



## Demonstration of Abnormal Cervical Change in Papanicolaou Smears by Liquid Base Cytology

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### Authors' contributions

*This work was carried out in collaboration among all authors. Author HMH designed the study, performed the statistical analysis. Authors AA, RA, BA, OA and EA wrote the protocol and wrote the first draft of the manuscript. Author KAI managed the analyses of the study. Authors RAR and OMK managed the literature searches. All authors read and approved the final manuscript.*

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### ABSTRACT

**Background:** Cervical cancer is considered one of the most important health problem affecting women health all over the world also it is preventable cancer as soon as it was discover early by cervical cytology using Papanicolaou (Pap) smears as it is an effective means of screening for cervical premalignant and malignant conditions such as Cervical intra-epithelial neoplasia (CIN). So this study aims to detect abnormal premalignant epithelial changes by liquid base Pap stained cervical smear in Taif city of Saudi Arabia.

**Methodology:** Cross sectional study is based on 100 females patients who attended the out-patient Department of Obstetrics and Gynecology in King Faisal hospital were randomly chosen as cross sectional study. Cervical smears were obtained and Pap smears were prepared from

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patients presenting with different complaints such as vaginal discharge, abnormal menstrual and vaginal bleeding and pain. After fixation and staining, each smear was carefully examined.

**Results:** showed that epithelial cell abnormalities were found in 7% of smears, age rang of the patients was between 20-50 years old and the main complaint was abnormal vaginal discharge. Also our study established the high frequency of abnormal cervical cytology in females used contraception as well as early marriage as a risk factors.

**Conclusion:** In Taif City, a conservative community, premalignant and malignant cervical lesions are relatively high. Pap smear cervical cytology is an easy, safe and effective test for early detection of pre-malignant and malignant lesions of the cervix, thereby allowing clinicians to treat patients early and more effectively.

*Keywords: Cervical cancer; cervical intraepithelial neoplasia; Papanicolaou smear.*

## 1. INTRODUCTION

Cervical cancer is consider the second most common cancer in women in the world, around 15% of all cancers' in females are cervical cancers, the prevalence increases in developing countries while in Southeast Asia, cancer cervix accounts for 20% of all cancers'. Unlike most other malignancies, cervical cancer is readily preventable when effective programs are conducted to detect and treat its precursor lesions. Since the introduction of Pap test, a dramatic reduction has been observed in the incidence and mortality of invasive cervical cancer worldwide [1].

Various agents have been reported either as an association or cause of cervical cancer. These include ethnic factors, number of partners, and use of contraception, the age of first sexual intercourse, the age of first birth, and infectious agents like human papilloma virus (HPV) and infectious agents such as human papilloma virus (HPV), herpes simplex virus type 2 and Chlamydia trachomatis, among others. As HPV infection is considered a sexually transmitted disease, investigations to reveal sexual behavioral risk factors have been conducted. Overall, women who had first sexual intercourse at an early age or who have had multiple sexual partners have an increased risk of developing cervical cancer. Apart from sexual behavior, smoking, nutrition, parity and oral contraceptive use have been reported as major environmental risk factors for cervical cancer. However, to date, there has been no clear-cut proven evidence of a biologic basis for these agents and the incidence rate of cervical cancer varies greatly from one population to another, depending on the prevalent risk factors mostly influenced by life style. These factors are well established in many countries [2].

In Saudi Arabia, cervical cancer ranks as the eighth most common cancer in females with a mean age of 53 years. Cervical cancer for the Saudi nationals represented 33.5% of all genital cancers. Current estimates indicate that every year, 271 Saudi women are diagnosed with cervical cancer, with 68 (25.1%) cases occurring in women of child-bearing age. Of these 271 women, 143 (52.8%) will die due to the disease, including 27 (39.7%) at the child-bearing age [3]. A dramatic increase in the incidence of cervical cancer in Saudi Arabia is anticipated [4].

The dysplastic changes in the cervical squamous epithelium is known as cervical intraepithelial neoplasia (CIN), that graded (CIN1) when dysplastic changes was mild, and with extensive and sever changes (CIN graded II and III). The extensive changes also known as high-grade squamous intraepithelial lesions (HSIL). More than 25% of cases with HSIL will progress to invasive cervical cancer if not discovered and treated so the identification of risk factors for HSIL is of great importance [5].

The prevalence of atypical epithelial cells abnormalities in Pap smear of Saudi patients was found to be 4.3% (841/19,650) Saudi patients were found with atypical epithelial cells abnormalities). Its prevalence in the years 2008 was 5.7%, 2009 was 4.9%, 2010 was 4.2%, and 2011 was 2.5%. Presence of abnormal cervical appearance was associated with increased epithelial cell abnormalities. Squamous cell abnormalities were identified in 767 out of 841 (91%) of studied patient, and the cervical glandular epithelial abnormalities were appeared in 74 out of 841 (9%) of patients [6]. The patients with early invasive cervical cancer are asymptomatic and the cervical malignant changes not visible clinically and can be detected only during routine cervical cytological screening. The most common symptoms in patient with

visible malignant lesion are discharge and bleeding especially post coital. Pain is not a common symptom in patient with early cervical cancer. In exophytic cervical cancer the symptoms (bleeding and discharge) may be worse, whereas in endophytic malignant growth the symptoms were minimal (Eifel, et al. 2006).

Cytology, either conventional or liquid-based cytology (LBC), is meant to detect cervical premalignant lesions that histologically as cervical intraepithelial neoplasia (CIN) from the cervix. Pap smear involves collection of exfoliated cells from the cervix onto glass slides which are processed in the laboratory and examined for the presence of cervical premalignant cells (Kinfolarin, et al. 2017).

Pap smear can be used as a screening test, however is false negative in about half of instances of cervical premalignant and malignant lesions. Affirmation of the analysis of cervical malignant or premalignant requires a biopsy of the cervix to be examined histologically. This is frequently done through colposcopy. Imaging modalities such as ultrasound, CT and MRI have been used to search for tumor spread and impact on nearby structures [7].

The premalignant and malignant cervical changes can be detected early by simple Pap smear test and this well lead to more efficient management of the patients so the aim of our study is to detect the abnormal cervical epithelium change by liquid base cervical Pap smear.

## 2. MATERIALS AND METHODS

Cross section study was conducted on 100 females patients attending the outpatient Department of Obstetrics and Gynaecology in king Faisal hospital hospitals from September 2018 to June 2019. Our cases includes female patients complaining of vaginal discharge, abnormal vaginal bleeding and pain. Some important clinical data from patient data sheet were collected including patient age, marital status, duration of marriage, history of contraception and complaint After cervical smears collection, brush heads were transferred directly into a vial with BD-SurePath preservative fluid [8]. From the fluid containing the cellular material, a liquid-based cytology sample was prepared with the robotic BD PrepStain Slide Processor (BD Diagnostics - TriPath, Burlington, NC, USA) [9]. Each specimen was smeared on a clean grease free slide. All the slides have been stained with Pap staining. The stained smears were examined under light microscope for the presence of cytological changes by two pathologists.

## 3. RESULTS

Cross section study included 100 female patients, their ages ranging from 20 to 50 years. They were divided into three age groups first group from 20-30, second from 31-40 and third from 41-50. The 1<sup>st</sup> include 45 (45%) patients, 2<sup>nd</sup> include 45 (45%) patients and 3<sup>rd</sup> include 10(10%) patients.

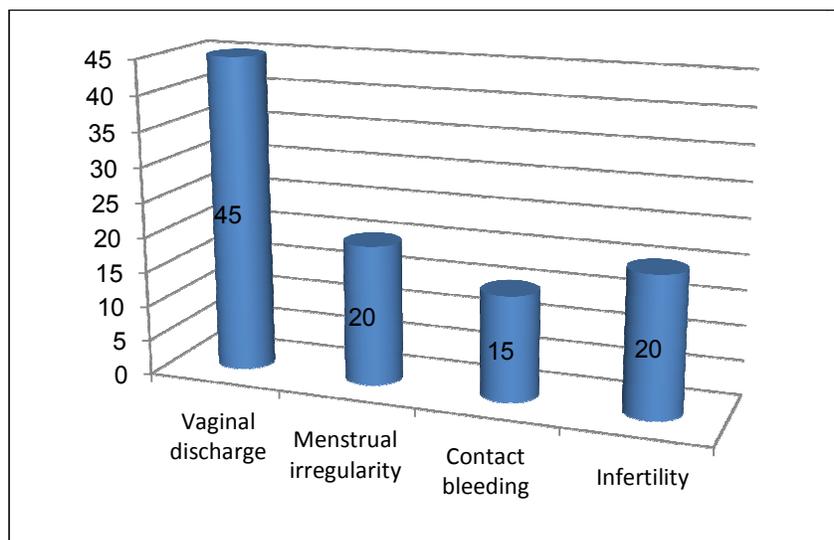
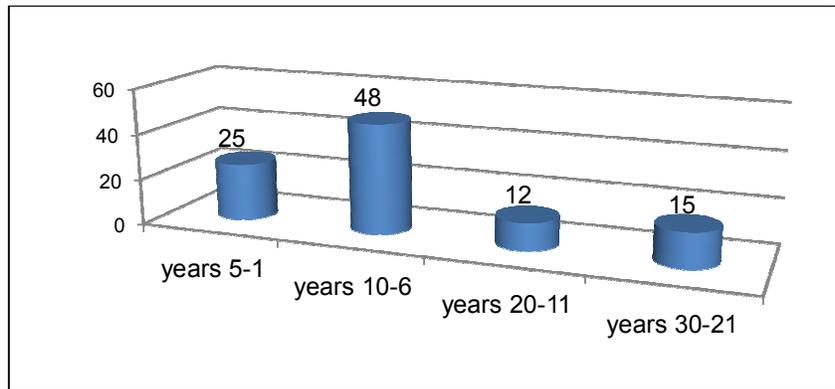
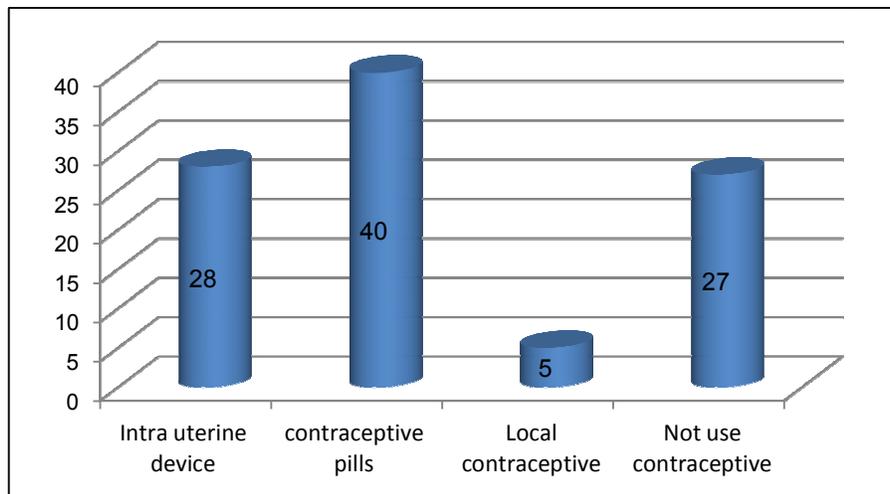


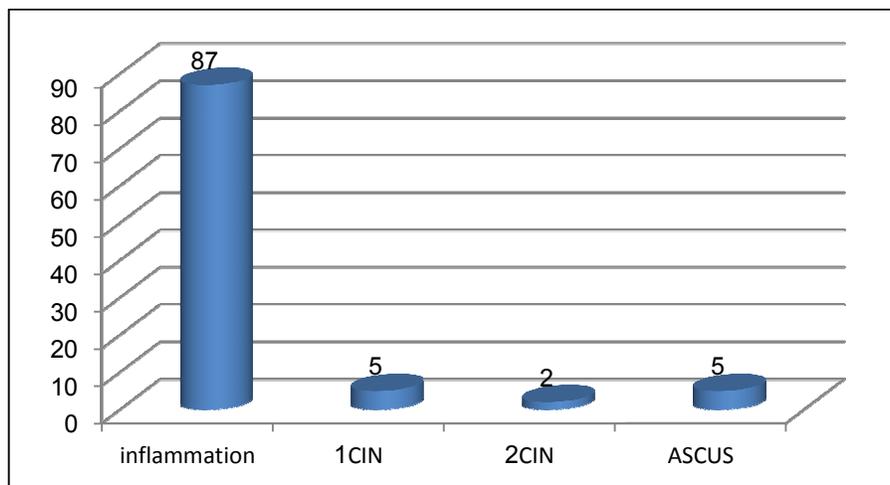
Fig. 1. Frequency of different types of patients complains



**Fig. 2. Frequency of duration of marriage of patients under study**



**Fig. 3. Frequency of contraceptive use in patients under study**

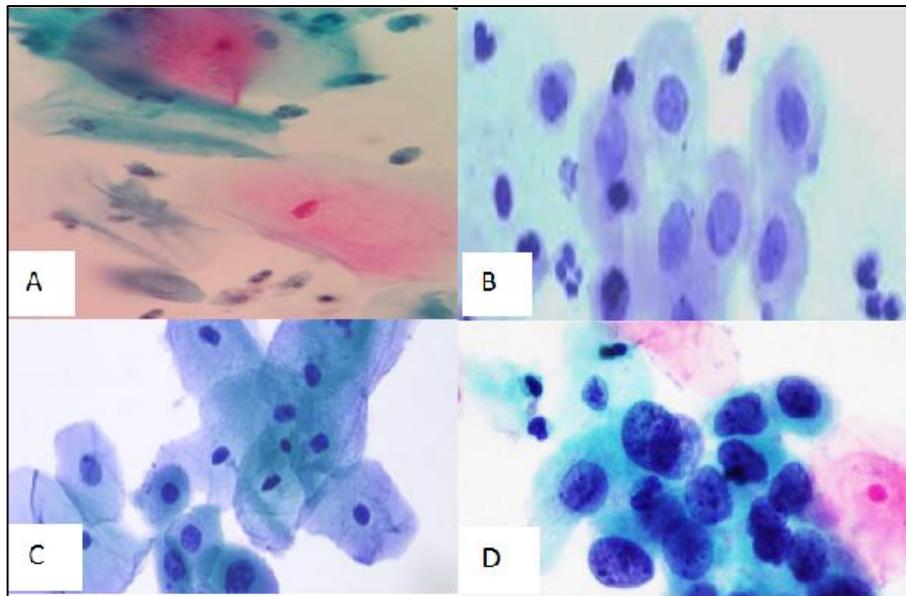


**Fig. 4. The microscopic examination of the cervical smears taken from the patients and stained by Pap stain revealed moderate to severe acute and chronic inflammatory infiltrate in 87 samples, mild dysplastic changes (CIN1) in 5 smears and moderate atypical changes (CIN2) in 2 smears and atypical squamous changes of undetermined significance (ASCUS) in 5 cases**

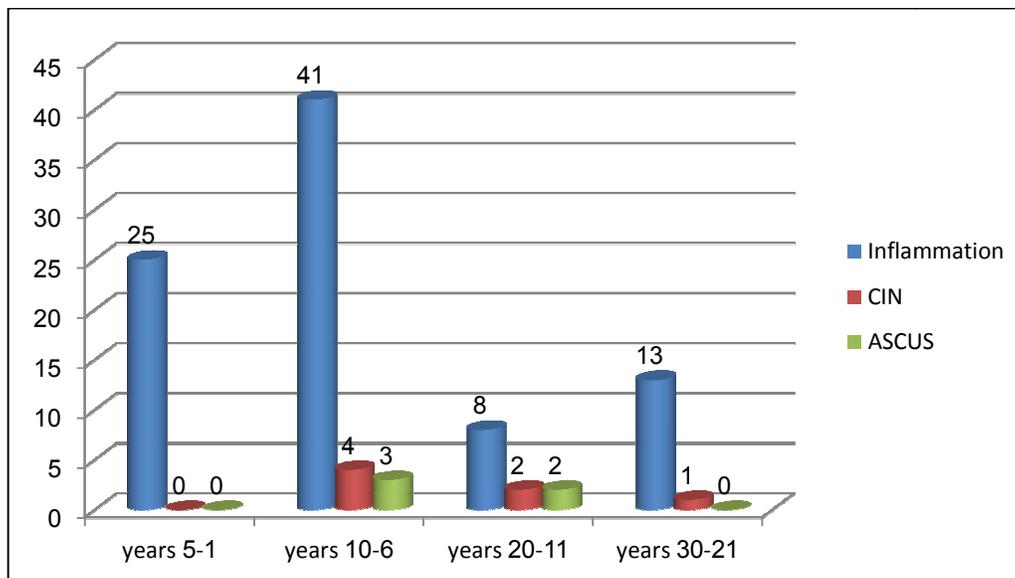
**Table 1. Association between vaginal discharge and CIN**

	Vaginal discharge No %	No vaginal discharge No %	Total No %	$\chi^2$	P-value
CIN change	6 (86%)	1(14%)	7(100%)	5.04	< 0.05*
CIN No change	39 (42%)	54 (58%)	93(100%)		

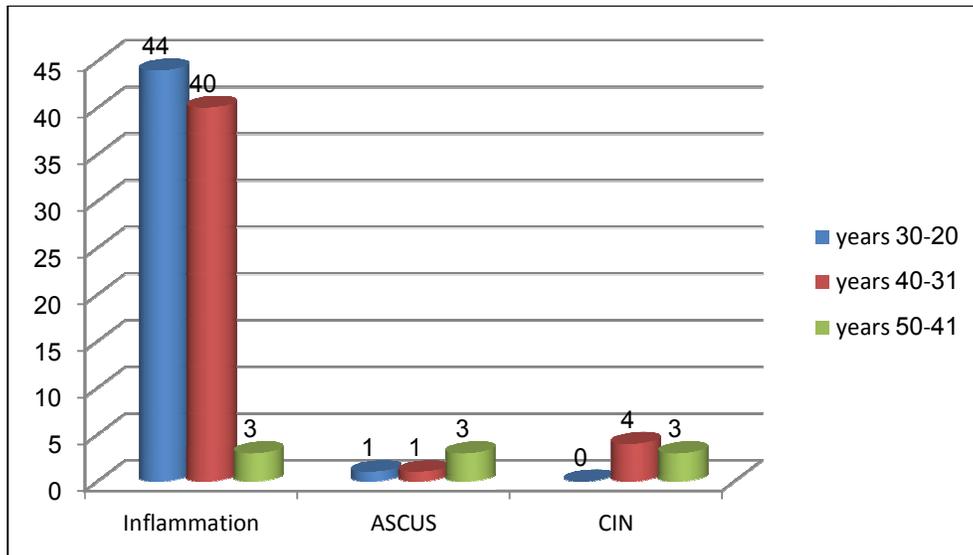
\* Significant difference. There was significant increase in CIN in patients with vaginal discharge in comparison to those without vaginal discharge ( $p < 0.05$ )



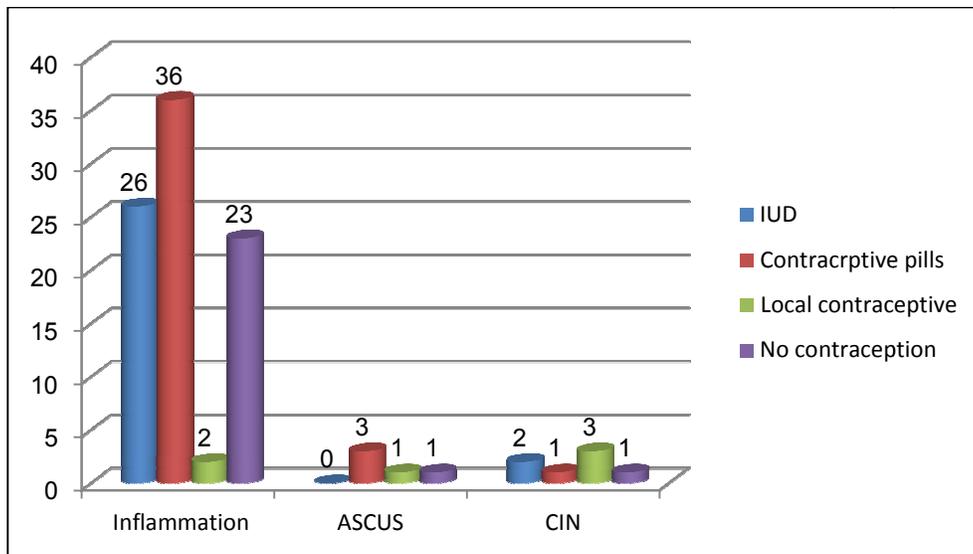
**Fig. 5. Shows A) Inflammatory smear with normal cervical epithelial cells. B) Inflammatory smear with mild reparative epithelial atypia (ASCUS). C) Mild dysplastic epithelial changes (CIN1). D) Moderate dysplastic epithelial changes (CIN2)**



**Fig. 6. Frequency of pathological changes in Pap smear and patient's duration of marriage**



**Fig. 7. Frequency of pathological changes in Pap smear with patient ages**



**Fig. 8. Frequency of pathological changes in Pap smear with contraceptive used**

#### 4. DISCUSSION

The change from premalignant to malignant cervical lesion take relatively long period in which these changes can be detected and managed, so the cervical cancer is the most female malignancy suitable for screening for detection of this premalignant changes [10].

Cervical cancer differ from most other malignancy, it can be prevented by establishing effective screening programmers for detection and treatment of its premalignant lesion. The use

of Pap test as a screening method for early detection of cancer cervix leads to considerable reduction in morbidity and mortality of this cancer [11].

In our study the prevalence of abnormal cervical epithelial changes detected in smear of included patients were 7 cases (7%). Our results is in agreement with Balaha, et al. 2011 who done an analysis of the cervical Pap smear reports from the Eastern region of Saudi Arabia, and represented 9.29% of abnormal Pap smears also the previously published studies from Saudi

Arabia Jamal, et al. [12] and Elhakeem, et al. [13] showed variable results. The prevalence rates of abnormal epithelial changes are in the range of 1.66-7.9%. The possible cause for presence of slight difference in our prevalence rate from other studies is that we studied symptomatic women and thus more chances of positive results. But the other studies were done on normal and abnormal cases also this may be explained by the different conditions prevalent in each study.

In our study the age of patients with abnormal cervical cytology in Pap smear (CIN) were ranged from 31 to 40 years with the mean of 36.4 years that age was clearly within the reproductive years), this finding was in agreement with Balaha, et al. 2011 study that showed The mean age of the cases diagnosed as abnormal cervical cytology was 35.8 years and with Bal, et al. [1] study in which the mean age of cases with low grade squamous intraepithelial lesion (LSIL) was 32.3 years and those with HSIL and invasive carcinoma were 40.5 years.

The mean age at marriage for cases of abnormal cervical cytology in the present study, was 21 years, the results was nearly in agreement with Bal, et al. [1] study as the mean age at marriage for CIN patients was 19.5 years, also Khattak, et al. [14] and Sherwani, et al. [15] found CIN on cytology to be more prevalent in patients who started sexual activity around 20 years of age.

Our study emphasized the increase frequency of abnormal vaginal discharge with preneoplastic changes in the cervix. The results correspond with many previous studies [14,16].

The high frequency of the use of contraception and the development of abnormal cervical cytology was established in the present study as the case positive for CIN were patient using intrauterine device in 2 cases, contraceptive pills in one case, and local contraception in three cases, and this explained by the increased susceptibility to cervical infection and chronic inflammation as with intrauterine device use and proliferative hormonal effect as with contraceptive pills use.

## 5. CONCLUSION

Premalignant and malignant cervical lesions are relatively common in Taif region. The use of simple Pap smear test for cervical cytology is safe and effective screening method for early detection and efficient management of

pre-malignant and malignant cervical changes in high risk women.

## 6. RECOMMENDATION

The study supports the importance of early detection of precancerous lesions of the cervix by cytological examination using Pap smear. Also the awareness for screening programs must be increased to decrease the advanced cases.

## CONSENT AND ETHICAL APPROVAL

As per international standard guideline participant consent and ethical approval has been collected and preserved by the authors.

## COMPETING INTERESTS

Authors have declared that no competing interests exist.

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