ORIGINAL ARTICLE

SPECTRUM OF CERVICAL EPITHELIAL CELL ABNORMALITIES DIAGNOSED AT KING FAHD HOSPITAL OF THE UNIVERSITY, AL-KHOBAR, SAUDI ARABIA

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ABSTRACT

Introduction: Cervical cancer is the second most common cancer among women worldwide. It is an aggressive malignancy that is preventable if detected early. The best method of early detection of precancerous lesions of cervix is cytological examination of Pap smears. This study was undertaken to find out the pattern of epithelial cell abnormalities in Pap smears carried out in a tertiary care hospital of Eastern Region in Saudi Arabia.

Material & Methods: An analysis of the records of Pap smears carried out at the Pathology Department of King Fahd Hospital of the University of Dammam from January 2000 to December 2010 was undertaken. Cases with epithelial cell abnormalities were identified. The slides were retrieved from departmental record and diagnosis was re-evaluated as per revised Bethesda system.

Results: Out of a total of 7,772 Pap cytology cases available for study, epithelial cell abnormalities were seen in 101 (1.30%) cases. The abnormalities detected were ASCUS (0.48%), ACS-H (0.06%), LSIL (0.19%), HSIL (0.37%), SCC (0.10%), AGUS (0.25%), and adenocarcinoma (0.05%). Mean age of patients was 51.02±10.18 years.

Conclusion: An almost uniform spectrum of epithelial cell abnormalities was observed over a period of 11 years that was conspicuous with a lower frequency of epithelial cell abnormalities and a higher mean age as compared to other studies from Saudi Arabia and the Eastern Mediterranean Region.

Key Words: Pap cytology, epithelial cell abnormalities, Cervical cancer.

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INTRODUCTION

Cervical cancer is the third most common cancer in women, and overall the seventh one with an estimated 530,000 new cases and 275,000 deaths in 2008. Its mortality:incidence ratio stands at 52%. More than 85% of the global burden occurs in developing countries, where it is responsible for 13% of all female cancers. High-risk regions comprise Eastern, Western, Southern and Middle Africa, South-Central Asia and South America. Lowest rates are seen in Western Asia, Northern America and Australia/New Zealand.[1] It is an aggressive malignancy that may extend to involve vagina, vulva, bladder, rectum, lungs, bones and lymph nodes.[2] However, it is also one of the preventable cancers.[3] The best method for early detection of precancerous lesions of cervix is by cytological examination of cervical cytology by Pap (Papanicolaou) smears.[4]

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The Papanicolaou cervical cytology test has the potential of detecting cervical cancer at an early stage. Cytological screening for cervical cancer has been found very effective in countries where the disease is more common.[2] In the US and Canada, widespread introduction of cytological screening reduced the incidence of cervical cancer with a concomitant decrease in mortality.[5] It has been documented that the use of this simple and cost-effective technique has decreased the incidence of cervical cancer by at least 70%.[6]

In Saudi Arabia cervical cancer ranks as the 11th most frequent cancer among women in Saudi

Arabia, and the 8th most frequent cancer among women between 15 and 44 years of age.[1] A vast majority of the cervical cancers are caused by Human Papilloma Virus (HPV).[2,7] Data is not yet available on the HPV burden in the general population of Saudi Arabia.[8]

National Health Services (NHS) in United Kingdom deduced that any patient developing cervical cancer at the average age 46–50 had carcinogenesis initiating two decades earlier, i.e., at the age of 26–30 years. Therefore screening should preferably be started at around 25 years of age.[9] In Saudi Arabia, merely 35% of cervical cancer cases present at an early stage.[10]

The cervical epithelial cell abnormalities originate in the squamous or glandular cells and in the Pap smears range from atypia and mild-to-severe dyskaryosis to invasive cancer.[11] The significance as well as consequence of these cytological diagnoses have been extensively elaborated in the 2001 Bethesda System.[12] The category of Atypical Squamous Cells (ASC) includes ASC-US (ASC of undetermined significance) and ASC-H (ASC cannot exclude High Grade Squamous Intraepithelial Lesion, HSIL). The term squamous intraepithelial lesion (SIL) is subdivided into lesions showing perinuclear halo (HPV-human papilloma virus associated) and mild dyskaryosis, termed as Low-grade squamous intraepithelial lesion (LSIL) and lesions showing moderate-to-severe dyskaryosis and carcinoma in situ, termed as HSIL. The category of atypical glandular cells is abbreviated as AGC. Smears showing no epithelial abnormalities are depicted under the category of 'Negative for Intraepithelial Lesion or Malignancy' (NILM), in the revised Bethesda system.[13,14]

It is imperative to delineate the precise burden of cervical pre-neoplastic lesions in each geographical region to develop strategies for awareness about screening. In Saudi Arabia there is paucity of such studies, with just a few documented studies from the Western[7,15–17] and Southwestern region[18], and only one from a small city of the Eastern region[3]. The present study was undertaken to find out the pattern of epithelial cell abnormalities in Pap smears, in a tertiary hospital of Eastern Region in Saudi Arabia.

MATERIAL AND METHODS

This study was carried out at King Fahd Hospital of the University (KFHU), Al-Khobar, Saudi Arabia. This is a tertiary care teaching hospital in Eastern Region of the Kingdom. The protocol was approved by the research and ethical committee of University of Dammam. Records of all Pap smears conducted at the Pathology Department of KFHU over a period of 11 years, from January 2000 to December 2010 were reviewed. Pap cytology reports of all these cases was retrieved from record. Total number of cases recorded in each year was counted. Cases with epithelial cells abnormalities were identified. These cases were re-evaluated and reported according to revised Bethesda system.[12] In addition to the known cases 10% of the cervical smears of each year were cytologically re-examined as quality control. Ages of all the patients with epithelial cells abnormalities were recorded to determine age range.

RESULTS

A total of 7,772 Pap smears were analysed during this period of 11 years. The yearly breakdown of these cases is given in Table-1. Out of these 101 (1.30%) were diagnosed to have epithelial cells abnormalities. The yearwise break down of these abnormal cases is presented in Table-2.

DISCUSSION

In this study epithelial cell abnormalities comprised 1.30% of total Pap cytology cases in patients with mean age of 51.02±10.18 years**.** The low frequency of epithelial lesions is in accordance with widely reported and recognised low frequency in WHO Eastern Mediterranean Region, of which Saudi Arabia is a constituent part.[19] In addition persistent low trend of cytological abnormalities and malignancy in Pap smears over a time span of 11 years is a very significant proof of general attribute of low frequency of this particular cancer in women sexually restricted by religious and social obligations.

Different regional and international studies have reported highly variable frequency of epithelial cell abnormalities. In Saudi Arabia, a few studies have been reported from Western region and one from the Eastern region. Regarding the Eeastern region the current study has a notably longer review period and a much bigger sample size. Jamal and Al-Maghrabi in a 16 years (1984–2000) study from King Abdul-Aziz University Hospital, Jeddah (Western Region of KSA) reported an overall frequency of 1.66% abnormal Pap smears.[15] In another study carried out in the Western region at King Khalid National Guard Hospital, Jeddah, in eight-year period (Jan 1990–Dec 1997) 2.2% of epithelial cell abnormalities were reported.[7] Same author, in a later two part study reported a frequency of 1.4% in its multicenter study from Jeddah and Abha region with a total of 45,596 cases carried out from 1990 to 2004. In the prospective part of study conducted in King Abdul Aziz University Hospital and a private Lab in a time period 1999–2004 the epithelial cell abnormalities were reported to be 4.7%.[16] Another study from Western region in King Abdul Aziz Medical City Jeddah (Jan 1998–Aug 2008), re-

Table 1: Yearwise distribution of Pap smear cases according to cytological diagnosis

Year	Total Satisfactory smears	Negative	Benign cellular/ reactive changes	Total epithelial cell abnormalities
2000	318	293	25	7 (2.20%)
2001	610	557	50	10 (1.64%)
2002	665	619	39	4 (0.60%)
2003	792	747	38	10 (1.26%)
2004	822	761	51	6 (0.73%)
2005	701	656	37	9 (1.28%)
2006	652	615	25	13 (1.99%)
2007	824	749	64	11 (1.33%)
2008	801	751	33	7 (0.87%)
2009	800	704	34	9 (1.13%)
2010	787	730	42	15 (1.90%)
Total	**7772**	**7192 (92.53%)**	**414 (5.75%)**	**101 (1.30%)**

Table 2: Yearwise distribution of Pap smear cases with epithelial cell abnormalities according to revised Bethesda system.

Year	ASCUS	ASC-H	LSIL	HSIL	SCC	AGUS	Adeno-carcinoma	Total
2000	3 (42.86%)	Nil	1 (14.29%)	2 (28.57%)	1 (14.29%)	Nil	Nil	7
2001	5 (50%)	Nil	Nil	1 (10%)	3 (30%)	Nil	1 (10%)	10
2002	2 (50%)	Nil	1 (25%)	1 (25%)	Nil	Nil	Nil	4
2003	4 (40%)	1 (10%)	1 (10%)	1 (10%)	3 (30%)	Nil	Nil	10
2004	2 (33.33%)	1 (16.67%)	Nil	2 (33.33%)	Nil	Nil	1 (16.67%)	6
2005	4 (44.44%)	1 (11.11%)	2 (22.22%)	Nil	1 (11.11%)	Nil	1 (11.11%)	9
2006	6 (46.15%)	1 (7.69%)	1 (7.69%)	5 (38.46%)	Nil	Nil	Nil	13
2007	3 (27.27%)	Nil	1 (9.09%)	7 (63.64%)	Nil	Nil	Nil	11
2008	1 (14.29%)	Nil	2 (28.57%)	4 (57.14%)	Nil	Nil	Nil	7
2009	3 (33.33%)	Nil	2 ((22.22%)	3 (33.33)	Nil	1 (11.11%)	Nil	9
2010	5 (33.33%)	1 (6.67%)	4 (26.67%)	3 (20%)	Nil	1 (6.67)	1 (6.67%)	15
Total	38 (37.62%)	5 (4.95%)	15 (14.85%)	29 (28.71%)	8 (7.92%)	2 (1.98%)	4 (3.96%)	101 (100%)

ASCUS: Atypical squamous cell of undetermined significance
ASC-H: Atypical squamous cells cannot exclude HSIL
LSIL: Low grade squamous intraepithelial lesion
HSIL: High grade squamous intraepithelial lesion
SCC: Squamous cell carcinoma
AGUS: Atypical glandular cells of undetermined significance

Table 3: Comparative analysis of age range in different epithelial cell abnormalities.

Cytological diagnosis	Age in current study group (year)	Saudi western region[17] Average (Average Range)	Saudi south western region (Average Range)	Saudi eastern region[3] Average (Average Range)
Epithelial cell abnormalities	51.02±10.18	—	—	—
ASCUS	49.64±8.34	42 (19-65)	34.5 (30-39)	45 (19-79)
ASC-H	61.83±7.07	53 (36-70)	Nil	45.3 (29-46)
LSIL	49.56±10.21	38 (29-47)	54.5 (50-59)	55 (one case only)
HSIL	48.78±6.30	42.5 (18-67)	44.5 (40-49)	35.8 (19-48)
SCC	58.25±10.48	59 (30-88)	54.5 (50-59)	46.8 (42-55)
AGUS	49.33±10.21	57.5 (26-89)	—	34 (one case only)
Adeno-carcinoma	63.55±10.63	52.5 (27-78)	—	—

Table 4: Comparison of frequencies of individual epithelial cell abnormalities with other studies.

Epithelial cell abnormalities (%)	Current study n=7772 11 years	Western region n=3088 8 years[7]	Western region n=5590 7.5 years[17]	South western region n=2100 10 years[18]	Eastern region n-1171 7 years[3]	Kuwaiti n=83,052 13 years[20]	Turkish n=32026 4 years[22]	Pakistani n=1000 2.5 years[6]
ASCUS	0.48	0.45	1.84	2.76	2.99	2.20	1.90	1.00
ASC-H	0.06	—	0.10	0.19	0.60	—	0.10	—
LSIL	0.19	0.93	1.00	1.30	0.09	1.00	0.50	4.60
HSIL	0.37	0.55	0.55	0.66	0.08	0.20	0.10	2.20
SCC	0.10	0.13	0.37	0.33	0.34	0.05	0.0094	1.40
AGUS	0.25	0.13	0.19	2.57	0.09	0.80	0.20	0.40
Adeno-carcinoma	0.05	0.03	0.25	Nil	Nil	0.05	Nil	0.60

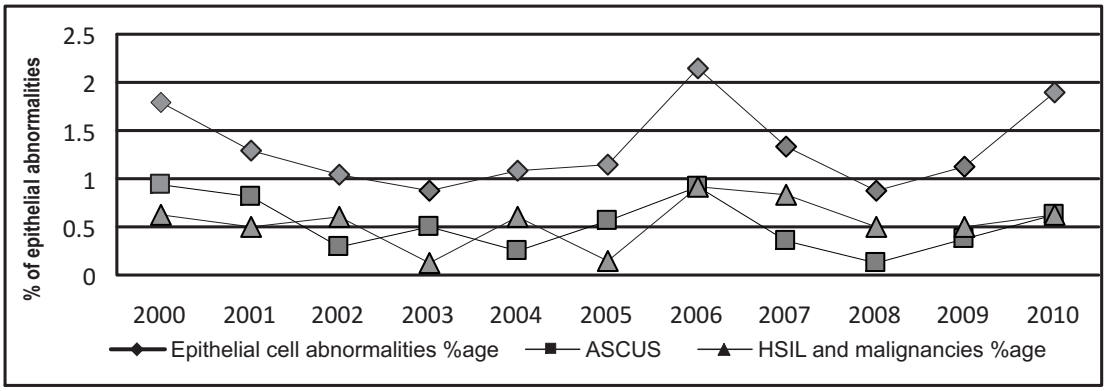

Fig 1: Evolving trends of epithelial cell abnormalities, ASCUS and HSIL with malignancies, (2000–2010).

ported the percentage of epithelial cell abnormalities as 5%.[17]

In a 10 year study from Al-Baha (Southwestern region) Elhakeem et al. reported epithelial cell abnormalities to be 7.9% in the period from 1994 to 2003.[18] This frequency is hitherto the highest reported from Saudi Arabia.

Another study with relatively high frequency is a 7 year (2003–2010) analysis of Pap smear from Eastern region of Saudi Arabia (Al Ahsa) that found 4.95% of epithelial cell abnormalities in 1,171 total cases reported.[3] The frequency of epithelial cell abnormalities in our study is much lower than this only study from a closeby city of the same region. The reason for this disparity could be a far less yearly turn over in the Al Ahsa study.

Likewise, other studies from the region have reported variable frequencies of epithelial cell abnormality in the Pap smear, like 4.3% from a Kuwaiti tertiary care hospital[20], 0.95% in Jewish Israeli women[21], 8.18% from Bangladesh[14], 10.2% from Pakistan[6], and 2.8% from Turkey.[22]

The mean ages in which different epithelial cell abnormalities were seen in the current study are presented in Table 3 and compared to other studies from Saudi Arabia. Regarding age pattern distribution in other Saudi studies the western region study by Abdullah[17] shows the prevalence in younger age group except SCC that is seen in the same age group and AGUS in an older age group than ours. In the Saudi southwestern region study by Elhakeem et al.[18] almost similar age range is seen in LSIL, HSIL and SCC and a lesser age range in ASCUS. In Saudi eastern region study by Balaha et al[3], a lesser age group was seen in most of the reported lesions besides ASCUS and LSIL which are at par with the current study. In a Kuwaiti study LSIL and HSIL was seen in a lesser age group of 25–34 years.[20] In a study from Pakistan the overall age of epithelial cell abnormalities was (44.7±15.63) the same as ours with neoplastic gynecological lesions seen in 50–59 years of age group.[6] In a Bangladeshi study a younger age distribution was seen, as bimodal age distribution was detected in the epithelial cell abnormality, with one peak seen in 22–44 years of age and the bulk being diagnosed in patients aged 45 or above.[14]

The frequency pattern of individual epithelial cell abnormalities is also some what less than in other Saudi and regional studies, however some of the entities are harmonious in distribution in this comparative analysis as depicted in Table 4. This variability may again be attributed to marked variation in sample size and time span of different studies or inherent ethnic and regional variation in lesion distribution. This variation also emphasises the need for more well-organised, prospective studies and cervical screening programs with a much lager cohorts.

In the present study over a span of 11 years, a more or less consistent frequency distribution of epithelial cell abnormalities is seen with a slight peak in 2000, 2006 and 2010 as shown in Figure-1. No particular reason can be attributed to this slightly higher frequency pattern. This persistent pattern is in harmony with the Kuwaiti study that although revealed a significant increase in ASCUS and AGUS in the study period but the percentages of LSIL, HSIL and carcinoma detected in PAP smears remained the same.[20]

CONCLUSION

This study highlights a low frequency of cervical epithelial cell abnormalities in Pap smears and in addition also demonstrates the persistence of this low trend of cytological abnormalities over a time span of 11 years.

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CONFLICT OF INTEREST
Authors declare no conflict of interest.
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