

Accuracy of Pap smear in cervical cancer screening

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Abstract

Introduction: Globally, cancer of the cervix is the second leading cancer in females. The sensitivity of conventional Pap smear in diagnosing cervical lesions before development of cervical cancer is fifty one percent, which indicates that false negative results is forty nine percent. The aim of this research is to compare two methods for cervical cancer screening (conventional Pap smear and colposcopy).

Methods: This was a cross sectional study carried out on 38 patients who presented to the private clinic, during the period 1st January-1st September 2018. All cases underwent Pap smear, a colposcopy, and a cervical biopsy, with the latter being considered as the gold-standard test. Inclusion criteria include married for at least 3 years, non pregnant, age ≥ 21 years. The exclusion criteria were the following; women with active vaginal bleeding, hysterectomy, women with frank growth and/or who had never been sexually active or had undergone prior treatment for CIN or cancer of cervix, or had unsatisfactory Pap smear. Pathological study was done by histopathology specialist. Conventional Pap smear was used, using a smear made on a glass slide for CPS and fixed. Cytology was reported using Bethesda system and histology reporting was done using CIN terminology.

Results: Most of the cases were Atypical Squamous Cell Undetermined Significant (ASCUS) 15 (39.5%). Histopathological study of the biopsy taken from the patient revealed that: Squamous cell carcinoma was found among 2 (5.3%) of the patients, CIN3 2 (5.3%), 4 (10.5%), and CIN1 7 (18.4%). The overall sensitivity of Pap smear was (93%), with the largest sensitivity among those aged ≤ 44 years (100%), while among those aged ≥ 45 years it was decreased (86%).

Conclusion: The sensitivity and specificity results indicate that the cytologists need more training as it is operator dependent.

Key words: conventional Pap smear, colposcopy, cervical cancer, sensitivity, specificity

Introduction

Globally cancer of the cervix is the second most prevalent cancer affecting women; the incidence of cervical cancer is 1.3 per 100,000 women in Iraq [1]. The prevention or cure of cervical cancer has the best prospects because there is a high rate of early diagnosis when it still has a high cure rate. Developing countries contain 80% of cases of cervical cancer occurrence, and it is the important reason for women's death [2, 3]. The Papanicolaou (Pap) smear is a unique, widely used, and cost effective method for diagnosing cancer of cervix, and it has been successful in prevalence, and mortality rates reduction of this cancer in women [4]. Pap smear has succeeded in reduction of cervical cancer rate and its mortality rate by 79%, and 70% respectively [5]. Patients with frequent Pap smears have increased incidence of cervical cancer [6]. Pap smear sensitivity in diagnosing lesions before stage cancer of cervix is found is half of the cases, which indicates false negative results of this conventional Pap smear is 49% [7]. Pap smear specificity and sensitivity in diagnosing (high-grade lesions of cervical intraepithelial neoplasia)+8 (CIN II and CIN III) have found around 55% and 97%, respectively [8]. Iranian researchers found that less than 2% of cervical cancer patients had undergone a Pap test in the previous 10 years [9, 10]. Human papilloma virus (HPV) is the primary reason behind cervical intraepithelial neoplasia (CIN) and cervical cancer. Researchers found that in females infected with HPV high-risk, their progression from CIN to cancer was of a higher rate, with three hundred-fold elevation in the risk of high-grade disease [6, 11, 12]. Although, HPV infections usually are not persistent, it can remain latent, maybe for many years. Exposed women are asymptomatic, and HPV infection is either suppressed or eliminated by the immune system [6, 7]. In another percentage of affected females, there may be occurrence of low-grade cervical lesions, which regress spontaneously. Mostly, the infections clear in 9-19 months [6, 13]. Limited percentages of females exposed to HPV, infection of persistent type may develop to CIN [6, 7]. Recently, prophylactic HPV vaccination has been initiated, but such vaccinations are not used in Iraq, so we do not have the benefit of its effective role in decreasing the incidence of persistent HPV infection [6]. The aim of this research is study the accuracy of Pap smear in cervical cancer screening.

Patients and method

Cross sectional study of 38 patients presented to the private clinic, during the period 1st January -1st September 2018. Inclusion criteria included married for at least 3 years, non pregnant, age \geq 21 years. Women with active vaginal bleeding, hysterectomy, and women with frank growth and/or who had never been sexually active or had undergone prior treatment for CIN or cancer of cervix, or had unsatisfactory Pap smear were excluded from the study. Pap smear colposcopy and cervical biopsy was done for all the patients. Pathological study was done by histopathology specialist. Conventional Pap smear was

used, using a smear made on a glass slide for CPS and fixed. Cytology was reported using Bethesda system and histology reporting was done using CIN terminology. Preparation of the single combined smear, was obtained through use of endocervical brush, taking a sample. The brush was inserted to the external os and the device rotated gently by use of $\frac{1}{4}$ or $\frac{1}{2}$ turn to get the cellular sample (being careful as bleeding may be caused by over rotation).

The following protocol was used: Firstly, do not smear, but allow the material to stay on brush. Then scraping of the ectocervix with a spatula and spreading of the material quickly onto a slide at its upper end. Then, rapidly roll the endocervical brush through the ectocervical material to a slide at its upper end. This technique, should be performed quickly to prevent drying artifacts. As soon as possible spray fix by thoroughly soaking the cellular sample while holding the spray fixative container about 6-8 inches from the slide. Allow spray fixative to evaporate.

Sensitivity, specificity, positive predictive value (PPV), negative productive value (NPV), and accuracy, was calculated by comparing the Pap smear results with biopsy results, as the latter is the gold test.

Statistical analysis and data management: The Statistical Package for Social Sciences (SPSS, version 18) was used for data entry and analysis. Chi (χ^2) square test, and t- test were used to compare means and proportions of different factors among different groups of study sample. P value of \leq 0.05 was regarded as statistically significant. Bar charts and tables were used to present the data.

Results

Table 1 shows the Pap smear results: most of the cases were Atypical Squamous Cell Undetermined Significant (ASCUS) 15 (39.5%), followed by Low-grade squamous intra-epithelial lesion (LSIL) 14 (36.8%), and High-grade squamous intra-epithelial lesions (HSIL) 6 (15.8%). Squamous cell carcinoma was found among 2 (5.3%) of the cases.

Histopathological study of the biopsy taken from the patient revealed that: Squamous cell carcinoma found among 2 (5.3%) of the patient, CIN3 2 (5.3%), 4 (10.5%), and CIN1 7 (18.4%), as shown in Table 2.

For testing the sensitivity and specificity the Pap smear result was regarded as: negative included (normal, inflammatory and ASCUS), while positive included (LSIL, HSIL, and carcinoma). The pathological results were also divided as; negative included (normal, inflammatory and ASCUS), while positive included (CIN1-3, and carcinoma). The correlation between Pap smear cytology and pathological result show that concordance in negative results was found among 15 (39.5%) of the total sample, and positive results found among 14 (36.8%). This relation was statistically significant, as shown in Table 3.

Table 1: The cytological results of the Pap Smear

Pap Smear cytology results	Frequency	%
Normal	1	2.6
Atypical Squamous Cell Undetermined Significant (ASCUS)	15	39.5
Low-grade squamous intra-epithelial lesion (LSIL)	14	36.8
High-grade squamous intra-epithelial lesions (HSIL)	6	15.8
Squamous cell carcinoma	2	5.3
Total	38	100%

Table 2: The Pathological results of the biopsy

Biopsy results	Frequency	%
Normal	17	44.70%
Atypical Squamous Cell Undetermined Significant (ASCUS)	6	15.80%
CIN1	7	18.40%
CIN2	4	10.50%
CIN3	2	5.30%
Squamous cell carcinoma	2	5.30%
Total	38	100.00%

Table 3: The correlation of Pap smear results with the Biopsy results

Pap smear results	Biopsy Results			
	Negative		Positive	
	Frequency	%	Frequency	%
Negative	15	39.5	1	2.6
Positive	8	21.1	14	36.8
Total	23	60.5	15	39.5

$\chi^2=12.77$, $df=1$, P value= <0.05 (significant)

Table 4: Comparison of Pap smear results with Biopsy results according to age of patient

Age	Pap smear results	Biopsy results				P- value
		Negative		Positive		
		Frequency	%	Frequency	%	
≤44	Negative	5	25	0	0.0	0.05*(significant)
	Positive	7	35	8	40	
	Total	12	60	8	40.0	
≥45	Negative	10	55.6	1	5.6	0.002*(significant)
	Positive	1	5.6	6	33.3	
	Total	11	61.1	7	38.9	

* Fisher's Exact Test

Table 5: The efficacy of the Pap Smear in diagnosing cervical carcinoma

Pap test efficacy	Sensitivity	Specificity	False +ve	False -ve	Accuracy	PPV ¹	NPV ²
Pap test efficacy in aged ≤44	100	42	58	0	65	53	100
Pap test efficacy in aged ≥45	86	91	9	14	89	86	90.9
Pap test regardless age	93	65	35	7	76	64	93.8

The correlation between Pap smear cytology and pathological result stratified by age, show that among those aged ≤ 44 years: the concordance in negative results was found among 5 (25%) of those aged ≤ 44 years, and positive results found among 8(40%). In the age group ≥ 45 years, the concordance found among 10 (55.6%), and 6 (33.3%) regarding negative and positive results among this age group. These relations were statistically significant, as shown in Table 4.

The overall sensitivity of Pap smear was (93%), with largest sensitivity among those aged ≤ 44 years (100%), while among those aged ≥ 45 years was decreased (86%). The largest specificity found among those aged ≥ 45 years (91%), and lowest among those aged ≤ 44 years (42%), the overall specificity was (65%). The overall positive predictive value (PPV) was (64%), (86%), and (53%), among all cases, those aged ≥ 45 years, and aged ≤ 44 years, respectively, while regarding Negative predictive value is (93.8%), (90.9%), and (100%) among all cases, aged ≥ 45 years, and aged ≤ 44 years, respectively, as shown in Table 5.

Discussion

In this study the overall sensitivity of Pap smear was (93%), and this is higher than results of previous studies which found that cervical cytology's specificity and sensitivity were somewhat low, because sensitivity ranges from 30-87% and specificity is 86-100% [13]. The unique finding of this study, was the differences in sensitivity and specificity with age. The largest sensitivity was among those aged ≤ 44 years (100%), while among those aged ≥ 45 years was decreased (86%). The largest specificity found among those aged ≥ 45 years (91%), and lowest among those aged ≤ 44 years (42%). The overall specificity in this study was (65%).

In this study, the sensitivity is more among those aged < 44 years which indicates that the cytologist pays attention when they see positive results in the younger age group, while they are not concentrating as much on the slide examination at age 44 years and above. While among those aged 45 years or above the cytologist may search thoroughly, therefore the specificity is higher. The sensitivity and specificity results indicate that the cytologist needs more training as it is operator dependent. The need for more training was also reported by Abedalrahman SK. [14].

The overall positive predictive value (PPV) was (64%), (86%), and (53%), among all cases, cases aged ≥ 45 years, and cases aged ≤ 44 years, respectively, while regarding Negative predictive value is (93.8%), (90.9%), and (100%) among all cases, aged ≥ 45 years, and aged ≤ 44 years, respectively. This is different from the results of Karimi-zarchi M, et al who found that Pap smears sensitivity, specificity, and the positive and negative predictive values were determined to be as follows; (18.2, 98.5, 85.7, and 71.3%), respectively. Karimi-zarchi M, et al found that colposcopy sensitivity, specificity, and the positive and

negative predictive values were as follows (66.7, 98.94, 80, and 97.9%), respectively. [16] For that reason, in case of finding of Pap abnormality, a set of (colposcopy, cervical biopsy, and endocervical curettage) are indicated for cervical cancer detection [15].

Histopathological study of the biopsy taken from the patient revealed that: Squamous cell carcinoma was found among (5.3%) of the patients, CIN3 (5.3%), CIN2 (10.5%), and CIN1(18.4%). This figure was higher than found by Karimi-Zarchi M 2015 [15] CIN3 (1%), CIN2(4%), CIN1(27.7%), normal (67.3%), and from Arvind B Set al 2016 who found, malignant (10%) CIN2-3 (11.5%), CIN1(16.5%), normal(3%) [16]. The greater figure of high and low grade, indicates the high prevalence of intraepithelial lesions among private clinic attendance in Iraq, which needs more attention for implementation of cervical cancer screening program [1] and coordination among private and public health sectors to overcome this problem.

Conclusion: The study has shown a relatively high prevalence of epithelial abnormalities in cervical smears in the studied population. The overall specificity and sensitivity was good with better results among women older than 45 years old. The sensitivity and specificity results indicate that the cytologist needs more training as it is operator dependent.

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