3)
High-grade intraepithelial lesion encompassing moderate & severe dysplasia, CIS/CIN 2 AND CIN 3	0	3	8	3	0	0	0	0	14	(8.4)	(0.7)
Squamous cell carcinoma	0	0	2	4	1	0	0	0	7	(4.2)	(0.3)
Atypical endocervical cells (NOS)	3	24	14	10	0	1	2	0	54	(32.5)	(2.6)
Endometrial cells (NOS)	0	0	1	0	1	0	0	0	2	(1.2)	(0.1)
<b>Total number of epithelial abnormalities</b>	<b>33</b>	<b>55</b>	<b>51</b>	<b>37</b>	<b>13</b>	<b>3</b>	<b>4</b>	<b>0</b>	<b>166</b>		<b>(7.9)</b>
ASCUS - atypical squamous cells of undeterminate significance, AGUS - atypical glandular cells of undeterminate significance, CIN - cervical intraepithelial neoplasia, CIS - carcinoma in situ, HPV - human papilloma virus, HSIL - high squamous intraepithelial lesion, API - age peak incidence, NOS - not other wise specified											

between 30-39 compared to 9.75% by Mount Papillo<sup>18</sup> and lower than the figures reported also by others.<sup>19,21</sup> Women with ASCUS should be managed using program of 2 repeat cytology tests, immediate colposcopy, or DNA testing for high-risk types of HPV. Patients follow up were diagnosed with ASCUS reveal that HSIL had developed in 9% of women.<sup>22</sup> In our study, LSIL including HPV/mild dysplasia/CIN I was seen in 27 cases (1.3%) with API between 50-59. High squamous intraepithelial lesion encompassing moderate to severe dysplasia, CIS/CIN II was seen in 14 cases (0.7%) with API between 40-49. The highest rate of squamous intraepithelial lesion (SIL) was found in the subset of patient's age 10-19 years.<sup>18</sup> In South African, Fonn et al<sup>23</sup> found that 2.4% of women screened by Pap smear have LSIL and the average age of these women was 33.1 years and that 1.8% had HSIL. In the same study, they demonstrated that 0.5% were found to have cytologically diagnosed invasive cancer. Ollayos and Swogger<sup>24</sup> found HSIL and LSIL present in 0.3% and 2.5% of the screened women. Edelman et al<sup>20</sup> reported 0.6% for HGSIL and 2.5% for LSIL. Mount and Papillo<sup>18</sup> demonstrated in adolescent the presence of SIL in 3.8% and atypical glandular cells of undetermined significance in 0.1%. In the current study, squamous cell carcinoma was seen in 0.3% of the cases with API between 50-59. This compared to the prevalence of 0.5% by Fonn et al.<sup>23</sup> We conclude that with an agreement with the others<sup>15,17,25</sup> we do have relatively lower prevalence cervical lesions and cervical carcinoma. That is most likely related to the sexual behavior under the Islamic roles; however, other practice such as male circumcision, which is well established in our country, may play an important role as well. There is a wide range of age compared to the United States and South Africa. The low prevalence rate of SIL among Saudi females with the wide range of age distribution in comparison with other population, should call for further nationwide study of the characteristics of this low-risk community. Management of women with cervical cytological abnormalities according to American Society for Polposcopy and Cervical Pathology (ASCCP) is as follows: women with atypical squamous cells (ASC) depends on whether Papanicolaou test is subcategorized as of undetermined significance (ASCUS) or as cannot exclude HSIL (ASC-H). Women with ASCUS should manage using program of 2 repeat cytology tests, immediate colposcopy, or DNA testing for high-risk types of HPV. Testing for HPV DNA is the preferred approach when liquid-based cytology is used for screening. In most instances, women with ASC-H, low grade squamous intraepithelial lesion HSIL and atypical glandular cells should be referred for immediate colposcopic evaluation.<sup>26-28</sup> In the current study, we identified 5 cases (0.002%) that shows cellular

changes consistent with Herpes simplex virus. This is much lower than the frequency reported in the western countries and from 12% in Thailand,<sup>29</sup> 3.9% in Algeria<sup>30</sup> and 4.2% in others.<sup>31</sup> However, it is relatively higher than our reported figure from the Western province (0.00005%).<sup>15</sup> Trichomonas vaginalis was seen in 1.3% which also less than the reported figures in the literature.<sup>32,33</sup> Manji et al demonstrated that treatment outcomes at King Faisal Specialist Hospital and Research Center, Riyadh, KSA match those achieved in developed countries, but two-thirds of patients (rather than one-third) present with advanced disease at diagnosis.<sup>34</sup> Therefore, any improvement in overall outcomes will require early detection.

We conclude that SIL, ASCUS and sexual related infectious diseases are less frequently encountered in Saudi women. Cervical intraepithelial neoplasia and invasive cervical carcinoma are also less common in KSA and occur at older age compared to the western countries, however, cervical screening programs are necessary nationwide to estimate the actual magnitude of cervical carcinoma and its precursor lesions. Our results indicated that early diagnosis and improvement of patients care of cervical neoplasm can be achieved only through an effective screening program. Health education is very important to encourage Saudi female to have the screening Pap smear particularly in this region of KSA.

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