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Cervical Pap Smear Cytological Changes with Clinicopathological Correlation in Iraqi Patients

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Abstract

Objectives: This study aimed to evaluate the role of Pap test in detecting pre-cancerous lesions, correlate the pap result with patient's age, parity, number of births, number of abortions, chief complaint, and clinical cervical exam and to evaluate the diagnostic accuracy of the pap test in correlation to histopathological examination among Iraqi women aged 45 years to 85 years.

Methods: Women who attended the outpatient gynaecological clinic of the Department of Obstetrics and Gynaecology at Baghdad medical city, Baghdad, Iraq, from January 2019 to January 2020 who had different chief complaints were selected for the study. Women who are 45 years to 85 years old were included in the study. A Pap smear was used for all women to screen for cervical cancer and the results were reported according to the 2014 Bethesda system. The data analysis was done utilizing statistical package for social sciences version 24 (SPSS v24).

Results: Total number of pap smears analyzed were 510, NILM (negative for intraepithelial lesions or malignancy) constituted major group 464/510 (91%) and epithelial cell abnormality were 46/510 (9%), age is significantly correlated with increasing rate of pre-neoplastic and neoplastic lesions in women and the significance of vaginal discharge & postmenopausal bleeding and its association with premalignant changes in the cervix. The sensitivity of Pap test is 94%, the specificity was 60% and accuracy rate 74%.

Conclusion: There is significant correlation between Pap smear abnormality and increasing age, vaginal discharge and postmenopausal bleeding, were evident in this study.

Keywords: Pap smear, Bethesda system, cervical cancer screening

Introduction

In 2018, an estimated 5,70,000 women were diagnosed with cervical cancer worldwide and about 3,11,000 women died from the diseasee. Hence, cervical cancer is considered a major health problem worldwide.[1] It's a common practice in developing countries that women only attend the clinic when they have different complaints, such as discharge and abnormal bleeding.[2] The risk of precancerous lesions of the cervix to progress to an invasive cervical cancer is time dependent, where 4% became invasive by end of one year and 11% by end of 3 years; as much as 22% reach invasive stage by 5 years and 30% by 10 years.[3] Due to the long latent phase of the precancerous lesions, the identification of these lesions can be made before progression to an invasive cancer.[4] Since the time of discovering the effectiveness and accuracy of pap smear testing, the test has broadly used as a main procedure in detecting epithelial changes in the uterine cervix in their precancerous stages.[5] Recent data had shown more than 50% decrease in the incidence of cervical cancer in the past 30 years due to the adoption use of screening of the cervix.[6] Pap smear is an uncomplicated procedure, economically effective screening test that is carried out by experienced doctors to diagnose epithelial cells abnormality.[7] Regular and systematic use of Pap smear screening could decrease cervical cancer death rate by 80%.[8] There are two types of cervical cancer screening tests broadly used which are Papanicolaou test (also known as the Pap smear) and HPV test.[9] The positive results of Pap smear should be proceeded by further investigation like colposcopy, cervical biopsy and fractional curettage. The Pap smear has the capability to diagnose 70–95% of cancer of the cervix and about 70% of endometrial cancer as stated in different studies.[10] In order to prevent early death among women due to cervical cancer, there are three essential measures which can be summarized in the following:

1. Prevention.
2. Early detection.
3. Control and treatment of the pre-invasive uterine cervical lesions.[11]

Based on the aforementioned, this study aims at finding out the prevalence of an abnormal Pap smear, in a tertiary hospital of a Iraq, and to conduct in depth analysis of clinicopathological and demographical in order to establish the pattern of epithelial cell abnormality in a Pap smear.

Method

This is a retrospective study of cervical pap smears of females aged (45 years to 85 years old) who attended Gynecology outpatient department in medical city from January 2019 to January 2020 were included in the study that satisfied exclusion and inclusion criteria. The Pap smears were interpreted in the department of pathology according to Bethesda system (TBS) 2014. Statistical package for social sciences version 24 (SPSSv24) used to analyze data. Continuous variables presented as means with standard deviation and discrete variables presented as numbers and percentages. Chi-square test for independence used to test the significance of association between discrete variables. T test for independent samples and Mann-Whitney tests used as appropriate to test the significance of difference in means of independent variables. Level of significance was set at $P < 0.05$.

Inclusion Criteria

- Women of age 45 years and older.
- Women with symptoms like vaginal discharge, postcoital bleeding, postmenopausal bleeding, intermenstrual bleeding.
- Women attained for regular checkup.

Exclusion Criteria

- Women aged younger than 45 years and unsatisfactory smears.

Results

This study enrolled 510 women aged from 45 to 85 years with mean age of 52.6 ± 6.9 years. The age group 45–55 years comprised the majority (73.9%) of the sample. Participants gave births in a median of 5 births and multiparous women constituted 91.8% of the sample. Sampled women have one abortion as a median reading in this study Table 1.

Regarding the characteristics of those with significant Pap smear: They were significantly older (mean age 55 years compared to 52.3 years in non-significant Pap group) ($P < 0.05$) and proportion of older age groups as well is significantly higher in those with significant Pap (patient older than 55 year is 43.5% compared to 24.3% in those with non-significant Pap ($P < 0.05$). Number of birth and abortions did not vary significantly between the two groups of Pap results ($P > 0.05$).

Significant finding were observed in 46 patients (9.0%) of the sample. High grade squamous intraepithelial lesion was the most observed significant finding (3.7%) out of the total sample, then low grade squamous intraepithelial lesion (2.2%). Atypical squamous cells of undetermined significance (1.6%), adenocarcinoma (0.6%), squamous cell carcinoma (0.6%), endometrial carcinoma (0.4%). Among non-significant results, non-specific findings were the frequent observation in this study (60%), then atrophic vaginitis (16.9%), squamous metaplasia (7.5%), endometrial cells shedding (5.5%) and viral infection (1%) Table 2.

Most frequent chief complaint was discharge (38.2%) then postmenopausal bleeding (19%) and intermenstrual bleeding (15.1%), then post coital bleeding (88.2%) and pelvic pain (0.2%). Pelvic pain was encountered only in one patient. Around halve the sample had normally looking cervix and around 29.8% had bleeding on touch, erosions and polyps were encountered in 9% and 4.9% of the sample respectively, total hysterectomy observed as follow: normal vault (3.1%), vault growth (0.2%). One patient had bleeding from vault on touch and one patient had a mass. Regarding the most frequent presentation, 39.1% of the significant Pap result group was postmenopausal bleeding and discharge was 39.7% in the non-significant pap result group. Upon examination, those with significant Pap result, bleeding on touch was 32.6% of the sample, normal appearance 28.3%, followed up erosions 23.9%, while those with non-significant Pap result appeared as normal (53.2%), bleed to touch (29.5%), or eroded (7.5%) in addition to other findings Table 3.

In the present study 27 cases of epithelial cells abnormality on pap smear results (significant pap result), 17 of them were having pre/malignant changes in histopathology (correlated) and the other 10 cases were negative in histopathology (non-correlated). And 16 cases with negative for intraepithelial lesions or malignancy result in pap smear (not significant), 15 cases were having non neoplastic lesions in histopathology (correlated) and only one case was non correlated (showing premalignant changes) Table 4.

Table 1. **Socio-demographic and fertility characteristics of studied patients**

			Pap smear				
	All		Significant		Not significant		
Variables	*N* = 510	100.0%	*N* = 46	100.0%	*N* = 464	100.0%	*P*-value
Age (y)							0.013
Mean ± SD	52.6 ± 6.9		55.0 ± 8.0		52.3 ± 6.7		
Min-Max, Median	45 – 85, 50		45 – 80, 52		45 – 85, 50		
Age group							0.015
45–55 y	377	73.9%	26	56.5%	351	75.6%	
56–65 y	106	20.8%	15	32.6%	91	19.6%	
> 65 y	27	5.3%	5	10.9%	22	4.7%	
Number of births							0.634
Mean ± SD	5.3 ± 2.7		5.5 ± 3.0		5.3 ± 2.7		
Min-Max, Median	0 – 16, 5		0 – 13, 5		0 – 16, 5		
Parity categories							0.433
Nulliparous	19	3.7%	3	6.5%	16	3.4%	
Primiparous	23	4.5%	1	2.2%	22	4.7%	
Multiparous	468	91.8%	42	91.3%	426	91.8%	
Number of abortions							0.500
Mean ± SD	1.1 ± 1.5		1.1 ± 1.3		1.1 ± 1.5		
Min-Max, Median	0 – 10, 1		0 – 4, 1		0 – 10, 1		

SD, standard deviation.

Regarding the performance of Pap smear to detect malignant condition of the cervix, this study found the sensitivity of Pap is 94% (95% CI 71%–100%). Specificity was 60% (95% CI 39%–78%) and accuracy rate as 74% (95% CI 59% to 86%) Table 5.

Table 2. **Results of cytological examination of Pap smears**

Result of Pap smears	*N* = 510	100.0%
Significant		
HSIL	19	3.7%
LSIL	11	2.2%
ASCUS	8	1.6%
Adenocarcinoma	3	0.6%
SCC	3	0.6%
Endometrial carcinoma	2	0.4%
Subtotal	46	9.0%
Not Significant		
Nonspecific cervicitis	306	60.0%
Atrophic vaginitis	86	16.9%
Squamous metaplasia	38	7.5%
Endometrial cells shedding	28	5.5%
Viral infection	5	1.0%
Subtotal	464	91.0%

HSIL, High grade squamous intraepithelial lesion; LSIL, Low grade squamous intraepithelial lesion; ASCUS, Atypical squamous cells of undetermined significance; SCC, Squamous cell carcinoma.

Discussion

In the present study, the mean age of the women was 52.6 ± 6.9 with a range of 45–85 years, the fundamental reasons for selected this age group are that most women attending the gynaecological department are in the perimenopausal period for symptomatic reasons, Cervical cancer usually occurs between 40 and 50 years as shown in the study by Shanmugham et al.[12] Ninety one percent of the Pap smears results were in the Negative for Intraepithelial Lesion or Malignancy category and 9% of the result were in the Epithelial Cell Abnormality category, this result comparable to those studies in Table 6 (Studies comparing prevalence of epithelial abnormalities in different countries). This may be explained by the fact that most patients who visited the gynecology clinic only when they have major complaints, such as, abnormal vaginal bleeding or discharge. It is obvious that they had come to visit the hospital when the atypical changes in the cervical epithelium had established. The reasons for these variations may be due to different inclusion criteria and sample size. Considering all lesions together, the most frequent epithelial abnormality in our study was HSIL (high grade squamous intra epithelial lesion). This may be explained by the fact that patients did not visit the gynaecological department for cancer screening purpose, but rather with specific complaints emphasizing the need for more public awareness.

It was worth noting that in the majority of studies including this study, prevalence of invasive carcinoma formed less than 1% of the abnormal smears except in Pakistan were the prevalence was 1.4%[20] and Bangladesh were the prevalence was 1.5.[18] In the present study, most of the epithelial cell abnormality (56.5%) was detected in patients in the age group

Table 3. **Observations related to complaints and appearance**

Complaint & appearance	All patients		Significant pap smear: Yes		Significant pap smear: No	
	N = 510	100.0%	*N* = 46	100.0%	*N* = 464	100.0%
Chief complaint						
Discharge	195	38.2%	11	23.9%	184	39.7%
Post-menopausal bleeding	97	19.0%	18	39.1%	79	17.0%
Inter-menstrual bleeding	77	15.1%	5	10.9%	72	15.5%
Post coital bleeding	42	8.2%	5	10.9%	37	8.0%
Pelvic pain	1	0.2%	0	0.0%	1	0.2%
No complain	98	19.2%	7	15.2%	91	19.6%
Cervical appearance						
Normal appearance	260	51.0%	13	28.3%	247	53.2%
Bleeding on touch	152	29.8%	15	32.6%	137	29.5%
Eroded	46	9.0%	11	23.9%	35	7.5%
Polyp	25	4.9%	3	6.5%	22	4.7%
Total hysterectomy, normal vault appearance	16	3.1%	2	4.3%	14	3%
Total hysterectomy vault growth	1	0.2%	1	2.2%	0	0.0%
Vault bleeding on touch	1	0.2%	0	0.0%	1	0.2%
Mass	1	0.2%	1	2.2%	0	0.0%
Others	8	1.6%	0	0.0%	8	1.7%

between 45–55 years, this result is consistent with the study by Bukhari et al[20] and to the study by Nair et al[24] who found epithelial abnormality was more prevalent in peri-menopausal age group with mean age of 50.89 years old. It is interesting to note that 73.9% of the patients included in this study are within the 45–55 year age group, and are within the peri-/postmenopausal age. Both low- and high-grade lesions of the cervix were more commonly seen in these patients than in any other age group. This finding could be explained by the fact observed from previous studies that older age groups are among the least users of the screening program.[25] Vaginal discharge was the most common complaint of the women in our study at 38.2%, similar to the rate in other studies.[26,27] A total of 13 patients with abnormal Pap results had a healthy-looking cervix and 194 patients had abnormal cervical appearance but with negative pap smears. This signifies that cervical cancer screening, based only on clinical impression and visual examination, is sort of unpredictable in reference to cytological screening. This also connotes the worth of universal cervical cancer screening, regardless of an unhealthy or healthy looking cervix. The results of this study show that parity have no effect on pap smear abnormality, this result oppose with a study done by EM Ikeanyi et al.[28] This might be explained by the fact that 91.8% of the sample are multiparous which lead to no real comparison between nulli and multipara as a risk factor, and also the mode of delivery is unknown in these patients (either normal vaginal delivery or caesarean section), as stated by the Canadian Cancer Society that women who have caesarean sections do not have a higher risk of developing cervical cancer.[29] This study emphasized the significance of vaginal discharge & postmenopausal bleeding and its association with premalignant changes in the cervix. Results came corresponding with other studies.[30,31] In the present study 27 cases of epithelial cells abnormality on pap smear results, 17 of them were having pre/malignant changes in histopathology (63% correlated) and the other 10 cases were negative in histopathology (37% non-correlated). And 16 cases with negative for intraepithelial lesions or malignancy result in pap smear, 15 cases were having non neoplastic lesions in histopathology (94% correlated) and only one case (6%) was non correlated (showing premalignant changes). This study found the sensitivity of Pap test is 94% which was comparable with Tamboli et al,[32] However the sensitivity was lower as in study by Jain V et al,[33] which was 78%. Specificity was 60% which was comparable to study by Anschau et al[34] and accuracy rate as 74%. In study by Nasreen et al,[18] Jain et al,[33] Tamboli et al,[32] diagnostic accuracy was 79.09%, 73.2%, 90.4% respectively. Histological follow up (either by colposcopic biopsy or fractional curettage) of benign endometrial cells shedding shows 64% non-significant diagnosis (hormonal imbalance) and 36% shows significant endometrial diseases. This is much lower than the reported frequency of detecting endometrial disease in women shedding normal endometrial cells. Ng[35] detected endometrial pathology in 54.3% of postmenopausal women with benign endometrial cells and this result is also in contrast to Yancey et al[36] found endometrial disease in 13.5% of postmenopausal women while Cherkis et al[37] found disease in 35.7% of women with abnormally shed normal endometrial cells which are comparable to this study result. In most of women they are physiological (the woman is cycling, naturally or because of hormone replacement therapy) or a result of benign endometrial pathology (e.g., an endometrial polyp). For this reason, an endometrial sampling is not indicated for all women with this diagnosis. The gynecologist, who

Table 4. **Performance of Pap test as a screening for malignant/premalignant changes of the cervix**

		Histopathology		Total
		Pre/Malignant changes	Other findings	
Pap smear	Significant	17	10	27
	Not significant	1	15	16
Total		18	25	43

Table 5. **Screening indicators value**

Screening indicators	Value	[95% CI]
Sensitivity	0.94	0.71–1.00
Specificity	0.60	0.39–0.78
Accuracy	0.74	0.59–0.86

Table 6. **Studies comparing prevalence of epithelial abnormalities in different countries**

Ref No	Author	Year	Place	Total no of patients	Total prevalence	ASCUS	LSIL	HSIL	SCC
13	Edelman	1999	Bronx, New York	271	13.2	9.9	2.5	0.6	0.2
14	Fonn S	2002	S. Africa	20603	5.09		2.42	1.8	0.47
15	Afrakhteh	2007	Iran	13315	1.18	0.63	0.21	0.13	0.2
16	Deshou	2009	China	31500	3.12	2.3	0.41	0.28	0.02
17	Balaha	2011	Saudi Arabia	1171	4.95	2.99	0.09	0.68	0.34
18	Nasreen	2011	Bangladesh	550	16.2	0.5	12	1.8	1.5
19	Atilgan	2012	Turkey	32026	2.8	1.9	0.5	0.1	0
20	Bukhari	2012	Pakistan	1000	10.2	1	4.5	2.2	1.4
21	Marahatta Khanal	2014	Nepal	1751	1.14	0.45	0.85	0.28	0
22	Mufti	2014	Iran	15721	14.52	7.1	2.2	0.8	0.06
23	Kapila	2015	Kuwait	135766	4.43	2.37	0.97	0.22	0.09
	Present study	2019	Iraq	510	9	1.6	2.2	3.7	0.6

knows her menstrual and menopausal status, clinical risk factors for endometrial cancer, and whether she is on hormone replacement therapy, should use his or her clinical judgment in deciding whether to take a histologic endometrial sample. Consensus guidelines recommend endometrial assessment for women who are postmenopausal.[38] From this study it is evident that Pap smear cytology-based screening is not well-organized enough in Iraq, with only symptomatic women being the main user of the screening test. A study was conducted to assess the awareness of Arab countries including Iraq, Jordan, Qatar and UAE about cervical cancer, HPV and vaccination, the study showed that Iraq is one of the countries with low level of education and awareness about cervical cancer.[39] In the perspective of a developing country like Iraq, the reasons may be, the poor awareness about cervical cancer screening, and shortage of health centers specialized for cancer screening which can cover a large area of the country including the rural and suburban areas.

Conclusion

In conclusion, this study has shown that age is significantly correlated with increasing rate of precancerous and cancerous lesions in women of perimenopausal and postmenopausal periods, the significance of vaginal discharge & postmenopausal bleeding and its association with premalignant changes in the cervix. Furthermore, the statistical analysis of the data used in this study revealed that the sensitivity value of Pap test is 0.94, the Specificity was 0.60 and accuracy rate 0.74.

Recommendations

1. Increase women awareness especially woman at the reproductive age about the importance of the pap screening test.
2. Establish pap screening program in the primary health institutions in order to make the access to pap test easier to the women especially in the rural areas.
3. HPV testing should be included too in the screening program.
4. Emphasizing on the importance of providing a full clinical history of the patients by the treating physician in the request form.

Conflicts of Interest Disclosure

No conflicts of interest.

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