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Prevalence of Cervical Cellular Abnormalities by Liquid Based Cytology in Taif Province: A Hospital Based Study

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Abstract

Aim of the work: The aim of this study was to determine the prevalence of the cervical cellular Abnormalities using liquid based thin-layer preparations as screening test for women who attended the gynaecology outpatient clinic at King Abdul Aziz Specialist Hospital, Taif, Saudi Arabia.

Material and method: In this retrospective chart review study, we reviewed the records and data of all women for whom liquid base cytological studies were performed as screening test to detect the cervical cellular abnormalities at King Abdul Aziz Specialist Hospital, Taif, Saudi Arabia from June 2010 to June 2012.

Results: The total number of women for whom liquid base, thin-layer cytological studies were performedwas 2168 patients 79.9% of them were symptomatic. The mean age was 38.6 years. Liquid based thin-layer preparations were used for all patients. Cervical abnormality was seen in 25.6% of the patients, of which 6.5% were malignant or premalignant and 19.1% were of benign nature.

Conclusion: Liquid-based, thin-layer cytology reduces sampling and preparation errors of the conventional smear; however, screening should include human papilloma virus (HPV), DNA testing to increase the sensitivity and specificity of primary screening.

Introduction

Since the introduction of Papanicolaou (Pap) smear as a screening test for cervical cellular abnormalities in 1960s, deaths due to squamous cell carcinoma of the cervix have fallen by 75% in the western world (1). The traditional Pap smear had a sensitivity of about 70% for detecting clinically significant precancerous lesions and cancer because of sampling and interpretive errors, however, the introduction of 2 liquid-based Pap smear collection systems in the 1990s, especially the thin-layer cytology preparations has reduced these errors in addition that, screening time of a thin-layer slide is also considerably shorter compared with the conventional smear (2& 3). Liquid-based Pap smear collection systems have improved the specimen adequacy and sensitivity for the detection of cervical cancer and the precancerous, squamous intraepithelial lesions (SILs) in addition to the detection of the benign cellular changes (which have no malignant potential) as bacterial and fungal vaginosis or inflammation(3). Recent studies show that high risk (oncogenic) human papilloma virus (HR-HPV) types are strongly associated with severe squamous intra-epithelial lesions (SILs) and the subsequent progression to cancer and the majority of SILs without a HR-HPV type usually regress (4). In Saudi Arabia, most centre are using conventional cytology for opportunistic screening for cervical cancer, however some centres (including our hospital) have adopted the use of liquid based cytology as a methods of screening in addition tothe use of HPV testing as a triage and co-testing (5). According to Cancer Incidence Report Saudi Arabia 2005, data about the prevalence of cervical cellular abnormality and the human papilloma virus (HPV) burden in the general population of Saudi Arabia are still lacking (5).The aim of this study was to determine the prevalence of the cervical cellular Abnormalities using liquid based thin-layer preparations as screening test for women who attended the gynaecology outpatient clinic at King

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Abdul Aziz Specialist Hospital, Taif, Saudi Arabia.

Material and method: In this retrospective chart review study, we reviewed the records and data for all women for whom the thin layer liquid base cytological studies were performed as screening test to detect the cervical cellular abnormalities at King Abdul Aziz Specialist Hospital, Taif, Saudi Arabia from June 2010 to June 2012. The inclusion criteria of this test include; married or previously married symptomatic or non symptomatic women, above age of 20 years, who accepted to perform the test (with a written consent).The test is done every 3-5 years till the age of 65 years, however if there is a history of abnormal smear, it has to be continued without upper age limit. The exclusion criteria include; women, below 20 years and thoseabove 65 years without history of abnormal smears, females who never had sexual contact and women who had total hysterectomy.

Statistical analysis: Results were expressed as mean± standard deviation using SPSS program version 15. Pearson and spearman's correlation test were used to correlate ages with cervical cellular changes in women to differentiate between positive and negative correlations and to find significant difference. $P<0.05$ was considered as statistically significant.

Results: The total number of women for whom liquid base cytological studies were performedwas 2168 patients and 79.9% of them were symptomatic. Table 1 shows demographic data of all women involved in this study with summary of the main presenting symptoms. The mean ages is shown in table 2. Liquid based thin-layer preparations were used for all patients. Cervical abnormality (table 3), was seen in 555/2168 patients (25.6%) of which 414 patients (19.1%) of benign nature and 141 patients (6.5%) of malignant and pre malignant nature.Adenocarcinoma was detected in 3 patients (0.14%), high grade squamous intra-epithelial lesion (HSIL) in 1 patient (0.046%), atypical squamous cells of undetermined significance (ASCUS) 132 patients (6.2%), of which ASCUS alone is detected in 27 patients, ASCUS with inflammation in 97 patients, ASCUS with bacterial vaginosis in 2 patients, ASCUS with bacterial inflammation in 6 patients, ASCUS with fungal inflammation in 2 patients, atypical squamous cell-cannot rule out high grade lesion (ASC-H) in 2 patients (0.092%), atypical glandular cells of undetermined significance (AGUS) in 1 patient (0.046%), bacterial vaginosis in 374 patients (17.25%), fungus without cellular changes in 19 patients (0.9%), actinomyces in 6 patients (0.28%) inflammation without isolated organisms in 15 patients (0.7%).

No significant correlation ($p > 0.05$) was seen between age and the type of abnormality (benign, malignant and premalignant) in women proved to have cervical cellular changes (table 4), however, the cases proved to be malignant were above 60 years (mean age; 69±7.55).Figure 1, shows comparison between numbers of different cellular changes with total number of women and figure 2& 3 show the normal and different cervical cellular abnormalities.

Discussion:

Cervical cancer is the 7th most frequent cancer in Saudi Arabian women and the third most common cancer among women in developed world, however, data about the exact prevalence of precancerous lesions of this disease in the general population of Saudi Arabia is not yet available(5). Screening for abnormal cervical cytology is the corner stone for early detection and prevention of carcinoma of the cervix (2). The use of liquid-based preparations (LBPs) which have largely replaced conventional Papanicolaou smears (CPS) for cervical samples in the western countries and in Saudi Arabia, has reduced the number of inadequate samples from over 9 per cent before LBC to 2.5 per cent in 2009 (1-5). The technique has considerably shorter Screening time compared with the conventional smear in addition to the reduction of the anxiety in women and decreasing the need to repeat tests with

quick results and overall cost reduction (4). In this study the thin-layer technique was used and the numbers of inadequate samples are about 3.5% which is comparable to other studies (1-5). Independent studies have shown that the thin-layer cytology has improved specimen sensitivity for the detection of cervical cancer and its cytological precursors, including atypical squamous cells of undetermined significance (ASCUS) and HSIL(2, 6 & 7). Altaf,(8), found in the prospective part of her study which evaluated 5132 cases, that the real percentage of abnormal smears that has premalignant or malignant cellular abnormalities was 4.7% after exclusion of benign cellular changes. In our study the total number of women for whom liquid base cytological studies were performedwas 2168 patients. Premalignant cervical abnormality was seen in 141/2168 patients (6.5%) which is similar to Altaf study but much more higher than recorded in the second part of her study where the total number of cases reported in the literature were 45596 and the percentage of abnormal smear was 1.4 %. The higher incidence in our study may be related to the difference in methodology where she used the conventional Pap smear method in addition to smaller number of patients in our series, however; cultural and environmental factors must be considered. The percentage of abnormal smears in other 2 studies using also conventional method, was 1.6% when the number of patients was 22089 (9) and raised to 7.9% in a series of 2100 patients (10), which is comparable to our study. In this study the adenocarcinoma was detected in 3 patients (0.14%), however; no other malignant variant was recorded. In other studies adenocarcinoma was reported in 0.02% (8), 0.023% (9) and 0.095% (10) and the reported incidence of squamous cell carcinoma in these studies were 0.8%, 0.33% and 0.12% respectively. High grade squamous intra-epithelial lesion (HSIL) was detected in 1 patient (0.046%) of our study which is significantly lower than other studies which varied from 0.33%-0.67% (8-10). In the present study atypical squamous cells of undetermined significance (ASCUS) was detected in 132 patients (6.2%), a finding which is significantly higher than other studies where it was 1.1% in Altaf study (8), 0.5% in Jamal et al, study (9) and 2.7% in El Hakeem et al series (10). Atypical squamous cell-cannot rule out high grade lesion (ASC-H) was recorded in 2 patients (0.092%) of our patient but not recorded in the previous studies; however this finding is comparable to that reported in the literature (11). Atypical glandular cells of undetermined significance (AGUS) were found in 1 patient (0.046%) of this study, while in other studies it was slightly higher (8-11). The variation in the results between different studies may be related to methodological and environmental factors, however much more studies applying the Liquid based thin-layer preparations technique, are required to find the actual burden of these cellular changes in Saudi Arabia.

In the present series, the benign cellular abnormalities were 414/2168 patients (19.1%), where bacterial vaginosis was detected in 374 patients (17.25%), fungus without cellular changes in 19 patients (0.9%), actinomyces in 6 patients (0.28%) and inflammation without isolated organisms in 15 patients (0.7%). This data are comparable to that reported in other studies (8-11)

Therecognized obstacles to cytology-based screening, include the need for required laboratory infrastructure, trained specialists for processing and reporting, quality control, and a system of communication to the women screened so that they may receive sufficient treatment in addition to the necessity for multiple visits which may result in significant loss to follow-up (12). In our study the majority of women (79.9%) were symptomatic and accepted the test as part of their management in contrast to the western countries where the majority of screening candidates are non-symptomatic, however in these countries, most of them have a history of HPV infection (4).

Cervical cancer is caused by sexual exposure to an oncogenic type of the human papillomavirus (HPV), usually types 16 and 18 and detection of high-risk HPV (HR-HPV) types is of diagnostic and prognostic value, recent studies show that HR-HPV types are strongly associated withsevere squamous intra-epithelial lesions (SILs) and the subsequent progression to cancer and the majority of SILs without a HR-HPV type usually regress (4 &13). Used as an adjunct to liquid-based cytology, HPV DNA testing has the potential to increase the sensitivity and specificity of primary screening and the predictive value of the combined test may improve cost-effectiveness by permitting screening intervals to be lengthened (14). Sait *et al*, (11), recommended starting screening at a later age (25-30 years) and with HPV testing and the secondary testing could be with cytology in women older than 35 years of age. The mean age of patients in our study was 38.6 ± 9.7 years and the screening test was done to women above 20 years and involved the performance of HPV-DNA testing for women with cervical cellular abnormalities proved by thin layer LBC,however; changing the protocol to start screening at latter age with performance of HPV testing as first triage test must be taken to consideration.

Sait *et al*. (11) concluded that in Saudi Arabia; the low prevalence of cervical cellular abnormalities may be related to that colposcopy services for the triage of patients with abnormal screening examinations are not widely available with some concern regarding the quality assurance of cytology findings. Recent data indicate that HPV testing may be used efficiently in the management of ASCUS cases by referring to cytological examination only those women who test positive (15). However in our hospital, gynaecologicand laboratory services are well developed with good quality assurance and quality control levels.

Visual inspection after the application of 3% to 5% acetic acid (VIA) when used in combination with HPV DNA testing and cytological examination using thin layer LBC has shown great promise and could help to obtain improved levels of prognostic information and accuracy (16).

Conclusion: Liquid-based, thin-layer cytology reduces sampling and preparation errors of the conventional smear; however, screening should include human papilloma virus (HPV), DNA testing to increase the sensitivity and specificity of primary screening.

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Table1:Demographic data.

Total number of women	2168
Mean age ± SD (Years)	38.6 ± 9.7
Nationality (No)	**Saudi:** 1714 (79%) **Non Saudi:** 454 (21%)
Marital status:	**Married:** 1812 (83.6%)
	Previously married: 356 (16.4%)
Mean age ± SD of 1st pregnancy (years)	22.6 ± 4.5
Presentation: number	**Symptomatic:** 1733 (79.9%) **Main presenting symptoms** Vaginal discharge and itching: 928 Pain including dyspareunia: 324 Infertility(primary and secondary):222 Bleeding: 143 Others: 116 **Non symptomatic:** 435 (20.1%)

Table 2: Mean age (± SD) of each lesion

Lesion	Mean age ± SD (years)
Glandular Cell Adenocarcinoma	69±7.55
ASCUS	38.4±13.1
HSIL	38
AGUS	58
ASC-H	38.2
Bacterial vaginosis	41.1±11.6
Fungal (Candida)	47.4±6.4
Inflammation	43.1±9.8
Actinomyces	45.2±7.8

Mean age of all cases	41.6±10.6

Table 3: Cervical cellular abnormalities.

Lesion	Number (%)
Total number of Cases	**2168(100)**
Malignant and premalignant lesions	**141(6.5)**
Glandular Cell Adenocarcinoma	3(0.14)
ASCUS Total number With no other abnormality With inflammation With bacterial vaginosis With fungal inflammation With bacterial inflammation	 134(6.2) 27(1.25%) 97(4.5) 2(0.092) 2(0.092) 6(0.28)
HSIL	1(0.046)
ASC-H	2(0.092)
AGUS	1(0.046)
Benign cellular changes	**414(19.1)**
Fungal (Candida)	19(0.9)
Bacterial vaginosis	374(17.25)
Inflammation	15(0.7)
Actinomyces	6(0.28)
Normal	**1613**

Table 4: correlation between age and cellular abnormalities

	Cellular abnormalities	
Age	**No**	**555**
	r=	**0.063**
	p- value	**NS**

NS: considered non significant as p>0.05.

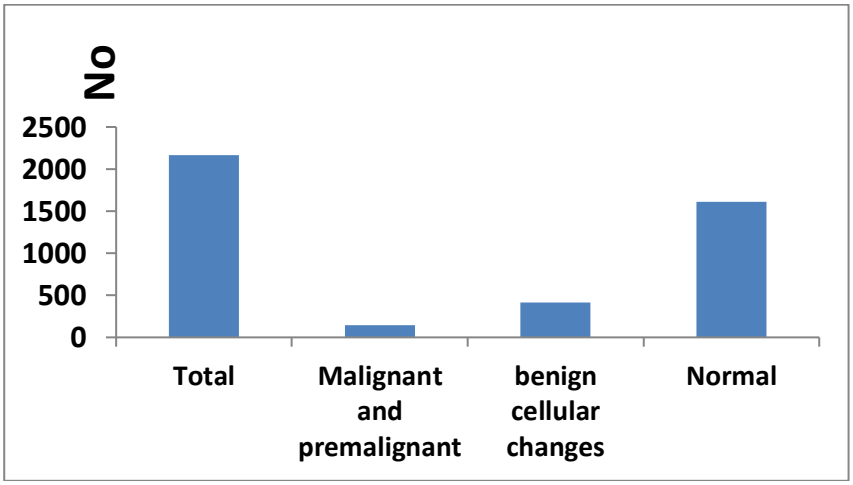
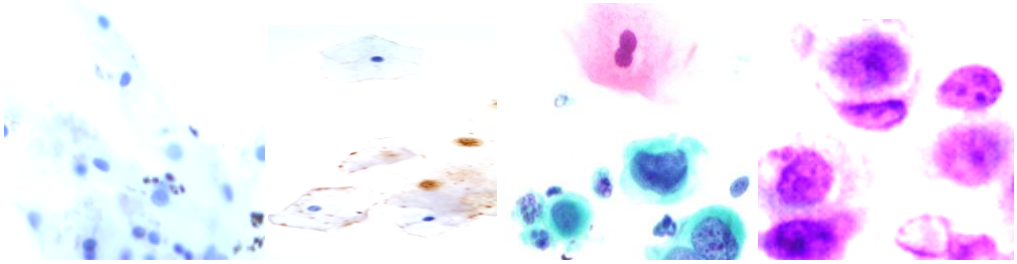
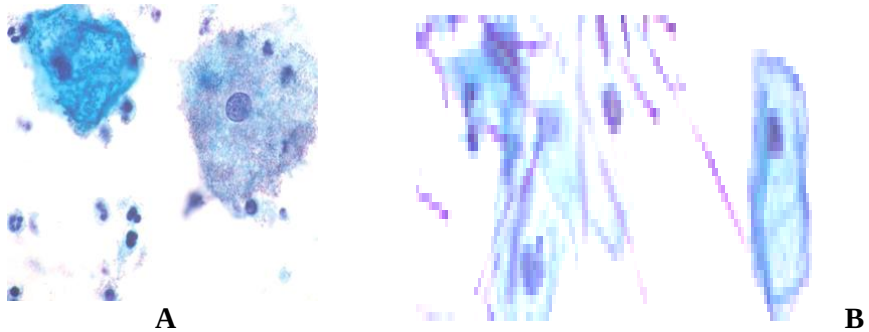


Figure 1: comparison between numbers of different cellular changes with total number of women



A B C D

Figure 2: Normal cytology (A), ASCUS (B), HSIL (C) and adenocarcinoma (D).



A B

Figure 3: Bacterial vaginosis (A) and Candida infection (B).