

PATTERN OF CERVICAL SMEAR CYTOLOGY IN THE WESTERN REGION OF SAUDI ARABIA

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In 1941, Papanicolaou described cervical mass screening for sexually active women for early detection of cervical cancer.¹ In 1980, cervical carcinoma was the second most frequent cancer in women throughout the world, accounting for 15% of all malignancies. Because of widespread differences in the availability of screening programs and the prevalence of risk factors, there is a marked variation in the relative frequency of cervical cancer in developing countries. The highest incidence rates have been reported from sub-Saharan Africa, Central and South America, Southeast Asia and Brazil. The lowest reported incidence rates are from the Middle East, where the incidence is particularly low among Muslims and Jews, as compared to other religious groups.^{2,3}

Sexual habits (age of first sexual intercourse and number of sexual partners), as well as human papilloma virus infection, play a major role in the pathogenesis of cervical cancer.⁴ In Saudi Arabia, carcinoma of the cervix ranks ninth in the frequency of carcinomas among Saudi females, with a prevalence rate of 3.6%.⁵ The pathogenesis of cervical cancer in Muslim countries might be different from that of Western societies because some risk factors, such as number of sexual partners, differ. The objective of this study is to evaluate the importance of cervical Pap smear in the early detection of carcinoma of the cervix and its precursors in our society, and to address the need for cancer screening programs in Saudi Arabia in order to properly estimate the magnitude of cervical cancer prevalence in the Kingdom.

Materials and Methods

This is a retrospective study of previous Pap smears performed at the Pathology Department at King Khalid National Guard Hospital, Jeddah, in an eight-year period from January 1990 to December 1997. Data recorded from all re-screened patients included clinical presentation and symptoms, specimen adequacy and cytological diagnosis. Some of the patients presented with gynecological

TABLE 1. *Descriptive diagnoses of Bethesda system.*

Benign cellular changes
<i>Trichomonas vaginalis</i>
Fungal
<i>Coccobacilli</i> consistent with shift in vaginal flora
Bacteria consistent with <i>Actinomyces</i> spp.
Cellular changes associated with herpes simplex virus
Other
Reactive changes
Reactive cellular changes associated with:
- inflammation
- atrophy
- radiation
- intrauterine contraceptive device
- others
Epithelial cell abnormalities
Squamous cell
Atypical squamous cell of undetermined significances (ASCUS); low-grade squamous intraepithelial lesion (LSIL)=CIN or HPV changes; high-grade squamous intraepithelial lesion (HSIL)=CIN 2 or CIN3 or carcinoma in situ (CIS); squamous cell carcinoma.
Glandular cell
Endometrial cells, cytologically benign, in a postmenopausal woman; atypical glandular cells or undetermined significance (AGUS); endocervical adenocarcinoma; endometrial adenocarcinoma; extrauterine adenocarcinoma; adenocarcinoma, NOS.
Other malignant neoplasms
Specify

symptoms, while others presented for either routine check-up and/or postpartum care. Specimen adequacy was assessed based on the presence of endocervical cells and/or metaplastic cells, as well as adequate numbers of squamous epithelial cells, i.e., more than 10% of the slides containing squamous cells.

A total of 3088 cases were available for the study. All the abnormal smears were re-examined and classified according to the Bethesda System of TBS diagnosis (Table 1).⁶ In addition, 10% of the cervical smears of each year were cytologically re-examined as quality control. The following cytological diagnoses were used: benign cellular changes including infection and reactive changes; and epithelial cell abnormalities including squamous and glandular cells.

Results

The total number of abnormal cervical smears was 97, i.e., 3.14% of all screened cytology cases. The average age

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TABLE 2. *The number of Muslims and Non-Muslims with abnormal cervical smears.*

Year	Muslim	Non-Muslim	Total no. of abnormal	Total no. of cases	Percentage of abnormal smears/year
90	7	3	10	287	3.5
91	5	2	7	256	2.7
92	11	1	12	365	3.3
93	6	2	8	377	2.1
94	8	0	8	362	2.0
95	8	4	12	309	3.9
96	13	2	15	454	3.3
97	24	1	25	678	3.7
Total	82	15	97	3,088	

TABLE 3. *The disease categories of abnormal cervical smear cases according to the Bethesda System.*

Disease categories	Age range	Number of patients	Prevalence of the disease (n=3088)
Benign cellular changes/infection			
Herpes	31-35	3	0.09%
Benign reactive changes			
Cervicitis/inflammation	20-56	19	0.60%
Atrophy	50	1	0.03%
Radiation	44-61	4	0.13%
Repair	43	1	0.03%
Epithelial cell abnormalities			
ASCUS	29-53	14	0.45%
LSIL CIN+HPV	24-49	29	0.93%
HSIL CIN2+CIN3+CIS	23-44	17	0.55%
Invasive squamous cell	44-55	4	0.13%
AGUS	23-61	4	0.13%
Adenocarcinoma	39	1	0.03%
Total		97	3.1%

TABLE 4. *Risk factors associated with cancer of the cervix.*

Sexual activity
Number of sexual partners
Early sexual activity (especially less than 16 years of age)
Sexually transmitted diseases
Human papilloma virus
Herpes simplex virus
Early age of first pregnancy
Parity
Low socioeconomic class
Cigarette smoking
Human immunodeficiency virus
Immunosuppression from any cause
Vitamin deficiencies
Interval since last Pap smear
Oral contraceptive use

of the patients was 43.2 years, and 84.5% of the patients with abnormal smear were Muslims (Table 2). The abnormal cervical smear results were reclassified by the TBS and cervical intraepithelial neoplasia (CIN) methods. The disease categories are listed in Table 3 with their percentages compared to the total number of cervical smears performed during the period of the study.

Discussion

It is well established in the literature and in clinical practice that the best method of early detection of precancerous lesions of cervical cancer is by cytological examination of cervical cytology by Pap smear. Visual inspection of the cervix has been proposed as an alternative to cervical cytology for the early detection of cervical cancer. Unaided direct visual inspection, referred to frequently as "downstaging," involves naked eye examination of the cervix by speculum examination to detect early disease. Unmagnified visual inspection of the cervix after the application of 3%-5% acetic acid, which is known as visual inspection of cervix with acetic acid wash (VIA), also known as cervicoscopy, seems to be potentially useful. A study performed by University of Zimbabwe showed VIA was more sensitive than cytology, but less specific. VIA sensitivity was estimated to be 76.7%, while cytology examination was 44.4%. The specificity of VIA was 84.1% and 90.6% for cytology.⁷⁻⁹

There is little doubt that cytological screening programs play a major role in reducing both the incidence and mortality of invasive cervical cancer. In the US and Canada, widespread introduction of cytological screening decreased the incidence of cancer of the cervix that was paralleled by a reduction in mortality.¹⁰⁻¹² According to the American Cancer Society, only 30% of US women had a Pap smear in 1961, but this number increased to 87% in 1987. In 1940, the incidence of cervical cancer in the US was 32.8/100,000, but by 1984, the figure had reached 8.3/100,000. In 1991 there were only 13,500 cases of invasive cervical cancer, with 4500 cancer deaths.¹³

Over the last decade there has been an explosion of information about the etiology of cervical cancer and its precursor lesion. The risk factors of carcinoma of the cervix are well documented in the literature⁴ (Table 4). Sexual activity and human papilloma virus infection (HPV) are the most important risk factors in the pathogenesis of cervical cancer. It is now widely accepted that both squamous cell carcinoma and adenocarcinoma of cervix, as well as their respective precursor lesions, are caused by specific HPV that infects the genital tract. HPV subtypes 6 and 11 cause benign lesions such as flat condyloma and mild atypia, whereas HPV 16, 18 and 31, that are called "oncogenic virus," produce high-grade cytological atypia (CIN 2, 3). By using Pap smear and colposcopy without biopsy in large-scale studies of patients who had had two or three abnormal cervical smears and who were followed for nine years, Richart¹⁴ found that 50% of women with CIN 1 progressed to CIN 3, and 16% progressed to CIN 2. The remaining 28% persisted at the same grade CIN 1 and only 6% of the patients regressed. Follow-up examination also showed that the rate of progression increased and the transit time decreased, depending on the grade of severity of the lesions. The transit time of conversion of CIN 1 to CIN 3 was approximately 5 years, and from CIN 2 to CIN 3 was 2 years. The average time for CIN 1 and CIN 2 together to

convert to CIN 3 was 4 years. In this study, if the percentage of categorized diagnoses against the total number of abnormal smears are compared, the percentage of patients with benign and reactive cellular changes is 29% (28/97). Those with low-grade lesions, including condyloma and CIN 1, ASCUS and AGUS, make up 48.5% (47/97), and the percentage of high-grade lesions which are noninvasive cancer is 17.5% (17/97). The percentage of invasive squamous and adenocarcinoma is 5.15% (5/97). The prevalence of CIN 1 and CIN 2 in our patients was 1.2% (38/3088), with an age range of patients between 23 and 53 years. The prevalence of CIN 3 was 0.19% (6/3088), with an age range of 35 to 51 years. If the results are compared with the literature,^{14,17} they reveal that the prevalence of CIN 1 and CIN 2 is lower than in other developed countries, i.e., 1.2% vs. 2.6%, with a wider range of age population of 23-53 years in our series compared to 25-29 years in the literature. The prevalence of CIN 3 in our population was approximately 0.2%, with an age range of 35-51 years, as against 0.5% and age range of 35-39 years in the literature. It would seem, therefore, that we have a lower prevalence of CIN 1 and CIN 2, with a wider age range in our society, compared to that of the developed countries, although we have a comparable prevalence of CIN 3 and a wide age range.

It is important to note that the precursors of cervical cancer are present in our society, and that the real incidence can be ascertained by designing screening programs that would involve the collaboration of all health sectors in the Western Region of the Kingdom. Health service providers should organize joint committees to tackle the problem. The major role of the committees is to establish a protocol for screening. The duration of the program, funding and methods of education should be considered, as these would be essential components of the screening program. The age of patients involved in the study should be predetermined, as well as the type of cervical examination (i.e., either by inspection only or VIA with or without colposcopic examination).

Education would play a major role in the success of a screening program. It is important to educate the public about cervical cancer and its precursors and encourage them to get involved in the screening program. Lectures and tutorials utilizing audiovisual facilities in hospital waiting areas would be helpful. Also, teaching health personnel, especially laboratory technicians, secretaries, and cytotechnicians, the most appropriate methods in performing cervical examination and reporting the results is also desirable. The interpretation of the cytological finding should follow a unified reporting system and unified methods of follow-up of normal or abnormal results. All abnormal cytology should be examined by a qualified pathologist or cytopathologist. It is important to set up a

unified protocol of treatment plans based on the cytological examination and/or colposcopic examination with or without biopsy.¹⁸

In the US, the treatment of CIN carries a 100% cure rate through three outpatient therapies of cryotherapy, laser vaporization and loop electrosurgical excision procedure (LEEP).⁹ Radiotherapy or surgical removal of cancer should also be considered when needed. Quality control methods should always form part of the examination and follow-up procedures and the results should be audited. As well, all results should be filed in computerized format to facilitate follow-up, results retrieval and data analysis. The prevalence of CIN 1, 2, and 3 will thus be properly estimated in the region, enabling such screening programs to be applied nationwide.

References

1. Papanicolaou GN, Traut H. The diagnostic value of vaginal smears in carcinoma of the uterus. *Am J Obstet Gynecol* 1941;42:193-205.
2. Christopherson WM, Lundin FE Jr, Mendez WM, et al. Cancer cervical control. Study of morbidity and mortality trends over a twenty-one-year period. *Cancer* 1976;38:1357-66.
3. Walton RJ. Cervical cancer screening program I. Epidemiology and history of carcinoma of cervix. *CMJ* 1976;114:1003-12.
4. Blaustein's Pathology of the Female Genital Tract, 4th edition. Springer-Verlag, 1994:289.
5. Cancer incidence in Saudi Arabia. The National Cancer Registry Report, 1994:12.
6. Kurman RJ, Solomon D. The Bethesda System for Reporting Cervical/Vaginal Cytology. Diagnosis, definitions, criteria and explanatory notes for terminology and specimen adequacy. New York:Springer-Verlag, 1993.
7. University of Zimbabwe/JHPIEGO Cervical Project. Visual inspection with acetic acid for cervical cancer screening test qualities in a primary care setting. *Lancet* 1999;353:869-73.
8. Kitchener HC, Symonds P. Detection of cervical intraepithelial neoplasia in developing countries (commentary). *Lancet* 1999;353:856-7.
9. Cox TJ. Management of cancer intraepithelial lesion. *Lancet* 1999;353:941-9.
10. Devesa SS. Descriptive epidemiology of cancer of uterine cervix. *Obstet Gynecol* 1984;63:605.
11. Devesta SS, Young JL, Brinton LA, et al. Recent trends in cervix uterine cancer. *Cancer* 1989;64:2184-90.
12. Miller AB, Lindsay J, Hill GB. Mortality from cancer of uterus in Canada and relationship to screening for cancer of cervix. *Int J Cancer* 1976;17:602-12.
13. American Cancer Society, 1998 Report.
14. Richart RM. Colpomicroscopic studies of cervical intraepithelial neoplasia. *Cancer* 1966;19:395.
15. Blaustein's Pathology of the Female Genital Tract, 4th edition. Springer-Verlag, 1994:246-55.
16. Meisels A. Cytological diagnosis of human Papilloma virus. Influence of age and pregnancy stage. *Acta Cytol* 1992;36:480-2.
17. Richart RM. The influence of diagnostic and therapeutic procedures on the distribution of cervical intraepithelial neoplasia. *Cancer* 1966; 19:1935.
18. Tomatis L. Cancer: causes, occurrence and control. Lyon: World Health Organization International Agency for Research on Cancer, 1990