

Profile of Pap smear cytology in the Western region of Saudi Arabia

Awatif A. Jamal, MD, FRCPC, Jaudah A. Al-Maghrabi, MD, FRCPC.

ABSTRACT

Objective: Cervical carcinoma is an important women's health problem in the Western countries. There are only few published data on this disease in the Kingdom of Saudi Arabia (KSA). The aim of this study is to evaluate the abnormal cytological entities detected by cervical Pap smear in Western region of KSA and to discuss the importance of Pap smears screening programs.

Methods: Retrospective review of all the cervical smears present at the King Abdul-Aziz University Hospital, Jeddah, KSA from 1984 to 2000. The reports of 22089 smears were retrieved from the file of the pathology department.

Results: There were 368 (1.66%) abnormal Pap smears out of 22089 smears. Out of these 368 abnormal Pap smears there were 62 (16.8%, mean age 37 year) cervical intraepithelial neoplasia grade 1, 45 (12.2%, mean age 38.5) cervical intraepithelial neoplasia grade 2, 27 (7.3%, mean age 40.5) cervical intraepithelial neoplasia grade 3, 22 (6%,

mean age 38.5) positive for malignant cells, 36 (9.8%, mean age 40.5) atypical endocervical cells, 88 (23.9%, mean age 39) atypical squamous cells, 9 (2.4%, mean age 40.5) squamous metaplasia with atypia, 26 (7.1%, mean age 45) squamous cell carcinoma, 6 (1.6%, mean age 36.5) reparative atypia, 2 (5.4% mean age 35) herpes virus changes, 19 (5.1%, mean age 37.5) human papilloma virus changes, 5 (1.4%, mean age 55) adenocarcinoma of endometrium, and 7 (1.9%, men age 43.5) adenocarcinoma of endocervix.

Conclusion: Cervical intraepithelial neoplasia and invasive cervical carcinoma are less common in KSA compared to the Western countries, however, cervical screening programs are necessary nationwide to estimate the actual magnitude of cervical carcinoma and its precursor lesions.

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In 1941 Papanicolaou¹ described cervical mass screening for sexually active women for early detection of cancer cervix and early pre-cancerous lesions. Until the early 1970s, approximately 75-80% of cervical cancer in the United States of America (USA) was invasive at the time of diagnosis.² Today, the vast majority of cervical cancer cases are diagnosed at the in-situ stage.^{2,3} 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.^{2,4} In some developing countries, it is the most

common cancer despite advances in the detection and management of cervical carcinoma.^{2,4} In the USA, the statewide screening program improved detection of breast and cervical cancer and helped reduce the incidence of advanced stages of breast cancer in a relatively short time period.⁵ The greatest barrier to effective cervical screening is patient ignorance.⁶ An accurate estimate of the prevalence of cervical intraepithelial neoplasia (CIN) in the Kingdom of Saudi Arabia (KSA) is not available. This is caused by many factors, which include (a) CIN is not reportable disease (b) apparent prevalence rates are dependent on

From the Department of Pathology, Faculty of Medicine, King Abdul-Aziz University Hospital, Jeddah, Kingdom of Saudi Arabia.

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Address correspondence and reprint request to: Dr. Awatif Jamal, Associate Professor and Consultant Pathologist, Department of Pathology, Faculty of Medicine, King Abdul-Aziz University Hospital, PO Box 80205, Jeddah 21589, Kingdom of Saudi Arabia. Tel. +966 (2) 6401000 Ext. 18434. Fax. +966 (2) 6403975. E-mail: awajamal@hotmail.com

the extent, which the population is screened. However, carcinoma of the cervix ranks eighth in the National Registry of Saudi Arabia in its frequency with prevalence of 3.8%.⁷ 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 in essentially all countries with a functioning screening program.⁸ It is the most successful cancer prevention program of all times. Consequently, 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.⁸ The rate of abnormal Pap smear in KSA was reported as 0.2%⁹ and 18.1%.¹⁰ The major risk factors for cervical cancer are well documented and include early age at initiation of sexual activity, sexual habits (age of first sexual intercourse and number of sexual partners), infection with human papilloma virus (HPV)^{11,12} and cigarette smoking. The pathogenesis of cervical cancer and pre-cancerous lesions in Muslim countries might be different compare to Western societies due to the difference in the risk factors. The objective of this study is to evaluate the abnormal cytological entities detected by cervical Pap smear in Western region of KSA and to discuss the importance of Pap smears screening programs.

Methods. A retrospective study is designed to review the previous reports of Pap smear in the archives of Pathology Department of King Abdul-Aziz University Hospital, Jeddah, KSA over the last 16 years, starting from January 1984 to December 2000. The information was collected from the reports and it includes clinical presentation for routine or for gynecology investigation, specimen adequacy and cytological diagnosis. Specimen adequacy was properly assessed only the last few years and it was based on the presence of endocervical cells or metaplastic cells as well as adequate number of squamous epithelial cells namely the slide contains more than 10% squamous cells. Prior to Bethesda system there was no specific criteria and adequacy was assessed subjectively. A total number of 22089 Pap smears were available for the study. The cytological information collected from the reports included these major categories: CIN I, CIN II, CIN III; positive for malignant cells; atypical endocervical cells (AGUS); atypical squamous cells (ASCUS); squamous metaplasia with atypia; reparative atypia; inflammatory atypia; HPV changes; herpes virus changes; squamous cell carcinoma; adenocarcinoma of endometrium and adenocarcinoma of endocervix. We noticed that no specific classification scheme was followed in the reporting of these smears, although all the known abnormalities were identified and stated in these reports.

Results. A total of 22089 cases of cervical Pap smears were seen in 16 years. The data of abnormal Pap smear and the age distribution was tabulated in **Table 1**. There were 368 (1.7%) abnormal Pap smears out of 22089 smears. Of these 368 abnormal Pap smears there were 62 (16.8%, mean age 37 year) CIN I, 45 (12.2%, mean age 38.5) CIN II, 27 (7.3%, mean age 40.5) CIN III, 22 (6%, mean age 38.5) positive for malignant cells, 36 (9.8%, mean age 40.5) AGUS, 88 (23.9%, mean age 39) ASCUS, 9 (2.4%, mean age 40.5) squamous metaplasia with atypia, 26 (7.1%, mean age 45) squamous cell carcinoma, 6 (1.6%, mean age 36.5) reparative atypia, 2 (5.4% mean age 35) herpes virus changes, 19 (5.1%, mean age 37.5) HPV changes, 5 (1.4%, mean age 55) adenocarcinoma of endometrium and 7 (1.9%, mean age 43.5) adenocarcinoma of endocervix.

Discussion. The literature overwhelmed with evidence supporting the importance of early detection of precancerous lesions in the cervix by cytological examination using Pap smear. Visual inspection of the cervix has been found to be a good alternative to cervical cytology for the early detection of cervical cancer.¹³ However, there is a little doubt that cytological screening programs play a major role in reducing both the incidence and mortality of invasive cervical cancer.^{14,15} Declining trends in cervical cancer in USA appear to be compared to the widespread use of cervical cytological screening programs, which have counteracted increases anticipated from changes in risk factor prevalence.¹⁶ The prevalence rate of dysplasia and carcinoma in situ was 18.8/1,000 for ages 15-19 and 28.8/1,000 for ages 20-24.¹⁷ Biopsy-proved cases of all grades of cervical intraepithelial neoplasia in the teenage population indicate a prevalence of 13.3/1,000.¹⁷ Over the last decade there has been an explosion of information on the etiology of cervical cancer and its precursor lesion. However, the sexual activity and HPV infection are the most important risk factors in the pathogenesis of cancer cervix. It is now widely accepted that both squamous cell carcinoma and adenocarcinoma of cervix as well as their pre-cursor lesions are caused by specific HPV that infects the genital tract. Human papilloma virus subtype 6 and 11 cause benign lesion such as flat condyloma and mild dysplasia whereas HPV 16, 18 and 31 called "oncogenic viruses" are implicated in high-grade dysplasia (CIN II and III) and squamous cell carcinoma as well as endocervical carcinoma.² In our study (**Table 1**), we found that there were 368 (1.66%) abnormal Pap smears out of 22089 smears. The rate of abnormal Pap smear in KSA was reported as 0.2%⁹ and 18.1%.¹⁰ The percentage of patient with benign and reactive cellular changes is 5.4% (0.9% of total Pap smears). Those with low-grade lesions including condyloma and CIN I, ASCUS, squamous metaplasia with atypia and AGUS represent 58.1%

Table 1 - Cytological diagnosis of Pap smears with their age distribution, mean age and percentage distribution.

Cytological diagnosis	Age groups							Mean age	Total	Abnormal Pap smear* %	Total Pap smear†
	20-29	30-39	40-49	50-59	60-69	70-79	80-89				
CIN I	13	18	22	6	3	-	-	37	62	16.8	0.28
CIN II	10	19	9	4	3	-	-	38.5	45	12.2	0.2
CIN III	5	8	11	1	1	1	-	40.5	27	7.3	0.12
Positive for malignant cells	4	4	6	5	1	2	-	45.5	22	6	0.09
Atypical endocervical cells	5	14	13	1	2	1	-	40.5	36	9.8	0.16
Atypical squamous cells	21	32	21	9	4	-	1	39	88	23.9	0.39
Squamous metaplasia with atypia	1	2	6	-	-	-	-	40.5	9	2.4	0.04
Squamous cell carcinoma	2	9	6	5	3	1	-	45	26	7.1	1.17
Reparative atypia	1	3	2	-	-	-	-	36.5	6	1.6	0.03
Inflammatory atypia	4	3	5	2	-	-	-	38.5	14	3.8	0.06
HPV changes	2	11	5	1	-	-	-	37.5	19	5.2	0.08
Herpes changes	1	-	1	-	-	-	-	35	2	0.5	0.009
Adeno carcinoma of endometrium	-	1	-	2	2	-	-	55	5	1.4	0.02
Adeno carcinoma of endocervix	-	3	2	2	-	-	-	43.5	7	1.9	0.03
Total	69	127	109	38	19	5	1		368	100	1.66

*percentage out of 398 abnormal PAP smears, †percentage out of 22089 Pap smears, HPV - human papilloma virus
 CIN I - cervical intraepithelial neoplasia, grade 1, CIN II - cervical intraepithelial neoplasia, grade 2, CIN III - cervical intraepithelial neoplasia, grade 3

Table 2 - Comparison of significant difference in prevalence and age range among 2 local studies with one study from the United States of America.

Studies	Cytological diagnosis			
	CIN I and CIN II Prevalence %	CIN II Age range (years)	CIN III Prevalence %	CIN III Age range (years)
<i>Kingdom of Saudi Arabia</i>				
Present study	0.5 (107/22089)	22-63	0.1 (27/22089)	25-71
Altaf ²¹	1.2 (38/3088)	23-53	0.2 (6/3088)	35-51
<i>United States of America</i>				
Richart ¹¹	2.6	25-29	0.5	35-39

CIN I - cervical intraepithelial neoplasia, grade 1, CIN II - cervical intraepithelial neoplasia, grade 2, CIN III - cervical intraepithelial neoplasia, grade 3

(214/368, 1% of total Pap smears). The high-grade intraepithelial lesions yet non-invasive cancer is CIN II and CIN III represent 19.5% (72/368, 0.3% of total Pap smears). The prevalence of CIN I and CIN II in our patient is 0.5 (107/22089) with an age range of patient between 22-63 years and the prevalence of CIN III is 0.1% (27/22089) the age range of 25-71 years. If we compare this results with the literature,¹¹ it reveals that the prevalence of CIN I and CIN II is lower than that reported in other developed countries as 0.5% in our study compared to 2.6% in USA and wider range of age in our study 22-63 years as compared to 25-29 years in USA¹¹ with wider age range of 22-63 versus 25-29. In general, the prevalence of CIN in the USA in teenagers and young adults aged 15-19 years is 1.8%.¹⁷ Study from southern Australia revealed that the prevalence of CIN I increased from 0.6% in 1978 to 5.6% in 1988.¹⁸ Similarly studies from Jewish Israeli women have indicated a substantial increase in the incidence of CIN and invasive cervical carcinoma in that population,^{12,19,20} historically at low risk for development of cervical carcinoma. The incidence of cervical cancer in all ages of Israeli-born Jewish women rose from 2.7/100,000 in 1960-1966 to 4.6/100,000 in 1972-1976.^{12,19,20} These epidemiological changes have been attributed to changes in sexual behavior. Bar-Am et al¹² found that the prevalence of abnormal cytology among the Israeli women was almost the same as that of the non-Jewish group: 24/1000 and 26/1000. Significant statistical differences were found between the following risk factors: number of sexual partners, age at first intercourse, and age at first pregnancy. Moreover, they found that there was an increase of 29.2% (from 17/1000 to 24/1000) in the prevalence of cervical premalignant lesions among the Israeli women and concluded that this population can no longer be considered as being at low risk for this disease.¹² Regarding CIN III the prevalence in our population is approximately 0.1% compared to 0.5% in the USA and with our wider age range of 25-71, as compared to 35-39 years in the USA. It seems from this statistic that in our society we have lower prevalence of CIN with wide range age compared to the developed countries. We have compared our results with another local study from King Khalid Hospital,²¹ Jeddah, KSA and with the result from the USA in **Table 2**. The prevalence in the local study by Altaf²¹ revealed a prevalence of CIN I and II of 1.2 (38/3088) and CIN III was 0.2% (6/3088). The difference between the 2 studies performed in different hospitals but in the same region could be explained partly by the much larger number presented by this study and difference in the patient selection category. In USA treatment of CIN give 100% cure rate by cryotherapy, laser vaporization and loop electrosurgical excision procedure.^{2,22} Cervical conization is a good choice for patient with CIN III and desired childbearing.²³ Radiotherapy or surgical removal of cancer is also carried out.

We conclude that with an agreement with the others^{10,21} we do have relatively lower prevalence of cervical carcinoma and cervical lesions in general, 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. From the findings, it is clear that our society have lower prevalence of CIN I and CIN II and that is in agreement with the other.²¹ There is a wide range of age compared to the USA although we have a bit comparable prevalence of CIN III but with a wide age range. Better estimates of the prevalence of cervical disease can be obtained from large, population-based surveys. Until now, no such studies are available in KSA. We also speculate that may be different level of interaction between the risk factors determining the development of the cervical low and high lesions in this region of the world. The low prevalence rate of CIN 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. A good centrally organized cytological cervicovaginal screening program, implemented by the public sector, is recommended. Visual inspection aided by application of acetic acid is an alternative to cytology screening, yet new techniques such as HPV DNA testing can be used to identify cervical lesions without reliance on cytology.²⁴

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